8500 **Oral Abstract Session, Sat, 1:15 PM-4:15 PM**

Tolerability and activity of combinations of the PI3Kδ inhibitor idelalisib (GS-1101) with rituximab and/or bendamustine in patients with previously treated, indolent non-Hodgkin lymphoma (iNHL): Updated results from a phase I study.

John Leonard, Nina D. Wagner-Johnston, Steven E. Coutre, Ian Flinn, Marshall T. Schreeder, Nathan Hale Fowler, Jeff Porter Sharman, Ralph V. Boccia, Jacqueline Claudia Barrientos, Kanti Roop Rai, Thomas E. Boyd, Richard R. Furman, Leanne Holes, David Michael Johnson, Yeonhee Kim, Roger D. Dansey, Wayne R. Godfrey, Sven De Vos; Weill Cornell Medical College, New York, NY; Washington University School of Medicine in St. Louis, St. Louis, MO; Stanford Cancer Institute, Stanford, CA; Sarah Cannon Research Institute, Nashville, TN; Clearview Cancer Institute, Huntsville, AL; The University of Texas MD Anderson Cancer Center, Houston, TX; Willamette Valley Cancer Institute/US Oncology Research, Springfield, OR; Center for Cancer and Blood Disorders, Bethesda, MD; Hofstra North Shore-LIJ School of Medicine, Hyde Park, NY; Yakima Valley Memorial Hospital/North Star Lodge Cancer Center, Yakima, WA; Gilead Sciences, Inc., Seattle, WA; University of California, Los Angeles Medical Center, Los Angeles, CA

Background: PI3K-delta signaling is critical for activation, proliferation and survival of B cells, and is hyperactive in many B-cell malignancies. Idelalisib is a first-in-class, selective, oral inhibitor of PI3Kδ that has shown considerable monotherapy activity in recurrent iNHL (Kahl, ICML 2011), as well as combination therapy (Fowler, ASCO 2012). **Methods:** This phase I study evaluated the activity of continuous (48 weeks) idelalisib (Id), 100/150 mg BID, in combination with rituximab (R) (375 mg/m^2 weekly x 8 doses) (Id+R), with bendamustine (B) (90 mg/m^2 x 2, for 6 cycles) (Id+B), or in combination with R (375 mg/m^2 monthly x 6) and B (90 mg/m^2 x 2), for 6 cycles (Id+BR). Investigators assessed response according to standard criteria (Cheson 2007). Patients who continued to benefit were able to enroll on an extension study. **Results:** Study enrolled 78 pts with relapsed/refractory iNHL, with 34 (44%) pts continuing on treatment in the ongoing extension protocol. The 3 cohorts included Id+R (N=30), Id+B (N=34), and Id+BR (N=14). Pts were 67% male, median age [range] of 62 [37E84] years, 41% with refractory disease, 88% stage III/IV, and 36% of FL with high FLIPI scores. The median [range] number of prior therapies was 3 [1E10]. The median [range] duration of treatment was 10.6 [0.5-29.2] months. Overall response rate (ORR) was 63/78 (81%), with 22/78 (28%) CR. The ORR/CR for Id+R was 77%/20%, Id+B was 85%/29%, and Id+BR was 79%/43%. At 20 months, the PFS was 66%. For responders, 73% were progression-free at 20 months. Most common adverse events included (total%/≥G3%) pyrexia (56/4), fatigue (45/4), nausea (41/0), rash (40/8), cough (37/0), diarrhea (36/8), chills (18/0), URI (18/1), and pneumonia (17/15). Lab abnormalities included (total%/≥G3%) ALT/AST elevations (56/17). **Conclusions:** Idelalisib-based combination therapy is highly active and well tolerated in patients with relapsed/refractory iNHL. These data support further clinical development. Phase III trials evaluating the efficacy of idelalisib in combination with R, or BR in iNHL are ongoing (NCT01732913, NCT01732926). Clinical trial information: NCT01732913, NCT01732929.

8501 **Oral Abstract Session, Sat, 1:15 PM-4:15 PM**

Preliminary results of PI3Kδ inhibitor idelalisib (GS-1101) treatment in combination with everolimus, bortezomib, or bendamustine/rituximab in patients with previously treated mantle cell lymphoma (MCL).

Nina D. Wagner-Johnston, Sven De Vos, John Leonard, Jeff Porter Sharman, Marshall T. Schreeder, Ralph V. Boccia, Jacqueline Claudia Barrientos, Steven E. Coutre, Ian Flinn, Thomas E. Boyd, Leanne Holes, David Michael Johnson, Yeonhee Kim, Roger D. Dansey, Wayne R. Godfrey, Nathan Hale Fowler; Washington University School of Medicine in St. Louis, St. Louis, MO; University of California, Los Angeles Medical Center, Los Angeles, CA; Weill Cornell Medical College, New York, NY; Willamette Valley Cancer Institute/US Oncology Research, Springfield, OR; Clearview Cancer Institute, Huntsville, AL; Center for Cancer and Blood Disorders, Bethesda, MD; Hofstra North Shore-LIJ School of Medicine, Hyde Park, NY; Stanford Cancer Institute, Stanford, CA; Sarah Cannon Research Institute, Nashville, TN; Yakima Valley Memorial Hospital/North Star Lodge Cancer Center, Yakima, WA; Gilead Sciences, Inc., Seattle, WA; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: PI3K-delta is critical for activation, proliferation and survival of B cells and plays a role in homing and retention in lymphoid tissues. PI3Kδ signaling is hyperactive in many B-cell malignancies. Idelalisib is a first-in-class, selective, oral inhibitor of PI3Kδ that has shown monotherapy activity in recurrent MCL (Kahl, ICML 2011). **Methods:** This phase 1 study is evaluating the activity of continuous idelalisib (Id), 150 mg BID, in combination with everolimus (E) (10 mg PO qD) (Id+E regimen), with bortezomib (V) (1.3 mg/m^2 SC day 1, 8, 15 per 28 day cycle) (Id+V regimen), or with rituximab (R) (375 mg/m^2, on Day 1) and bendamustine (B) (90 mg/m^{2}x 2), for 6 cycles (Id+BR regimen). Investigators assessed response according to standard criteria (Cheson 2007). **Results:** Study enrolled 22 patients with relapsed/refractory MCL. Results are from 14 Jan 2013 data cutoff. The 3 cohorts included Id+E (N=12), Id+V (N=6), and Id+BR (N=4). Patients were 73% male, median age [range] of 68 [47E79] years, 32% with refractory disease and 73% stage III/IV. The median [range] number of prior therapies was 3 [1E7]. The median [range] duration of treatment was 2.5 [0.5-8.3+] months. Overall response rate (ORR) was 10/22 (46%), with 2 CR (9%). The ORR/CR for Id+E, was 25%/0%, Id+V was 50%/0%, and Id+BR was 100%/50%. The median duration of response (mDOR) and median PFS (mPFS) were not reached. Most common adverse events included (total%/≥G3%) diarrhea (41/9), fatigue (41/0), rash (27/14), cough (27/0), decreased appetite (23/0), and epistaxis (23/0). Lab abnormalities included (total%/≥G3%) thrombocytopenia (82/27), neutropenia (32/14), and ALT/AST elevations (50/5). **Conclusions:** Preliminary data indicates idelalisib-based combination therapy is active in patients with relapsed/refractory MCL. All combinations were tolerable. These data support further clinical development in larger trials to further characterize safety and response duration. Clinical trial information: NCT01088048.

8502 **Oral Abstract Session, Sat, 1:15 PM-4:15 PM**

Phase Ib study combining ibrutinib with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in patients with CD20-positive B-cell non-Hodgkin lymphoma (NHL).

Anas Younes, Ian Flinn, Jesus G. Berdeja, Jonathan W. Friedberg, Sara Alberti, Catherine Thieblemont, Franck Morschhauser, Peter Hellemans, Brett Hall, Johan Smit, Donna Skee, Ronald de Vries, Marija Todorovic, Imran Khan, Nele Fourneau, Yasuhiro Oki; The University of Texas MD Anderson Cancer Center, Houston, TX; Sarah Cannon Research Institute, Nashville, TN; Sarah Cannon Research Institute; Tennessee Oncology, Nashville, TN; University of Rochester, Wilmot Cancer Center, Rochester, NY; Assistance Publique–Hôpitaux de Paris, Hôpital Saint Louis, Paris, France; Centre Hospitalier Régional Universitaire de Lille, Hôpital Claude Huriez, Service Maladies du Sang, Lille, France; Janssen Research & Development, LLC, Beerse, Belgium; Janssen Research & Development, LLC, Spring House, PA; Janssen Research & Development, LLC, Raritan, NJ; Janssen Research & Development, LLC, Belgrade, Serbia

Background: Ibrutinib, a first-in-class oral Bruton's tyrosine kinase inhibitor, has demonstrated single-agent activity in a variety of relapsed or refractory B-cell malignancies with limited toxicity, making it an appropriate drug to combine with standard R-CHOP chemotherapy in patients with previously untreated NHL. **Methods:** Patients received oral daily dose of ibrutinib (280, 420, or 560 mg) in combination with standard doses of R-CHOP (rituximab, cyclophosphamide, doxorubicin, and vincristine on day 1, and prednisone on days 1 through 5 of each 21-day cycle for up to 6 cycles). The primary objective was to determine the recommended phase 2 dose (RP2D) of ibrutinib in combination with standard R-CHOP (IR-CHOP). The secondary objectives were to assess safety, overall response rate, pharmacokinetics, and pharmacodynamic biomarkers. **Results:** Seventeen patients (7, 4, and 6 in increasing ibrutinib doses) were enrolled: 59% male, median age 65 (range 46-81) years, diffuse large B-cell lymphoma 47%, mantle cell lymphoma 29% and follicular lymphoma 24%. In the 280 mg cohort, 2 patients had dose-limiting toxicity (DLT): 1 with transient syncope and 1 with periorbital cellulitis; at 560 mg, 1 patient had gastritis (grade 2). The RP2D was established at 560 mg ibrutinib. The most common ($\geq$ 20% of patients) adverse events (AEs) were neutropenia (77%), thrombocytopenia (65%), vomiting (59%), anemia (53%), nausea (47%), fatigue (35%), headache (29%), constipation (24%), diarrhea (24%), and dizziness (24%). To date, 6 patients completed 6 cycles of treatment, and 2 patients discontinued treatment (1 due to noncompliance with the study drug and 1 due to non-DLT AE). At the time of this analysis, of the 10 patients had at least one post baseline tumor, the overall response rate was 100% (7 complete and 3 partial responses). **Conclusions:** The combination of IR-CHOP has an acceptable safety profile. No new toxicities were noted with adding ibrutinib to R-CHOP. An expansion cohort 560 mg ibrutinib (RP2D) is being opened to further explore the safety and efficacy of IR-CHOP in patients with newly diagnosed diffuse large B-cell lymphomas. Clinical trial information: NCT01569750.

8503 **Oral Abstract Session, Sat, 1:15 PM-4:15 PM**

Preventing hepatitis B reactivation in HBsAg-positive patients with untreated diffuse large B-cell lymphoma with R-CHOP chemotherapy: A prospective study to compare entecavir and lamivudine.

He Huang, Xue Ying Li, Hao Ran Li, Dr.Prem Raj Shrestha, Cheng-cheng Guo, Chao Yong Liang, Tingzhi Liu, Mengping Zhang, Huang Ming Hong, Jia Tian Lin, Jia Jia Huang, Ying Tian, Tongyu Lin; Sun Yat-sen University Cancer Center, Guangzhou, China; Cancer Center, Sun Yat-Sen University, Guangzhou, China; Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China

Background: Hepatitis B reactivation is a serious complication in lymphoma patients treated with rituximab-contained chemotherapy despite lamivudine prophylaxis. The optimal prophylactic antiviral protocol is undetermined. This prospective study was designed to compare the efficacy of prophylactic entecavir and lamivudine in preventing hepatitis B reactivation in HbsAg-positive patients with untreated diffuse large B cell lymphoma (DLBCL) under R-CHOP treatment. **Methods:** HBsAg carriers with untreated DLBCL, normal liver function and low serum HBV DNA levels (less than 10^3copys/ml)were randomized to receive entecavir or lamivudine during R-CHOP treatment and for 6 months after completion of chemotherapy. HBsAg, HBsAb, HBeAg, HBeAb and HBcAb were performed prior to initiation of treatment. Serum alanine aminotransferase (ALT), and HBV-DNA levels were prospectively monitored before every cycle of chemo and every month after completion of chemotherapy. **Results:** Between February 2008 and December 2012, a total of 229 patients older than 18y with newly diagnosed DLBCL were included. The present analysis is based on 121 HBsAg-positive patients, including 61 patients randomly assigned to entecavir and 60 patients to lamivudine .The primary efficacy end point was the incidence of HBV-related hepatitis. The secondary end point was chemotherapy disruption due to hepatitis. Compared with the lamivadine group, the entecavir group had significantly lower rates of hepatitis(8.2% vs 23.3%,P=0.022), hepatitis B reactivation (0 vs 13.3%,P=0.003),HBV reactiviation(6.6% vs 30.0%,P=0.001), delayed HBV-related hepatitis (0 vs 8.3%,P=0.027) and disruption of chemotherapy (1.6% vs 18.3%,P=0.002). 7 of 8 patients with hepatitis B reactivation had advanced stage(III–IV) disease. **Conclusions:** In HBsAg-positive DLBCL patients undergoing R-CHOP chemotherapy, entecavir is more effective than lamivudine in preventing hepatitis B reactivation. For patients with advanced stage disease, entecavir should be considered the primary preventive therapy. Clinical trial information: CTR-TRC-11001687.

8504 **Oral Abstract Session, Sat, 1:15 PM-4:15 PM**

Utility of post-therapy surveillance scans in DLBCL.

Carrie A. Thompson, Matthew J. Maurer, Herve Ghesquieres, William R Macon, Thomas Matthew Habermann, Thomas E. Witzig, James Robert Cerhan, Brian K. Link; Mayo Clinic, Rochester, MN; Centre Léon Bérard, Lyon, France; University of Iowa Hospitals and Clinics, Iowa City, IA

Background: Diffuse large B-cell lymphoma (DLBCL) is an aggressive lymphoma. The optimal follow-up strategy for patients (pts) in remission is not clear. The goal of this study is to determine the utility of surveillance scans in a large, prospective, multi-institutional cohort of DLBCL pts. **Methods:** Patients were enrolled in the University of Iowa/Mayo Clinic SPORE Molecular Epidemiology Resource (MER), a prospective cohort of newly diagnosed lymphoma pts. All pts were followed for events including relapse, re-treatment, and death with events verified by medical records. Patients eligible for this study had biopsy proven DLBCL and were treated with anthracycline based immunochemotherapy (IC). Initial and post-treatment management was per treating physician. Medical records were re-reviewed in pts with events for clinical details at relapse and relationship to planned follow-up visits and surveillance scans. **Results:** 644 pts with DLBCL treated with IC were enrolled in MER from 2002-2009. Median age was 63 years (range 18-92), 54% were men, and median f/u was 59 months (range 8-116). 537 pts entered post-treatment observation; 109 (20%) of the 537 pts relapsed and 41 died from other causes. 42% of relapses were in the first 12 months following diagnosis, 27% between 12-24 months, and 31% $>$24 months. In the 109 who relapsed, 62% of pts (62/100, 9 unknown) presented to their physician earlier than a planned follow-up visit due to symptoms. At the time of relapse, 68% were symptomatic, 42% of pts had abnormal physical exam, and 55% had elevated LDH; 87% of pts had $\geq$1 of these features. Of the 38 pts with relapse detected at a planned visit, 26 had clinical features of relapse and 12 pts had relapse detected solely by planned surveillance scan; 4 pts had relapse of low-grade or other subtype and 8 had DLBCL relapse (4 of whom had equivocal/positive PET at the end of IC). Thus, surveillance scanning detected DLBCL relapse prior to clinical manifestations in only 8/537 pts (1.5%) observed post DLBCL therapy. **Conclusions:** The vast majority of DLBCL relapses occur outside of planned follow-up visits and are accompanied by symptoms, physical exam, or laboratory abnormalities. Routine surveillance scans post-therapy add little to detection of DLBCL relapse.

8505 **Oral Abstract Session, Sat, 1:15 PM-4:15 PM**

Clinical or survival benefit to routine surveillance imaging for classical Hodgkin lymphoma patients in first complete remission.

Sai Ravi Pingali, Sarah Jewell, Luiza Havlat, Martin Bast, Jonathan Thompson, Daniel Eastwood, Nancy Bartlett, James O. Armitage, Nina Wagner-Johnston, Julie Vose, Timothy S. Fenske; Medical College of Wisconsin Affiliated Hospitals, Milwaukee, WI; Washington University in St. Louis, St. Louis, MO; University of Nebraska Medical Center, Omaha, NE; Medical College of Wisconsin, Milwaukee, WI; Washington University School of Medicine in St. Louis; Siteman Cancer Center, St. Louis, MO; Nebraska Medical Center, Omaha, NE

Background: Routine surveillance imaging (RSI) for patients in complete remission from classical Hodgkin lymphoma (cHL) is common practice. RSI offers the theoretical benefit of detecting asymptomatic relapse, which may allow for more successful second-line therapy. Despite this, evidence for a clinical benefit of RSI is lacking. We compared outcomes in cHL patients undergoing RSI versus clinical surveillance (CS) in which scans are only obtained to evaluate concerning signs or symptoms. **Methods:** Patients with cHL diagnosed at three tertiary care centers from 2001-2010, who achieved complete remission (CR) following frontline therapy, were analyzed retrospectively. Patients were stratified into two groups based on the surveillance strategy employed. Baseline patient characteristics, prognostic features, treatment records, and outcomes were collected. The primary objective was to compare overall survival for patients undergoing RSI versus CS. As a secondary objective we compared the success of second-line therapy for relapsed patients in each group. **Results:** 207 patients met eligibility criteria, with 131 RSI patients and 76 CS patients. Patient characteristics (age, gender, stage, sedimentation rate, Hasenclever index, bulky disease and B symptoms) were similar in each group. Chemotherapy consisted of ABVD in 79% and Stanford V in 15%. Patients in the RSI group more commonly received ABVD (91% vs. 57%) and less often radiation therapy (38% vs. 68%). Mean number of scans was 4.77 in RSI and 1.11 in CS groups, respectively. With a median follow up of 4 years, the overall survival was similar in both groups ($p=0.74$), with 5 (3.8%) deaths in the RSI group and 4 (5.3%) in the CS group. Six (4.6%) relapses occurred in the RSI group (4 of which were detected by RSI), and 5 (6.6%) in the CS group ($p=0.64$ for relapse at 5 years). All relapsed patients achieved second CR with second-line therapy. **Conclusions:** RSI did not yield a survival advantage in cHL patients who achieved CR after frontline therapy.Given the radiation exposure, cost, and risk for additional procedures associated with RSI, we conclude CS is the preferred strategy in cHL patients in first complete remission.

8506 **Oral Abstract Session, Sat, 1:15 PM-4:15 PM**

Randomized phase II study of mogamulizumab (KW-0761) plus VCAP-AMP-VECP (mLSG15) versus mLSG15 alone for newly diagnosed aggressive adult T-cell leukemia-lymphoma (ATL).

Tatsuro Jo, Takashi Ishida, Shigeki Takemoto, Hitoshi Suzushima, KImiharu Uozumi, Kazuhito Yamamoto, Naokuni Uike, Yoshio Saburi, Kisato Nosaka, Atae Utsunomiya, Kensei Tobinai, Hiroshi Fujiwara, Kenji Ishitsuka, Shinichiro Yoshida, Naoya Taira, Yukiyoshi Moriuchi, Kazunori Imada, Toshihiro Miyamoto, Masao Tomonaga, Ryuzo Ueda; Department of Hematology, Japanese Red Cross Nagasaki Genbaku Hospital, Nagasaki, Japan; Department of Medical Oncology and Immunology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; Department of Hematology and Institute for Clinical Research, National Hospital Organization Kumamoto Medical Center, Kumamoto, Japan; Department of Hematology, Kumamoto Shinto General Hospital, Kumamoto, Japan; Department of Hematology and Immunology, Kagoshima University Hospital, Kagoshima, Japan; Department of Hematology and Cell Therapy, Aichi Cancer Center Hospital, Nagoya, Japan; Department of Hematology, National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan; Department of Hematology, Oita Prefectural Hospital, Oita, Japan; Cancer Center, Kumamoto University Hospital, Kumamoto, Japan; Department of Hematology, Imamura Bun-in Hospital, Kagoshima, Japan; Department of Hematology, National Cancer Center Hospital, Tokyo, Japan; Department of Bioregulatory Medicine, Ehime University Graduate School of Medicine, Toon, Japan; Department of Internal Medicine, Division of Medical Oncology, Hematology, and Infectious Diseases, Fukuoka University, Fukuoka, Japan; Department of Hematology, National Hospital Organization Nagasaki Medical Center, Ohmura, Japan; Department of Internal Medicine, Heartlife Hospital, Okinawa, Japan; Department of Hematology, Sasebo City General Hospital, Sasebo, Japan; Department of Hematology, Kokura Memorial Hospital, Kitakyushu, Japan; Department of Medicine and Biosystemic Science, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan; Department of Tumor Immunology, Aichi Medical University School of Medicine, Nagoya, Japan

Background: Mogamulizumab (Moga), a defucosylated humanized anti-CCR4 antibody, was approved for the treatment of relapsed/refractory ATL in Japan in 2012. This multicenter, randomized, phase II trial was conducted to examine the efficacy of the combination of Moga with standard chemotherapy for untreated aggressive ATL. **Methods:** Previously untreated patients (pts) with CCR4-positive ATL were randomly assigned to receive mLSG15 plus Moga (arm A) or mLSG15 alone (arm B). The primary endpoint was CR rate (%CR), and secondary endpoints included ORR, PFS, OS and safety. Pts received 4 courses of mLSG15 regimen, with or without a total of 8 doses of Moga (1.0 mg/kg) once every 2 weeks. The planned sample size, 22 pts per arm, provided a probability of 80% that %CR in arm A would have larger %CR when true %CR for arm A is 15% better than that for arm B. **Results:** Of 54 pts randomized, 53 were treated (arm A: 29; arm B: 24). Male/female ratio was 53/47%, median age was 63 (37-81), and subtype was acute/lymphoma/unfavorable chronic, 70/25/6%. %CR and ORR in arms A and B was 52% (95%CI [CI]; 33, 71) vs. 33% (CI; 16, 55) and 86% (CI; 63, 96) vs. 75% (CI; 53, 90), respectively. The results in arm B were similar to the previously reported %CR of 40% and ORR of 72% with mLSG15 (Tsukasaki et al, JCO 2007). ORR according to the disease subtype, in arms A and B, was 55% vs. 29% for acute, 50% vs. 43% for lymphoma and 33% vs. 0% for unfavorable chronic. Median PFS was 259 days (CI; 197, -) for arm A and 192 days (CI; 147, -) for arm B. Median OS was not reached in both arms. The most common treatment-related AEs in each arm were neutropenia (100%, 96%), thrombocytopenia (100%, 96%), leukopenia (100%, 92%), lymphocytopenia (97%, 96%), anemia (97%, 92%) and febrile neutropenia (90%, 88%). In arm A, skin disorders were more frequent but manageable, and no serious skin disorder like Stevens-Johnson syndrome was observed. There was one treatment-related death, which was not related to Moga. **Conclusions:** The combination of Moga with mLSG15 was well tolerated and the study met its primary endpoint. These results suggest that Moga with mLSG15 is a rational treatment option for newly diagnosed aggressive ATL. Clinical trial information: NCT01173887.

8507 **Oral Abstract Session, Sat, 1:15 PM-4:15 PM**

Belinostat, a novel pan-histone deacetylase inhibitor (HDACi), in relapsed or refractory peripheral T-cell lymphoma (R/R PTCL): Results from the BELIEF trial.

Owen A. O'Connor, Tamás Masszi, Kerry J. Savage, Lauren C. Pinter-Brown, Francine M. Foss, Leslie Popplewell, Amanda F. Cashen, Jeanette Doorduijn, Shanta Chawla, Poul Knoblauch, Pier Luigi Zinzani, Peter Brown, Georg Hess, Achiel Van Hoof, Steven M. Horwitz, Andrei R. Shustov; Center for Lymphoid Malignancies, Columbia University Medical Center, New York, NY; St. István and St. László Hospital, Budapest, Hungary; Department of Medical Oncology, British Columbia Cancer Agency Centre, Vancouver, BC, Canada; Geffen School of Medicine at UCLA, Los Angeles, CA; Yale Cancer Center, New Haven, CT; City of Hope, Duarte, CA; Washington University in St. Louis, St Louis, MO; Erasmus MC, Rotterdam, Netherlands; Spectrum Pharmaceuticals, IRVINE, CA; TopoTarget, Copenhagen, Denmark; Dipartimento di Ematologia e Scienze Oncologiche, Bologna, Italy; H:S Rigshospitalet, The Finsen Centre, KAT, Haematology Department 4241, Copenhagen, Denmark; Klinikum Johannes-Gutenberg -Universitaet, III. Medizinische Klinik und Poliklinik, Mainz, Germany; University Hospital St-Jan, Brugge, Belgium; Memorial Sloan-Kettering Cancer Center, New York, NY; University of Washington Medical Center, Seattle, WA

Background: Therapies approved in US for R/R PTCL have overall response rates (ORR) of 25%-27%. The need for new therapies persists. BELIEF is a pivotal, single-arm study of belinostat in patients with R/R PTCL after failure of ≥1 prior systemic therapies. **Methods:** Entry criteria were measurable PTCL, platelets ≥ 50,000/μL, no prior HDACi therapy, and adequate organ function. PTCL was confirmed by central pathology review (CPRG). Belinostat 30 min IV infusion at 1000 mg/m^{2}was administered on days 1–5 of a 3 week cycle until progression or unacceptable toxicity. Tumor response was assessed by Cheson 2007 criteria. The primary endpoint was ORR. **Results:** Patients with R/R PTCL (N=129, 53% male, median age 63 y) received belinostat a median of 2 cycles (range 1–33). The median number of prior therapies was 2 (1-8) including CHOP/CHOP-like (96%) and stem cell transplant (23%). The median administered dose intensity was 98%. One and two dose reductions of 25% occurred in 12% and 1% of patients, respectively, due to adverse events (AEs). For patients with CPRG confirmed PTCL (N=120), the ORR was 26% (n=31; 10% CR; 16% PR). The median time to response was 5.6 weeks (range 4.3-50.4). The median duration of response (DoR) was 8.3 months; longest DoR was 29.4 months. Seven patients remain on study in response. For the subgroup of patients with CPRG confirmed PTCL and baseline platelets ≥100,000/μL (N=100) ORR was 28% (CR 11%; PR 17%). The most frequent (≥ 5%) grade 3-4 treatment emergent AEs were thrombocytopenia (13%), neutropenia (13%), anemia (10%), dyspnea (6%), pneumonia (6%), and fatigue (5%). Patients with platelets <100K tolerated belinostat, with 98% dose intensity. Belinostat was well tolerated with a low incidence of myelosuppression. Discontinuations were due to PD (64%), death (11%), AEs (7%), patient request (8%), and other (4%). **Conclusions:** Belinostat demonstrated a 26%-28% ORR in BELIEF and was well tolerated with a favorable safety profile in patients with R/R PTCL including those with low platelets. The low incidence of myelosuppression observed warrants further investigation of belinostat combination therapy to develop new treatment paradigms for R/R PTCL. Clinical trial information: NCT00865969.

8508 **Oral Abstract Session, Sat, 1:15 PM-4:15 PM**

Phase II/III randomized trial of CID-ATT with radiotherapy compared with CHOP with radiotherapy as first-line treatment for previously untreated early staging extranodal NK/T-cell lymphoma, nasal type (ENKL).

Tongyu Lin, He Huang, Chao Yong Liang, Chengcheng Guo, Ying Tian, Tingzhi Liu, Xue Ying Li, Mengping Zhang, Huang Ming Hong, Dr.Prem Raj Shrestha; Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China; Sun Yat-sen University Cancer Center, Guangzhou, China; Cancer Center, Sun Yat-Sen University, Guangzhou, China

Background: Extranodal NK/T cell lymphoma, nasal type (ENKL) is more prevalent in Asia and has worse prognosis than B-NHL. No therapeutic strategy is currently identified for ENKL. This phase II/III study was undertaken to compare CHOP-B/IMVD/DHAP-Alternating Triple Therapy (CID-ATT) and standard CHOP regimen as first-line treatment prospectively. **Methods**:109 patients (pts) initially diagnosed as ENKL (16-70 ys old) with Ann Abor Stage I to II were randomized to receive CID-ATT or CHOP regimen from Jan 2006 to Jan 2012. CID-ATT alternated among CHOP-B, IMVD, and DHAP, given in alternating sequence for a total of 6 courses (2 circle). Involved field radiation was administered after 6 courses(2 circle) of CID-ATT regimen or 6 cycles of CHOP regimen. All pts received prophylactic granulocyte colony-stimulating factor, interleukin-11and thrombopoietin for each DHAP cycle. **Results:** 109 pts were evaluable (54CID-ATT; 55 CHOP). With a median follow-up of 40.3months,OS and PFS was significantly prolonged with CID-ATT compared with CHOP (1yOS :80.2% vs 78.6%, 3yOS:68.0% vs 42.3%, 5yOS: 64.2% vs 34.5%,P=0.023; 1yPFS: 74.9% vs 59.6%, 3yPFS:60.5% vs 32.0%, 5yPFS: 60.5% vs 32.0% ; P=0.016). Compared to CHOP group, CID-ATT group has a much higher complete remission rate (CID-ATT:47/54,87.0 % vs CHOP:29/55,52.7%, P<0.001). The survivals for pts who achieved CR after One circle (3 courses) were significantly better than those who were in non-CR group.(5yOS: CR group in ATT:75.3%, non-CR group in ATT:51.5%, CR group in CHOP:39.3%, non-CR group in CHOP:31.0%; P=0.003). No treatment related death was observed, although Grade III/IV neutropenia (30/54,55.6%) and thrombocytopenia (33/54,61.1%) were observed in CID-ATT regimen, especially in DHAP cycle. **Conclusions**: Our study has demonstrated that the CID-ATT regimen as an optimal first-line therapy achieved promising clinical activity with safe and tolerated toxicity under close monitoring and good supportive care of untreated early staging ENKL pts. CR of induce chemotherapy following radiotherapy is very important for ENKL survival. Clinical trial information: CSWOG0002.

8509 **Oral Abstract Session, Mon, 8:00 AM-11:00 AM**

Melphalan/prednisone/lenalidomide (MPR) versus high-dose melphalan and autologous transplantation (MEL200) plus lenalidomide maintenance or no maintenance in newly diagnosed multiple myeloma (MM) patients.

Mario Boccadoro, Federica Cavallo, Francesca Maria Gay, Francesco Di Raimondo, Arnon Nagler, Vittorio Montefusco, Francesca Patriarca, Paola Tacchetti, Tommasina Guglielmelli, Pellegrino Musto, Luca Baldini, Claudia Crippa, Marina Ruggeri, Fabiana Gentilini, Maide Cavalli, Dina Ben Yehuda, Tommaso Caravita, Giovannino Ciccone, Izhar Hardan, Antonio Palumbo; Myeloma Unit, Division of Hematology, University of Torino, Torino, Italy; Italian Multiple Myeloma Network, GIMEMA, Italy, Italy; Hematology Division, BMT and Cord Blood Bank, Chaim Sheba Medical Center, Tel-Hashomer, Israel; Hematology Division, Hadassah Medical Center, Jerusalem, Israel; Cancer Epidemiology Unit, CeRMS and CPO Piemonte, Città della Salute e della Scienza, University of Torino, Torino, Italy; Hematology Division, Meir Medical Center, Kfar-Saba, Israel; Division of Hematology, University of Turin, Turin, Italy

Background: The incorporation of new drugs into induction, consolidation, and maintenance therapy is changing the treatment paradigm of MM. **Methods:** At diagnosis, 402 pts (< 65 years) were randomly assigned to receive six MPR cycles (N=202) or tandem MEL200 (N=200). After MPR or MEL200, pts were further randomized, within each group, for no maintenance (N=204) or lenalidomide maintenance (N=198). A 2x2 factorial randomized trial was designed. The primary end point was PFS. An enrolment of 170 pts/arm was required to demonstrate a 15% improvement of PFS at 2 years (2-sides a = 0.05, 1- β 80%). **Results:** After a median follow-up of 45 mos from diagnosis, the median PFS was 25 mos with MPR and 39 mos with MEL200 (p=.0002). Median PFS were 37.5 mos for maintenance and 25.7 mos for no maintenance (p=.0008). The 4-year OS from diagnosis was 71% with MPR and 72% with MEL200 (p=0.71), 76% for maintenance and 68% for no maintenance (p=.08). After a median follow-up of 32 mos from start of maintenance, the median PFS was for 41 mos for maintenance and 18 mos for no maintenance (p<.0001). The 3-year OS from start of maintenance was 81% for maintenance and 72% for no maintenance (p=.04). **Conclusions:** MEL200 significantly prolonged PFS in comparison with MPR. Lenalidomide maintenance significantly reduced the risk of progression independently from the previous treatment. OS is similar between MPR and MEL200, with a trend for an improved OS in pts receiving lenalidomide as maintenance therapy. Clinical trial information: NCT00551928.

	First randomization			Second randomization		
	MPR	**MEL200**	**HR (95%CI; p value)**	**MAINT**	**No MAINT**	**HR (95%CI; p value)**
From diagnosis						
Median PFS (mos)	25	39	1.66 (1.27-2.18; .0002)	37.5	25.7	0.63 (0.48-0.83;.0008)
4-ys OS	71	72	1.08 (0.72-1.63;.71)	76	68	0.68 (0.45-1.04;.08)
	First randomization			Second randomization		
Start of maintenance	MPR	MEL200	HR (95%CI;p value)	MAINT	No MAINT	HR (95%CI; p value)
Median PFS (mos)	18	41	2.01 (1.45-2.79;<.0001)	41	18	0.50 (0.36-0.69;<.0001)
3-ys OS	77	76	0.98 (0.61-1.58;.94)	81	72	0.60 (0.37-0.97;.04)

8510 **Oral Abstract Session, Mon, 8:00 AM-11:00 AM**

MM-003: A phase III, multicenter, randomized, open-label study of pomalidomide (POM) plus low-dose dexamethasone (LoDEX) versus high-dose dexamethasone (HiDEX) in relapsed/refractory multiple myeloma (RRMM).

Jesùs F. San-Miguel, Katja C. Weisel, Philippe Moreau, Martha Lacy, Kevin W. Song, Michel Delforge, Lionel Karlin, Hartmut Goldschmidt, Anne Banos, Albert Oriol Rocafiguera, Xin Yu, Lars Sternas, Christian Jacques, Mohamed H. Zaki, Meletios A. Dimopoulos; Hematology, Hospital Universitario de Salamanca, Salamanca, Spain; Hematology & Oncology, Department of Medicine, University Hospital Tuebingen, Tuebingen, Germany; Hematology, University Hospital Hotel-Dieu, Nantes, France; Mayo Clinic, Rochester, MN; Vancouver General Hospital, Vancouver, BC, Canada; Department of Hematology, University Hospital Leuven, Leuven, Belgium; Centre Hospitalier Lyon Sud/Hospices Civils de Lyon, Pierre-Bénite, France; Universitätsklinikum Heidelberg, Heidelberg, Germany; Hematology, Centre Hospital de la Côte Basque, Bayonne, France; Institut Catala d'Oncologia, HGTiP, Barcelona, Spain; Celgene Corporation, Summit, NJ; Alexandra Hospital, Athens, Greece

Background: RRMM patients (pts) who have exhausted treatment (Tx) with bortezomib (BORT) and lenalidomide (LEN) or thalidomide have a poor prognosis with short overall survival (OS). HiDEX is a well-established standard Tx in RRMM. POM has demonstrated clinical efficacy in pts refractory to LEN and BORT. MM-003 compared POM + LoDEX vs. HiDEX in RRMM pts who failed LEN and BORT and who progressed on their last Tx. **Methods:** Pts must have been refractory to last prior Tx (progressive disease [PD] during Tx or within 60 days) and failed LEN and BORT after ≥ 2 consecutive cycles of each (alone or in combination). Pts were randomized 2:1 to receive 28-day cycles of POM 4 mg D1–21 + DEX 40 mg (20 mg for pts aged > 75 y) weekly or DEX 40 mg (20 mg for pts aged > 75 y) D1–4, 9–12, and 17–20. Tx continued until PD or unacceptable toxicity. The primary endpoint was progression-free survival (PFS). Secondary endpoints included OS, overall response rate (ORR; ≥ partial response), and safety. Analyses were based on intent to treat. **Results:** 455 pts were randomized to POM + LoDEX (n = 302) or HiDEX (n = 153). The median number of prior Tx was 5 (range 1-17). 72% were refractory to LEN and BORT. Median follow-up was 4 months. POM + LoDEX significantly extended median PFS (3.6 vs. 1.8 months, HR = 0.45, $P < .001$) and OS (not reached vs. 7.8 months, HR = 0.53, $P < .001$) vs. HiDEX. The OS benefit was observed despite 29% of HiDEX pts receiving POM after PD. The trial met the primary endpoint of PFS, crossed the upper boundary for OS superiority, and the Data Monitoring Committee recommended crossover from HiDEX to POM ± DEX. With updated data, the ORR was 21% for POM + LoDEX vs. 3% for HiDEX ($P < .001$) and 24% vs 3% for pts randomized ≥ 6 months post-enrollment ($P < .001$). The most frequent grade 3/4 adverse events (AEs) for POM + LoDEX vs. HiDEX were neutropenia (42% vs. 15%), anemia (27% vs. 29%), and infection (24% vs. 23%). Discontinuation due to AEs was infrequent (7% vs. 6%). Updated data will be presented. **Conclusions:** POM + LoDEX significantly extended PFS and OS vs. HiDEX in pts who failed LEN and BORT. POM + LoDEX should become a standard of care in RRMM pts who have exhausted Tx with LEN and BORT. Clinical trial information: NCT01311687.

8511 **Oral Abstract Session, Mon, 8:00 AM-11:00 AM**

Prognostic value of deep sequencing method for minimal residual disease (MRD) detection in multiple myeloma.

Joaquin Martinez-Lopez, Ramon Garcia-Sanz, Francois Pepin, Rosa Ayala, Maria Angeles Montalban, Bruno Paiva, Li Weng, Santiago Barrio, Laura Montejano, Immaculada Rapado, Rafael Martinez, Maria Jesus Blachard, Pedro Sanchez-Godoy, Joan Blade, Jesùs F. San-Miguel, Malek Faham, Juan José Lahuerta; Hematology, Hospital 12 de Octubre, Madrid, Spain; University Hospital of Salamanca, Salamanca, Spain; Sequenta, Inc., South San Francisco, CA; Hospital 12 de Octubre, Madrid, Spain; Hospital Clinic of Madrid, Madrid, Spain; Hospital Ramon y Cajal, Madrid, Spain; Hospital Severo Ochoa de Leganes, Madrid, Spain; Hospital Clinic de Barcelona, Barcelona, Spain; Hematology, Hospital Universitario de Salamanca, Salamanca, Spain

Background: Most multiple myeloma (MM) patients will relapse due to persistence of residual tumor cells, or MRD. We compared the prognostic value of traditional response criteria and MRD measurement by a sequencing-based method, LymphoSIGHT, and multiparameter flow cytometry (MFC) in a cohort of 68 uniformly-treated MM patients from the Spanish Myeloma Group trials. **Methods:** Bone marrow samples were obtained from 68 patients at diagnostic and post-treatment time points on GEM clinical trials (GEM00 and GEM05). All patients were in CR or VGPR at the post-treatment time point. Using sequencing, we identified clonal rearrangements of immunoglobulin (*IGH-VDJ, IGH-DJ*, and *IGK*) genes in diagnostic samples. We assessed MRD in follow-up samples, analyzed concordance between sequencing and MFC MRD results, and compared the prognostic value of each method with traditional response criteria. **Results:** The sequencing assay detected a myeloma-specific gene rearrangement in diagnostic samples from 59 of 68 (87%) patients. We tested MRD in follow-up time points in 56 of the 59 patients. We observed high correlation between MFC and sequencing MRD results ($r^2=0.86$), with MFC underestimating the myeloma burden (Slope=0.4). Of the 56 patients, 45 were positive by sequencing at MRD levels of 10^{-5} or higher and 11 were MRD negative. There was significantly improved overall survival (OS) in the MRD negative group versus the MRD positive group (median not reached vs. 86 mos, p=0.026). Similar differences were found in progression free survival. When limiting the analysis to the 35 patients in conventional CR, 24 of 35 patients were positive by sequencing at MRD levels at 10^{-5} and higher and 10 were MRD negative. There was significantly improved OS in the MRD negative group versus the MRD positive group (median not reached vs. 80.92 mos, p=0.041). **Conclusions:** Our data shows high correlation between MFC and sequencing MRD levels in MM patients. For patients in CR by traditional response criteria, the presence or absence of MRD by sequencing delineated 2 groups of patients with significantly different OS. MRD negativity by sequencing may be a better prognostic indicator than CR by traditional response criteria.

8512^ **Oral Abstract Session, Mon, 8:00 AM-11:00 AM**

Phase I/II dose-escalation study of daratumumab in patients with relapsed or refractory multiple myeloma.

Henk M Lokhorst, Torben Plesner, Peter Gimsing, Hareth Nahi, Monique Minnema, Ulrik Niels Lassen, Jakub Krejcik, Jacob Laubach, Steen Lisby, Linda Basse, Paul Gerard Guy Richardson; UMC Utrecht, Utrecht, Netherlands; Vejle Hospital, Vejle, Denmark; Copenhagen University Hospital, Copenhagen, Denmark; Karolinska Universitetssjukhuset-Huddinge, Huddinge, Sweden; Rigshospitalet, Copenhagen, Denmark; Jerome Lipper Multiple Myeloma Center, Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA; Genmab A/S, Copenhagen, Denmark; Dana-Farber Cancer Institute, Boston, MA

Background: Daratumumab (DARA) is a human CD38 monoclonal antibody (mAb) with broad-spectrum killing activity. Preliminary safety and efficacy data from this first-in-human dose-escalation study of DARA in pts with relapsed or refractory (RR) multiple myeloma (MM) have previously been published. Here, we present safety and efficacy data from the finalized part 1 and preliminary safety data from the ongoing part 2 of the study. **Methods:** Pts ≥18 years requiring systemic therapy and considered RR to at least 2 prior lines of therapy and ineligible for ASCT were enrolled. In part 1, a 3+3 dose-escalation design was applied and DARA was administered over a 9-week period as 2 pre- and 7 full doses. The phase II dose was determined to 8mg/kg and these pts receive DARA weekly for 8 weeks followed by dosing every 2nd week for 16 weeks and every 4th week until disease progression, toxicity or for max. 24 months. **Results:** Data from 32 pts included in part 1 are presented. In part 2, 7/16 pts have been recruited: all available data will be presented at the meeting. In part 1, the median number of prior treatment lines was 6. PK analysis showed plasma peak levels as expected but relatively rapid clearance at low dose levels. At doses ≥4mg/kg, observed PK values approximated model-predicted values. Efficacy evaluation from part 1 was based on IMWG guidelines. In the ≥4mg/kg groups (n=12), 5 PRs and 3 MRs were observed. 7 of these pts had a 50-100% concomitant reduction in bone marrow plasma cells. Median PFS in the ≥4mg/kg dose groups was not reached (median follow-up at data cut-off was 3.8mths (range: 0-9.6mths). No ADA responses were detected. In part 1, the most common adverse events reported were infusion related (IRE) which occurred predominantly during the first full infusion. 44% of subjects across all dose groups had IREs grade 1-3, of which 2 were grade 3. Six related SAEs (1 anemia, 1 thrombocytopenia, 2 bronchospasm, 1 cytokine release, 1 AST increase) were reported. **Conclusions:** DARA induced a marked reduction in paraprotein and bone marrow plasma cells at doses ≥4mg/kg in heavily pretreated RR MM pts. In addition, high response rates and encouraging PFS data were observed. This is unprecedented for single-agent mAb treatment of MM. Clinical trial information: NCT00574288.

8513 **Oral Abstract Session, Mon, 8:00 AM-11:00 AM**

Effect of CMP, carfilzomib (CFZ) plus melphalan-prednisone (MP), on response rates in elderly patients (pts) with newly diagnosed multiple myeloma (NDMM): Results of a phase (Ph) I/II trial.

Cyrille Touzeau, Brigitte Kolb, Cyrille Hulin, Denis Caillot, Lotfi Benboubker, Mourad Tiab, Xavier Leleu, Murielle Roussel, Carine Chaleteix, Michel Attal, Thierry Facon, Philippe Moreau; Hôpital Hôtel Dieu, CHU Nantes, Service d'Hématologie, Nantes, France; University Hospital, Reims, France; Hematology Department, University Hospital, Nantes, France; Hematology Department, CHU Le Bocage, Dijon, France; Centre Hospitalier Universitaire Tours-Hopital Bretonneau, Tours, France; Hematology Department, University Hospital, La Roche Sur Yon, France; Service des Maladies du Sang, Hôpital Claude Huriez, Lille, France; Hematology Department, CHU Purpan, Toulouse, France; University Hospital, Clermont-Ferrand, France; Centre Hospitalier Universitaire Purpan, Toulouse, France; Hôpital Claude Huriez, Lille, France; Hematology, University Hospital Hotel-Dieu, Nantes, France

Background: MP+thalidomide (MPT) and MP+bortezomib (MPV) have shown significant progression-free survival and overall survival (OS) benefits in NDMM pts > 65 years (y) but are associated with peripheral neuropathy (PN). CFZ, a novel proteasome inhibitor, has shown promising activity and a favorable toxicity profile with low PN rates. **Methods:** This PhI/II study in NDMM >65y was designed to determine maximum tolerated dose (MTD) of CMP and assess safety and efficacy. In PhI, CFZ was started at 20mg/m^2, then escalated to 27, 36, and 45mg/m^2, given IV in 42-day (D) cycles (C) on D1/2/8/9/22/23/29/30 for 9C. Melphalan 9mg/m^2 and prednisone 60mg/m^2 were given PO D1–4 of every 45-day cycle. MTD was based on dose-limiting toxicity (DLT) in C1 defined as any grade (G) 4 hematologic adverse event (AE), any hematologic AE preventing aministration of ≥ 2 C1 CFZ doses except G4 thrombocytopenia without bleeding or G4 neutropenia ≤7D, ≥G3 febrile neutropenia, or any ≥G3 nonhematologic AE. **Results:** As of Jan 6, 2013, 24 pts have been enrolled in PhI: 6 for each dose level. There were 2 DLTs at 45mg/m^2(fever, hypotension) resulting in a MTD of 36mg/m^2. In PhII, 45 additional pts received CMP at 36mg/m^2 CFZ for N=69 total PhI/II pts (median age 74y). ORR was 89% with 51% ≥VGPR. With median follow-up of 12 mo, the projected 2y OS was 89.9%. CMP was well tolerated without PN ≥G2. **Conclusions:** These results compare favorably to those of MPV, MPT, MP+lenalidomide (R), and R+dex in similar pts (ORR 71% San Miguel NEnglJMed2008, 76% Facon Lancet2007, 80% Palumbo JClinOncol2007 and 85% Rajkumar LancetOncol2010, respectively). CFZ 36mg/m^2 +MP is tolerable and effective in elderly NDMM pts. Treatment is ongoing. Final safety and efficacy data will be presented during the meeting. Clinical trial information: NCT01279694.

8514 **Oral Abstract Session, Mon, 8:00 AM-11:00 AM**

Weekly MLN9708, an investigational oral proteasome inhibitor (PI), in relapsed/refractory multiple myeloma (MM): Results from a phase I study after full enrollment.

Shaji Kumar, William Bensinger, Todd M. Zimmerman, Craig B. Reeder, James R. Berenson, Deborah Berg, Ai-Min Hui, Neeraj Gupta, Alessandra Di Bacco, Jiang Yu, Yaping Shou, Ruben Niesvizky; Mayo Clinic, Rochester, MN; Clinical Division, Fred Hutchinson Cancer Research Center, Seattle, WA; Department of Medicine, University of Chicago, Chicago, IL; Division of Hematology/Oncology, Mayo Clinic, Scottsdale, AZ; Institute for Myeloma and Bone Cancer Research, West Hollywood, CA; Millennium Pharmaceuticals, Inc., Cambridge, MA; Center of Excellence for Lymphoma and Myeloma, Weill Medical College of Cornell University, New York Presbyterian Hospital, New York, NY

Background: MLN9708 is an investigational, orally bioavailable, potent, reversible, specific inhibitor of the 20S proteasome that has demonstrated antitumor activity in in vivo models of MM. We report safety, activity and pharmacokinetics (PK) of weekly oral MLN9708 in a phase 1 trial in patients (pts) with relapsed and/or refractory MM after full enrollment (NCT00963820). **Methods:** Pts received MLN9708 (days 1, 8, 15; 28-day cycles) at 0.24–3.95 mg/m^2 (dose-escalation phase) and at the MTD, 2.97 mg/m^2, in relapsed and refractory (RR), bortezomib (btz)-relapsed, PI-naïve, and prior carfilzomib (CZ) expansion cohorts. Adverse events (AEs) were graded by NCI-CTCAE v3.0. Response was assessed by IMWG uniform criteria. **Results:** 60 pts (33 male, median age 64 yrs [40–79]) were enrolled, 32 in the dose-escalation phase and 31 to the expansion cohorts (11 RR, 10 btz-relapsed, 6 PI-naïve, 4 CZ; 2 RR and 1 btz-relapsed pts included from MTD dose-escalation cohort). Median time from MM diagnosis was 4.9 yrs (1.5–18.8). Median number of prior regimens was 6 (2–18), including btz, lenalidomide, thalidomide, and CZ in 83%, 95%, 52%, and 13%, respectively; 76% were refractory to last therapy (17% btz-refractory). At data cut-off (Nov 29, 2012) pts had received a median of 2 cycles (1–11); 5 pts remained on treatment. All-grade/grade $\geq$3 drug-related AEs were seen in 83%/52% of pts; common drug-related grade $\geq$3 AEs were thrombocytopenia (33%), diarrhea, neutropenia (17%), decreased appetite, fatigue, and lymphopenia (8%). 6 pts (10%) had drug-related PN (no grade $\geq$3). 5 pts discontinued due to drug-related AEs; 1 pt died on study due to an unrelated AE. By investigator assessment in 41 evaluable pts, responses included1 VGPR, 5 PR, 1 MR, and 15 with SD. MLN9708 was rapidly absorbed, with a terminal half-life of 4–12 days (supporting weekly dosing) and a proportional increase in plasma AUC with dose (0.8–3.95 mg/m^2). PK data were similar across expansion cohorts. **Conclusions:** Current data suggest weekly oral MLN9708 is generally well tolerated with infrequent PN, and shows activity in this heavily pretreated population with prior exposure to immunomodulatory drugs and btz. Clinical trial information: NCT00963820.

8515 **Oral Abstract Session, Mon, 8:00 AM-11:00 AM**

Clinical, genomic, and imaging predictors of malignancy: Analysis of the first U.S. cooperative group prospective clinical trial in asymptomatic monoclonal gammopathies (SWOG S0120).

Madhav V. Dhodapkar, Rachel Sexton, Sarah Waheed, Saad Zafar Usmani, Xenofon Dimitrios Papanikolaou, Bijay P. Nair, Nathan Petty, John D. Shaughnessy, Antje Hoering, John Crowley, Robert Z. Orlowski, Bart Barlogie; Yale Cancer Center, New Haven, CT; Cancer Research and Biostatistics, Seattle, WA; Myeloma Institute for Research and Therapy, Little Rock, AR; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Asymptomatic monoclonal gammopathies (AMG) are the most common plasma cell dyscrasia classified as either monoclonal gammopathy of undetermined significance (MGUS) or asymptomatic multiple myeloma (AMM). Clinical outcome in AMGs can be highly variable and there is an unmet need to identify newer clinical, genomic and imaging parameters from prospective studies to guide patient management. **Methods:** We analyzed clinical, genomic and imaging data from AMG patients (n=334) enrolled in a prospective observational clinical trial (S0120) conducted under the auspices of SWOG. Baseline data from clinical variables, as well as gene expression profiles of purified tumor cells and the findings on magnetic resonance imaging (MRI) were correlated with the risk of progression to symptomatic myeloma (MM) requiring therapy. **Results:** In addition to serum M spike, percent bone marrow plasma cells and the ratio of involved/uninvolved serum free light chains, the level of serum beta-2-microglobulin was associated with an increased risk of progression to clinical myeloma requiring therapy. Gene expression profiles (GEP) of purified tumor cells revealed that all of the known molecular GEP subtypes of human MM are also represented in the precursor phase. An increased risk score (> - 0.26) based on a 70-gene signature (GEP70) was an independent predictor of the risk of progression to clinical MM requiring therapy. The presence of focal lesions on MRI also conferred an increased risk of disease progression but was not independent of other clinical and genomic features. **Conclusions:** These data represent the first comprehensive evaluation of clinical, genomic and imaging features of AMGs in the context of a prospective US-cooperative group trial, and demonstrate that while all genetic subtypes of MM have a precursor phase, genetic signatures previously associated with high risk myeloma also predict the risk of progression to clinical malignancy requiring therapy. These findings suggest the need to integrate both clinical assessment of tumor bulk and genomic properties of tumor cells in the clinical management of these patients. Clinical trial information: NCT00900263.

8516 Oral Abstract Session, Mon, 8:00 AM-11:00 AM

Definition of a high-risk population among patients with AL amyloidosis not undergoing autologous stem cell transplantation using bone marrow plasmacytosis and the presence of CRAB.

Taxiarchis Kourelis, Morie Gertz, Martha Lacy, Francis Buadi, Suzanne R. Hayman, Shaji Kumar, Steven R. Zeldenrust, Nelson Leung, Robert A. Kyle, Stephen Russell, David Dingli, John Anthony Lust, Yi Lin, Prashant Kapoor, Vincent Rajkumar, Angela Dispenzieri; Mayo Clinic, Rochester, MN; Division of Hematology, Mayo Clinic, Rochester, MN

Background: There is consensus that light chain amyloidosis (AL) patients with CRAB criteria (abnormal calcium or renal function, anemia or lytic bone lesions) also have multiple myeloma (MM). These patients are typically excluded from AL trials; however, AL patients with >= 10% bone marrow plasma cells (BMPC) in the absence of CRAB are included in trials along with AL with < 10% BMPC. We postulated that the currently used dichotomy may be incorrect and examined the spectrum of AL with and without MM. **Methods**: We identified 1,272 patients with AL seen within 90 days of diagnosis, between January 1, 2000, and December 31, 2010. We defined the population of patients with coexisting MM based on the existence of CRAB (AL-CRAB-MM). Patients without CRAB were divided into two groups, AL-only (<10% BMPC) and AL-PC-MM (>=10% BMPC). **Results**: Among the 1,272 patients, 117 (9%) had AL-CRAB-MM, 476 (37%) had AL-PC-MM, and 679 (53%) had AL only. Their respective median overall survivals (OS) were 16.2, 15.8, and 28.4 months ($p<0.0001$). Autologous stem cell transplant (ASCT) was performed in 203 (30%), 138 (29%) and 23 (20%) patients respectively. Since the outcomes of AL-CRAB-MM and AL-PC-MM were similar, they were pooled for univariate and multivariate analyses. On multivariate analysis, AL-CRAB-MM and AL-PC-MM retained negative prognostic value independent of age, cardiac stage, prior autologous stem cell transplant (ASCT), beta 2 microglobulin, and dFLC. We next considered whether patients received ASCT as part of their treatment. For those patients who never received ASCT, the 5-year OS were 19%, 14%, and 31%, $p<0.001$, for AL-CRAB-MM, AL-PC-MM, and AL only respectively. In contrast, for those patients who received ASCT, the respective 5-year OS were 46%, 56%, and 73%, $p<0.001$. **Conclusions**: AL patients with >=10% BMPCs have a poor prognosis similar to patients with AL-CRAB-MM and should therefore be considered as AL with MM.

8517 **Oral Abstract Session, Mon, 8:00 AM-11:00 AM**

Second primary malignancies (SPM) in newly diagnosed myeloma (MM) patients treated with lenalidomide (Len): Meta-analysis of 6,383 individual patient data (IPD).

Antonio Palumbo, Sara Bringhen, Vincent Rajkumar, Giulia Lupparelli, Saad Zafar Usmani, Anders Waage, Alessandra Larocca, Bronno van der Holt, Pellegrino Musto, Andrea Evangelista, Sonja Zweegman, Meletios A. Dimopoulos, Roman Hajek, Michele Cavo, Sagar Lonial, Giovannino Ciccone, Mario Boccadoro, Bart Barlogie, Pieter Sonneveld, Philip L. McCarthy; Division of Hematology, University of Turin, Turin, Italy; Myeloma Unit, Division of Hematology, University of Torino, Torino, Italy; Mayo Clinic, Rochester, MN; Myeloma Institute for Research and Therapy, Little Rock, AR; St. Olav's Hospital/NTNU, Trondheim, Norway; Erasmus MC, Rotterdam, Netherlands; Department of Onco-Hematology, IRCCS-CROB, Referral Cancer Center of Basilicata, Rionero in Vulture, Italy; Cancer Epidemiology Unit, CeRMS and CPO Piemonte, Città della Salute e della Scienza, University of Torino, Torino, Italy; VU University Medical Center, Amsterdam, Netherlands; Department of Clinical Therapeutics, University of Athens School of Medicine, Athens, Greece; School of Medicine, University of Ostrava; Institute of clinical haematology, University Hospital Ostrava, Ostrava, Czech Republic; Bologna University School of Medicine, Seràgnoli Institute of Hematology, Bologna, Italy; Emory University School of Medicine, Atlanta, GA; Roswell Park Cancer Institute, Buffalo, NY

Background: An increased risk of SPM in MM pts treated with len has been reported. We performed an IPD metanalysis to estimate the incidence of SPM according to len exposure. **Methods:** Randomized studies of MM, from PubMed and ASCO/IMW/ASH (after 2000), that met the following criteria, were included: randomization to treatment with len (len-trials); randomization to treatment including new drug but not len (no-len-trials); available SPM data. Primary aim was to estimate cumulative incidence of SPMs by len exposure, corrected for death (competing event). **Results:** Data from 6,383 pts (3,218 from 8 len-trials, 3,165 from 10 no-len-trials) were analyzed. Median age was 69 years. During follow-up (median=30 mos) 420 (6.6%) SPMs were reported: 188 (2.9%) hematologic and 232 (3.6%) solid cancers. Solid tumors occurred with similar incidence in all groups. Incidence of hematologic SPM was significantly higher in patients receiving len (3.2 vs 1.1, p=0.04), but risk is limited to patients treated with melphalan+len (4.1, 95%CI: 2.4-5.8) with no excess in other combinations (len without melphalan: 1.2, 0.0-2.6; melphalan without len: 1.1, 0.0-2.7) (p=0.003). The cumulative incidence of death for any cause was much higher than the risk of SPM. **Conclusions:** The risk of hematologic SPMs was higher in pts receiving melphalan+len. The benefit/risk profile of len treatment remains positive. Cumulative incidence (%) of SPMs and death (95%CI).

	3-year			5-year		
	Len randomized trials		No len trials	Len randomized trials		No len trials
	Len arms	No len arms		Len arms	No len arms	
SPM						
Overall	5.2 (4.0-6.3)	3.8 (2.2-5.4)	3.2(2.4-4)	10.2 (8.0-12.4)	7.2 (4.1-10.3)	6.2(5.1-7.4)
Hematologic	1.4 (0.8-2.1)	0.3 (0.0-0.8)	1(0.6-1.5)	3.2 (2.0-4.4)	1.1 (0.0-2.7)	2.6(1.8-3.3)
Solid	3.7(2.8-4.7)	3.5(1.9-5.1)	2.2(1.5-2.8)	7(5.1-8.9)	6.1(3.4-8.8)	3.7(2.8-4.5)
Death						
All causes	23.3 (21.2-25.6)	24.8 (21-29.2)	36.6 (34.5-38.8)	47 (43.1-51.2)	64.8 (54-75.5)	56.2 (53.9-58.6)
Toxicity (Infection, cardiac, etc)	6.6(5.4-7.8)	6.6(4.2-8.9)	8.2(7-9.4)	9.8(8-11.7)	17.5(11.4-23.6)	10.8(9.4-12.2)
MM	13.2(11.4-15)	14.9(11.6-18.2)	14.8(13.2-16.4)	25.9(22.6-29.2)	35.4(25.6-45.2)	24.4(22.4-26.3)

8518 **Clinical Science Symposium, Mon, 11:30 AM-1:00 PM**

Preliminary safety and efficacy of IPI-145, a potent inhibitor of phosphoinositide-3-kinase-δ,γ, in patients with relapsed/refractory lymphoma.

Steven M. Horwitz, Ian Flinn, Manish R. Patel, Anas Younes, Francine M. Foss, Yasuhiro Oki, Jennifer Sweeney, Kerstin Allen, Joi Dunbar, Patrick Francis Kelly, Brad S. Kahl; Memorial Sloan-Kettering Cancer Center, New York, NY; Sarah Cannon Research Institute, Nashville, TN; Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL; The University of Texas MD Anderson Cancer Center, Houston, TX; Yale Cancer Center, New Haven, CT; Infinity Pharmaceuticals, Inc., Cambridge, MA; University of Wisconsin Carbone Cancer Center, Madison, WI

Background: Phosphoinositide-3-kinases (PI3Ks) are pivotal in cell signaling and regulate a variety of cellular functions relevant to oncogenesis. IPI-145, a potent oral inhibitor of the PI3KEδ and PI3K-γ isoforms, is in clinical development for patients (pts) with hematologic malignancies. Early results in pts with relapsed/refractory lymphoma from an ongoing Phase 1 study are reported here. **Methods:** This dose-escalation study evaluates the safety, maximum tolerated dose (MTD), clinical activity, and pharmacokinetics (PK) of IPI-145. Expansion cohorts (EC) $<$ MTD are allowed. IPI-145 is given orally twice daily (BID) in 28-day cycles. Tumor response is based on standard disease-specific criteria. **Results:** 55 pts have been dosed with IPI-145. PK, available through 50 mg BID, are linear with complete inhibition of PI3K-δ at doses $>$ 15 mg BID and increasing suppression of PI3K-γ with increasing dose. In the 36 pts with lymphoma who received 15 mg to 75 mg BID, the median [range] number of cycles was 2.4 [0.1–10] and 67% remain on study. Treatment-related adverse events (TRAEs) occurred in 50% of pts with lymphoma. Neutropenia and increased ALT were the most common $\geq$ Grade 3 TRAEs (4 pts each) and were not associated with increasing dose. $>$ Grade 3 ALT elevations were more common in lymphoma pts (18%) compared to non-lymphoma pts (5%). Among evaluable pts with lymphoma (n=27), early clinical activity was observed in T-cell (n=6, 1 CR, 1 PR, 1 SD) and aggressive/indolent B-cell (n=21, 2 CR, 9 PR, 5 SD) lymphoma pts at $\leq$ 75 mg BID. 92% of responses were observed by 3 months. **Conclusions:** IPI-145 appeared well tolerated and has shown clinical activity in pts with relapsed/refractory advanced B- and T-cell lymphoma across the range of doses examined. The single agent MTD has not been determined and dose escalation continues. Updated safety and efficacy data from pts with lymphoma enrolled in dose escalation or ECs evaluating 25 mg BID and a higher dose ($<$ MTD) of IPI-145 will be presented. Clinical trial information: NCT01476657.

8519 **Clinical Science Symposium, Mon, 11:30 AM-1:00 PM**

Final results of a phase I study of idelalisib, a selective inhibitor of phosphatidylinositol 3-kinase P110δ (PI3Kδ), in patients with relapsed or refractory mantle cell lymphoma (MCL).

Stephen Edward Forbes Spurgeon, Nina D. Wagner-Johnston, Richard R. Furman, Ian Flinn, Steven E. Coutre, Jennifer R. Brown, Don M. Benson, John C. Byrd, John Leonard, Sissy Peterman, David Michael Johnson, Jessie Gu, Roger D. Dansey, Wayne R. Godfrey, Brad S. Kahl; Oregon Health & Science University, Portland, OR; Washington University School of Medicine in St. Louis, St. Louis, MO; Weill Cornell Medical College, New York, NY; Sarah Cannon Research Institute, Nashville, TN; Stanford Cancer Institute, Stanford, CA; Dana-Farber Cancer Institute, Boston, MA; The Ohio State University, Columbus, OH; Gilead Sciences, Inc., Seattle, WA; University of Wisconsin Carbone Cancer Center, Madison, WI

Background: PI3K-delta signaling is critical for activation, proliferation and survival of B cells and plays a role in homing and retention in lymphoid tissues. PI3Kδ signaling is hyperactive in many B-cell malignancies. Idelalisib is a first-in-class, selective, oral inhibitor of PI3Kδ. Initial response rate of 42% was previously reported in MCL (Kahl, ICML 2011). Long-term follow-up is now presented. **Methods:** This phase 1 study evaluated the activity of continuous (48 weeks) idelalisib monotherapy in pts with relapsed or refractory hematologic malignancies. Doses ranged from 50 mg BID to 350 mg BID in 8 cohorts. Response was based on investigator assessments using standard criteria (Cheson et al, 2007). Patients who continued to benefit were able to enroll in an extension study. **Results:** 40 patients with recurrent MCL enrolled. Patients were 88% male, median age [range] of 69 [52-83] years, 43% with refractory disease. The median [range] number of prior therapies was 4 [1E14]. The median [range] duration of idelalisib treatment was 3.5 [1-26+] months, with 6 (15%) patients continuing on treatment in the extension protocol. Overall response rate (ORR) was 16/40 (40%), with 2/40 CR (5%). The median duration of response (mDOR) was 2.7 months, and median PFS (mPFS) was 3.7 months. The 1-year PFS was 22%. For patients dosed with ≥100 mg BID, ORR was 12/23 (52%), for patients dosed with ≥150 mg BID, ORR was 11/16 (69%) including both CR (12.5%). Most common adverse events included (total%/≥G3%); diarrhea (40/18), nausea (33/5), pyrexia (28/0), fatigue (25/3), rash (25/3), decreased appetite (20/15), URI (20/0), and pneumonia (13/13). Abnormal lab values included (total%/≥G3%) ALT/AST elevations (65/20). 6/40 (15%) patients discontinued therapy due to AEs, potentially treatment related. **Conclusions:** The oral PI3Kδ inhibitor idelalisib (GSE1101) is active and well tolerated in heavily pre-treated pts with MCL. A proportion of patients have long-term (>1 year) clinical benefit. These data support further clinical evaluation of idelalisib in MCL. Clinical trials with idelalisib in combination with other agents are in progress. Clinical trial information: NCT00710528.

8520 **Clinical Science Symposium, Mon, 11:30 AM-1:00 PM**

Updated results of a phase I first-in-human study of the BCL-2 inhibitor ABT-199 (GDC-0199) in patients with relapsed/refractory non-Hodgkin lymphoma (NHL).

Matthew Steven Davids, John Francis Seymour, John F. Gerecitano, Brad S. Kahl, John M. Pagel, William G. Wierda, Mary Ann Anderson, David E. Darden, Cathy E. Nolan, Lori A. Gressick, Jianning Yang, Brenda J. Chyla, Todd A. Busman, Alison M. Graham, Elisa Cerri, Sari H. Enschede, Rod A. Humerickhouse, Andrew W Roberts; Dana-Farber Cancer Institute, Boston, MA; Peter MacCallum Cancer Center, Melbourne, Australia; Memorial Sloan-Kettering Cancer Center, New York, NY; University of Wisconsin Carbone Cancer Center, Madison, WI; University of Washington, Seattle, WA; The University of Texas MD Anderson Cancer Center, Houston, TX; Royal Melbourne Hospital; Walter and Eliza Hall Institute of Medical Research, Parkville, Australia; AbbVie, Inc, North Chicago, IL; Royal Melbourne Hopsital, Parkville, Australia

Background: BCL-2 is highly expressed in NHL, including mantle cell lymphoma (MCL), and is a promising therapeutic target as it is involved in NHL pathogenesis and mediates resistance to many cytotoxics. ABT-199 is a second generation inhibitor with 500-fold higher affinity for BCL-2 (K_i<0.10 nM) than BCL-X_L (K_i=48 nM). **Methods:** Objectives of this Ph 1 dose-escalation study include evaluations of safety, pharmacokinetics and preliminary efficacy in patients (pts) with relapsed or refractory (R/R) NHL. A single oral dose (50-400 mg) was administered followed by 6 days off drug prior to the initiation of continuous once daily dosing. Due to concerns of potential tumor lysis syndrome (TLS), a 2 to 3 wk lead-in period with step-wise escalation to the target cohort dose was implemented. Dose cohorts up to 900 mg have been evaluated to date. **Results:** As of January 2013, 31 pts have been enrolled (median age 68 y (range 35-85); 20 males; median prior therapies 3 (range 1-7). 13 (42%) and 4 (13%) had bulky adenopathy (>5 and >10 cm, respectively). The most common AEs (≥15% of patients) were nausea (36%), diarrhea (26%), dyspepsia, vomiting, fatigue, pyrexia and cough (16% each). Gr 3/4 AEs occurring in >1 patient were anemia, neutropenia (4 pts each), and febrile neutropenia (2 pts). Two of 14 pts in cohort 5 experienced DLTs at the target dose of 600 mg: Gr 3 febrile neutropenia and Gr 4 neutropenia. Although Gr 3/4 thrombocytopenia was observed in 3 pts, it was not dose dependent. Gr 3 TLS was seen after the initial dose in 1 pt with very bulky MCL (>10 cm). With a median follow-up of 5 months (range 0.5-15), 17 have discontinued: 13 due to PD, 2 due to AEs and 2 who received a BMT. Of the 29 pts evaluable for efficacy, the overall best response rate was 55% with 1 DLBCL pt achieving a CR and 15 (52%) a PR (8/8 MCL, 3/3 Waldenstrom macroglobulinemia, 2/7 follicular lymphoma and 2/7 DLBCL pts). **Conclusions:** ABT-199 is highly active in R/R NHL, particularly in MCL. Additional dosing and scheduling modifications are currently being explored to optimize the efficacy/safety profile of this active new agent. ABT-199 warrants further single-agent and combination trials in NHL. Clinical trial information: NCT01328626.

8521 Poster Discussion Session (Board #1), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

A phase II trial of ifosfamide, methotrexate, etoposide, and prednisolone (IMEP) for previously untreated stage I, II extranodal natural killer/T-cell lymphoma, nasal type (NTCL): A multicenter study of the Korean Cancer Study Group.

Tae Min Kim, Dong-Wan Kim, Yoon-Koo Kang, Goon Jae Cho, Hong-Suk Song, Hyo Jung Kim, Byung Soo Kim, Jong-Seok Lee, Hawk Kim, Sung Hyun Yang, Young Jin Yuh, Sung Hwa Bae, Kyung-Hee Lee, Yoon-Kyung Jeon, Chul Woo Kim, Dae Seog Heo; Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea; Seoul National University Hospital, Seoul, South Korea; Asan Medical Center, Seoul, South Korea; Pusan National University Hospital, Busan, South Korea; Dongsan Medical Center, Keimyung University, Daegu, South Korea; Department of Internal Medicine, Hallym University Medical Center, Hallym University College of Medicine, Anyang, South Korea; Korea University Medical Center, Seoul, South Korea; Seoul National University Bundang Hospital, Bundang City, South Korea; Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, South Korea; Department of Internal Medicine, Korea Cancer Center Hospital, Seoul, South Korea; Inje University Sanggye Paik Hospital, Seoul, South Korea; Daegu Catholic University Hospital, Daegu, South Korea; Yeungnam University Medical Center, Daegu, South Korea; Department of Pathology, Seoul National University Hospital, Seoul, South Korea

Background: Combination chemotherapy of IMEP was active as a first-line as well as a second-line treatment for NTCL in a retrospective analysis. Thus, we conducted a prospective, multicenter, phase II study of IMEP chemotherapy in previously, untreated stage I/II NTCL. **Methods:** Patients with chemonaïve stage I/II NTCL were enrolled between December 2004 and February 2009 and they received 6 cycles of IMEP (ifosfamide 1.5 g/m^2 on days 1 to 3; methotrextate 30mg/m^2 on days 3 and 10; etoposide 100mg/m^2 on days 1 to 3; and prednisolone 60mg/m^2/day on days 1 to 5) followed by involved field radiotherapy (IFRT). Response was evaluated every 2 cycles of chemotherapy and 4 to 8 weeks after completion of IFRT using modified Response Evaluation Criteria in Solid Tumors. **Results:** Overall, 44 patients including 29 males were analyzed by the intent-to-treat principle. Overall response rates were 73% (complete remission [CR], 11 [27%] of 41 evaluable patients) after IMEP chemotherapy and 78% (CR, 18 [67%] of 27) after IMEP followed by IFRT. Grade 3 to 4 neutropenia and thrombocytopenia were documented in 33 (75%) and 7 (16%) patients, respectively. Only 8 (18%) patients experienced grade 3 febrile neutropenia. 2-year progression-free survival (PFS) and overall survival (OS) were 56% and 66%, respectively. High Ki-67 ($\geq$ 70%) and Ann Arbor stage II independently reduced PFS (hazard ration [HR]=5.6, 95% confidence interval [CI] 1.8-17.6; P=.004) and OS (HR=4.8, 95% CI 1.9-12.2; P=.001), respectively. **Conclusions:** IMEP followed by IFRT is active and safe against patients with previously untreated stage I/II NTCL.

8522 Poster Discussion Session (Board #2), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Phase I expansion trial of an oral TORC1/TORC2 inhibitor (CC-223) in diffuse large B-cell lymphoma (DLBCL) and multiple myeloma (MM).

Andre Goy, Vincent Ribrag, Andrea Varga, Thomas E. Witzig, Enrique M. Ocio, Luis G. Paz-Ares, Monica M. Mita, Tim Meyer, Pamela N. Munster, Amit Mahipal, Jean-Pierre Delord, Hendrik-Tobias Arkenau, Martin Gutierrez, Angela James, Lilly Wong, Shuichan Xu, Xiaoling Wu, James Carmichael, Rajesh Chopra, Kristen Hege; John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; Institut Gustave Roussy, Villejuif, France; Mayo Clinic, Rochester, MN; Hospital Universitario de Salamanca, Salamanca, Spain; Hospital Universitario Virgen del Rocío, Seville, Spain; Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA; University College London Cancer Institute, London, United Kingdom; UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA; H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; Institut Claudius Regaud, Toulouse, France; Sarah Cannon Research UK, London, United Kingdom; Hackensack University Medical Center, Hackensack, NJ; Celgene Corporation, Summit, NJ; Celgene Corporation, San Diego, CA; Celgene Corporation, Basking Ridge, NJ; Celgene SL, Madrid, Spain; Celgene Corporation, San Francisco, CA

Background: CC-223 is an ATP-competitive inhibitor of the mTOR kinase, including both TORC1 and TORC2 complexes. CC-223 was selected to address resistance of rapamycin analogues mediated by TORC2 activation. **Methods:** Following establishment of the MTD (reported at ASCO 2012), subjects with advanced DLBCL, MM and select solid tumors were enrolled in parallel expansion cohorts of up to 20 evaluable subjects. CC-223 was dosed at 45 mg once daily in 28 day cycles until disease progression. **Results:** As of 09 January, 2013, 35 subjects were enrolled including DLBCL (21) and MM (14). Results in solid tumor cohorts are reported separately. The most common ($>$ 20%) related adverse events (all grades) were fatigue, hyperglycemia, rash, anorexia, nausea, vomiting and diarrhea. In addition, related serious adverse events included infection (2), pneumonitis (1), renal insufficiency (2), pancreatitis (1) and thrombocytopenia (1). CC-223 dose reduction was required in 9 subjects (27%), usually during cycle 1 or 2, and 4 additional subjects with DLBCL dropped out during cycle 1 due to toxicity. Systemic exposure was similar between the two tumor cohorts and was associated with inhibition of TORC1 (p4EBP1) and TORC2 (pAKT) biomarkers in blood cells. Reduction in glucose uptake (32 – 98% decrease) on PET imaging at day 15 was observed in 7/7 DLBCL subjects with results currently available. Three of 17 evaluable subjects with DLBCL had partial responses (PR) after 2 cycles; two with rapid and near complete regression ($>$ 90%) of target lesions by CT and PET with PR confirmed and treatment ongoing at 6 and 8 cycles. Both had failed multiple prior treatment regimens (5 and 3, respectively), including autologous stem cell transplant (ASCT). No responses were observed in 10/14 evaluable subjects with MM although 2 subjects have prolonged stable disease (SD) with treatment ongoing at 12 and 14 cycles. **Conclusions:** Encouraging signals of biomarker and clinical activity were observed in DLBCL, including two near complete responses, which are ongoing. Due to dose reductions and interruptions, a starting dose of 30 mg QD is recommended for future studies. Clinical trial information: NCT01177397.

8523 Poster Discussion Session (Board #3), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

A phase I study of ISIS 481464 (AZD9150), a first-in-human, first-in-class, antisense oligonucleotide inhibitor of STAT3, in patients with advanced cancers.

David S. Hong, Anas Younes, Luis Fayad, Nathan Hale Fowler, Fredrick B. Hagemeister, Reena Mistry, John J. Nemunaitis, Mitesh J. Borad, Alan H. Bryce, Mason Yamashita, Steven George Hughes, Theodore Jesse Kwoh, A. Robert MacLeod, Dan Norris, Ron Baldwin, Gene Hung, Brett P. Monia, Razelle Kurzrock; The University of Texas MD Anderson Cancer Center, Houston, TX; Memorial Sloan-Kettering Cancer Center, New York, NY; Mary Crowley Cancer Research Center, Dallas, TX; Mayo Clinic, Scottsdale, AZ; Isis Pharmaceuticals, Inc, Carlsbad, CA; University of California, San Diego, San Diego, CA

Background: ISIS 481464 is a synthetic bicyclic nucleic acid-containing antisense oligonucleotide that is complementary to the mRNA for signal transducer and activator of transcription 3 (STAT3). **Methods:** Primary objective of the dose-escalation study (3+3 design) was to establish the maximum tolerated dose (MTD) and recommended phase II dose (RP2D). Secondary objectives included safety, tumor response, pharmacokinetics (PK), and pharmacodynamics (PD) using IL-6 and tumor markers. Patient (pt) eligibility included : >18 yrs old, solid tumors or lymphomas refractory to at least 1 prior systemic therapy. ISIS 481464 was administered IV as a loading dose on Days 1, 3, and 5 and then weekly. **Results:** 15 pts were dosed (4 at 2 mg/kg and 11 at 4 mg/kg). 6 pts had advanced lymphoma (3 DLBCL, 2 Hodgkin's lymphoma, 1 mantle cell lymphoma) and 9 pts solid tumors. There was one dose limiting toxicity (DLT), a possibly related thrombotic microangiopathy at 4 mg/kg. Treatment emergent thrombocytopenia was observed with an average reduction of approximately 70% from baseline. Three pts, 1 at 2 mg/kg and 2 at 4 mg/kg, experienced nadirs in platelet count below $50x10^9$/L (range 16 to $33x10^9$/L). MTD was not reached; however, given the thrombocytopenia at 4mg/kg, the RP2D was 2mg/kg. Partial responses were observed in 2/3 DLBCL pts. The 1st DLBCL pt (2 mg/kg) with 10 prior treatments had a durable 55% reduction in tumor size and is ongoing treatment at 11 months. This pt had a 76% reduction in IL-6. The 2nd DLBCL pt (4 mg/kg) with 2 prior treatments had a 65% reduction for 4 months and was able to undergo autologous stem cell transplantation. There were no responses in the solid tumor pts. PKs revealed increased plasma trough levels (indicative of tissue concentrations) with increased dose. **Conclusions:** ISIS 481462 was well-tolerated and the RP2D was determined to be 2 mg/kg. Initial tumor activity was observed in DLBCL pts and a dose expansion in advanced lymphomas is ongoing. Clinical trial information: NCT01563302.

8524 Poster Discussion Session (Board #4), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

A pooled analysis of 1,546 patients with AIDS-related lymphoma (ARL): An assessment of prognostic factors by treatment era.

Stefan K. Barta, Michael Samuel, Xiaonan Xue, Jeanette Y. Lee, Nicolas Mounier, Lawrence D. Kaplan, Josep-Maria Ribera, Michele Spina, Umberto Tirelli, Rudolf Weiss, Lionel Galicier, Francois Boue, Wyndham Hopkins Wilson, Christoph Wyen, Kieron Dunleavy, Richard F. Little, Scot C. Remick, Mendel Goldfinger, Ariela Noy, Joseph A. Sparano; Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY; Montefiore Medical Center, Bronx, NY; Albert Einstein College of Medicine, Bronx, NY; Department of Biostatistics, University of Arkansas for Medical Sciences, Little Rock, AR; Centre Hospitalier Universitaire l'Archet, Nice, France; University of California, San Francisco, San Francisco, CA; Hospital Universitari Germans Trias i Pujol, Barcelona, Spain; National Cancer Institute, Aviano, Italy; Private Practice for Hematology, Oncology, and Infectious Diseases, Bremen, Germany; Hopital St Louis, Assistance Publique-Hopitaux de Paris, Paris, France; Hopital Antoine Béclère, Clamart, France; National Cancer Institute, Bethesda, MD; University Hospital Cologne, Cologne, Germany; Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD; NCI, Bethesda, MD; Mary Babb Randolph Cancer Center, West Virginia University School of Medicine, Morgantown, WV; Memorial Sloan-Kettering Cancer Center, New York, NY

Background: Management of ARL evolved in the last 2 decades. We previously reported prognostic factors in a pooled analysis of 1,546 patients with ARL, and here present analysis of these factors over time to determine if their prognostic significance has changed. **Methods:** Following a systematic review, we assembled individual patient data from 19 prospective phase 2/3 clinical trials (published 1993-2010) for ARL (n=1,546). Factors analyzed include age, sex, histology, CD4 count, prior history of (h/o) AIDS, & age-adjusted (aa) IPI. The endpoint was overall survival (OS) expressed as the hazard ratio (HR) for death. We used separate Cox proportional hazard models adjusted for the other covariates to determine the significance of each variable in the following time periods: pre-cART [combination antiretroviral therapy] (<1996; n=388), early cART ('96-'00; n=694), modern cART ('01-'04; n=282) & current era ('05-'10; n=182). We also combined all enrollments in one Cox model to test for difference in association with OS over enrollment periods. **Results:** Rituximab use was limited in the early cART (20%) compared with the modern cART (83%) and current (93%) eras. Histology & sex were not significantly associated with OS in any time period. Increasing age was associated with worse OS in the pre-cART (HR 1.02; $p<0.01$) and current (HR 1.05, $p=0.04$) eras. A prior h/o AIDS increased risk of death during early cART (HR 1.31, $p=0.047$) but was not significant after 2000. Meanwhile, baseline CD4 count <50 was a poor prognostic factor during early (HR 1.78, $p<0.01$) and modern cART (HR 2.76, $p=0.001$) eras, but not in the current era. The aaIPI predicted worse OS in each time period (pre-cART: HR 1.54, $p<0.0001$; early cART: HR 1.49, $p<0.0001$; modern cART: HR 1.52, $p<0.01$; current era: HR 2.34, $p<0.0001$). No significant interaction between each prognostic factor with enrollment was found. **Conclusions:** In this pooled analysis of 1,546 patients with ARL, aaIPI was the only consistently significant prognostic factor and its effect was magnified in the current era. HIV-related factors gained prognostic relevance in the early and modern cART era but may not be as relevant with current treatment strategies.

8525 Poster Discussion Session (Board #5), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Phase II study of chidamide (CS055), a new subtype-selective oral histone deacetylase inhibitor, in patients with relapsed or refractory peripheral T-cell lymphoma.

Yuan-Kai Shi, Mei Dong, Xiao-Nan Hong, Wei-Jing Zhang, Ji-Feng Feng, Jun Zhu, Li Yu, Xiao-Yan Ke, Hui-Qiang Huang, Zhi-Xiang Shen, Yun Fan, Wei Li, Xie-Lan Zhao, Lu-Gui Qiu, He Huang; Cancer Institute & Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China; Fudan University Shanghai Cancer Center, Shanghai, China; 307 Hospital of PLA, Beijing, China; Jiangsu Cancer Hospital, Nanjing, China; Beijing Cancer Hospital, Beijing, China; Chinese PLA General Hospital, Beijing, China; Peking University Third Hospital, Beijing, China; Sun Yat-sen University Cancer Center, Guangzhou, China; Ruijin Hospital, Medical College, Shanghai Jiao Tong University, Shanghai, China; Zhejiang Cancer Hospital, Hangzhou, China; The First Hospital of Jilin University, Changchun, China; Xiangya Hospital Central-South University, Changsha, China; Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China; The First Affiliated Hospital of College of Medicine, Zhejiang University, Hangzhou, China

Background: Chidamide (CS055) is a new benzamide type of histone deacetylase (HDAC) inhibitor with subtype selective activity against HDAC1, 2, 3 and 10. Chidamide has shown well-tolerated and favorable PK profiles in patients (pts) with advanced solid tumors and lymphomas. This phase II study was to evaluate the efficacy and safety of chidamide in relapsed or refractory peripheral T-cell lymphoma (PTCL). **Methods:** 102 PTCL pts were enrolled. In the exploratory trial, pts were randomized to receive chidamide 30mg or 50mg twice per week for 2 weeks, followed by 1 week of rest. In the pivotal trial, chidamide was administered 30mg twice per week w/o drug-free holiday. The primary endpoint was overall response rate (ORR). Responses were assessed using IWC criteria. **Results:** In the exploratory trial, 19 pts were enrolled with 9 and 10 to the 30mg and 50mg arms, respectively. ORR was 11.1% (1 CR) in the 30mg arm and 40.0% (1 CR, 1 CRu, 2 PR) in the 50mg arm. One pt in the 50mg arm experienced drug-related grade 4 thrombocytopenia. In the pivotal trial, 83 pts were enrolled. Most pts were stage III (35.2%) or IV (45.9%). 23 pts (29.1%) had confirmed responses out of 79 evaluable pts in the pivotal trial (8 CR, 3 CRu, and 12 PR). Responses of 19 pts (24.1%) maintained for $\geq$12 weeks. ORR with 27.8% was obtained by the Independent Review Committee. 68 pts (81.9%) experienced at least 1 AE in the pivotal trial, with 52.9% of AEs $\leq$ grade 2. The most common AEs were thrombocytopenia (50.6%), leucocytopenia (39.8%), neutropenia(21.7%), and fatigue (9.6%). 1 pt had a grade 3 QTc prolongation. 7 pts (8.4%) experienced at least one SAE, in which a grade 4 thrombocytopenia was considered to be drug-related. 2 pts with responses (CR) have received chidamide for $>$ 43 months w/o evidence of cumulative toxicity. **Conclusions:** Chidamide as an oral single agent had significant and durable activity in pts with relapsed or refractory PTCL. Toxicities with the therapy were generally tolerable and manageable. The overall differences in pathological subtypes of pts enrolled and clinical profiles between chidamide and the two existing drugs, pralatrexate and romidepsin, will be discussed. Clinical trial information: ChiCTR-TNC-10000811.

8526 Poster Discussion Session (Board #6), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Final results of a phase I study of idelalisib, a selective inhibitor of PI3Kδ, in patients with relapsed or refractory indolent non-Hodgkin lymphoma (iNHL).

Don M. Benson, Brad S. Kahl, Richard R. Furman, Jennifer R. Brown, Nina D. Wagner-Johnston, Steven E. Coutre, Stephen Edward Forbes Spurgeon, John C. Byrd, John Leonard, Sissy Peterman, David Michael Johnson, Yoonjin Cho, Roger D. Dansey, Wayne R. Godfrey, Ian Flinn; The Ohio State University, Columbus, OH; University of Wisconsin Carbone Cancer Center, Madison, WI; Weill Cornell Medical College, New York, NY; Dana-Farber Cancer Institute, Boston, MA; Washington University School of Medicine in St. Louis, St. Louis, MO; Stanford Cancer Institute, Stanford, CA; Oregon Health & Science University, Portland, OR; Gilead Sciences, Inc., Seattle, WA; Sarah Cannon Research Institute, Nashville, TN

Background: PI3K-delta signaling is critical for activation, proliferation and survival of B cells, plays a role in homing and retention in lymphoid tissues, and is hyperactive in many B-cell malignancies. Idelalisib (GS-1101) is a first-in-class, selective, oral inhibitor of PI3Kδ. Initial response rate of 38% was reported previously in iNHL (Kahl, ICML 2011). Long-term follow-up is now presented. **Methods:** This phase 1 study evaluated the activity of continuous idelalisib monotherapy in pts with relapsed hematologic malignancies. Doses ranged from 50 to 350 mg QD or BID in 8 cohorts. Response was evaluated based on investigator assessments using standard criteria (Cheson, 2007). Pts who continued to benefit were able to enroll in an ongoing extension study. **Results:** Study enrolled 64 pts with indolent iNHL. iNHL subtypes included 38 FL, 11 SLL, 9 LPL/WM, and 6 MZL. Pts were 69% male, median age [range] of 64 [32E91] years, 58% with refractory disease and 53% with bulky disease (LN diameter ≥5 cm). The median [range] number of prior therapies was 4 [1E10]. The median [range] duration of treatment was 3.8 [0-41] months, with 19 (30%) pts continuing on treatment extension protocol. ORR across all cohorts were 31/64 (48%), with 1 CR (1.6%). The median duration of response (mDOR) was 18.4 months, and median PFS (mPFS) was 7.6 months. For pts dosed with ≥100 mg BID (N=36); the ORR was 24/36 (67%), the mDOR was 15.4 months, and the mPFS was 16.6 months. The ORR for iNHL subtypes was: FL (45%), SLL (64%), LPL/WM (56%), and MZL (33%). Adverse events included (total%/≥G3%) diarrhea (36/8), fatigue (36/3), rash (27/3), nausea (25/2), pyrexia (20/3), chills (20/0), cough (19/2), pneumonia (17/16), and URI (17/0). Lab abnormalities included (total%/≥G3%) ALT/AST elevations (56/25). 8/64 (12.5%) pts discontinued therapy due to potentially treatment-related adverse events. **Conclusions:** The oral PI3Kδ inhibitor idelalisib is active in heavily pretreated pts with iNHL, can produce durable responses, and has a favorable safety profile. These data support further clinical development; phase 2 and 3 trials in iNHL are ongoing (NCT01732913, NCT01732926). Clinical trial information: NCT00710528.

8527 Poster Discussion Session (Board #7), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Pomalidomide plus low-dose dexamethasone (POM + LoDEX) versus high-dose dexamethasone (HiDEX) in relapsed/refractory multiple myeloma (RRMM): MM-003 analysis of patients (pts) with moderate renal impairment (RI).

Katja C. Weisel, Meletios A. Dimopoulos, Philippe Moreau, Martha Lacy, Kevin W. Song, Michel Delforge, Lionel Karlin, Hartmut Goldschmidt, Anne Banos, Albert Oriol Rocafiguera, Xin Yu, Lars Sternas, Christian Jacques, Mohamed H. Zaki, Jesùs F. San-Miguel; Hematology & Oncology, Department of Medicine, University Hospital Tuebingen, Tuebingen, Germany; Alexandra Hospital, Athens, Greece; Hematology, University Hospital Hotel-Dieu, Nantes, France; Mayo Clinic, Rochester, MN; Vancouver General Hospital, Vancouver, BC, Canada; Department of Hematology, University Hospital Leuven, Leuven, Belgium; Centre Hospitalier Lyon Sud/Hospices Civils de Lyon, Pierre-Bénite, France; Universitätsklinikum Heidelberg, Heidelberg, Germany; Hematology, Centre Hospital de la Côte Basque, Bayonne, France; Institut Catala d'Oncologia, HGTiP, Barcelona, Spain; Celgene Corporation, Summit, NJ; Hematology, Hospital Universitario de Salamanca, Salamanca, Spain

Background: Pts who have exhausted lenalidomide (LEN) and bortezomib (BORT) treatment (Tx) have a poor prognosis. A significant proportion of pts have RI with increasing incidence during disease course. POM + LoDEX has demonstrated efficacy in pts with prior LEN and BORT, including those with RI. MM-003 is an open-label, multicenter, phase 3 trial comparing POM + LoDEX vs HiDEX in RRMM pts who failed LEN and BORT and progressed on their last Tx. **Methods:** Pts must have failed LEN and BORT after ≥ 2 consecutive cycles of each (alone or in combination) and must have been refractory to last prior Tx (progressive disease [PD] during Tx or within 60 days). Pts with creatinine clearance (CrCl) < 45 mL/min were excluded. Randomization was 2:1 to POM 4 mg D1–21 + DEX 40 mg (20 mg for pts aged > 75 y) qw; or DEX 40 mg (20 mg for pts aged > 75 y) D1–4, 9–12, and 17–20 (28-D cycles). Tx continued until PD or unacceptable adverse event (AE). The primary endpoint was progression-free survival (PFS). Secondary endpoints included overall survival (OS) and AEs. This analysis examined pts with or without moderate RI (CrCl < 60 vs ≥ 60mL/min). **Results:** 302 pts received POM + LoDEX; 153 pts received HiDEX, 31% and 39% had moderate RI, respectively. Pts with moderate RI were more likely to be older (64% vs 36% aged > 65 y) vs no RI. Median follow-up was 4 mo. Median PFS and OS were significantly longer with POM + LoDEX vs HiDEX regardless of RI (Table). Similar AE rates for POM + LoDEX as well as HiDEX Tx were seen in pts with and without moderate RI (Table). Discontinuation due to AE was 5% vs 7% (no moderate RI) and 11% vs 5% (moderate RI). **Conclusions:** POM + LoDEX significantly extended PFS and OS vs HiDEX in pts with or without moderate RI. Tolerability of POM + LoDEX was acceptable across subgroups, with few discontinuations due to AE. Clinical trial information: NCT01311687.

	≥ 60 mL/min			< 60 mL/min		
CrCl	POM + LoDEX	HiDEX	HR (P)	POM + LoDEX	HiDEX	HR (P)
Efficacy (mo)						
Median PFS	3.7	1.8	0.47 (<.001)	3.2	1.6	0.44 (< .001)
Median OS	Not reached	9.2	0.57 (.021)	10.3	4.6	0.51 (.008)
Grade 3/4 AEs (%)						
Neutropenia	41	15	—	44	15	—
Anemia	24	26	—	33	34	—
Infection	23	23	—	28	24	—

8528 Poster Discussion Session (Board #8), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Pomalidomide plus low-dose dexamethasone (POM + LoDEX) versus high-dose dexamethasone (HiDEX) in relapsed/refractory multiple myeloma (RRMM): Impact of cytogenetics in MM-003.

Hartmut Goldschmidt, Meletios A. Dimopoulos, Katja C. Weisel, Philippe Moreau, Martha Lacy, Kevin W. Song, Michel Delforge, Lionel Karlin, Anne Banos, Albert Oriol Rocafiguera, Xin Yu, Lars Sternas, Christian Jacques, Mohamed H. Zaki, Jesùs F. San-Miguel; Universitätsklinikum Heidelberg, Heidelberg, Germany; Alexandra Hospital, Athens, Greece; Hematology & Oncology, Department of Medicine, University Hospital Tuebingen, Tuebingen, Germany; Hematology, University Hospital Hotel-Dieu, Nantes, France; Mayo Clinic, Rochester, MN; Vancouver General Hospital, Vancouver, BC, Canada; Department of Hematology, University Hospital Leuven, Leuven, Belgium; Centre Hospitalier Lyon Sud/Hospices Civils de Lyon, Pierre-Bénite, France; Hematology, Centre Hospital de la Côte Basque, Bayonne, France; Institut Catala d'Oncologia, HGTiP, Barcelona, Spain; Celgene Corporation, Summit, NJ; Hematology, Hospital Universitario de Salamanca, Salamanca, Spain

Background: RRMM patients (pts) who fail lenalidomide (LEN) and bortezomib (BORT) have poor prognosis. High-risk cytogenetics predict shorter survival. POM + LoDEX has demonstrated efficacy in pts with prior LEN and BORT and high-risk cytogenetics. MM-003 is an open-label, multicenter, phase III trial comparing POM + LoDEX vs. HiDEX in RRMM pts who failed LEN and BORT treatment (Tx) and have progressed on their last therapy. **Methods:** Pts must have been refractory to the last prior Tx (progressive disease [PD] during or within 60 days) and failed LEN and BORT after $\geq$ 2 consecutive cycles of each (alone or in combination). Randomization was 2:1 to POM 4 mg D1–21 + DEX 40 mg (20 mg for pts aged $>$ 75 y) weekly; or DEX 40 mg (20 mg for pts aged $>$ 75 y) D1–4, 9–12, and 17–20 (28-day cycles). Tx continued until PD or unacceptable adverse events (AEs). The primary endpoint was progression-free survival (PFS). Secondary endpoints included OS and AEs. This analysis examined pts meeting modified high-risk cytogenetic criteria—del(17p13) and/or t(4p16/14q32). **Results:** 302 pts received POM + LoDEX, and 153 pts received HiDEX. 225 and 107 pts, respectively, were evaluable for cytogenetics. Baseline characteristics were similar. Median PFS and OS were significantly longer with POM + LoDEX vs. HiDEX, regardless of cytogenetic risk (Table). The most common grade 3/4 AEs were neutropenia, anemia, and infection (Table). Discontinuation due to AE was low: 4% vs. 6% (high risk) and 10% vs. 4% (standard risk). **Conclusions:** Median PFS and OS were significantly longer with POM + LoDEX vs. HiDEX in pts with cytogenetically-defined high-risk disease, consistent with results from the intent-to-treat population. Tolerability was acceptable. POM + LoDEX should be considered a new Tx option in pts failing LEN and BORT. Clinical trial information: NCT01311687.

	High			Standard		
Cytogenetic risk	POM + LoDEX (n = 77)	HiDEX (n = 35)	HR (P)	POM + LoDEX (n = 148)	HiDEX (n = 72)	HR (P)
Efficacy (mo)						
Median PFS	3.1	1.2	0.39 (< .001)	4.0	2.1	0.46 (< .001)
Median OS	11.1	4.5	0.48 (.017)	Not reached	9.0	0.60 (.050)
Grade 3/4 AEs (%)						
Neutropenia	50	29	–	44	13	–
Anemia	37	37	–	27	29	–
Infection	20	23	–	31	19	–

8529 Poster Discussion Session (Board #9), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Final results from the phase Ib/II study (PX-171-006) of carfilzomib, lenalidomide, and low-dose dexamethasone (CRd) in patients with relapsed or progressive multiple myeloma.

Michael Wang, Thomas Martin, William Bensinger, Melissa Alsina, David Samuel DiCapua Siegel, Edward Kavalerchik, Ruben Niesvizky; Department of Lymphoma and Myeloma, University of Texas M. D. Anderson Cancer Center, Houston, TX; University of California, San Francisco, San Francisco, CA; Fred Hutchinson Cancer Research Center, Seattle, WA; H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; Onyx Pharmaceuticals, Inc., South San Francisco, CA; Center of Excellence for Lymphoma and Myeloma, Weill Medical College of Cornell University, New York Presbyterian Hospital, New York, NY

Background: Carfilzomib (CFZ) is approved in the US as single-agent treatment for patients with multiple myeloma (MM) who have progressed after bortezomib (BTZ) and an IMiD and are refractory to last line of treatment. We previously reported interim data from PX-171-006 (NCT00603447), a Ph 1b/2 study of CRd in relapsed or progressive MM (Wang et al. ASCO 2011). Herein we report final results. **Methods:** Patients (1–3 prior treatments) received CRd in 28-day (D) cycles—CFZ IV on D1, 2, 8, 9, 15, 16, lenalidomide (LEN) PO D1–21, and dexamethasone (dex) wkly. In phase 1, CFZ (15–27 mg/m^2) and LEN (10–25 mg) doses were escalated to determine the maximum tolerated dose (MTD) with a maximum planned dose (MPD) of CFZ 20 mg/m^2 D1, 2 of Cycle 1 and 27 mg/m^2 thereafter, LEN 25 mg/d, and dex 40 mg/wk, followed by phase 2 expansion at MTD/MPD. Endpoints included IMWG overall response rate (ORR), duration of response (DOR), progression-free survival (PFS), and safety. **Results:** A total of 84 patients were enrolled since June 2008. Overall, prior treatment included BTZ (77%/18% refractory) and LEN (70%/35% refractory); 20% had high-risk cytogenetics/FISH. MTD was not reached in Ph 1, supporting expansion at the MPD (n=52, 23% BTZ refractory and 42% LEN refractory). As of Nov 2012 (median follow-up 24.4 mo): ORR was 69% overall and 76.9% at MPD with very good partial response in 36.9% and 38.5% and stringent complete response in 3.6% and 3.8%, respectively; median DOR was 18.8 (95% CI 9.7–41.5) and 22.1 mo (95% CI 9.5–NE) respectively; median PFS was 11.8 (95% CI 7.6–20.7) and 15.4 mo (95% CI 7.9–NE), respectively. Seven responders at MPD pursued other therapy and were censored for PFS.A median of 8.5 (range 1−46) CFZ cycles were started; 4% required CFZ dose reductions; 15% discontinued CFZ due to adverse events (AEs). Grade 3/4 AEs were generally consistent with earlier studies in advanced MM that used similar doses of single-agent CFZ; grade 3/4 peripheral neuropathy was 1%. **Conclusions:** CRd was well tolerated, providing robust and durable responses in this pt population where 35% were LEN refractory. This combination is being further evaluated in several ongoing phase 2/3 trials. Clinical trial information: NCT00603447.

8530 Poster Discussion Session (Board #10), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Phase Ib dose escalation study of oral quisinostat, a histone deacetylase inhibitor, in combination with bortezomib and dexamethasone for patients with relapsed multiple myeloma.

Xavier Leleu, Cyrille Touzeau, Lotfi Benboubker, Thierry Facon, Martine Delain, Nele Fourneau, Charles Phelps, Ann Forslund, Peter Hellemans, Johan Smit, Julie Badamo-Dotzis, Philippe Moreau; Service des Maladies du Sang, Hôpital Claude Huriez, Lille, France; Hôpital Hôtel Dieu, CHU Nantes, Service d'Hématologie, Nantes, France; Centre Hospitalier Universitaire Tours-Hopital Bretonneau, Tours, France; Janssen Research & Development, LLC, Beerse, Belgium; Janssen Research & Development, LLC, Raritan, NJ; Quintiles, Providing Services On Behalf of Janssen Research & Development, Division of Janssen-Cilag, Issy-Les-Moulineaux, France

Background: Aggresome formation is a mechanism of resistance to agents (e.g., bortezomib) which block proteasome activity. HDACi (e.g., quisinostat) prevents aggresome formation by deacetylation of tubulin that allows the transport of unfolded proteins to lysosomes for degradation. **Methods:** Patients received quisinostat (Q) at escalated doses (6, 8, 10 and 12 mg) on days 1, 3, and 5 weekly, subcutaneous VELCADE (V) at 1.3 mg/m^{2}on days 1, 4, 8, and 11 of a 3-week cycle, and oral dexamethasone (D) at 20 mg on the day of and the day after VELCADE dosing. The primary endpoint was the maximum tolerated dose (MTD) of Q in the combination (Q+V+D). The secondary endpoints included safety, overall response rate, and pharmacodynamic biomarkers. **Results:** Eighteen patients (3, 3, 6, and 6 in increasing Q doses) were enrolled: 56% male; median age = 69 (range 50-82) years; multiple myeloma stage: IA = 11% and IIIA = 89%; prior lines of therapy: 1 = 100%, 2 = 55.6%, and 3 = 11.1%; prior VELCADE treatment = 50%. At the highest dose (12 mg) 2 patients had dose-limiting toxicity, 1 with QTc prolongation and 1 with atrial fibrillation. The MTD was established at the 10 mg Q for the Q+V+D regimen. The most common adverse events ($\geq$ 10% of patients) were diarrhea (39%), asthenia (33%), peripheral oedema (22%), nausea (17%), thrombocytopenia (17%), alopecia (11%), constipation (11%), and vomiting (11%); most were grade 2 or lower in toxicity. To date, 13 patients have discontinued treatment, of which 5 completed 11 cycles of treatment. The overall response rate was 87.5% (14/16, 95% CI: 61.7% to 98.5%), including 1 complete response, 2 very good partial response, and 11 partial responses. Most patients (9/11) showed a decrease in number of circulating multiple myeloma cells after 1 cycle. Two of 5 patients showed an increase in acetylated histone 3 from baseline as measured in peripheral blood mononuclear cells. **Conclusions:** The MTD is 10 mg quisinostat in combination with VELCADE and dexamethasone. The combination is active in the treatment of relapsed multiple myeloma and has an acceptable safety profile. Clinical trial information: NCT01464112.

8531 Poster Discussion Session (Board #11), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Clinical response by baseline characteristics in patients (pts) with relapsed and bortezomib (BTZ)-refractory multiple myeloma treated with panobinostat (PAN), BTZ, and dexamethasone (DEX; PANORAMA 2).

Melissa Alsina, Paul Gerard Guy Richardson, Robert L. Schlossman, Donna M. Weber, Steven E. Coutre, Cristina Gasparetto, Sutapa Mukhopadhyay, Michael S. Ondovik, Mahmudul H Khan, Carole S. Paley, Sagar Lonial; H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; Dana-Farber Cancer Institute, Boston, MA; The University of Texas MD Anderson Cancer Center, Houston, TX; Stanford Cancer Institute, Stanford, CA; Duke University Medical Center, Durham, NC; Novartis Pharmaceuticals Corp, East Hanover, NJ; Emory University School of Medicine, Atlanta, GA

Background: In PANORAMA 2, PAN + BTZ + DEX recaptured responses in heavily pretreated pts with BTZ-refractory MM; overall response rate (ORR), clinical benefit rate (CBR), and progression-free survival (PFS) were 34.5%, 52.7%, and 5.4 months, respectively. Here, we evaluate clinical response per baseline characteristics. **Methods:** Response was based on European Group of Blood and Marrow Transplantation 1998 criteria. High-risk cytogenetics was defined as del(17p), t(4;14), or t(14;16). Quality of life (QoL) was measured with Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity (FACT/GOG-Ntx) v4.0 scale. **Results:** Response rate trended higher in pts whose prior BTZ therapy was not their last line of therapy (Table). Although no trend in response rate was noted, PFS appeared longer in pts progressing within 60 days of their last BTZ-containing regimen than in those progressing on their last BTZ-containing regimen. In the 14 pts with high-risk cytogenetics, ORR was 42.9% and CBR was 71.4%. The mean FACT/GOG-Ntx subscale did not exhibit a clinically meaningful change from baseline (mean ± standard deviation [SD], 114.2 ± 21.1; n = 41) to cycle 9 day 1 (day 169; 104.2 ± 15.4; n = 16) as determined by 50% SD threshold for minimally important difference. Other QoL parameters were similarly unchanged. **Conclusions:** PAN + BTZ + DEX demonstrated activity regardless of baseline demographics in heavily pretreated pts with BTZ-refractory MM. Clinical trial information: NCT01083602.

	n	ORR, % (95% CI)	CBR, % (95% CI)	PFS, months (95% CI)
Disease progression				
On BTZ	40	37.5 (22.7-54.2)	55.0 (38.5-70.7)	4.2 (2.6-5.8)
Within 60 days of BTZ	15	26.7 (7.8-55.1)	46.7 (21.3-73.4)	7.6 (6.7-9.0)
BTZ in last prior line of therapy				
Yes	27	25.9 (11.1-46.3)	48.1 (28.7-68.1)	4.9 (2.1-7.6)
No	28	42.9 (24.5-62.8)	57.1 (37.2-75.5)	6.0 (3.9-7.6)
DEX in last BTZ-containing regimen				
Yes	45	26.7 (14.6-41.9)	46.7 (31.7-62.1)	4.9 (2.6-6.7)
No	10	70.0 (34.8-93.3)	80.0 (44.4-97.5)	6.2 (2.6-8.3)
DEX in last prior line of therapy				
Yes	37	32.4 (18.0-49.8)	54.1 (36.9-70.5)	4.2 (2.6-6.7)
No	18	38.9 (17.3-64.3)	50.0 (26.0-74.0)	6.5 (2.6-9.7)

8532 Poster Discussion Session (Board #12), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Pomalidomide (POM) with or without low-dose dexamethasone (LoDEX) in patients (Pts) with relapsed and refractory multiple myeloma (RRMM): MM-002 phase II age subgroup analysis.

Sundar Jagannath, Craig C. Hofmeister, Rachid C. Baz, David Samuel DiCapua Siegel, Ravi Vij, Christine Chen, Sagar Lonial, Kenneth Carl Anderson, Min Chen, Mohamed H. Zaki, Paul Gerard Guy Richardson; Mount Sinai Medical Center, New York, NY; Ohio State University Medical Center, Columbus, OH; H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; Washington University in St. Louis, St Louis, MO; Princess Margaret Hospital, Toronto, ON, Canada; Emory University School of Medicine, Atlanta, GA; Dana-Farber Cancer Institute, Boston, MA; Celgene Corporation, Summit, NJ

Background: POM demonstrated clinical efficacy and favorable tolerability in RRMM pts previously treated with lenalidomide (LEN) and bortezomib (BORT), in the randomized, multicenter, open label MM-002 phase II trial. This analysis evaluated whether the efficacy and tolerability of POM+LoDEX treatment is consistent across age subgroups. **Methods:** Pts with RRMM who had received $\geq$ 2 prior therapies, including LEN and BORT, and were refractory to their last regimen were randomized to either POM+LoDEX (POM 4 mg/day, days 1–21 of a 28-day cycle; LoDEX 40 mg/week) or POM alone. End points included progression-free survival (PFS), response rate (based on EBMT criteria), response duration, and safety. A post-hoc analysis based on age ($\leq$ 65 vs. $>$ 65 yrs) was conducted. **Results:** A total of 221 pts with a mean age of 64 yrs (range 34–88) were randomized to POM+LoDEX (n = 113) or POM (n = 108). The efficacy outcomes and the most common treatment emergent grade 3/4 adverse events (AEs) for the age subgroups according to treatment arm are presented in the Table. **Conclusions:** Regardless of age ($\leq$ 65 vs. $>$ 65 yrs), POM with or without LoDEX was effective and generally well tolerated in heavily pretreated RRMM pts who had already received LEN and BORT. POM with or without LoDEX represents a new clinical option for pts previously treated with numerous lines of therapy. Updated data will be presented at the meeting. Clinical trial information: NCT00833833.

Efficacy and safety outcomes.

	≤ 65 yrs		> 65 yrs	
Efficacy	**POM+LoDEX (n = 62)**	**POM (n = 69)**	**POM+LoDEX (n = 51)**	**POM (n = 39)**
≥ PR (%)	31	13	37	18
≥ MR (%)	47	23	43	44
Median DoR (months[a])	10.1	8.3	7.7	10.6
Median PFS (months, range)	4.7 (3.7–6.7)	1.9 (1.8–2.7)	3.7 (2.1–5.5)	3.3 (2.8–5.5)
Safety	**POM+LoDEX (n = 61)**	**POM (n = 68)**	**POM+LoDEX (n = 51)**	**POM (n = 39)**
Hematologic AEs (%)				
Neutropenia	46	40	35	59
Anemia	26	24	18	26
Thrombocytopenia	18	24	20	21
Nonhematologic AEs (%)				
Pneumonia	16	10	29	21
Urinary tract infection	10	3	8	0

[a] For pts who achieved ≥ PR. DoR, duration of response; MR, minimal response; PR, partial response.

8533 Poster Discussion Session (Board #13), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Combined analysis of single-agent lenalidomide in relapsed/refractory mantle cell lymphoma.

Thomas E. Witzig, Julie Vose, Pier Luigi Zinzani, Thomas Matthew Habermann, Joseph M. Tuscano, Rajni Sinha, Michael E. Williams, Johannes W. Drach, Rod Ramchandren, Sevgi Kalayoglu Besisik, Lei Zhang, Sherri Cicero, Tommy Fu, Andre Goy; Mayo Clinic, Rochester, MN; Nebraska Medical Center, Omaha, NE; Institute of Hematology "Seràgnoli", University of Bologna, Bologna, Italy; UC Davis Comprehensive Cancer Center, Sacramento, CA; Emory University Winship Cancer Institute, Atlanta, GA; University of Virginia Medical Center, Charlottesville, VA; Medical University of Vienna, Oncology, Vienna, Austria; Karmanos Cancer Institute, Wayne State University, Detroit, MI; Istanbul University Faculty of Medicine, Istanbul, Turkey; Celgene Corporation, Summit, NJ; John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ

Background: Mantle cell lymphoma (MCL) is an aggressive form of non-Hodgkin lymphoma (NHL) with poor prognosis. The immunomodulatory agent lenalidomide shows consistent activity with tolerable safety in multiple phase II studies of relapsed/refractory aggressive NHL (NHL-002 and NHL-003) and MCL post-bortezomib (MCL-001). This pooled analysis further examined the efficacy and safety of single-agent lenalidomide in patients with relapsed/refractory MCL. **Methods:** Single-agent lenalidomide was given 25 mg/d PO on days 1-21 of 28-day cycles as tolerated for 52 weeks (NHL-002) or until disease progression (NHL-003 and MCL-001). All MCL patients received ≥1 prior treatment, including bortezomib in MCL-001. Efficacy data were examined by independent central review for MCL-001 and NHL-003 and by investigators for NHL-002. **Results:** 206 patients with relapsed/refractory MCL were studied. The median age was 67 y (range 33-84; 63% ≥65 y), 91% stage III/IV disease and 51% had received ≥4 prior regimens (76% prior bortezomib). Overall response rate (ORR) with lenalidomide was 32% (10% CR/CRu), with a median time to response of 2.1 months and median duration of response (DOR) of 16.6 months (not yet reached in patients with CR/CRu; Table). Kaplan-Meier estimates for median PFS and OS were 5.4 and 23.9 months, respectively. Mean daily dose of lenalidomide was 21 mg. Grade 3/4 AEs included neutropenia (44%), thrombocytopenia (29%), anemia (11%), and fatigue (7%). Other any-grade AEs included tumor flare reaction (7%), venous thromboembolic events (7%), and invasive second primary malignancies (3%). **Conclusions:** Lenalidomide produced rapid and durable responses in patients with relapsed/refractory MCL, and exhibited a predictable safety profile among 3 phase II studies of lenalidomide in heavily pretreated patients, including prior treatment with bortezomib. Clinical trial information: MCL-001: NCT00737529; NHL-002: NCT00179660; NHL-003: NCT00413036.

Efficacy of lenalidomide in relapsed/refractory MCL.

Efficacy outcomes	(N=206)
ORR, % (95% CI)	32 (25-38)
CR/CRu, % (95% CI)	10 (6-15)
Median time to response, mo (95% CI)	2.1 (1.6-24.2)
Median DOR, mo (95% CI)	16.6 (9.2-32.4)
Median PFS, mo (95% CI)	5.4 (3.7-6.7)
Median OS, mo (95% CI)	23.9 (19.0-34.9)

8534 Poster Discussion Session (Board #14), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Lenalidomide in relapsed/refractory mantle cell lymphoma post-bortezomib: Subgroup analysis of the MCL-001 study.

Michael E. Williams, Andre Goy, Rajni Sinha, Sevgi Kalayoglu Besisik, Johannes W. Drach, Rod Ramchandren, Lei Zhang, Sherri Cicero, Tommy Fu, Thomas E Witzig; University of Virginia Medical Center, Charlottesville, VA; John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; Emory University Winship Cancer Institute, Atlanta, GA; Istanbul University Faculty of Medicine, Istanbul, Turkey; Medical University of Vienna, Oncology, Vienna, Austria; Karmanos Cancer Institute, Wayne State University, Detroit, MI; Celgene Corporation, Summit, NJ; Mayo Clinic, Rochester, MN

Background: Lenalidomide, an immunomodulatory agent with antitumor and antiproliferative effects, demonstrated rapid and durable efficacy in patients with relapsed/refractory mantle cell lymphoma (MCL) post-bortezomib in the phase II multicenter MCL-001 study. The objective of this analysis was to explore the efficacy of lenalidomide across patient subgroups. **Methods:** Single-agent lenalidomide was administered at 25 mg/d PO on days 1-21 of a 28-day cycle until disease progression or intolerability; primary endpoints were overall response rate (ORR) and duration of response (DOR) determined by an independent central review committee per modified IWG criteria. Exploratory analyses of ORR and DOR for subgroups were predefined and prospectively conducted. **Results:** Patients with relapsed/refractory MCL (N=134) had a median age of 67 y, with a median of 4 prior therapies (range, 2-10). The ORR was 28% (7.5% CR/CRu) and DOR was 16.6 months (95% CI, 7.7-26.7). Lenalidomide treatment provided consistent ORR and DOR across all subgroups analyzed by demographics, baseline disease status and prior therapy (Table). High vs normal baseline LDH was the only significant factor by univariate and multivariate logistic regression analysis of ORR (odds ratio=0.193; p=0.002). **Conclusions:** Single-agent lenalidomide provided consistent clinical benefit in patients with relapsed/refractory MCL post-bortezomib irrespective of patient subgroups at baseline with the exception of LDH. Clinical trial information: NCT00737529.

Subgroup analysis of lenalidomide in MCL.

Subgroup	n	ORR, n (%)	Median DOR, mo (95% CI)
Median age (≥65 years)	85	22 (26)	9.2 (5.8-16.7)
Sex	108	28 (26)	16.7 (9.2-NA)
Male	26	9 (35)	7.7 (2.1-20.5)
Female			
High MIPI	39	10 (26)	7.7 (3.6-NA)
Normal LDH	84	32 (38)	16.7 (14.8-NA)
High LDH	47	5 (11)	5.8 (1.7-7.7)
High tumor burden*	77	22 (29)	14.8 (5.8-26.7)
Bulky disease†	44	13 (30)	14.8 (5.7-NA)
Refractory to bortezomib	81	22 (27)	20.5 (7.7-NA)
Refractory to last therapy	74	20 (27)	26.7 (5.6-NA)
Time from last systemic anti-lymphoma therapy	96	23 (24)	7.7 (3.6-26.7)
<6 mo	36	14 (37)	16.7 (14.8-NA)
≥6 mo			
Prior high-dose/high-intensity treatment	44	12 (27)	16.7 (3.6-16.7)

*At least 1 lesion ≥5 cm or ≥3 lesions each ≥3 cm. [†]At least 1 lesion ≥7 cm.

8535 Poster Discussion Session (Board #15), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

A phase II study of single agent mocetinostat, an oral isotype-selective histone deacetylase (HDAC) inhibitor, in patients with diffuse large cell B-cell (DLBCL) and follicular (FL) lymphomas.

Michael Crump, Charalambos Andreadis, Sarit E. Assouline, David Rizzieri, Amanda Copeland, Richard H. C. Van Der Jagt, Susan Fox, Gregory K. Reid, Jeffrey M. Besterman, Robert E. Martell, Anas Younes; Princess Margaret Hospital, Toronto, ON, Canada; University of California, San Francisco, San Francisco, CA; Clinical Research Unit, Segal Cancer Center, Lady Davis Institute, Jewish General Hospital, Montreal, QC, Canada; Duke University Medical Center, Raleigh, NC; The University of Texas MD Anderson Cancer Center, Houston, TX; Ottawa Hospital, General Campus, Ottawa, ON, Canada; Hôpital Charles LeMoyne, Greenfield Park, QC, Canada; MethylGene Inc., Montreal, QC, Canada

Background: Mocetinostat (MGCD0103) is an orally available, isotype-selective, non-hydroxamate HDAC inhibitor targeting HDACs 1,2, 3 and 11 with single-agent activity in Hodgkin's lymphoma and in AML and MDS (in combination with 5-azacitidine). More than 430 patients have been treated to date. **Methods:** This open-label, phase II trial enrolled patients with DLBCL and FL. Patients received mocetinostat at doses ranging from 70-110 mg 3x/wk every 28 days. Anticancer activity, safety, pharmacokinetics and pharmacodynamics were evaluated. **Results:** Sixty-nine patients with DLBCL (n=41) and FL (n=28) were enrolled for treatment at starting doses of 85-110 mg. Median age was 62 years (range: 32 to 81). Median duration of treatment was ~3 months (range: <1 to 24). Objective response rate in DLBCL and FL, respectively, was 7/41 (17%; including 2 unconfirmed PRs) and 3/28 (11%; including 1 CR). Median time to response was 2.0 mos (range 1.7-21.0) and 5.3 mos (range 4.3-6.0) respectively. Stable disease was achieved by 13/41 (32%) and 14/28 (50%), respectively, for a disease control rate of 49% and 61%, respectively. Mean duration of SD in patients with DBLCL was ~4.5 mos (range 2-12 mos), with 10 patients remaining stable for ≥3 mos. Among FL patients, mean duration of SD was approximately 4.1 mos (range 1.7-13 mos), with 9 patients remaining stable for ≥3 mos. The FL CR occurred in a 62-year-old female with paratracheal, subcarinal and portal target lesions who achieved a PR after 4 cycles and CR after 12 cycles that persisted through the remaining 4 mos on study. Study drug was discontinued for adverse events in 19/69 (28%). Fatigue, weight loss or anorexia were most common (n=4 each). A total of 26 drug-related SAEs were reported among 12 patients (17%; 1-6 events per pt). There were no drug related deaths. Enrollment is complete and final data will be presented. **Conclusions:** Single-agent mocetinostat has activity in DLBCL and FL. Fatigue, gastrointestinal, and cardiac symptoms are the most common adverse events resulting in discontinuation of dosing. Based on the acceptable tolerability and clinical activity further development is warranted. Clinical trial information: NCT00359086.

8536 Poster Discussion Session (Board #16), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Long-term follow-up of the GELA LNH 03-7B study: A prospective phase II study of 150 patients over 80 years with diffuse large B-cell lymphoma (DLBCL) treated with RminiCHOP.

Frederic Peyrade, Olivier Fain, Bettina Fabiani, Frederic Bauduer, Eric Van Den Neste, Margaret Macro, Alain Devidas, Joelle Collignon, Christian Rose, Sophie Bonnet, Marie Maerevoet, Hilde Demuynck, Rene-Olivier Casasnovas; Centre Antoine Lacassagne, Nice, France; Hôpital Jean Verdier, Bondy, France; Hôpital Saint Antoine, Paris, France; Centre Hospitalierde La Cote Basque, Bayonne, France; Cliniques universitaires UCL Saint-Luc, Bruxelles, Belgium; Centre Hospitalier Universitaire de Caen, Caen, France; Hôpital Gilles de Corbeil, Corbeil, France; Centre Hospitalier Universitaire Sart-Tilman, LIEGE, Belgium; Centre Hospitalier Universitaire, Lille, France; Centre Hospitalier Universitaire, Liege, Belgium; Centre Hospitalier Universitaire, Ottignies, France; Heilig Hartziekenhuis Roeselare, Roeselare, Belgium; Hôpital Le Bocage, Dijon, France

Background: We report the outcome of patients included in the LNH 03-7B prospective phase II study of the GELA group which evaluated the tolerance and efficacy of a reduced dosage chemotherapy regimen (miniCHOP) associated with full dose rituximab in patients aged over 80 years with DLBCL. **Methods:** Patients were between 80 and 95 years (median 83 years), had disease stage I Bulky to IV and 65% had poor risk lymphoma according to IPI. Perfomance status was 0-2 in all cases. The majority of deaths and grade III/IV toxicity occurred during cycle 1 and 2. Response to treatment and early survival analyses were previously presented with 20 months median follow-up (Lancet oncol 2011;12:460-468). **Results:** At the time of this analysis, The median follow-up time was 41 months and 75 (50%) patients were alive. The 4-year estimated overall survival (OS) was 49.3% [95% CI: 40.8-57.3%] and the median OS was 38 months. The 4-year estimated PFS, EFS and DFS were 41.4% [95% CI: 33.1-49.5%], 39.4% [95% CI : 31.2-47.5%] and 57.9% [95% CI : 47.3-67.2%] respectively.]. During the additional follow-up, 8 patients relapsed (10% of CR patients) and 17 died. No long term toxicity was recorded. In a multivariate analysis an albumin level $>$35 g/l remained significantly associated with a longer survival. **Conclusions:** These results show that very old patients with DLBCL treated with RminiCHOP could express long-term survival and probably be cured. Regarding the DFS and despite the early toxicity, it seems crucial to obtain the best possible response. This long term analysis confirm that in patient aged over 80y with DLBCL and with PS from 0 to 2, RminiCHOP is the treatment cornerstone. Clinical trial information: NCT01087424.

8537 Poster Discussion Session (Board #17), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Secondary efficacy subanalysis by histology from the phase III BRIGHT study: First-line bendamustine-rituximab (BR) compared with standard R-CHOP/R-CVP for patients with advanced indolent non-Hodgkin lymphoma (NHL) or mantle cell lymphoma (MCL).

Ian Flinn, Richard H. C. Van Der Jagt, Brad S. Kahl, Peter Wood, Tim E. Hawkins, David MacDonald, Mark Hertzberg, Yiu-Lam Kwan, David Simpson, Michael Craig, Kathryn S. Kolibaba, Samar Issa, Regina Clementi, Doreen M. Hallman, Mihaela C. Munteanu, Ling Chen, John M. Burke; Sarah Cannon Research Institute, Nashville, TN; Ottawa Hospital, General Campus, Ottawa, ON, Canada; University of Wisconsin Carbone Cancer Center, Madison, WI; Princess Alexandra Hospital, Woolloongabba, Australia; Auckland Hospital, Auckland, New Zealand; Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada; Westmead Hospital, Wentworthville, Australia; Concord Repatriation General Hospital, Concord West, NSW, Australia; North Shore Hospital, Takapuna, New Zealand; Osborn Hematopoietic Malignancy and Transplant Program, West Virginia University, Morgantown, WV; Compass Oncology, Vancouver, WA; Middlemore Hospital, Auckland, New Zealand; Teva Pharmaceuticals, Inc., Frazer, PA; Rocky Mountain Cancer Centers, Aurora, CO

Background: BR was previously reported to be statistically noninferior to R-CVP/R-CHOP for complete response rate in the treatment of patients with indolent NHL or MCL. Evaluation of time-to-event outcomes is immature. This subanalysis reports response by histology. **Methods:** Indolent NHL or MCL was histologically confirmed <6 months before study enrollment in patients who were therapy-naïve. Patients were stratified according to predetermined standard treatment (R-CHOP or RECVP) and lymphoma type, then assigned to receive BR (28-day cycles: bendamustine 90 mg/m^2 on days 1 and 2, rituximab 375 mg/m^{2}on day 1) or standard treatment (21-day cycles at standard doses) for 6-8 cycles. Responses were assessed by a blinded independent review committee. The primary efficacy measure was noninferiority of BR complete response (CR) rate for evaluable patients with ≥1 postbaseline efficacy assessment. If the noninferiority threshold was met, superiority was assessed. Secondary measures included tolerability. **Results:** Of 447 patients enrolled in the study, 213 receiving BR and 206 receiving R-CHOP/R-CVP were evaluable with postbaseline data (Table). BR achieved a statistically noninferior CR rate compared with R-CHOP/R-CVP in patients with indolent NHL and MCL. **Conclusions:** In patients with treatment-naïve indolent NHL and MCL, BR achieved the primary endpoint of noninferior CR rate. Most CR rates were numerically, but not significantly, higher with BR. Small subgroup results should be interpreted with caution. Support: Teva BPP R&D, Inc. Clinical trial information: NCT00877006.

Response rates.

	CR			CR + partial response	
n/N (%)	BR	R-CHOP/R-CVP	CR ratio [95% CI]	BR	R-CHOP/R-CVP
Indolent NHL	49/178 (28)	43/174 (25)	1.11 [0.78, 1.59]	173/178 (97)	160/174 (92)
Follicular	45/148 (30)	37/149 (25)	1.23 [0.85, 1.78]	147/148 (>99)	140/149 (94)
Lymphoplasmacytic	0/5	1/6 (17)	0.39 [0.02, 7.88]	3/5 (60)	6/6 (100)
Marginal zone	5/25 (20)	4/17 (24)	0.84 [0.26, 2.66]	23/25 (92)	12/17 (71)
MCL	17/34 (50)	9/33 (27)*	1.76 [0.91, 3.42]	32/34 (94)	28/33 (85)*

* R-CHOP, n = 22.

8538 Poster Discussion Session (Board #18), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Changes in the tumor microenvironment associated with transformation in follicular lymphoma.

Jacob Paul Smeltzer, Jason Michael Jones, Steven Ziesmer, Deanna Grote, Zhi Zhang Yang, Anne Novak, Bing Xiu, Kay Ristow, Stephen Maxted Ansell; Mayo Clinic, Rochester, MN

Background: Follicular lymphoma (FL) is a heterogeneous disease with a variable prognosis. Transformation to an aggressive lymphoma is associated with a poor prognosis. Previous studies have identified tumor microenvironment cells such as CD68+ macrophages, PD-1+ and FOXP3+ cells as prognostic in FL. However, results have been conflicting and infrequently address the risk of transformation. In this study we analyzed various components of the microenvironment and their association with transformation. **Methods:** Patients with FL that later transformed were identified through Mayo Clinic lymphoma database. Tissue specimens at diagnosis were stained with CD68, CD11c, CD21, CXCL13, FOXP3, PD-1 and CD14 and characterized by pattern of location and semi-quantitative cell content. Time to transformation (TTT) and overall survival (OS) were assessed by Kaplan-Meir analysis. Significant variables were further analyzed by cox proportional hazards model. **Results:** 58 patients were included with a median TTT of 4.7 years (range, 0.4-20). Presence of CD14+ cells vs absence and their location (follicular vs non-follicular) were associated with shorter TTT (4.5 vs 6.2 yrs., p=0.037 and 3.8 vs 5.9 yrs. p= 0.027, respectively). The quantity of PD-1+ cell content was not associated with TTT or OS. However, localization of PD-1 to the follicle compared to diffuse was associated with a longer TTT (6.1 vs 3.6 yrs. p=0.033) and superior OS (9.7 vs 4.6 yrs. p=0.009). On multivariate analysis, the pattern of CD14 and PD-1 staining remained significantly associated with shorter TTT (Table). **Conclusions:** In follicular lymphoma, a diffuse pattern of PD-1+ cells is associated with inferior TTT and OS. CD14+ cells localized to the follicle is associated with a shorter TTT. After accounting for FLIPI score, both these factors remained significant. These results identify two independent predictors of the rate of transformation in follicular lymphoma and suggest it is location rather than quantity of CD14+ or PD-1+ cells that influence outcomes.

Multivariate analysis.

	TTT		OS	
	HR	P value	HR	P value
FLIPI	2.3 (CI 1.4-3.8)	0.001	1.7 (CI 1.0-2.9)	0.05
PD-1	1.9 (CI 1.0-3.4)	0.045	2.5 (CI 1.2-4.8)	0.012
CD14	3.0 (CI 1.5-6.1)	0.004	1.4 (CI 0.6-2.9)	0.37

8539 Poster Discussion Session (Board #19), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Total therapy 5 (TT5) for newly diagnosed high-risk multiple myeloma (HRMM): Comparison with predecessor trials total therapy 3a and 3b (TT3 a/b).

Saad Zafar Usmani, Sarah Waheed, Frits Van Rhee, Alan Mitchell, Alejandro Restrepo, Monica Grazziutti, John Crowley, Bart Barlogie; Myeloma Institute for Research and Therapy, Little Rock, AR; Cancer Research and Biostatistics, Seattle, WA

Background: HRMM has not benefited from advances achieved in the remainder 85% with low-risk MM. In order to guard against relapses during previous drug-free intervals in TT3, TT5 was designed as a dose-dense and less dose-intense program. Here we are reporting for the first time on the TT5 outcomes in comparison with TT3a/b results in HRMM. **Methods:** TT5 called for M-VTD-PACE induction with HPC collection. This was followed by tandem autologous stem cell transplants (ASCT) with hybrid regimens Mel80 plus VRD-PACE, sandwiched in between were 2 inter-transplant cycles of MEL20-VTD-PACE. Maintenance consisted of 3 years of alternating VRD and VMD (M, melphalan). As relapses were observed during maintenance, bortezomib was increased from 1.3mg/m2 to 1.5mg/m2 weekly. Results were compared with HRMM treated with TT3a/b (n=40/37). Data were compared with TT3 HRMM, involving 77 patients. Overall survival and progression free survival was analyzed employing Kaplan-Meier curves. Cox regression modeling was done for univariate and multivariate analyses. **Results:** Of 59 patients enrolled in TT5, CR was 66% including 10% with s-CR. The 18-mo OS was 92% v 74% with TT3 (p=0.009), whereas PFS was similar at 67% and 69%, respectively. A newly developed GEP-5 model distinguished 8 patients with a 36-mo OS estimate of 20% versus almost 90% for the remainder (p=0.04). On multivariate analysis that included TT5 and TT3, our GEP80 low-risk score, TT5 (vs TT3) and age <65yr were independent features linked to superior OS. **Conclusions:** This isthe first report of a dose-dense chemotherapeutic approach for newly diagnosed HRMM, which also introduced a hybrid Mel80-VRDPACE hybrid preparative regimen for ASCT. TT5 represents an advance in the management of GEP70-defined HRMM compared to predecessor trials TT3a/b for similar patients, with significant improvement in overall survival and tolerability compared with TT3 a/b. Clinical trial information: NCT00081939, NCT00572169, NCT00869232.

8540 Poster Discussion Session (Board #20), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Early versus delayed autologous stem cell transplant (ASCT) in patients receiving induction therapy with lenalidomide, bortezomib, and dexamethasone (RVD) for newly diagnosed multiple myeloma (MM).

Ajay K. Nooka, Amelia A. Langston, Edmund K. Waller, Leonard T. Heffner, Charise Gleason, Samatha Muppidi, Melanie Watson, Daniela Casbourne, Lawrence Boise, Jonathan L. Kaufman, Sagar Lonial; Division of BMT, Emory University, Winship Cancer Institute - Hematology and Medical Oncology, Atlanta, GA; The Winship Cancer Institute of Emory University, Atlanta, GA; Emory University, Atlanta, GA; Emory University School of Medicine, Atlanta, GA

Background: Lenalidomide, bortezomib and dexamethasone (RVD) is an active, tolerable induction regimen with superior response rates (≥VGPR rates of 80%) in newly diagnosed MM pts. However, the optimal timing of ASCT with this triplet combination is uncertain. We have evaluated our institutional experience to provide an insight for the best timing of ASCT, where specific patients were offered delayed ASCT based on risk, response and toxicity of therapy. **Methods:** 222 consecutive transplant-eligible pts with newly diagnosed MM that received at least 3 cycles of RVD and harvested stem cells were included in the analysis from May 2007 until October 2011. Patients underwent early ASCT (received planned ASCT immediately after stem cell harvest, n=136) or delayed transplant (received planned maintenance therapy after collection with intent to proceed with ASCT at first relapse, n=86). **Results:** Median age of the patients at the time of diagnosis is 60.5 yrs (32-77) vs. 60 yrs (22-73) for early vs. delayed groups. ISS stage 3 disease was seen in 31% patients and 10% patients; high risk cytogenetics were seen in 11% and 7% patients in early vs. delayed groups, respectively. Median time from initiation of induction therapy to ASCT in early group is 5.45 months (range, 3.19-12.68 months). In the delayed SCT group, 28 patients underwent ASCT at a median time of 26.21 months (range, 13.67-41.72 months) from initiation of therapy. At a median follow up of 32 months, 5-year overall survival from diagnosis was 68% and 88% in patients undergoing early and delayed ASCT, respectively ($p = 0.106$). **Conclusions:** Transplantation-eligible patients who receive RVD as initial therapy followed by early vs. delayed ASCT result in comparable overall survival. In carefully selected newly diagnosed myeloma patients with lower ISS stage receiving RVD as induction therapy, planned delayed ASCT results in 5-year survival rates close to 90%.

8541 Poster Discussion Session (Board #21), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Beneficial effect of complete response and type of therapy in multiple myeloma.

Shivlal Pandey, S. Vincent Rajkumar, Angela Dispenzieri, Martha Lacy, Morie Gertz, Francis Buadi, David Dingli, Suzanne R. Hayman, Stephen J. Russell, John Anthony Lust, Steven R. Zeldenrust, Prashant Kapoor, Arleigh Robertson McCurdy, Robert A. Kyle, Shaji Kumar; Mayo Clinic, Rochester, MN

Background: Achievement of a complete response (CR) to treatment is an important predictor of outcome for patients (pts) with myeloma (MM). The goal of the current study was to assess whether the treatment that resulted in CR has any impact on the outcomes. **Methods:** We identified 462 pts with MM, who fulfilled the IMWG criteria for CR, seen at Mayo Clinic between 1991 and 2011. The treatment was classified into groups by the regimen that led to CR (Table), and also based on whether an autologous stem cell transplant (ASCT) was part of the regimen. The remaining 21 pts had a variety of regimens and are not included in the Table. **Results:** The median age at diagnosis was 58.5 yrs (27.1–82.3 yrs) with 56% males. The overall survival (OS) from diagnosis for the entire cohort was 10.7 yrs (95% CI; 9.3, NR). The median interval from diagnosis to the recorded CR was 10.3 mos (range 1- 170), with 272 (58.4%) and 385 (82.7%) obtaining a CR in $<$12 mos and $<$24 months from diagnosis. We first compared the outcomes based on whether ASCT was part of the regimen; 328 had an ASCT while 117 pts received only chemotherapy. Median time to progression (TTP) following a CR was 5.1 yrs for the ASCT group compared with 5.5 yrs for the rest (P=0.3). Median OS from CR was 9.1 yrs for the ASCT group and 7.5 yrs for the rest (P=0.5) and OS from diagnosis was 10.1 yrs for the ASCT group and 12.6 for the rest (P=0.5). Examining the outcomes based on the regimen utilized showed that the TTP and OS from CR as well as OS from diagnosis were similar for all the groups (Table). Among pts who had a CR within a year of diagnosis, there were no differences in terms of the TTP or OS from the onset of CR or from diagnosis between the ASCT vs. chemotherapy groups or between the different regimens (P=NS for all comparisons). **Conclusions**: The current study highlights an important message regarding CR in MM. The results suggest that the prognostic value of CR is independent of the nature of therapy, and likely reflects the contribution of disease biology to obtaining a CR.

		Median from CR (yrs)		Median from diagnosis (yrs)
Regimen	N	TTP	OS	OS
Dexamethasone only	48	4.8	8.0	8.7
Lenalidomide based	145	5.5	NR	NR
Bortezomib based	101	4.5	NR	9.2
Lenalidomide + bortezomib based	41	3.5	NR	NR
Thalidomide-based	72	5.0	8.7	10.7
VAD	36	4.3	12.1	12.6

8542 Poster Discussion Session (Board #22), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Phase (Ph) I/II study of elotuzumab (Elo) plus lenalidomide/dexamethasone (Len/dex) in relapsed/refractory multiple myeloma (RR MM): Updated Ph II results and Ph I/II long-term safety.

Sagar Lonial, Sundar Jagannath, Philippe Moreau, Andrzej J. Jakubowiak, Marc S. Raab, Thierry Facon, Ravi Vij, Eric Bleickardt, Donna Ellen Reece, Lotfi Benboubker, Jeffrey A. Zonder, Wei Deng, Anil K. Singhal, Paul Gerard Guy Richardson, on behalf of the 1703 Study Investigators; Emory University School of Medicine, Atlanta, GA; Multiple Myeloma Research Consortium, Norwalk, CT/Mount Sinai Medical Center, New York, NY; Hematology, University Hospital Hotel-Dieu, Nantes, France; Multiple Myeloma Research Consortium, Norwalk, CT/University of Chicago, Chicago, IL; Universitaetsklinikum Heidelberg, Heidelberg, Germany; Hôpital Claude Huriez, Lille, France; Multiple Myeloma Research Consortium, Norwalk, CT/Washington University School of Medicine, St. Louis, MO; Bristol-Myers Squibb, Wallingford, CT; Princess Margaret Hospital, Toronto, ON, Canada; Centre Hospitalier Universitaire Tours-Hopital Bretonneau, Tours, France; Multiple Myeloma Research Consortium, Norwalk, CT/Karmanos Cancer Institute, Detroit, MI; AbbVie Biotherapeutics Incorporated, Redwood City, CA; AbbVie Biotherapeutics Corporation, Redwood City, CA; Multiple Myeloma Research Consortium, Norwalk, CT/Dana-Farber Cancer Institute, Boston, MA

Background: Elotuzumab (Elo) is a humanized anti-CS1monoclonal antibody that enhances natural killer cell mediated antibody dependent cellular cytotoxicity of CS1 expressing myeloma cells. This study included a dose finding Ph I cohort (N=28) and a Ph II cohort (N=73). Here we update Ph II data and provide long term safety data from both cohorts. **Methods:** Patients (pts) treated with ≥1 (Ph I) or 1–3 (Ph II) prior therapies received Elo + Len/dex as described previously (Lonial JCO 2012; Richardson ASH 2012) until disease progression, unacceptable toxicity, or death. All pts received a premedication regimen including methylprednisolone, diphenhydramine or equivalent, ranitidine or equivalent, and acetaminophen to mitigate infusion reactions. Adverse events (AEs) in Ph I/II pts occurring ≤18 months (mo) (N=98) were compared to AEs with a >18 mo onset in a subgroup of pts treated >18 mo (n=49). This safety analysis excluded 3 Ph I pts treated with Elo 5 mg/kg. **Results:** In the Ph II cohort (median 63 yr), objective response rate (ORR) was 84%; 92% with 10 mg/kg (n=36) and 76% with 20 mg/kg (n=37). At a median follow-up of 20.8 mo, median progression free survival (PFS) was not reached (10 mg/kg) and 18.6 mo (20 mg/kg). Most common treatment emergent grade ≥3 AEs were lymphopenia (19%), neutropenia (18%), thrombocytopenia (16%) and anemia (14%). Most common grade 3/4 AEs emerging ≤18 vs >18 mo in Ph I/II cohorts are shown (Table). 15 pts discontinued due to AEs; none after 18 mo of treatment. There were 4 second primary malignancies; none were reported after 18 mo. **Conclusions:** Elo 10 mg/kg + Len/dex was generally well tolerated and resulted in a high ORR and encouraging PFS in pts with RR MM. AEs emergent after 18 mo of therapy were consistent with AEs during the initial 18 mo. Updated Ph II safety/efficacy data and long term safety data from Ph I/II cohorts will be presented.

8543 Poster Discussion Session (Board #23), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Treatment outcome with the combination of carfilzomib, lenalidomide, and low-dose dexamethasone (CRd) for newly diagnosed multiple myeloma (NDMM) after extended follow-up.

Andrzej J. Jakubowiak, Dominik Dytfeld, Kent A. Griffith, Jagoda Jasielec, Kathryn McDonnell, Daniel Lebovic, David H Vesole, Sundar Jagannath, Elaine G. Chottiner, Tara B. Anderson, Kristen Detweiler-Short, Keith Stockerl-Goldstein, Asra Z. Ahmed, Terri L. Jobkar, Diane E. Durecki, Melissa A Mietzel, Daniel R. Couriel, Ravi Vij, Mark Stefan Kaminski; University of Chicago Medical Center, Chicago, IL; Poznan University of Medical Sciences, Poznan, Poland; University of Michigan Comprehensive Cancer Center, Ann Arbor, MI; University of Chicago, Winooski, VT; The University of Chicago Medicine and Biological Sciences, Chicago, IL; University of Michigan, Ann Arbor, MI; John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; Mount Sinai Medical Center, New York, NY; University of Michigan Medical Center, Ann Arbor, MI; Washington University School of Medicine in St. Louis, St. Louis, MO; University of Michigan Hospital, Ann Arbor, MI; Washington University in St. Louis, St Louis, MO

Background: We previously reported results from a phase 1/2 trial of CRd in NDMM (NCT01029054), demonstrating a high rate (42%) of stringent complete response (sCR) and overall favorable efficacy /safety after a median of 12 cycles of treatment (tx) and a median follow-up of 13 mo (Jakubowiak et al Blood, 2012). Here we report updated results after extended tx and additional 12 mo of follow-up. **Methods:** Patients (pts) received 28-day (d) cycles of carfilzomib (CFZ) 20–36 mg/m^2 IV (d1, 2, 8, 9, 15, 16), lenalidomide (LEN) 25 mg PO (d1–21), and dexamethasone 40/20 mg PO wkly (cycles 1–4/5–8). For cycles 8–24, CRd was given with a modified CFZ schedule (d1, 2, 15, 16) and then LEN alone after cycle 24. Stem cell transplant was an option after cycle 4. Response was assessed by IMWG plus nCR. **Results:** As of Nov 2012, 53 pts had received a median of 22 CRd cycles (range 2–24); 7 pts opted for transplant; 24 continued LEN maintenance for median 8 mo (range 1–10). Median follow-up was 25 mo (range 5–37). With extended tx, the CR rate was 64%; sCR improved from 42% to 53%, ≥nCR from 62% to 72%, and ≥VGPR from 81% to 87% (follow-up 13 vs 25 mo); ≥PR remained at 98%. Immunophenotypic CR (IMWG) was achieved in 22/26 evaluated pts. Of pts in sCR, 25% had high-risk cytogenetics per IMWG. In pts who did not proceed to transplant (n=46), the sCR was 59%, CR 70%, ≥nCR 78%, ≥VGPR 91%, and ≥PR 100%. Over the course of tx, depth of response improved. Median time to ≥VGPR was 4 cycles (range 2–17), ≥nCR 4.5 cycles (range 2–15), and sCR 10 cycles (range 4–30); 2 pts converted to sCR during LEN maintenance. At 2 years, the estimated PFS rate was 94% and OS was 98%; for pts with sCR, rates were 96% and 100%, respectively. Adverse event types, rates, and dose modifications during extended tx were comparable with those previously reported. There was 1 death off study due to disease progression. **Conclusions:** Extended follow-up showed that depth of response continued to improve over the course of prolonged CRd tx, resulting in exceptional CR, sCR, and PFS. Extended tx continued to be well tolerated. The results compare favorably with historical studies in both transplant and non-transplant NDMM. Clinical trial information: NCT01029054.

8544 Poster Discussion Session (Board #24), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Lenalidomide (LEN)-melphalan-prednisone induction followed by LEN maintenance (MPR-R) in newly diagnosed multiple myeloma (NDMM) elderly patients (Pts) with moderate renal impairment (RI): MM-015 trial post-hoc analysis.

John V. Catalano, Antonio Palumbo, Katja C. Weisel, Meletios A. Dimopoulos, Michel Delforge, Joan Blade, Maria Teresa Petrucci, Martin Kropff, Roman Hajek, Christian Jacques, Zhinuan Yu, Lindsay Herbein, Michele Cavo; Frankston Hospital and Department of Clinical Haematology, Monash University, Melbourne, Australia; Division of Hematology, University of Turin, Turin, Italy; Hematology & Oncology, Department of Medicine, University Hospital Tuebingen, Tuebingen, Germany; University of Athens School of Medicine, Athens, Greece; Department of Hematology, University Hospital Leuven, Leuven, Belgium; Hospital Clínic de Barcelona, Barcelona, Spain; Department of Cellular Biotechnology and Hematology, Sapienza University of Rome, Rome, Italy; University of Muenster, Muenster, Germany; School of Medicine and Institute of Clinical Hematology, University Hospital Ostrava, Ostrava, Czech Republic; Celgene Corporation, Summit, NJ; Bologna University School of Medicine, Seragnoli Institute of Hematology, Bologna, Italy

Background: The MM-015 pivotal phase III trial showed significant PFS benefit for MPR-R (31 mos) vs. MPR (14 mos) or MP (13 mos; both $p < 0.001$) followed by placebo in NDMM pts aged ≥ 65 years. As NDMM pts with RI have poor prognosis, this retrospective analysis studied the efficacy and safety of MPR-R in pts with creatinine clearance (CrCl) $<$ 60 mL/min. **Methods:** LEN starting dose for induction/maintenance was 10 mg/day (D1–21 of a 28-day cycle). Dose adjustments were not recommended for pts with RI. CrCl was calculated using the Cockcroft-Gault equation. Pts with severe RI (serum Cr $>$ 2.5 mg/dL [221 μmol/L]) were excluded from the trial. **Results:** Pts with CrCl $<$ 60 mL/min (median 47, interquartile range [IQR] 38–55) were included in this analysis: 51% MPR-R, 45% MPR, and 49% MP. Median PFS was significantly higher with MPR-R (26 mos [95% CI 14–48]) vs. MPR (13 mos [95% CI 12–15]) or MP (14 mos [95% CI 12–16]; both $p < 0.001$). In a Cox proportional model of PFS, CrCl $<$ 60 mL/min was not identified as a negative prognostic factor ($p = 0.69$). The most common Gr 4 adverse events (AEs) were hematologic and occurred predominantly during induction and are shown in the Table for pts with or without moderate RI. The number of deaths on study was similar: 10% (MPR-R), 7% (MPR), and 8% (MP); deaths associated with RI or disease progression were reported in $\leq$ 1% of pts with RI across the arms. **Conclusions:** The benefit of continuous LEN treatment with MPR-R is not compromised in NDMM pts with moderate RI, consistent with the overall trial results. CrCl and AEs should be monitored closely in this population. Clinical trial information: NCT00405756.

AEs during induction according to baseline renal function

	MPR-R		MPR		MP	
CrCl (mL/min)	CrCl ≥ 60 (n = 71)	CrCl < 60 (n = 77)	CrCl ≥ 60 (n = 82)	CrCl < 60 (n = 69)	CrCl ≥ 60 (n = 77)	CrCl < 60 (n = 75)
Median CrCl (mL/min) (IQR)	84 (70–95)	47 (38–55)	76 (68–85)	46 (37–54)	79 (68–92)	47 (34–55)
Gr 4 hematologic AEs (%)						
Neutropenia	32	35	27	38	3	12
Thrombocytopenia	7	16	6	20	1	7
Anemia	1	4	1	4	1	1
Leukopenia	4	4	2	9	1	1
Febrile neutropenia	0	3	0	3	0	0
Gr 3–4 nonhematologic AEs (≥ 5%) (%)						
Pneumonia	1	1	1	9	5	1
Fatigue	1	9	0	4	0	5
Asthenia	0	4	1	6	1	0
Hypokalemia	3	4	2	6	0	1
Bone pain	1	4	4	4	5	3
Rash	4	5	2	9	3	1

8545 Poster Discussion Session (Board #25), Mon, 1:15 PM-5:15 PM and 4:45 PM-5:45 PM

Results after long-term follow-up from the CAN2007 phase I/II study of weekly or twice-weekly bortezomib in patients (pts) with relapsed systemic light-chain (AL) amyloidosis.

Donna Ellen Reece, Ute Hegenbart, Vaishali Sanchorawala, Giampaolo Merlini, Giovanni Palladini, Joan Blade, Jean-Paul Fermand, Hani Hassoun, Leonard Heffner, Lixia Pei, Christopher Enny, Dixie Esseltine, Helgi Van De Velde, Andrew Cakana, Raymond Comenzo; Princess Margaret Hospital, Toronto, ON, Canada; Amyloidosis Center, University of Heidelberg, Heidelberg, Germany; Boston University School of Medicine, Boston, MA; Amyloidosis Research and Treatment Center, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Policlinico San Matteo, University of Pavia, Pavia, Italy; Hematology Department, Institute of Hematology and Oncology, Institut d'Investigacions Biomèdiques August Pi i Sunyer, Hospital Clínic, University of Barcelona, Barcelona, Spain; Hôpital Saint Louis, Paris, France; Memorial Sloan-Kettering Cancer Center, New York, NY; Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA; Janssen Research & Development, LLC, Raritan, NJ; Millennium Pharmaceuticals, Inc., Cambridge, MA; Janssen Research & Development, LLC, Beerse, Belgium; Janssen Research & Development, LLC, High Wycombe, United Kingdom; Tufts Medical Center, Boston, MA

Background: Data from multiple studies suggest that bortezomib alone or in combination regimens is active in newly diagnosed and relapsed AL. CAN2007 (NCT00298766) was the first prospective study of single-agent bortezomib in relapsed AL. Here we report outcome data at study closure after a median follow-up of 51.8 mos (median 46.1–66.1 mos). **Methods:** 70 pts received bortezomib 0.7, 1.0, 1.3, or 1.6 mg/m^2 on days 1, 8, 15, and 22 of 35-day cycles (QW) or 0.7, 1.0, or 1.3 mg/m^2 on days 1, 4, 8, and 11 of 21-day cycles (BIW) for up to 8 cycles (or longer in pts with evidence of ongoing clinical benefit). The maximum tolerated dose was not reached on either schedule; 18 and 34 pts were treated at the maximum planned doses of 1.6 mg/m^2 QW and 1.3 mg/m^{2}BIW, respectively, and 18 pts were treated at lower doses. Post-treatment, pts were followed every 6 weeks until disease progression, and then every 3 mos for survival during the long-term follow-up phase. **Results:** Pts received a median (range) of 8 (1–39), 6 (1–57), and 8 (3–57) cycles of bortezomib in the 1.6 mg/m^2 QW, 1.3 mg/m^2 BIW, and lower-dose groups, respectively; overall, 32 (46%) pts received ≥8 cycles, and 4 pts were still on treatment and had received ≥39 cycles at study closure. Hematologic responses and outcomes are summarized below. Median (range) follow-up for survival was 51.8 (1–68), 46.1 (1–61), and 66.1 (2–80) mos, and 7, 12, and 9 pts have died, in the 1.6 mg/m^2 QW, 1.3 mg/m^{2}BIW, and lower-dose groups, respectively. Median overall survival (OS) in all 70 pts was 62.7 mos, and 4-yr OS rate was 67.3%; data by dose group are shown below. **Conclusions:** Single-agent bortezomib produces durable hematologic responses and promising long-term OS data in pts with relapsed AL. Clinical trial information: NCT00298766.

	Bortezomib dose groups		
	1.6 mg/m^2 QW, N=18	1.3 mg/m^2 BIW, N=34	Lower doses, N=18
Best confirmed hematologic response rate, %	68.8	66.7	38.9
Complete response, %	37.5	24.2	16.7
Hematologic response duration ≥1 yr, % of responders	80	80	83.3
Median (range) follow-up for hematologic disease, mos	21.6 (0–35)	11.3 (0–18)	9.9 (2–49)
2-yr hematologic disease progression-free rate, %	72.2	76.8	73.8
Median OS, mos	62.1	Not reached	63.2
4-yr OS rate, %	75.0	63.0	69.7

8546 General Poster Session (Board #47A), Sun, 8:00 AM-11:45 AM

Patterns of failure in advanced-stage diffuse large B-cell lymphoma (DLBCL) patients treated with R-CHOP chemotherapy and the emerging role of consolidative radiotherapy.

Zheng Jane Shi, Satya Das, Derick Okwan-Duodu, Natia Esiashvili, Christopher Flowers, Kun Jiang, Zhengjia Chen, Xiaojing Wang, Walter J. Curran, Mohammad K. Khan; Department of Radiation Oncology, Winship Cancer Institute, Emory University, Atlanta, GA; Emory University School of Medicine, Atlanta, GA; Department of Radiaiton Oncology, Winship Cancer Institute, Emory University, Atlanta, GA; Department of Medical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA; Department of Pathology, Emory University, Atlanta, GA; The Winship Cancer Institute of Emory University, Atlanta, GA; Department of Biostatistics and Bioinformatics, Winship Cancer Institute, Emory University, Atlanta, GA; Radiation Therapy Oncology Group; Department of Radiation Oncology, Winship Cancer Institute of Emory University, Atlanta, GA

Background: The role of consolidative radiotherapy (RT) after a complete response (CR) to R-CHOP for stage III-IV DLBCL patients is unclear. The goal of our study is to evaluate the Emory experience when consolidative RT is delivered to initial presenting nodal and extranodal sites or bulky sites in these patients. **Methods:** From 01/2000 to 05/2012, 211 histologically confirmed DLBCL patients with stage III-IV disease who received R-CHOP were identified at Emory University. Patterns of failure for patients who achieved CR to R-CHOP were analyzed. Local control (LC), distant control (DC), progression free survival (PFS) and overall survival (OS) were estimated using Kaplan-Meier method and compared between patients who received R-CHOP alone versus R-CHOP plus consolidative RT using Log-rank test. Multivariate analyses were also performed using Cox proportional hazards model. **Results:** 163 patients had detailed treatment records. After a median 6 cycles of R-CHOP, 110 patients (67.5%) achieved CR and were entered for analysis. Fourteen patients (12.7%) received consolidative RT to a median dose of 30.6 Gy as part of initial management. With a median follow up time of 32.9 months, 43.8% of patients who received R-CHOP alone failed at the initial presenting sites with or without distant recurrence (DR), whereas isolated DR only occurred in 3.2% of these patients. Consolidative RT was associated with significantly improved LC (91.7% vs 48.8%, $p<0.0001$), DC (92.9% vs 71.9%, $p<0.0001$), PFS (85.1% vs 44.2%, $p<0.0001$) and OS (92.3% vs 68.5%, $p<0.0001$) at 5-years when compared to patients with R-CHOP alone. In addition, the in-field control rate was 100% within irradiated sites for patients who received consolidative RT. On multivariate analysis, consolidative RT and non-bulky disease were predictive of increased LC and PFS, whereas bone marrow involvement was associated with increased risk of DR and worse OS. **Conclusions:** 44% of patients with advanced stage DLBCL failed at initial presenting sites despite achieving a CR to R-CHOP. Incorporation of consolidative RT as part of upfront treatment in these patients was associated with improved LC and PFS.

8547 General Poster Session (Board #47B), Sun, 8:00 AM-11:45 AM

The LIMD1-MYBL1 index as a composite marker for subtype classification and survival prediction for diffuse large B-cell lymphoma patients.

Qinghua Xu, Cong Tan, Shujuan Ni, Lin Yuan, Fei Wu, Fang Liu, Xun Ye, Xia Meng, Weiqi Sheng, Xiang Du; bioMérieux (Shanghai) Co.,Ltd., Shanghai, China; Fudan University Cancer Hospital, Shanghai, China; Shanghai Jiaotong University Affiliated First People's Hospital, Shanghai, China; Institut Mérieux Laboratory, Fudan University Cancer Hospital, Shanghai, China

Background: Diffuse large B-cell lymphoma (DLBCL) is a heterogeneous group of B-cell lymphomas with wide variations in patient survival. Through gene expression profiling, DLBCL can be stratified into two major cell-of-origin subtypes with distinct prognoses: the favorable germinal center B-cell-like (GCB) and the unfavorable activated B-cell-like (ABC) DLBCLs. However, the current cell-of-origin signatures are not suitable for use in routine clinical practice. Our study aimed to identify a novel biomarker to facilitate the translation of research into clinical practice. **Methods:** We performed an integrative analysis of seven independent cohorts comprising 1,682 patients. The DLBCL-1 cohort was used for signature identification. The identified signature was then tested in the DLBCL-2 to DLBCL-7 cohorts. **Results:** Two genes (*LIMD1* and *MYBL1*) were significantly differentially expressed between the ABC and GCB subtypes. We integrated these genes into a composite marker, the *LIMD1-MYBL1* Index. In seven independent cohorts, the average concordance rate between the *LIMD1-MYBL1* Index and the cell-of-origin signature classification was 87% (range, 77% to 94%). Furthermore, the *LIMD1-MYBL1* index is an independent prognostic factor for patients from different populations and for patients treated with a variety of therapies (Table). **Conclusions:** We identified the *LIMD1-MYBL1* Index that has clinical value for DLBCL subtype classification and prognosis. Although little is known about the oncogenic roles of these genes, our findings prompt further research on the molecular mechanisms of DLBCL.

	Subtype classification			Survival prediction		
Cohort	Subtype	COO	LIMD1-MYBL1	Concordance	Hazard ratio (95%CI)	P value
DLBCL-1	ABC	167	208	87%	2.3 (1.7-3.2)	0.001
	GCB	183	206			
	Unclassified	64				
DLBCL-2	ABC	34	85	84%	2.1 (1.3-3.5)	0.004
	GCB	85	91			
	Unclassified	57				
DLBCL-3	ABC	55	84	89%	2.0 (1.2-3.4)	0.01
	GCB	74	82			
	Unclassified	37				
DLBCL-4	ABC	71	134	85%	NA	NA
	GCB	144	137			
	Unclassified	56				
DLBCL-5	ABC	20	31	88%	4.5 (1.3-16.5)	0.02
	GCB	40	38			
	Unclassified	9				
DLBCL-6	ABC	214	257	77%	NA	NA
	GCB	237	241			
	Unclassified	47				
DLBCL-7	ABC	59	45	94%	2.4 (1.0-5.6)	0.04
	GCB	13	43			
	Unclassified	16				

8548 General Poster Session (Board #47C), Sun, 8:00 AM-11:45 AM

Dexabeam versus ICE salvage regimen prior to autologous transplantation for relapsed or refractory aggressive peripheral T-cell lymphoma: A retrospective evaluation of parallel patient cohorts of one center.

Jan-Henrik Mikesch, Mareike Kuhlmann, Angela Demant, Utz Krug, Eva Schmidt, Torsten Kessler, Christoph Schliemann, Michele Pohlen, Michael Mohr, Gabriele Koehler, Johannes Wessling, Rolf M. Mesters, Carsten Mueller-Tidow, Wolfgang E. Berdel, Nils Heinrich Thoennissen; University Hospital Münster, Münster, Germany; University of Muenster Hospital, Muenster, Germany; University of Muenster, Muenster, Germany

Background: High-dose chemotherapy (HDT) followed by autologous stem-cell transplantation (ASCT) is considered standard in the treatment of patients with relapsed or refractory aggressive peripheral T-cell lymphoma (PTCL). However, the optimal salvage regimen before ASCT has not yet been established. **Methods:** We retrospectively analyzed 31 patients with relapsed or refractory aggressive PTCL after anthracycline based first-line chemotherapy who received either DexaBEAM (n=16) or ICE (n=15) regimen as first salvage chemotherapy followed by HDT and ASCT between 1996 and 2009. The median patient age was 46 years (range, 18-66) in the DexaBEAM group and 40 years (range, 17-59) in the ICE group. Patients were included independent of WHO stage and IPI score. **Results:** The overall response rate (OR) was significantly higher for patients treated with DexaBEAM (69%) as compared to the ICE group (20%; P=0.01), with higher complete response (CR; 38% vs. 7%) as well as partial response (PR; 31% vs. 13%) rate. Changing regimen due to failure of the first salvage therapy, 12 patients initially receiving ICE still achieved an OR of 58% (33% CR, 25% PR) with DexaBEAM as second salvage therapy, whereas in 3 patients receiving ICE after DexaBEAM failure only 1 patient achieved an OR (1 PR). Median progression-free survival (PFS) was significantly higher in the DexaBEAM group (6.4 vs. 2 months; P=0.01). Median overall survival (OS) was not different between the two groups (22.8 vs. 29.8 months; P=0.72), most likely due to the good response rate of patients to DexaBEAM as 2nd salvage regimen after failure of ICE chemotherapy. Major adverse event in both groups was myelosuppression with higher but tolerable treatment-related toxicity for patients in the DexaBEAM group. **Conclusions:** In this retrospective comparison DexaBEAM salvage chemotherapy was superior to ICE for patients with relapsed or refractory aggressive PTCL for remission induction prior to autologous transplantation, with higher but manageable treatment-related toxicity.

8549 General Poster Session (Board #47D), Sun, 8:00 AM-11:45 AM

Comparative outcomes of splenectomy and rituximab-based chemotherapy in elderly patients with splenic marginal zone lymphoma.

Adam J. Olszewski; Alpert Medical School of Brown University, Providence, RI

Background: Despite advances in diagnosis and therapy, over 50% of patients with splenic marginal zone lymphoma (SMZL) undergo splenectomy. The objective of this retrospective study was to compare outcomes in SMZL patients undergoing surgery or rituximab-containing chemoimmunotherapy (RCIT) based on the Surveillance, Epidemiology, and End Results-Medicare linked database. **Methods**: Records of 521 SMZL patients diagnosed between 2000 and 2007 were extracted, excluding cases with incomplete Medicare coverage. Two treatment arms were defined by receipt of RCIT or splenectomy within 2 years of diagnosis. Factors confounding treatment selection or prognosis were balanced in both arms using a propensity score. The primary endpoint was lymphoma-related death, estimated using competing risk models, with overall survival (OS) and toxicities as secondary endpoints. **Results**: Of the 341 eligible patients (median age, 77 years), 67 (20%) were untreated, while 169 (50%) underwent splenectomy and 97 (28%) chemotherapy (64% single-agent rituximab) at median 1.4 months from diagnosis. Stage IE, treatment in a teaching hospital and good performance status were associated with a preference for splenectomy. There was no evidence of significantly different risk of lymphoma-related death after treatment with RCIT rather than surgery (hazard ratio, HR, 1.10, 95%CI 0.56-2.18, P=0.78). There was an excess of early mortality after splenectomy (7% within 90 days) but more later events with RCIT (OS at 3 years 69% vs. 67%, respectively). More patients required chemotherapy after surgery (38%) than vice versa (14%, P<0.001). Nursing home admissions were more common after splenectomy (22%, P=0.03). There were more inpatient hospitalizations after multidrug RCIT (P=0.003), but not after rituximab alone (P=0.65). **Conclusions:** Although SMZL is considered indolent, most elderly patients required treatment soon after diagnosis in this population-based study. Survival outcomes were similar after either RCIT or splenectomy. Complications of surgery or combination chemotherapy are significant, suggesting rituximab alone as a more suitable option in elderly patients.

8550 General Poster Session (Board #47E), Sun, 8:00 AM-11:45 AM

Nodular lymphocyte-predominant and classical Hodgkin lymphoma subtypes: Differences in biology, survival, and impact of radiotherapy.

Shihab Ali, Adam J. Olszewski; Alpert Medical School of Brown University, Providence, RI

Background: Hodgkin lymphoma (HL) is a heterogeneous disease, but differences between nodular lymphocyte predominant (NLPHL) and classical (CHL) subtypes were previously studied in small cohorts preventing adjustment for confounders. We studied those differences based on the Surveillance, Epidemiology and End Results (SEER) program data. **Methods:** We analyzed SEER HL cases aged 16 years and over, diagnosed between 1995 and 2009. We studied the following endpoints: crude probability of HL-related death (HLRD), relative survival (using individual data in multivariate flexible parametric models) and risk of secondary malignancies (using competing risk regression). We studied the impact of radiotherapy (RT) in early-stage disease using a propensity score, adjusting for treatment selection and immortal time bias. **Results:** We identified 25,903 patients, with disparate age, race and stage distributions between subtypes. In a multivariate model, NLPHL demonstrated significantly better crude and net survival outcomes (Table), but in contrast to all CHL subtypes, it showed a steady increase in mortality rate after 2 years. The risk of secondary non-Hodgkin lymphoma was significantly higher in both NLPHL (hazard ratio, HR, 2.28, P=0.002) and lymphocyte-rich (LR) CHL (HR 2.08, P=0.01) than in nodular sclerosis (NS). The risk of other secondary malignancies did not differ between subtypes. After balancing confounding factors in treatment arms, RT in stage I/II was associated with improved survival in NS (HR, 0.78, P=0.001) and LR-CHL (HR 0.36, P<0.001), but not in NLPHL (HR 0.98, P=0.94) or in the remaining CHL subtypes. **Conclusions:** Studies of NLPHL and CHL subtypes should account for their disparate biology and clinical course. Prospective evaluation of NLPHL treatment strategies without RT is justified.

Subtype	N	5-year risk of HLRD (95% CI)	P	Excess HR (95% CI)	P
NLPHL	1,018	5.6% (3.7-8.0)	<0.001	0.29 (0.17-0.48)	<0.001
LR-CHL	806	14.6% (11.6-18.0)	0.44	0.82 (0.65-1.03)	0.09
NS-CHL	15,387	13.2% (12.6-13.9)	Reference	1	
Mixed cellularity	3,558	25.3% (23.6-27.1)	<0.001	1.18 (1.08-1.29)	<0.001
Lymphocyte-depleted	350	48.9% (42.8-54.7)	<0.001	2.17 (1.83-2.59)	<0.001

8551 General Poster Session (Board #47F), Sun, 8:00 AM-11:45 AM

Phase I study of a novel humanized anti-CD20 antibody, BM-ca, in patients (pts) with relapsed or refractory indolent B-cell non-Hodgkin lymphoma (B-NHL) pretreated with rituximab.

Kensei Tobinai, Michinori Ogura, Dai Maruyama, Tatsuya Suzuki, Yukio Kobayashi, Toshiki Uchida, Suguru Fukuhara, Takashi Oyama, Tomoharu Fukuzaki, Yasuhiko Komatsu; National Cancer Center Hospital, Tokyo, Japan; Nagoya Daini Red Cross Hospital, Nagoya, Japan; BioMedics Japan Inc., Tokyo, Japan

Background: BM-ca is a novel humanized type-I/II anti-CD20 antibody, which is effective against rituximab-resistant cell line RC-K8, and has more potent anti-cell-proliferation activity than rituximab or ofatumumab when combined with cancer chemotherapeutics. The aim of this study was to evaluate the safety, efficacy, and PK profile of BM-ca in pts with indolent B-NHL. **Methods:** A total of 12 pts {age: median 61 (50-73), number of prior regimens: median 2 (1-13)} with indolent B-NHL relapsed after or refractory to rituximab-containing therapy underwent treatment by IV infusion of BM-ca weekly for 4 weeks at a dose of 5, 10, or 15 mg/kg. Initially, 3 pts were to undergo BM-ca therapy at a dose of 5 mg/kg using the conventional 3+3 dose escalation design. To minimize infusion reactions (IRs), pts were pretreated with acetaminophen and d-chlorpheniramine maleate. Allopurinol and/or hydrocortisone were also administered if necessary. Infusion was started at 50 or 100 mg/h and was gradually increased to a maximum of 400 mg/h. Since no DLTs were observed, all 12 pts completed weekly 4 doses of BM-ca. **Results:** The most frequent AE was IRs (11 of 12 pts), which occurred mostly in the first infusion, and the highest grade of AE was neutropenia (grade 4 in one pt of 15 mg/kg after the last infusion). Anti-BM-ca antibodies were not detected. Of the 12 pts examined, 2 achieved CR (10 mg/kg) and 2 PR (15 mg/kg); these 4 pts had follicular histology. The remaining 8 pts including one each of extranodal marginal zone, nodal marginal zone, and small lymphocytic histology were judged to achieve SD. The CR states in 2 pts continued at least >14 and >11 months, respectively. The PK properties of BM-ca were comparable to those of other naked anti-CD20 antibodies including rituximab (AUC and C_{max} were proportional to the doses; $V_{dss} \approx 4$ L; $t_{1/2} \approx 750$ h). Since at 10 mg/kg the response was the best and no grade 4 AE observed, 10 mg/kg was suggested as a recommended phase II dose. **Conclusions:** Four weekly IV administration of BM-ca up to 15 mg/kg was well tolerated and safe with promising preliminary anti-lymphoma activity in pts with indolent B-NHL. Further evaluation is warranted. Clinical trial information: 000004805.

8552 General Poster Session (Board #47G), Sun, 8:00 AM-11:45 AM

Impact of time from diagnosis to initiation of curative chemotherapy on survival of patients with diffuse large B-cell lymphoma (DLBCL).

Kevin A. Hay, Benny Lee, Ozge Goktepe, Joseph M. Connors, Laurie Helen Sehn, Kerry J. Savage, Tamara Nina Shenkier, Richard John Klasa, Diego Villa; Department of Medicine, University of British Columbia, Vancouver, BC, Canada; Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada; Cancer Surveillance & Outcomes, British Columbia Cancer Agency, Vancouver, BC, Canada; British Columbia Cancer Agency/University of British Columbia, Vancouver, BC, Canada; Division of Medical Oncology, British Columbia Cancer Agency Centre for Lymphoid Cancer and the University of British Columbia, Vancouver, BC, Canada; Department of Medical Oncology, British Columbia Cancer Agency Centre, Vancouver, BC, Canada; British Columbia Cancer Agency, Vancouver, BC, Canada

Background: DLBCL is potentially curable with combination chemotherapy such as CHOP-R. Although it is generally regarded appropriate to start chemotherapy promptly after diagnosis, the impact of the time from diagnosis to treatment initiation on treatment outcome is unknown. **Methods:** Patients diagnosed with DLBCL and treated with at least one cycle of CHOP-R with curative intent during 2003 – 2008 in British Columbia were identified in the Lymphoid Cancer Database. Additional demographic data were obtained from the BC Cancer Registry. The BC Cancer Agency provincial pharmacy database was used to obtain dates of chemotherapy administration. The impact of the time interval from the date of pathologic diagnosis to treatment on overall survival (OS) and progression-free survival (PFS) was evaluated. **Results:** A total of 793 patients were identified: 199 (25%) received CHOP-R $<$2 weeks after diagnosis, 244 (31%) at 2-4 weeks, 293 (37%) at 5-8 weeks, and 57 (7%) at $>$8 weeks. High international prognostic index, primary mediastinal DLBCL, and hospitalization at the time of CHOP-R start were associated with earlier initiation of chemotherapy ($p<0.001$ for all factors). Distance to chemotherapy from home ($p=0.237$), rural vs. urban location ($p=0.952$), geographic region ($p=0.458$), and median household income ($p=0.127$) were not associated to treatment start. Five-year PFS and OS respectively were 54% (SD 4%) and 61% (SD 4%) for treatment $<$2 weeks, 63% (SD 3%) and 66% (SD 3%) for 2-4 weeks, 70% (SD 3%) and 74% (SD 3%) for 5-8 weeks, and 60% (SD 7%) and for 61% (SD 8%) $>$8 weeks, $p=0.006$ (PFS) and $p=0.024$ (OS). A multivariate analysis demonstrated no significant difference between the groups. **Conclusions:** In a publicly funded healthcare system, earlier initiation of chemotherapy was strongly associated with poor prognostic factors, as well as inferior PFS and OS. The timing of chemotherapy initiation appears to be related to clinical factors instead of system or socioeconomic barriers. Notwithstanding the lack of detrimental outcomes in those commencing CHOP-R after 8 weeks, clinicians should endeavor to initiate curative chemotherapy as soon as possible after a diagnosis of DLBCL is established.

8553 General Poster Session (Board #47H), Sun, 8:00 AM-11:45 AM

Radiotherapy for nasal cavity and Waldeyer ring natural killer/T-cell lymphoma: Analysis in 131 patients.

Yuan Zhu, Luying Liu, Jialing Luo; Zhejiang Cancer Hospital, Hangzhou, China

Background: Theaim of this study was to evaluate the efficacy and prognosis of chemotherapy and radiotherapy for patients with nasal cavity and Waldeyer ring natural killer/T cell lymphoma. **Methods:** Records of 131 patients who received chemotherapy or radiotherapy or chemoradiotherapy at Zhejiang Cancer Hospital between 2000 and 2010, were retrospectively reviewed. Ninety-eight patients received chemoradiotherapy. Thirty patients received radiotherapy, and three patients received chemotherapy. All patients had pathology and immunohistochemistry diagnosis. According to the Ann Arbor Staging System, majority of patients were staged as IE stage (116/131). 14 patients presented with IIE stage, and 1 IIIE stage. Thirty-four patients had B symptoms. **Results:** 109 patients were with nasal cavity NK/T cell lymphoma, and 22 patients with Waldeyer ring NK/T cell lymphoma. Complete response (CR) was achieved in 116 (89%) patients. The 5-year overall survival (OS) rate and disease-free survival (DFS) rate for all patients were 62.7% and 53.5%, respectively. 5-year OS in patients with RT dose ^{3}a50Gy and $<$ 50Gy were 64% and 45.4% respectively ($p = 0.024$). No survival difference was observed between patients with nasal cavity and Waldeyer ring, treated with radiotherapy and chemoradiotherapy, with or without B symptoms, CD56(+) and CD56(-), and between stage IE and IIE patients. On multivariate analysis, the level of lactate dehydrogenase (LDH) before treatment and dose of RT were correlated with prognosis ($p<0.05$). **Conclusions:** Radiotherapy, as the primary therapy, can result in a favorable outcome in the treatment of nasal cavity and Waldeyer ring natural killer/T cell lymphoma. The patients with the lower level of LDH before treatment, RT dose $\geq$50Gy had better prognosis. Addition chemotherapy to radiotherapy didn't improve the survival.

8554 General Poster Session (Board #48A), Sun, 8:00 AM-11:45 AM

Dose-dense R-CHOP (administered every 2 weeks) with sargramostim in patients with newly diagnosed diffuse large B-cell lymphoma.

Preeti Chaudhary, Susan G. Groshen, Denice D Tsao-Wei, Imran Siddiqi, Vinay Duddalwar, Nancy Berman, Christine Duran, Teh-Chun Wang, Anil Tulpule; University of Southern California Keck School of Medicine, Los Angeles, CA; University of Southern California Keck School of Medicine and Norris Comprehensive Cancer Center, Los Angeles, CA; Keck School of Medicine, University of Southern California, Los Angeles, CA; University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA; USC Norris Comprehensive Cancer Center, Los Angeles, CA; Norris Cancer Hospital, Los Angeles, CA

Background: R-CHOP administered every 3 weeks is standard of care for the treatment of diffuse large B-cell lymphoma (DLBCL). There are conflicting reports regarding the superiority of dose dense (DD) regimen (R-CHOP administered every 2 weeks), compared to the standard R-CHOP regimen. In a Phase II study, the tolerability and efficacy of DD-RCHOP+Sargramostim was evaluated. **Methods:** All patients received intravenous rituximab, 375 mg/m^2; cyclophosphamide, 750 mg/m^2; doxorubicin, 50 mg/m^2 and vincristine, 1.4 mg/m^2 on day 1; prednisone 100 mg orally on days 1-5 and sargramostim 250 mg/m^{2}subcutaneously on days 3-13. Chemotherapy cycles were repeated every 2 weeks. **Results:** We studied50 newly diagnosed, previously untreated DLBCL patients (median age 54.1 years, range 21.4-80.3 years). Stage III and IV disease was noted in 12 (24%) and 29 (58%) patients, respectively. Baseline characteristics included the following: high-intermediate or high-risk IPI score (n=38, 76%), extranodal involvement (n=32, 64%), bone marrow infiltration (n=5, 10%), B-symptoms (n=23, 46%), median LDH level (272, range 118-3797) and good baseline performance status (n=45, 90%). The median follow up from the start of treatment was 12.7 months (range 0.1-41.4 months). Among the 46 patients evaluated for response, complete response (CR) or unconfirmed CR (CRu) was observed in 36 (78%) patients, partial response (PR) or an unconfirmed PR in 9(20%) patients and 1 patient had stable disease. The probability of overall survival (OS) at 18 months was 0.84. The probability of disease free survival in complete responders at 9 months was 0.89. Neutropenia was the most common hematological toxicity and accounted for delays in 40 (20%) treatment cycles. There were no episodes of fever/sepsis in the 33 patients (66%) with grade 3 or 4 neutropenia. IgG, IgA and IgM levels decreased during therapy and returned to normal in 2-4 months post therapy. No opportunistic infections were reported. **Conclusions:** The administrationof DD-RCHOP+Sargramostim regimen is safe, tolerable and effective in patients with newly diagnosed DLBCL. However, neutropenic episodes were significant, accounting in many cases for treatment delays.

8555 General Poster Session (Board #48B), Sun, 8:00 AM-11:45 AM

Interim FDG PET/CT to predict progression-free survival (PFS) better than clinical and baseline metabolic measurements in Hodgkin lymphoma (cHL).

Ashley Knight-Greenfield, Richard Aaron Marshall, Martin Hutchings, John Doucette, Jamie Stern, Morton Coleman, Lale Kostakoglu; Icahn School of Medicine at Mount Sinai, New York, NY; Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; Mount Sinai Medical Center, New York, NY; Weill Cornell Medical College, New York, NY; Department of Radiology, Mount Sinai Medical Center, New York, NY

Background: Previous studies in cHL have demonstrated that conventional methods to risk stratify patients into various prognostic groups and predict PFS may not be sufficient to individualize therapy. Metabolic parameters using FDG-PET may be helpful for developing a prognostic algorithm and predict PFS. Objectives: To determine the best predictor of PFS among various variables of tm metabolic measurements at baseline and at interim PET/CT compared to conventional methods in cHL patients. **Methods:** Retrospective evaluation of prospectively acquired data in 58 cHL pts, all stages [IIB-IV:41%, >IPS-3:24%, unfavorable (UF):44%]. Eligibility: PET/CT prior to and after 1 cycle (PET1) ABVD therapy, imaging at 60min+15min, follow-up>24 mo. Baseline PET parameters including metabolic tumor volume (MTV), total lesion glycolysis (TLG), SUVmax, and SULpeak were determined using gradient method (PETVCAR2, GE Healthcare, WI). Data were also evaluated at PET1 for %ΔMTV, %ΔSUVmax, %ΔTLG, PERCIST criteria and visually with Deauville 5-PS. Variables were correlated with PFS. **Results:** Median follow-up: 32.2 mo. Of 58 pts 14 relapsed (median PFS:6.5 mo). Results for PFS are displayed in the Table. No baseline conventional (stage, IPS, UF vs F) or PET variable was associated with PFS. The best predictor of PFS was Deauville 5-PS at PET1. PERCIST and %ΔTLG using gradient method trended toward significance. **Conclusions:** Deauville 5-PS best predicts PFS at PET1 in cHL. Neither baseline PET nor conventional prognostic factors correlated with PFS in this group of cHL pts. Risk-stratification of cHL using tumor metabolic volumetry and PERCIST criteria may require a larger sample size and further assessment of various methodologies.

Variable	HR	Cutoff	P value
Gradient method			
Baseline MTV (mL)	1.74	132	0.34
Baseline SUVMAX	1.97	15.5	0.23
Baseline TLG	1.04	572	0.95
% decrease MTV	2.25	98%	0.15
% decrease SUVmax	2.43	83%	0.14
% decrease TLG	2.91	99%	0.06
PERCIST criteria			
Baseline SULpeak	1.98	9.15	0.23
% decrease SULpeak	3.09	84%	0.06
Deauville PET1	5.61	3	0.002
Conventional			
Stage III or IV	1.02		0.96
IPS >3	1.1		0.9
F vs UF (early stage only)	1.3		0.72

8556 General Poster Session (Board #48C), Sun, 8:00 AM-11:45 AM

Efficacy of radioimmunotherapy-based conditioning with high-dose chemotherapy and autologous stem cell transplantation for transformed lymphoma.

Amrita Y. Krishnan, Marielle Wondergem, Joycelynne Palmer, Avichai Shimoni, Andrew Antony Raubitschek, Auayporn Nademanee, Otto Visser, Jose M Zijlstra, Nicole Tsai, Arnon Nagler, Neil Martin Kogut, Jennifer Simpson, Stephen J. Forman; City of Hope, Duarte, CA; Hematologie VUMC, Amsterdam, Netherlands; Hematology Division and Bone Marrow Transplantation Department, Chaim Sheba Medical Center, Ramat-Gan, Israel; City of Hope Cancer Center/Beckman Research Institute, Duarte, CA; Hematology Department, VU University Medical Center, Amsterdam, Netherlands; VU University Medical Center, Amsterdam, Netherlands; City Of Hope, Duarte, CA; Hematology Division, BMT and Cord Blood Bank, Chaim Sheba Medical Center, Tel-Hashomer, Israel; Southern California Permanente Medical Group, Duarte, CA

Background: Transformed non-Hodgkin lymphoma (TF NHL) has a poor prognosis with median survival of 7-20 months. Studies have suggested the benefit of HDC. The series by Eide showed 47%, 5yr OS in 47 pts treated with HDC and ASCT (Br J Hem 2011). Our multicenter experience with RIT plus HDC (Yttrium 90 ibritumomab tiuxetan plus BEAM; carmustine, etoposide, cytarabine, melphalan ″ZBEAM″) demonstrated the safety and efficacy of the regimen in diffuse large cell lymphoma (DLCL). Therefore, the regimen was explored in other subtypes of NHL. Herein we report the outcome of 57 pts with TF NHL treated with ZBEAM conditioning and ASCT at three centers (City of Hope USA n=20, VUMC the Netherlands n=31, Chaim Sheba Med Center, Israel n=6.) between 2003- 2011. **Methods:** Histological confirmation of transformation was defined as dx of DLCL in pts with either a prior history or concomitant dx of follicular NHL. **Results:** Median age at ASCT was 59.6 yrs (range 41-69). Median number of prior regimens 2 (range 1-6), all pts received rituximab in at least one regimen. Disease status at ASCT: 1st CR 29, 1stPR 7,1st rel 9, IF 5, 2nd CR 5, 2nd rel 1, >3CR 1. Median time from TF NHL dx to ASCT was 7.7 mo (range 2.8-116). Pts engrafted white cells at median of 12 days (range 8-33). Non relapse mortality was 3.5%. There were two second malignancies: 1 MDS and 1 SCC Skin. Median f/u for living pts was 29 mo (range 7-100). Two year PFS was 69.67% (95%CI 59.39 - 77.83) and OS 90.29% (95% CI: 79.63 - 95.52). On univariate analysis, number of prior regimens, time from TF NHL dx to ASCT and history of marrow involvement were not significant for PFS and OS. Disease status at ASCT was significant for PFS in 1st CR vs relapse disease (p=0.03) The relapsed pts had a significant increase in risk of relapse/progression or death post ASCT compared to the 1CR patients. [HR = 2.9, (95% CI: 1.07 - 7.9)]. **Conclusions:** ZBEAM conditioning with ASCT is an active treatment for pts with TF NHL, and is particularly efficacious as consolidation for pts in 1st CR.

8557 General Poster Session (Board #48D), Sun, 8:00 AM-11:45 AM

Limited utility of surveillance imaging for detection of relapse in non-Hodgkin lymphoma.

Quoc Van Truong, Nilay Shah, Mark Knestrick, Brendan F. Curley, Michael Craig, Mehdi Hamadani; Mary Babb Randolph Cancer Center, West Virginia University School of Medicine, Morgantown, WV; Department of Internal Medicine, West Virginia University, Morgantown, WV; Mary Babb Randolph Cancer Center at West Virginia University, Morgantown, WV; West Virginia University, Robert C. Byrd Health Sciences Center, Morgantown, WV; Osborn Hematopoietic Malignancy and Transplant Program, West Virginia University, Morgantown, WV

Background: Surveillance imaging with computerized tomography (CT) and positron emission tomography with CT (PET/CT) scans during follow-up after first-line therapies in patients with non-Hodgkin lymphoma (NHL) is commonly used in practice. However, most guidelines do not recommend surveillance imaging. We aimed to determine the value of routine imaging for the detection of first relapse in NHL patients in complete remission (CR) after first-line therapies. **Methods:** We retrospectively analyzed NHL patients referred to our center, who achieved CR after first-line therapies and subsequently relapsed. We evaluated whether the relapse was detected solely by routine CT or PET/CT or by patient-reported symptoms. Subgroup analysis was performed according to baseline histology (indolent vs. aggressive NHL). Data were also collected to determine the number of additional imaging, number of false positive scans, invasive procedures and iatrogenic complications, directly resulting from an abnormality detected on surveillance imaging. **Results:** Seventy-seven patients with first relapse of NHL between January 1, 2000 and December 31, 2010 were included. Majority of the relapses were detected by patient-reported symptoms as opposed to surveillance imaging (79.2% (n=61) vs. 20.8% (n=16); $p<0.0001$). There was no overall survival difference between the two groups ($p=0.08$). Patient-reported symptoms led to the detection of majority of relapses in aggressive (86.4% (n=45) vs. 13.6% (n=6); $p<0.0001$) and indolent NHL (69.7% (n=32) vs. 30.3% (n=10); $p=0.037$). There were greater number of scans done after a suspected relapse in the imaging versus symptoms group (1.94 versus 0.97; $p=0.0004$). Surveillance imaging led to 2 false positive scans/invasive procedures with one case of iatrogenic pneumothorax. **Conclusions:** Our limited retrospective analysis suggests that there is a limited role of surveillance imaging by CT or PET/CT for the detection of relapse in patients with NHL. There was no difference in survival outcome in our study between the two groups.

8558 General Poster Session (Board #48E), Sun, 8:00 AM-11:45 AM

Long-term survival with ^{90}yttrium ibritumomab tiuxetan and rituximab as treatment for relapsed or refractory diffuse large B-cell lymphoma.

Jon E. Arnason, Katarina Luptakova, Jacalyn Rosenblatt, Jeffrey Zwicker, James D. Levine, Vassiliki Boussiotis, Michelle Kim, David Avigan, Robin Joyce; Beth Israel Deaconess Medical Center/ Harvard Medical School, Boston, MA

Background: Patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) are salvaged with high dose chemotherapy followed by autologous stem cell rescue. Ibritumomab tiuxetan is an anti-CD20 antibody conjugated to the radionuclide ^{90}yttrium. 90Y ibritumomab tiuxetan has demonstrated clinical efficacy in DLBCL with a favorable toxicity profile relative to transplant. **Methods:** This phase II trial investigated the overall response rate (ORR), event free survival (EFS), overall survival (OS) and toxicity of treatment with ibritumomab followed by rituximab in patients with relapsed or refractory DLBCL, not candidates for transplant. Patients were treated with an initial dose of rituximab (250 mg/m^2) followed one week later by ibritumomab (0.4 mCi^{90}Y/kg or 0.3 mCi^{90}Y/kg based on plateles) followed by 4 weekly doses of rituximab (375mg/m^2). All non-progressing patients received maintenance rituximab (375 mg/m^2) weekly for 4 doses every 6 months for 4 cycles. **Results:** 25 patients were enrolled. Median age was 79 (range 45-95). 12 of 25 (48%) had stage 3 or 4 disease. 13 (52%) had 2 or more prior regimens. At 12 weeks 5 patients (21%) had a complete response (CR), 3 (13%) a partial response, 2 (8%) stable disease and 14 (58%) progressed for an ORR of 32% (8/25). At best response 7 patients obtained a CR. Median EFS was 2.5 months. Median OS was 8.1 months. No patient who obtained CR later relapsed, with follow up of 18.3-100.1 months. Deaths unrelated to treatment occurred in remission in 5 patients. 2 patients remain free of disease at 67.4 and 100.1 months. 11 (65%) patients had grade 3 or 4 thrombocytopenia, but no significant bleeding was observed. 9 (36%) patients had grade 3 non-hematologic toxicity. Grade 1 and 2 fatigue occurred in 41%. Patients who progressed through a rituximab containing regimen were at high risk of early progression. **Conclusions:** The ORR of ibritumomab as salvage therapy for DLBCL compares favorably to other regimens with acceptable toxicity. Those patients with disease refractory to rituximab are not likely to benefit. For a subset of patients not candidates for salvage with autologous transplant, this treatment can produce a durable remission. Clinical trial information: NCT00110149.

8559 General Poster Session (Board #48F), Sun, 8:00 AM-11:45 AM

Certification and role of local pathologists for diffuse large B-cell lymphoma (DLBCL) subtyping and eligibility determination in the phase II PYRAMID study.

Jonathan W. Said, James Andrew Reeves, Ian Flinn, Anil Tulpule, Robert Leon Robles, Christopher Flowers, Nicholas J. DiBella, Kathryn S. Kolibaba, Parameswaran Venugopal, Tatjana Kolevska, Sven De Vos, David L. Jaye, Dixie Esseltine, George Mulligan, Maria Margarita Corvez, John R. Eckardt, Bryan Brockman, Isagani M. Chico, John Leonard, Steven Kussick; Department of Pathology and Laboratory Medicine, David Geffen School of Medicine, Los Angeles, CA; Hematology/Oncology, Sarah Cannon Research Institute – Florida Cancer Specialists, Fort Myers, FL; Oncology, Sarah Cannon Research Institute – Tennessee Oncology, PPLC, Nashville, TN; University of Southern California Norris Comprehensive Cancer Center and Hospital, Los Angeles, CA; Diablo Valley Oncology/Hematology Medical Group, California Cancer and Research Institute, Pleasant Hill, CA; Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA; Rocky Mountain Cancer Centers; US Oncology Research, Aurora, CO; Compass Oncology, Vancouver, WA; Rush University Medical Center, Chicago, IL; Department of Oncology, Vallejo Medical Center, Vallejo, CA; Hematology/Oncology, UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA; Department of Pathology and Laboratory Medicine, Winship Cancer Institute of Emory University, Atlanta, GA; Millennium Pharmaceuticals, Inc., Cambridge, MA; DAVA Oncology, Dallas, TX; Oncology Therapeutic Delivery Unit, Quintiles, San Francisco, CA; Center for Lymphoma and Myeloma, Weill Cornell Medical College, New York, NY; PhenoPath Laboratories, Seattle, WA

Background: The role of local pathologists in promoting patient (pt) accrual and evaluating eligibility criteria involving a complicated immunohistochemical (IHC) algorithm has rarely been investigated. The phase II PYRAMID trial (NCT00931918) is assessing R-CHOP ± bortezomib for newly diagnosed pts with non-germinal-center B-cell (non-GCB) subtype DLBCL. In this trial, local pathologists were encouraged to perform DLBCL subtyping at the point of biopsy, identify suitable pts for the trial, and facilitate accrual. **Methods:** Determination of GCB vs non-GCB subtype is per the Hans method, an algorithm based on IHC for CD10, BCL-6, and IRF4/MUM1. In stage 1, pathologists demonstrated IHC subtyping proficiency by evaluating a tissue microarray (TMA) of 12 DLBCL cases; those with ≥80% of samples in agreement with central lab results were certified for determining trial eligibility. In stage 2, to broaden participation, pathologist certification occurred via teleconference outlining trial eligibility criteria, tissue subtyping requirements, and determining pathologists' experience with the Hans method. **Results:** 182 pathologists have been certified for local subtyping, 50 via TMA and 132 by teleconference. 66/88 active study sites have ≥1 certified pathologist. Only 1 of the 10 top enrolling sites lacks a certified pathologist. 52% (84/162) of pts have been enrolled based on local pathologist subtyping prior to central lab confirmation. Discordance with central lab results occurred in 9/84 cases (11%). Enrollment rates pre- and post-local pathologist certification were 0.053 and 0.096 pts/site/month; an improvement of 81%. Trial accrual correlates with the presence of a certified local pathologist ($p=0.0026$). The rate of ineligible GCB cases sent for central lab testing was lower from sites with a certified pathologist (23% [69/299 cases] vs 38% [40/106 cases] for sites without). **Conclusions:** Engagement of local pathologists in trials requiring pathology selection can significantly improve accrual. This study demonstrates the effectiveness of various training modalities in improving selection by local pathologists using a complex IHC algorithm. Clinical trial information: NCT00931918.

8560 General Poster Session (Board #48G), Sun, 8:00 AM-11:45 AM

Y^{90}-ibritumomab tiuxetan (Y^{90}-IT) and high-dose melphalan as conditioning regimen before autologous stem cell transplantation (ASCT) for elderly patients with lymphoma in relapse or resistant to chemotherapy: A feasibility trial (SAKK 37/05).

Michele Voegeli, Stephanie Rondeau, Simona Berardi, Erika Lerch, Luciano Wannesson, Thomas Pabst, Jochen Rentschler, Mario Bargetzi, Lorenz M. Jost, Nicolas Ketterer, Angelika Bischof Delaloye, Michele E. G. Ghielmini; Medizinische Universitätsklinik, Liestal, Switzerland; SAKK - Swiss Group for Clinical Cancer Research, Coordinating Center, Berne, Switzerland; IOSI (Oncology Institute of Southern Switzerland), Bellinzona, Switzerland; IOSI (Oncology Insitute of Southern Switzerland), Bellinzona, Switzerland; Institute of Medical Oncology, Berne, Switzerland; Universitätsspital Basel, Basel, Switzerland; Kantonsspital Aarau, Aarau, Switzerland; Kantonsspital Bruderholz, Bruderholz, Switzerland; Hirslanden Lausanne, Lausanne, Switzerland; Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

Background: Standard conditioning regimens for ASCT are often not tolerated by elderly patients. Single agent high-dose melphalan has been shown to be safe and active in elderly patients with multiple myeloma. Y^{90}-IT is a well-tolerated lymphoma treatment and feasible in the transplantation setting. We therefore investigated this combination of high-dose melphalan and Y^{90}-IT as a conditioning regimen for elderly patients. **Methods:** Patients ≥65 years with relapsed or chemotherapy resistant CD20-positive lymphoma in PR or CR after salvage chemotherapy could be enrolled prior to stem cell mobilization. Myeloablation regimen consisted of standard dose Y^{90}-IT followed by melphalan at escalating doses (100, 140, 170 and 200mg/m^2, with a 3+3 phase I design) and by ASCT. The primary objective was to identify the MTD of melphalan in combination with standard dose Y^{90}-IT (as defined < 1 DLT in 3 patients); secondary endpoints were toxicity and CR rate 100 days after transplantation. **Results:** Between 2006-2012 twenty patients were included. Median age was 72 years (range 66-77). One patient was considered retrospectively ineligible and was evaluable for toxicity but not for DLT. Thirteen patients received the treatment and were transplanted. Eleven patients were evaluable for DLT. No DLT occurred. Non-hematological grade 3 or higher treatment related adverse events were: infection (n=6, including 2 cases of febrile neutropenia), diarrhea (n=3), mucositis, anorexia, viral hepatitis, hypokalemia, dehydration and multi-organ failure (n=1). Seven patients did not start treatment because of mobilization failure (n=3), progressive disease (n=2), worsening of cardiac failure (n=1) and grade 3 dyspnea (n=1). Seven patients achieved a CR/CRu and 2 patients were stable 100 days after transplantation. **Conclusions:** The combination ofstandard dose Y^{90}-IT and high dose melphalan (200mg/m^2) is a safe and feasible conditioning regimen before ASCT for patients ≥65 years. The results show promising activity. Clinical trial information: NCT00392691.

8561 General Poster Session (Board #48H), Sun, 8:00 AM-11:45 AM

Allogeneic hematopoietic cell transplantation (alloHCT) in diffuse large B-cell lymphoma (DLBCL) after nonmyeloablative (NMA) or reduced-intensity (RIC) conditioning: Long-term outcome in 116 patients.

L. M. Poon, Rima Saliba, Gabriela Rondon, Grace-Julia Okoroji, Yasuhiro Oki, Richard E. Champlin, Chitra Hosing, Ken H Young, Francesco Turturro, Issa F. Khouri; National University Cancer Institute, Singapore, Singapore; The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: The role of alloHCT and conditioning intensity in DLBCL remains unclear. In this retrospective study, we determined their effectiveness in 116 patients (pts) with DLBCL (de novo, n=59, transformed, n=57) receiving alloHCT at our institution, between 1998-2011. **Methods:** Median age was 51years (range, 19-70); median prior therapies was 4 (range 2-12). Disease status at alloHCT was complete response (CR) (n=22), partial response (PR) (n=58), stable (SD) (n=25) or progressive disease (PD) (n=11). 41 (35%) pts had previous autografts. 74 (64%) pts received RIC of melphalan/fludarabine (Flu) or BEAM, and 42 (36%) received a NMA conditioning of Flu/cyclophosphamide or cisplatin/cytarabine/Flu. Donor source was HLA-identical sibling (MRD) (65%), HLA-matched unrelated (MUD) (31%) or a 1-Ag mismatched donor (4%). **Results:** With median follow-up among survivors of 63 months (range 5-157), estimated 5-yr OS and PFS for the whole cohort was 41% and 34% respectively. On multivariate (MV) analysis, disease status was most significant predictor for OS, with chemo refractory disease (SD/PD) being associated with higher mortality rate (HR 3.7, 95% CI 1.6-8.6, p=0.002). Combined use of NMA conditioning and MRD was associated with significantly lower mortality rate (HR 0.4, 95% CI 1.6-8.6, p=0.005). OS was highest [69% (95% CI 49-82)} for pts in CR/PR after NMA with a MRD (n=29), and lowest [(12% (95% CI 3-29)] for SD/PD pts after RIC with a non MRD (n=32). Disease status was strongest predictor of PFS on MV analysis, with CR pts having improved PFS compared to SD/PD (5-year estimates of 58% and 13%, respectively (P<0.001). Pts in PR with early disease stage (< Stage 4) and negative PET at alloHCT had PFS comparable to pts in CR (56% at 5 yr HR=1.3, p=0.6), while all other PR pts had PFS comparable to SD/PD pts (PFS=20%, p 0.1). **Conclusions:** Our study shows disease status, donor type and conditioning intensity are predictors of outcomes after alloHCT in DLBCL. Pts with chemosensitive disease and receiving NMA, MRD had improved survival rates compared to RIC alloHCT. PR pts with low volume PR had similar outcomes to CR pts.

8562 General Poster Session (Board #49A), Sun, 8:00 AM-11:45 AM

Markers of angiogenesis and hypoxia to cell of origin (COO) subtypes of DLBCL: Correlative studies from S0515, a phase II trial of R-CHOP plus bevacizumab.

Ambuga R. Badari, Mohammad Abu Zaid, Joseph M. Unger, Lisa M. Rimsza, Marilyn Marron, Richard I. Fisher, Thomas P. Miller, Alison Stopeck; University of Arizona Cancer Center, Tucson, AZ; SWOG Statistical Center, Seattle, WA; University of Arizona Department of Pathology, Tucson, AZ; University of Rochester, Rochester, NY

Background: S0515 was a nonrandomized phase 2 trial of R-CHOP + bevacizumab in 64 patients with newly diagnosed DLBCL. No significant improvement in PFS or OS was observed compared with historic controls.Patients with higher baseline levels of plasma VCAM and urine VEGF had worse PFS and OS. Tumor-associated carbonic anhydrase, CA IX, is induced by hypoxia in various tumors and part of the hypoxia inducible factor -1/ hypoxia responsive element (HIF-1/HRE) system. We present additional correlative studies from S0515 including longitudinal plasma CAIX levels, and correlate expression of VEGF and VEGF receptors (VEGFR) to COO subtype [GCB vs. non-GCB] and urine VEGF and plasma VCAM. **Methods:** COO subtypes were determined by immunohistochemistry (IHC) using the Hans classification. VEGF and VEGFR expression was determined by IHC and scored on a scale of 0 (none) to +3 (strong). Plasma VCAM, CAIX, urine VEGF levels were measured by ELISA and samples collected at baseline and before cycles 4 and 8 of therapy. **Results:** Baseline CAIX levels did not predict PFS ($p = 0.95$) or OS ($p=.66$) or change with therapy. Patients with lower baseline CAIX levels (below the median) had a statistically significant increase in CAIX over the course of therapy (median 34.1 to 52.4, $p=.002$), whereas in patients with higher baseline CAIX, levels decreased (median 96.7 to 78.2, $p=.20$). CAIX correlated with plasma VCAM ($P=.006$), but not COO subtype. 33 lymphoma samples were classified as GCB ($n = 21$) or non-GCB ($n=12$). COO subtype did not predict difference in PFS ($p=.56$) or OS ($p=.67$). Median urine VEGF and plasma VEGF levels trended higher in non-GCB vs GCB tumors (181 vs 144pg/mL and 1499 and 821ng/mL, respectively). Lymphoma expression of VEGF did not correlate with plasma VCAM or urine VEGF. VEGR2 expression was higher in non-GCB vs GCB tumors (33% vs 5% expression). **Conclusions:** Plasma CAIX levels, a marker of hypoxia and HIF1alpha activation, increased only in those patients with lower baseline levels in response to therapy. COO by IHC did not predict PFS or OS. However, non-GCB tumors had higher expression of VEGFR2, plasma VCAM, and urine VEGF compared to GCB tumors consistent with increased angiogenesis. Clinical trial information: SWOG S-0515.

8563 General Poster Session (Board #49B), Sun, 8:00 AM-11:45 AM

Correlation of chemotherapy delivery and survival outcomes of follicular lymphoma in the immunchemotherapy era.

Kitsada Wudhikarn, Anna M Button, Brian J. Smith, Thomas Matthew Habermann, Carrie A. Thompson, James Robert Cerhan, Brian K. Link; University of Iowa Hospitals and Clinics, Iowa City, IA; College of Public Health, University of Iowa, Iowa City, IA; Mayo Clinic, Rochester, MN

Background: Optimal initial treatment of follicular lymphoma (FL) is unknown. Rituximab as monotherapy (R) or as a component of immunochemotherapy (R+Chemo) is established as effective and it is now reasonable to re-examine the role of chemotherapy dosing. We explored clinical features, systemic treatment and chemotherapy delivery with comparative effectiveness of delivered dose intensity (DDI) on outcomes. **Methods:** We reviewed the University of Iowa/Mayo Clinic SPORE Molecular Epidemiology Resource database along with medical records on newly diagnosed grade I-IIIa FL who received systemic therapy from 2002 to 2009. Presenting clinicopathologic factors, outcomes and systemic therapy details including doses of chemotherapy were collected. The event-free (EFS) and overall survival (OS) effects of systemic therapy and chemotherapy DDI were analyzed with multivariate Cox regression. Confounding effects of FLIPI, grade, stage, and age were considered in the analysis. **Results:** From 2002 to 2009, 631 newly diagnosed FL were enrolled. Median follow up duration was 52.7 months. We identified 322 grade I-IIIa FL treated with systemic therapy including 93 R and 229 R+Chemo. Age and stage were similarly distributed between the R and R+Chemo groups; however, patients in the R group had lower grade ($p<0.01$) and FLIPI ($p=0.03$). Multivariate analysis showed no significant differences in EFS (HR=1.24, $p=0.28$) or OS (HR=0.55, $p=0.13$) for R compared to R+Chemo. Among R-CVP or R-CHOP treated FL, DDI data were collected for 73 doxorubicin (dox) and 137 cyclophosphamide (cyc) patients. Eighty-five percent of patients received 90% or more pre-planned DDI. After controlling for confounding factors, higher cycDDI was associated with improved EFS (HR 0.55, P=0.04) and OS (HR 0.74, P=0.03). No significant OS or EFS effects of doxDDI were observed. **Conclusions:** Addition of chemotherapy to rituximab was not associated with a detectable difference in survival outcomes in grade I-IIIa FL at a median follow-up of 52.7 months. Among R+Chemo treated FL, chemotherapy was delivered completely in most patients and more completed delivery of cyclophosphamide was associated with improved EFS and OS.

8564 General Poster Session (Board #49C), Sun, 8:00 AM-11:45 AM

A phase II study of gemcitabine, ifosfamide, and oxaliplatin (GIFOX) as upfront treatment for high-risk, non-anaplastic large cell, peripheral T-cell lymphomas.

Gaetano Corazzelli, Gianpaolo Marcacci, Ferdinando Frigeri, Gaetana Capobianco, Francesco Volzone, Cristina Becchimanzi, Daniela Donnarumma, Rosa Azzaro, Rosaria De Filippi, Filippo Russo, Antonio Pinto; Hematology-Oncology and Stem Cell Transplantation Unit, Istituto Nazionale Tumori, Fondazione, Naples, Italy; Department of Hematology, Istituto Nazionale Tumori, Fondazione, Naples, Italy; Department of Clinical Medicine and Surgery, Naples, Italy

Background: Patients (pts) with peripheral T/NK cell lymphomas (PTCL) and intermediate-high/high IPI risk have a 5-yr overall survival < 20%. Current chemotherapy is unsatisfactory while benefit of upfront autologous transplantation (ASCT) is limited by high pre-transplant progression rates and pts advanced age. We evaluated efficacy and stem cells (SCs)-mobilizing activity of a biweekly regimen of gemcitabine (G), ifosfamide (Ifo) and oxaliplatin (Ox) (GIFOX), as an upfront strategy ensuring fast cytoreduction and early ASCT access or an effective alternative to CHOP-like programs in transplant-inelegible pts. **Methods:** Six biweekly courses of GIFOX [G 1000 mg/m2 D1, Ox 130 mg/m2 D2, Ifo 5 g/m2 D2 as 24h infusion (fractionated over days 2-4 in pts>65 yrs), G-CSF DD 7-11] were planned for all pts, with SCs mobilization at course 3 in ASCT-eligible pts. Simon's minimax two-stage design was adopted with the primary and secondary endpoints of response rate (RR) and progression-free survival (PFS), respectively. **Results:** Thirty-four pts (median age 63 yrs, r 42-80) [PTCL, nos (n=16), AITL (n=7), extranodal NK/T-cell (n=5), SS (n=6)], with IPI score intermediate-high (62%) or high (38%) were accrued [stage IV: 71%; BM involvement: 38%; E-site >1: 47%; hi LDH: 71%; ECOG>1: 38%; B-symptoms: 44%]. A total of 172 courses was delivered (median 6, r 2-6). Only 5 pts received <4 courses, due to progression (n=4) or early death (n=1). Overall RR was 82% [95% CI, 66-92; 22 complete (CR) and 6 partial (PR) responses]. Twelve pts mobilized SCs (median $CD34^+$ cells harvest: $4.36x10^6$/kg) and 8 (7CRs,1PR) underwent ASCT, 6 to 13 weeks after the 6th course. Estimated 5-yr PFS was 48% (95%CI: 28-65); median PFS for non-transplanted pts was 15 mo.s. Estimated 4-yr disease-free survival was 58%. Relevant toxicities were G4 thrombocytopenia (13%), G4 anemia (23%), G3/G4 infection (29%/6%), G3 encephalopathy (6%). **Conclusions:** Response and survival rates of GIFOX in high-risk PTCL compared more than favorably to CHOP-based regimens. Effective cytoreduction and prompt access to ASCT were ensured, together with safe delivery of a full induction program to transplant-ineligible pts.

8565 General Poster Session (Board #49D), Sun, 8:00 AM-11:45 AM

Different safety profiles of first-line bendamustine-rituximab (BR), R-CHOP, and R-CVP in an open-label, randomized study of indolent non-Hodgkin lymphoma (NHL) and mantle cell lymphoma (MCL): The BRIGHT study.

David MacDonald, Richard van der Jagt, John M. Burke, Brad S. Kahl, Peter Wood, Tim E. Hawkins, Mark Hertzberg, Yiu-Lam Kwan, David Simpson, Michael Craig, Kathryn S. Kolibaba, Samar Issa, Regina Clementi, Doreen M. Hallman, Mihaela C. Munteanu, Ling Chen, Ian Flinn; Dalhousie University, Halifax, NS, Canada; University of Ottawa, Ottawa, ON, Canada; Rocky Mountain Cancer Centers, Aurora, CO; University of Wisconsin Carbone Cancer Center, Madison, WI; Princess Alexandra Hospital, Woolloongabba, Australia; Auckland Hospital, Auckland, New Zealand; Westmead Hospital, Wentworthville, Australia; Concord Repatriation General Hospital, Concord West, NSW, Australia; North Shore Hospital, Takapuna, New Zealand; West Virginia University, Morgantown, WV; Compass Oncology, Vancouver, WA; Middlemore Hospital, Auckland, New Zealand; Teva Pharmaceuticals, Inc., Frazer, PA; Sarah Cannon Research Institute, Nashville, TN

Background: The BRIGHT study demonstrated that first-line BR was non-inferior to R-CHOP/R-CVP in terms of complete remission rate in indolent NHL and MCL. This is the first detailed analysis of the safety and tolerability of the study regimens. **Methods:** Patients were preselected for R-CHOP or R-CVP, and then randomized to 6-8 cycles of BR (28-d cycle) or the preselected standard regimen (21-d cycles). BR dosing was bendamustine 90 mg/m^2/d as a 30-min infusion on days 1 and 2 plus rituximab 375 mg/m^{2}given before bendamustine on day 1. Colony stimulating factors (CSFs) and antiemetics were given per local standards. **Results:** In patients preselected for R-CHOP, 103 received BR and 98 R-CHOP. In patients preselected for R-CVP, 118 received BR and 116 R-CVP. For all regimens, $\geq$ 88% of patients received the planned 6 cycles. Main differences in adverse events (AEs), all grades, are shown in the Table. Incidence of grade 3/4 AEs was 69% for R-CHOP vs 56% BR, and 50% for R-CVP vs 56% BR. Grade 3/4 drug hypersensitivity, neuropathy, and rash were infrequent. Antiemetic use was similar between groups except use of aprepitant as an adjunct to 5-HT3 antagonists was higher with R-CHOP (23% [19% in cycle 1]) than BR (9% [2%]) or R-CVP (3% [2%]). CSF use was higher with R-CHOP (61%) than BR (29%) or R-CVP (27%). Analyses of event prevalence over the treatment period and by region will also be presented. **Conclusions:** BR, R-CHOP, and R-CVP have significantly distinct AE profiles. More nausea, vomiting, and hypersensitivity occurred with BR while more constipation, neuropathy, and alopecia occurred with RECHOP/R-CVP. Support: Teva BPP R&D, Inc. Clinical trial information: NCT00877006.

All-grade AEs.

	Preselected for R-CHOP		Preselected for R-CVP	
	BR (n = 103) %	R-CHOP (n = 98) %	BR (n = 118) %	R-CVP (n = 116) %
Nausea	63	58	63	39 †
Vomiting	29	13 *	25	13 *
Constipation	32	40	27	44 *
Drug hypersensitivity [a]	17	6 *	13	3 *
Infection [a]	55	57	53	50
Grade ≥3 infection	12	5	7	7
Opportunistic infection [a]	10	7	12	9
Pneumonia / respiratory infection [a]	18	14	14	13
Peripheral neuropathy / paresthesia [a]	9	44 †	14	47 †
Rash / urticaria [a]	20	12	24	16
Alopecia	4	51 †	3	21 †

[a] From multiple preferred terms. * P <0.05; † P <0.005.

8566 General Poster Session (Board #50A), Sun, 8:00 AM-11:45 AM

The role of radiotherapy and intrathecal CNS prophylaxis in extralymphatic craniofacial diffuse large B-cell lymphoma.

Niels Murawski, Samira Zeynalova, Gerhard Held, Marita Ziepert, Barbara Kempf, Andreas Viardot, Mathias Haenel, Mathias Witzens-Harig, Christian Ruebe, Jochen Fleckenstein, Carsten Zwick, Bertram Glass, Norbert Schmitz, Michael Pfreundschuh, German Non-Hodgkin Lymphoma Study Group (DSHNHL); Saarland University Medical School, Homburg, Germany; Institute for Medical Informatics, Statistics and Epidemiology, Leipzig University, Leipzig, Germany; Klinikum Landshut, Landshut, Germany; University Hospital Ulm, Ulm, Germany; Chemnitz Hospital, Chemnitz, Germany; University Hospital Heidelberg, Heidelberg, Germany; Saarland University Medical School, Homburg/Saar, Germany; Asklepios Hospital St. Georg, Hamburg, Germany

Background: The role of radiotherapy and intrathecal prophylaxis in extralymphatic craniofacial involvement of aggressive B-cell lymphoma remains to be determined in the rituximab era. **Methods:** In a retrospective subgroup analysis of 9 consecutive prospective DSHNHL trials covering all DLBCL risk groups from 18 to 60 years of age, patients with and without craniofacial involvement were compared with respect to clinical presentation, event-free and overall survival. **Results:** 336 sites of extralymphatic craniofacial involvement were observed in 284/3840 (7.4%) patients (orbita: 30, paranasal sinuses: 90; main nasal cavity: 38, tongue: 26, remaining oral cavity: 99, salivary glands: 53). In a multivariable analysis adjusting for IPI risk factors the addition of rituximab improved EFS and OS in both patients with and without craniofacial involvement. The 141 responding patients who received radiotherapy to sites of craniofacial involvement had a similar 3-year event-free (79% vs 79%; p=0.835) and 3-year overall survival (88% vs. 85%; p=0.311) when compared with the 56 patients who did not receive radiotherapy. Without rituximab, the 2-year-rate of cumulative risk of CNS disease was increased in 205 patients with compared to 2586 patients without craniofacial involvement (4.2% vs. 2.8%; p=0.038), while this difference disappeared in patients who received CHOP(like) chemotherapy in combination with rituximab (1.7% in 77 patients with compared to 2.9% in 946 patients without craniofacial involvement; p=0.868). Of 85 patients with craniofacial involvement who received intrathecal prophylaxis with methotrexate, the 2-year-rate of cumulative risk of CNS disease was 4.3% compared to 2.3% in 189 patients who did not (p=0.995). **Conclusions:** Rituximab eliminates the increased risk for CNS disease in patients with craniofacial involvement. As a practical consequence intrathecal prophylaxis and radiotherapy to sites of craniofacial involvement should not be given any more.

8567 General Poster Session (Board #50B), Sun, 8:00 AM-11:45 AM

A matched pair analysis of conditioning BuEM versus BEAM in autologous haematopoietic cell transplantation for lymphomas in terms of toxicity and efficacy.

Ioanna Sakellari, Despina Mallouri, Ioannis Batsis, Chryssoula Apostolou, Varnavas Konstantinou, Elma Maria Abela, Vassiliki Douka, Anastasia Marvaki, Kyriakos Karypidis, Iskas Michail, Panayiotis Baliakas, Panayiotis Kaloyannidis, Evangelia Yannaki, George Kouvatseas, Christos Smias, Achilles Anagnostopoulos; George Papanicolaou Hospital, Thessaloniki, Greece; George Papanikolaou Hospital, Thessaloniki, Greece; Hellenic Cooperative Oncology Group (HeCOG), Athens, Greece

Background: In autologous hematopoietic cell transplantation (AHCT) for lymphomas, the optimal conditioning regimen is currently investigated. The standard conditioning used is BEAM. During 2009-2011 a new alternative Busulphan-based conditioning regimen constructed in our unit, consisting of Busilvex (9.6 mg/Kg), Etoposide (9.6 mg/Kg) and Melphalan (140mg/m^2) (BuEM) was used. We retrospectively analysed the outcome of patients (pts) conditioned with BEAM and BuEM regimen, in terms of toxicity and efficacy, in a matched pair analysis. **Methods:** A matched paired analysis on a 1:2 ratio was performed. Thus, 2 control cases (receiving BEAM regimen) were matched to each patient treated with BuEM according to: phase of transplant, age, lines of previous chemotherapy. The first 50 consecutive pts treated with BuEM were matched to a random sample from the historical BEAM control population. Ninety-three BEAM pts that fulfilled the matching criteria were eventually randomly selected. Concerning pts characteristics there were no statistical significant differences except from more chemoresistant disease in the BuEM cohort ($p=0.008$). Thus a second matched pair analysis was conducted upon stratification by disease chemosensitivity instead of age as a risk factor. **Results:** Progression free survival and overall survival (OS) were 70.6% and 81.8% for the BEAM vs 68.9% and 83% for the BuEM cohort respectively ($p=$ns). In the BuEM cohort a borderline significantly better OS was noted in Hodgkin's pts receiving BuEM ($p=0.05$). In terms of early toxicity a significantly faster neutrophil engraftment was found in the BEAM cohort, but there was a significantly less need of red blood cells, platelet transfusions and GCSF infusion in the BuEM cohort. BEAM regimen was also associated with: reduced incidence of infections ($p=0.02$), less severe (grade 3-4) mucositis ($p=0.000$) and liver toxicity ($p=0.004$). **Conclusions:** BEAM regimen was correlated with a favourable reduced early toxicity profile, ie severe mucositis and liver impairment. On the other hand, BuEM was found to be equally efficacious and moreover offered improved overall survival in Hodgkin's lymphoma pts.

8568 General Poster Session (Board #50C), Sun, 8:00 AM-11:45 AM

Screening for coronary artery disease after mediastinal irradiation in Hodgkin lymphoma survivors.

Laurien Aletta Daniëls, Augustinus Krol, Michiel A de Graaf, Arthur JHA Scholte, Hein Putter, Mars B van t Veer, Albert de Roos, Martin J Schalij, Carien L. Creutzberg; Leiden University Medical Center, Department of Clinical Oncology, Leiden, Netherlands; LUMC, Department of Cardiology, Leiden, Netherlands; Department of Medical Statistics, Leiden University Medical Center, Leiden, Netherlands; LUMC, Department of Hematology, Leiden, Netherlands; Leiden University Medical Center, Department of Radiology, Leiden, Netherlands

Background: Cardiovascular diseases are the most common non-malignant cause of death in Hodgkin Lymphoma (HL) survivors, especially those who had mediastinal irradiation as part of their treatment. We investigated the role of CT coronary angiography (CTA) as a screening tool for coronary artery disease (CAD) in asymptomatic HL survivors, related findings to stress testing and subsequent interventions. We also evaluated acceptance of screening. **Methods:** Patients were eligible if at least 10 years disease-free and treated with mediastinal radiotherapy. All patients were screened with ECG, stress testing and CTA. Primary endpoint was significant CAD (stenosis >50%) on CTA. A sample size of 50 patients would achieve ≥80% power to detect a difference of 13% (≥20% vs a population proportion of 7%) using a two-sided binominal test. Allowing for non-evaluable and false-positive scans, we considered CTA screening to be indicated for testing in a larger population if in ≥six patients revascularization would be necessary. **Results:** Fifty-two patients were included, 48 patients underwent CTA. Median age was 47 years, time since HL diagnosis 21 years. Most patients had no risk factors for CAD. There were 45 evaluable scans. Prevalence of significant CAD on CTA was found in 20% (N=9), and significantly increased compared to the 7% expected abnormalities (p=0.01, 95% CI 8.3-31.7%). In 5 of the 8 patients who underwent conventional angiography, significant CAD was confirmed, and revascularization performed. Two patients were started on medication. Stress testing was inaccurate for determining CAD: all participants were asymptomatic and 1 patient with significant CAD had signs of ischemia. Ninety percent of the participants were content with the screening offered in this study, regardless whether the CTA showed abnormalities or not. **Conclusions:** Prevalence of significant CAD among HL survivors is high. In our participants even the most severe and life-threatening CAD was not preceded by typical symptoms. In symptomatic cardiac patients revascularization improves survival. This might justify both screening by CTA and intervention in this asymptomatic population, but needs to be further evaluated in a larger cohort. Clinical trial information: NCT01271127.

8569 General Poster Session (Board #50D), Sun, 8:00 AM-11:45 AM

Association of 25-OH vitamin D deficiency with worse outcome for elderly patients with aggressive B-cell lymphomas treated with CHOP plus rituximab (R): An analysis of the RICOVER-60 trial of the German High-Grade Non-Hodgkin Lymphoma Study Group (DSHNHL).

Joerg Thomas Bittenbring, Marina Achenbach, Bettina Altmann, Marita Ziepert, Joerg Reichrath, Juergen Geisel, Evi Regitz, Niels Murawski, Carsten Zwick, Gerhard Held, Michael Pfreundschuh; Saarland University Hospital, Homburg, Germany; Institute for Medical Informatics, Statistics and Epidemology, Leipzig University, Leipzig, Germany; Institute for Medical Informatics, Statistics and Epidemiology, Leipzig University, Leipzig, Germany; Saarland University Medical School, Homburg, Germany; Saarland University Medical School, Homburg/Saar, Germany

Background: Vitamin D deficiency was shown to be is associated with a worse outcome in patients with non-Hodgkin's lymphoma (Drake et al., 2010) To study whether this observation could be confirmed in patients with aggressive B-cell lymphomas treated uniformly within a prospective trial, we analyzed 25-OH vitamin D serum levels in patients treated within the RICOVER-60 trial of the DSHNHL. **Methods:** 25-OH Vitamin D serum levels were determined with a commercial chemoluminescence immunoassay in the serum from elderly patients of the RICOVER-60 trial which compared 6 or 8 cycles of CHOP, both with and without rituximab. **Results:** 193 of 359 pts (53.8%) had vitamin D deficiency ($<$10 ng/ml) and 165/359 patients (46.0%) had vitamin D insufficiency (10-30 ng/ml) according to current definitions. When treated with R-CHOP, patients with vitamin D levels $\leq$8 ng/ml had a 3-year EFS of 59% compared to 79% of patients with vitamin D serum levels $>$8 ng/ml; the respective figures for 3-year overall survival were 70% and 82%, respectively. In R-CHOP pts these differences were significant in a multivariable analysis adjusting for IPI risk factors with a hazard ratio (HR) of 2.1 ($p=0.008$) for EFS and a HR of 1.9 ($p=0.040$) for OS. In pts treated without R effects of vitamin D deficiency were significant only for OS (HR 1.8; $p=0.025$), but not with respect to EFS (HR 1.2; $p=0.388$). These results were confirmed in an independent validation set of 63 patients treated within the prospective RICOVER-noRx study. **Conclusions:** Vitamin D deficiency is a significant risk factor for patients with aggressive B-cell lymphomas treated with R-CHOP. The stronger adverse effect of vitamin D deficiency in patients receiving rituximab suggests that vitamin D deficiency interferes with the R mechanisms of this antibody. A prospective study evaluating the effects of vitamin D substitution on outcome of patients receiving R-CHOP is warranted. Supported by Deutsche Krebshilfe.

8570 General Poster Session (Board #51A), Sun, 8:00 AM-11:45 AM

Differential impact of sex in young and elderly patients with DLBC: Correlation with rituximab (R) pharmacokinetics.

Michael Pfreundschuh, Carsten Mueller, Samira Zeynalova, Gerhard Held, Viola Poeschel, Carsten Zwick, Tanja Rixecker, Norbert Schmitz, Niels Murawski, German Non-Hodgkin Lymphoma Study Group (DSHNHL); Saarland University Medical School, Homburg, Germany; University Hospital, Cologne, Germany; Institute for Medical Informatics, Statistics and Epidemiology, Leipzig University, Leipzig, Germany; Asklepios Hospital St. Georg, Hamburg, Germany

Background: Sex and weight independently influence R clearance in elderly DLBCL pts (Mueller et al., Blood 2012). **Methods:** We analyzed the impact of sex on R pharmacokinetics and outcome of 1,222 elderly pts of the RICOVER-60, 823 young (18 to 60 years) aaIPI=0,1 pts of the MInT, and 375 aaIPI=2,3 pts of the Mega-CHOEP trials. R pharmacokinetics was determined by ELISA in 33 young and 49 elderly patients. Population pharmacokinetic modeling was performed with nonlinear mixed-effect modeling software (NONMEM VI). **Results:** R clearance was independent of tumor mass (IPI), but weakly correlated (0.2, R^2linear=0.045) with increasing age in male, and moderately inversely correlated (-0.5, R^2linear=0.207) with age in female DLBCL patients, resulting in similar R clearances in young female and male patients (9.88 vs. 10.38 ml/h; p=0.238), but a significantly faster R clearance in elderly males compared to females (10.50 vs 8.25 ml/h; p=0.006). In the RICOVER-60 trial, elderly females had a higher 3-year PFS (68% vs. 61%) and OS (74% vs. 68%) than male pts. due to a greater outcome improvement by the addition of R in females. In a multivariable analysis adjusting for IPI, the hazard for progression in male compared to female pts. was not significantly increased after CHOP (HR=1.1; p=0.348), but was significantly higher after R-CHOP (OR=1.6; p=0.004). In contrast, young males treated in the MInT and Mega-CHOEP trials benefitted as much as females from the addition of rituximab, with a similar hazard for male pts. after CHOP and R-CHOP (HR=1.2) with no significant difference to female patients (HR_{PFS}=1.2, p=0.552; HR_{OS}=1.0; p=0.898). **Conclusions:** While no differences in R clearance and benefit from rituximab were found in young female compared to male patients, the reduced benefit of adding R to CHOP in elderly male DLBCL pts. who have a shorter rituximab serum half life and hence lower serum levels suggests that this subpopulation is suboptimally dosed when R is given based on body surface area at 375 mg/m^2. Ongoing studies of the DSHNHL investigate whether higher R doses for pts. with a shorter R serum half life can improve the outcome of the respective patients. Supported by Deutsche Krebshilfe and Roche.

8571 General Poster Session (Board #51B), Sun, 8:00 AM-11:45 AM

Infectious disease associations in advanced stage, indolent lymphoma (follicular, FL, and nonfollicular, nFL): A prospective trial of antibiotic therapy.

Carol S. Portlock, Paul A. Hamlin, John F. Gerecitano, Ariela Noy, Maria Lia Palomba, Janelle Walkley, Stacie Corcoran, Genovefa A Papanicolaou, Arnold Markowitz; Lymphoma Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY; Memorial Sloan-Kettering Cancer Center, New York, NY

Background: The antigen-drive association of gastric MALT with H. pylori (HP) is well recognized. Successful antibiotic (Ab) can result in lymphoma remission. We have studied a 3 mo course of clarithromycin (substituting lansoprazole/amoxicillin/clarithromycin, Prevpak, in the first 2 wks if HP +) in non-bulky, advanced stage indolent lymphoma as the first step to such a lymphoma treatment/prevention strategy. **Methods:** Patients with new diagnosis indolent lymphoma (FL and nFL), stages II (abdominal), III and IV fulfilling GELF criteria for observation were eligible. Stool HP done in all patients. Hepatitis B and C positive excluded. All patients had CT and PET prior to and 1 mo post Ab. **Results:** 32 evaluable patients were enrolled: 14 females, 18 males; median age, 53.5 years (36- 81); 22 FL, 10 nFL; stage II (2), III (16), and IV (14). HP + patients: 4 (3 FL, 1 nFL). We have observed lymphoma responses 1 mo post Ab in 7 of 32 (Table). With continued followup post Ab, best response to date in 9 of 32: PET CR (2 FL; 2 nFL); CT CR/PR (1/3 FL, 1/0 nFL). Median followup for all patients, 23.7 mos; and for those not needing lymphoma treatment, 54.9 mos. To date, no patient with PET CR has required lymphoma treatment (22.5+ to 62.8+ mos). Among 22 with FL, 8 have progressed, 3 had histologic transformation, possibly suggesting a different biology. **Conclusions**: H pylori eradication/3 mos clarithromycin has achieved lymphoma responses in advanced stage indolent lymphoma. PET negative CRs have been durable for 22.5 – 62.8 + mos following Ab alone. This prospective study may be a first step toward developing a lymphoma prevention strategy and deserves further clinical/biological study. Clinical trial information: NCT00461084.

	PET neg CR	CT CR	CT PR
H Pylori + FL	1	1	0
H Pylori - FL	0	0	0
H Pylori + nFL	0	1	2
H Pylori - nFL	1	1	0

8572 General Poster Session (Board #51C), Sun, 8:00 AM-11:45 AM

Impact of rituximab on the course of low-grade follicular lymphoma.

Jairam Krishnamurthy, Fausto R. Loberiza, Martin Bast, Pavankumar Tandra, Vijaya Raj Bhatt, Gregory Bociek, Philip Jay Bierman, Julie Vose, James O. Armitage; University of Nebraska Medical Center, Omaha, NE; Nebraska Medical Center, Omaha, NE

Background: Rituximab has revolutionized the treatment of lymphomas and has been shown to improve clinical outcomes in patients with follicular lymphoma. Our study evaluated the progression free survival (PFS) and overall survival (OS) in patients with grades I and II follicular lymphoma when rituximab was used as initial therapy, as salvage or if no rituximab was used. **Methods:** Patients with grades I and II follicular lymphoma treated between June 1981 and January 2010 were included. Disease and treatment related variables were compared based on type of treatment (No rituximab-Group I, rituximab as salvage-Group II, Rituximab as initial treatment-Group III) using the Kruswal Wallis or chi-square tests. Univariate probabilities of PFS and OS were estimated using the Kaplan Meier method. Multivariate analyses were performed using Cox proportional hazards regression analysis to evaluate differences in risk of treatment failure and mortality in the three groups while adjusting for covariates. **Results:** There were 226 patients in group I, 84 in group II and 110 in group III. Significant differences were found in some of the disease and treatment related variables. Univariate analysis is shown in the Table. The relative risk of treatment failure for group II was 0.82 ($p=0.26$) and 2.63 ($p=0.0001$) respectively in the first 10 years and after 10 years while it was 0.52 ($p=0.0003$) and 3.97 ($p=0.001$) respectively for group III in the first 10 years and after 10 years. The relative risk of mortality in group II was 0.63 ($p=0.008$) and group III was 0.32 ($p<0.0001$). **Conclusions:** Overall survival for patients with low grade follicular lymphoma is significantly improved when rituximab is used as initial treatment or as salvage when compared with no rituximab.

Outcomes	Group I (95% CI)	Group II (95% CI)	Group III* (95% CI)	P value
PFS (years)				0.12
5	53(46-59)	65(54-74)	80(70-87)	
10	38(32-45)	43(32-54)	47(33-59)	
20	16(10-23)	1(<1-6)	Follow-up short	
Median (95% CI)	5.79(3.77-8.35)	9.72(7.68 – 10.50)	9.54(8.62-10.96)	
OS (years)				<0.0001
5	71(64-76)	90(82-95)	90(82-94)	
10	49(42-56)	68(56-77)	82 69-90)	
20	20(13-27)	22(6-43)	Follow-up short	
Median (95% CI)	9.78(8.16-11.50)	16.68(12.70-18.56)	Not yet attained	

* Longest follow-up is only up to 13.5 years.

8573 General Poster Session (Board #51D), Sun, 8:00 AM-11:45 AM

Prognostic value of PET/CT scans on early chemo-cycle in diffuse large B-cell lymphoma: Prospective study.

He Huang, Jia Tian Lin, Cheng-cheng Guo, Dr.Prem Raj Shrestha, Tingzhi Liu, Ying Tian, Chao Yong Liang, Xue Ying Li, Mengping Zhang, Huang Ming Hong, Tongyu Lin; Sun Yat-sen University Cancer Center, Guangzhou, China; Cancer Center, Sun Yat-Sen University, Guangzhou, China; Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China

Background: To evaluate the prognostic value of positron emission tomography/computed tomography (PET/CT) scan on early chemo-cycle in newly-diagnosed diffuse large B cell lymphoma (DLBCL) patients. Also to distinguish the variation in outcome of early-responder (ER), late-responder (LR) and non-responder (NR). **Methods:** Newly diagnosed 149 DLBCL patients were treated with R-CHOP regimen for 2-8 cycles (mean: 5.49 cycles) in our center (Feb 2008–Jan 2013). The median age at diagnosis was 47 years (range, 17-80 years); 78 males (52.35%) and 71 females (47.65%); 63 stage I-II (42.3%) and 86 stage III-IV (57.7%); 45 B symptoms (30.2%); 90 IPI 1-2 scores (60.4%) and 59 IPI 3-5 scores (39.6%). All the patients with bulky disease, extranodal invasions and residual disease underwent baseline PET/CT scan and repeated after every 2 chemo-cycles. **Results:** After 2 subsequent cycles, the PET/CT evaluation showed complete remission (CR) in 82/149 (early-responder, 55.03%), and non-CR in 67/149 (44.97%) patients. Among 67 non-CR patients, 39 achieved CR (late-responder), 21 partial remission (PR), 3 stable disease (SD) and 4 progressive diseases (PD) (non-responder). After a follow-up of median 618 days (range 45-1816 days), the 1st and 2nd year progression-free survival (PFS) rate in NR were significantly different from ER (61.3% vs 92.6% , 52.5% vs 86.6%, $p < 0.001$) and LR (61.3% vs 91.6%, 52.5% vs 75.9%, $p=0.023$), and no significant differences were found between ER and LR ($p=0.329$). The 1st and 2nd year overall survival (OS) were 98.5%, 91.9% in ER; 97.3%, 97.3% in LR and 89.8%, 60.0% in NR respectively with significant differences between NR and ER ($p=0.005$), between NR and LR ($p=0.008$), but there was no statistically significant difference between ER and LR ($p=0.558$). The 1st and 2nd year disease free survival (DFS) rate did not differ between ER and LR (92.6% vs 84.6%, 86.9% vs 76.7%, $p=0.250$). **Conclusions:** The PET/CT findings in early chemo-cycle response might predict PFS advantage, but the difference of DFS and OS between ER and LR were not so obvious, and NR showed poor prognosis according to our current data. Clinical trial information: CTR-TRC-11001687.

8574 **General Poster Session (Board #51E), Sun, 8:00 AM-11:45 AM**

Single ascending dose escalation study of the specific Syk inhibitor P505-15 investigating pharmacokinetics, pharmacodynamics, and safety in healthy male volunteers.

Greg Coffey, Aradhana Rani, Andreas Betz, Yvonne Pak, Anjali Pandey, Stanley Hollenbach, Daniel D. Gretler, Tim Mant, Stipo Jurcevic, Uma Sinha; Portola Pharmaceuticals, Inc., South San Francisco, CA; King's College London, London, United Kingdom; Quintiles Drug Research Unit at Guy's Hospital, London, United Kingdom

Background: The spleen tyrosine kinase (Syk) regulates immune cell activation in response to ligation of a variety of receptors, making it an intriguing target for inflammatory and autoimmune disorders, as well as certain B cell malignancies. Here we present data from our first human study aimed at characterizing the pharmacokinetics (PK), pharmacodynamics (PD), and safety of P505-15, a selective Syk inhibitor in male volunteers following single oral administration. **Methods:** This study was a single center, blinded, randomized, placebo-controlled, ascending, single dose study of oral P505-15 suspension or its matching placebo, administered to healthy male volunteers. Dosing was initiated at 3mg and escalated to 400mg over seven cohorts. Serial blood samples for PK and PD evaluations were analyzed. The PD assays were designed to determine the potency and specificity of Syk inhibition. Potency for Syk inhibition was determined by measuring B cell receptor- (BCR) mediated ERK Y204 phosphorylation and cellular activation (CD69), as well as FcεRI-mediated basophil degranulation. **Results:** PK data indicate that P505-15 has a long terminal half life (~50-60 hrs), a T_{max} of about 2 hrs, and oral exposure more than dose proportional up to the 200mg dose. Complete inhibition of all three Syk-dependent assays was observed in the 200mg and greater dose levels. PD effect in the basotest approximated IC_{50} at 24 hours post-dose, and returned to pre-dose levels by 72 hours. At all dose levels, no inhibition of PMA or fMLP induced signaling and leukocyte activation was observed, consistent with a high degree of selectivity for Syk. Analysis of the PK/PD relationship indicated an $IC_{50}$of 208nM (95% confidence interval of 190-225) for inhibition of BCR-mediated B cell activation, and 124nM (95% confidence interval of 117-131) for inhibition of FcεRI-mediated basophil degranulation. **Conclusions:** P505-15 was safe and well tolerated across the entire range of doses. These data show that P505-15 has a favorable PK profile, and demonstrate its utility to safely and potently suppress Syk kinase function in humans.

8575 General Poster Session (Board #52A), Sun, 8:00 AM-11:45 AM

A phase I dose-escalation trial of ublituximab (TG-1101), a novel anti-CD20 monoclonal antibody (mAb), for rituximab relapsed/refractory B-cell lymphoma patients.

Changchun Deng, Jennifer Effie Amengual, Marshall T. Schreeder, Sean Clark-Garvey, Molly Patterson, Hari Miskin, Peter Sportelli, Owen A. O'Connor; Columbia University Medical Center / New York Presbyterian Hospital, New York, NY; Clearview Cancer Institute, Huntsville, AL; TG Therapeutics, Inc., New York, NY

Background: Anti-CD20 therapy (rituximab or RTX) in treating patients (pts) with B-cell lymphomas has resulted in significant improvement in treatment response and clinical outcomes. Despite advances, pts continue to relapse from, or are refractory to, RTX-based regimens. Ublituximab (UTX) is a novel, chimeric mAb targeting a unique epitope on the CD20 antigen. UTX has been glycoengineered to enhance affinity for all variants of FcγRIIIa receptors, and therefore demonstrates greater ADCC activity than RTX (Le Garff-Tavernier, 2011). UTX displayed greater antitumor activity compared to RTX in NHL in vivo models and in low CD20 expressing tumors (ASH 2011). A phase I trial with UTX used as a single agent in pts with relapsed/refractory CLL reported a response rate of 45%. Herein we report on the phase I dose-escalation of UTX in pts with RTX relapsed/refractory B-cell lymphoma. **Methods:** Eligible pts have B-cell lymphoma relapsed or refractory to a RTX containing regimen. Pts are required to have measurable/evaluable disease, ECOG PS < 2 and no active hepatitis B/C. The phase I dose-escalation uses a sequential 3+3 design in dose cohorts of 450mg, 600mg and 900mg respectively. UTX is administered once weekly for 4 infusions followed by monthly maintenance therapy. PK and correlative PD data are being collected. Primary endpoint: Maximum Tolerated Dose (MTD) and Dose Limiting Toxicities (DLT). Efficacy is a secondary endpoint. **Results:** Nine pts (5 FL, 3 MZL, 1 MCL) have been enrolled (3 each cohort). Median age 63; 3/6 (M/F). Median prior Rx = 4 (2-6). RTX refractory (44%). 8/9 pts are evaluable for safety; no DLT's observed and no Grade 3/4 AE's to date. 7/9 pts have had at least one response assessment (8 wk scan), which includes: 1 CR (rituximab refractory MZL); 2 PR's (1 MZL, 1 FL); 2 SD (FL) and 2 PD (1 transformed FL, 1 MCL). PK analysis is ongoing. **Conclusions:** UTX has been well tolerated to date with no G 3/4 AE's with demonstrated early clinical activity at all doses. 7/9 patients continue to receive UTX treatment (range 1–25 wks). Enrollment in the 900mg expansion cohort is now open with an emphasis on RTX relapsed/refractory indolent or low CD20-expressing lymphomas. Clinical trial information: NCT01647971.

8577 General Poster Session (Board #52C), Sun, 8:00 AM-11:45 AM

Whole genome sequencing of sporadic Burkitt lymphoma in HIV-infected and uninfected patients.

Deborah Ritter, Kimberly Walker, Myoung Kwon, Premal Lulla, Catherine M. Bollard, Andrea Sheehan, Helen E. Heslop, Richard A. Gibbs, David A. Wheeler, Martha P. Mims; Baylor College of Medicine, Houston, TX; Human Genome Sequencing center, Houston, TX; Human Genome Sequencing Center, Houston, TX

Background: Burkitt Lymphoma is defined by canonical translocations between *MYC* and immunoglobulin *IgH, IgK* or *IgL* (8:14, 8:2, 8:22, respectively), and is commonly associated with HIV. The identification of HIV from sequenced samples is critical to understanding HIV-associated Burkitt Lymphoma. While recent novel gene mutations (*ID3* and *TCF3*) have been implicated in functional roles, concomitant genomic structural variants and the interaction of HIV with structural variation is less well defined. **Methods:** We sequenced the whole genomes of 15 patients with 100bp paired-end reads on Illumina Hi-Seq platform, resulting in an average insert size of 278 (+/- 63) and coverage of 60X tumor and 30X normal. We included 7 HIV-negative, and 8 HIV-positive subjects. Sequencing reads were mapped to the reference genome using BWA. Large-scale structural variation was detected by the BreakDancer and Crest programs. Functional annotation was used to prioritize structural variants for validation. Single nucleotide variants and small insertions and deletions were detected by CARNAC, a somatic variation discovery pipeline. The subset of WGS reads that failed to align to the human reference genome were tested for the presence of HIV sequences by comparing the unmapped reads to a database of viral DNA sequences which included the common subtypes of HIV defined by Los Alamos. Reads matching HIV or EBV with an expectation value of $<10^{-4}$ were analyzed to determine virus coverage and viral integration sites. **Results:** Canonical *MYC-IgH* translocations were identified in 9/15 (60%) tumor samples, with 2 additional subjects harboring either a deletion or an inversion near exon1 of *MYC*; 4 had no *MYC* rearrangement. *MYC* translocations occurred equally in both groups. *TP53* and *SMARC4* point mutations were observed recurrently in the HIV uninfected group but not in the HIV infected patients. Variable levels of HIV DNA sequence were observed in normal tissue of all HIV infected patients. **Conclusions:** Whole genome sequencing has identified known somatic variants in HIV infected and uninfected patients. Two genes, *TP53* and *SMARC4*, appear to be differentially mutated, but additional samples are needed to achieve statistical significance.

8578 General Poster Session (Board #52D), Sun, 8:00 AM-11:45 AM

EBV-negative post-transplant lymphoproliferative disorder: Clinical characteristics, response to therapy, and survival.

Daniel S. Heil, Marlise Rachael Luskin, Edward Allen Stadtmauer, Stephen J. Schuster, Donald Edward Tsai, Ran Reshef; Hospital of the University of Pennsylvania, Philadelphia, PA

Background: Post-transplant lymphoproliferative disorder (PTLD) is a potentially life-threatening complication of solid organ transplantation. PTLD is frequently linked with Epstein-Barr virus (EBV) and it was suggested that EBV negativity is associated with a poor prognosis and lack of response to reduction of immunosuppression (RI). We conducted a case-control study to identify the characteristics, outcome and response to therapy of EBVpos and EBVneg PTLD over a 20-year period. **Methods:** We reviewed data on patients diagnosed with PTLD at U. Penn. between 1982 and 2012. We determined EBV positivity on tumor samples according to WHO criteria. We compared clinical and pathologic characteristics, response to therapy, and survival of EBVpos and EBVneg patients. **Results:** Of 222 patients diagnosed with PTLD, we verified the EBV status of 169 patients, of whom 35% were EBVneg and 65% were EBVpos. Mean follow-up was 46.7 months. Median time from transplant to PTLD was 23.1 mo. in EBVpos vs. 59.3 mo. in EBVneg ($p=0.003$) with 42% of EBVpos patients being diagnosed within the first year after transplant vs. 15% in the EBVneg group ($p<0.001$). EBVneg PTLD was more likely to occur in non-thoracic vs. thoracic transplants ($p=0.006$). 28% of patients with EBVpos PTLD presented with disease originating from the graft vs. 14% in the EBVneg group ($p=0.03$). In terms of histology, 36% of EBVpos patients had polymorphic PTLD vs. 7% of EBVneg patients ($p<0.001$). Of patients who were treated with RI alone (40% of patients in both groups), the overall response rates were 50% and 48% in EBVpos and EBVneg patients respectively (p=NS). Response rates to rituximab were also similar. There was no difference in the mortality risk between groups (HR=1.04; $p=0.84$). The 5-year survival rates were 47% and 51% in EBVpos and EBVneg PTLD respectively (p=NS). **Conclusions:** In a large single-center series, EBVneg PTLD was associated with late occurrence after transplant, monomorphic histology and similar outcome in comparison with EBVpos PTLD. Importantly, the response of EBVneg PTLD to RI and rituximab was no different than EBVpos PTLD. These results have implications for the management of solid organ transplant recipients with PTLD.

8579 General Poster Session (Board #52E), Sun, 8:00 AM-11:45 AM

Effect of phosphotidylinositol 3-kinase-delta inhibitor idelalisib (GS-1101) on signaling in primary non-Hodgkin lymphoma cells: Correlative studies from NCT01306643.

Adriana Arita, Katherine Hanlon, Halina Chkourko, Brian Joseph Lannutti, David Michael Johnson, Janice Lynn Gabrilove, Eileen Scigliano, Samir S. Parekh, Joshua Brody; Mount Sinai Medical Center, New York, NY; Gilead Sciences, Inc., Seattle, WA; Icahn School of Medicine at Mount Sinai, New York, NY; Mount Sinai School of Medicine, New York, NY

Background: Studies of GS-1101, an oral phosphatidylinositol 3-kinase (PI3K)d-specific inhibitor, in heavily pre-treated patients with indolent-non-Hodgkin's lymphomas (iNHL) have shown marked clinical activity [Kahl BS, et al., *Blood* 2010]. We have shown that GS-1101 blocks both constitutive and inducible signaling events proximally downstream of PI3K [Lannutti BJ, et al., *Blood* 2011]. We hypothesized that flow-cytometric interrogation of PI3Kd-inhibition in iNHL samples might demonstrate signaling differences between patients that can be correlated with clinical outcomes. **Methods:** Single-cell suspensions of biopsy specimens from patients were incubated with or without GS-1101, B-cell receptor stimulated and stained with lineage markers and phospho-specific antibodies targeting signaling nodes proximally (e.g. pAkt S473) or distally (e.g. pS6 S235/6) downstream, or ″parallel″ to (e.g. pErk1/2) described PI3K pathways. **Results:** Healthy and iNHL B cells demonstrated complete or near-complete inhibition of PI3K *proximal* downstream signaling by GS-1101. PI3K *distal* downstream signaling was completely inhibited by GS-1101 in healthy B cells. The degree inhibition of distal downstream signaling was variable between iNHL patients. iNHL showed marked variability in the degree of PI3K distal downstream signaling amongst tumor cells within the same sample, suggesting an admixture of ″PI3K-dependent" and ″PI3K-independent″ tumor cells. We also observe variable PI3K-independence amongst other NHL histologies such as mantle cell lymphoma. Additionally, combining inhibition of PI3K with that of other signaling nodes shows additive distal downstream effects. **Conclusions:** We demonstrate that GS-1101 blocked both constitutive and invoked signaling proximally downstream of PI3K in primary iNHL cells. By correlating clinical outcomes in the ongoing study with signaling readouts between patients we may develop predictive rules for response. Ongoing studies will focus on studying the change in intratumoral cell subsets which develop in vivo as patients progress on PI3Kd inhibitor therapy.

8580 General Poster Session (Board #53A), Sun, 8:00 AM-11:45 AM

Use of stem cell transplantation (SCT) as initial therapy in multiple myeloma (MM) and impact of sociodemographic factors in the era of novel agents: Analysis of 137,409 patients using the National Cancer Data Base (NCDB).

Mohammed Al-Hamadani, Ronald S. Go; Gundersen Lutheran Medical Foundation, La Crosse, WI; Gundersen Lutheran Health System, La Crosse, WI

Background: Novel agents for MM became available in the past decade. Our study aim was to determine whether the rate of SCT utilization as part of initial therapy in patients with MM had changed in the US after the introduction of novel agents. We also determined the impact of various sociodemographic factors. **Methods:** De-identified patient level data were obtained from the NCDB bParticipant User File. NCDB is a nationwide oncology outcomes database, which comprises approximately 70% of all newly diagnosed cancer cases in the United States. **Results:** A total of 137,409 MM patients were included in the study. The median age was 68 years (range, 18-90+). The population was predominantly male (54%), white (79%), non-Hispanic (87%), and living in a metro (78%), low- or middle-income (annual income $<$ \$46,000; 63%), and low- or moderate-education ($>$ 14% without high school diploma; 66%) areas. Most patients had minimal or no co-morbidities (Charlson-Deyo score of 0-1; 93%) and treated in the community setting (62%). The rate of SCT use as initial therapy consistently increased annually from 5% in 1998 to 12% in 2010. This was true for all socio-demographic subgroups except for those who were age $>$ 75 years, treated in the Northeast, and the medically uninsured. Multivariate logistic regression showed that the following characteristics were significant main predictors of lower likelihood of SCT use (odds ratio): age $>$ 65 years (0.18), non-white race (0.57), Hispanic ethnicity (0.68), lack of high education (0.89), annual income $<$ \$30,000 (0.76), diagnosed before the era of novel agents (1998-2003) (0.70), covered by a non-managed care insurance (0.57), treatment in a non-academic facility (0.28), residence at a non-metro area (0.88), and treatment facility located outside of the Midwest or West (0.62). In contrast, sex was not significant. **Conclusions:** Even after the introduction of novel agents, the rate of SCT as initial therapy in MM continues to increase annually in the US. Significant disparity exists in the rate of SCT use by demographic, social, and geographic factors as well as the type of treatment facility.

8581 General Poster Session (Board #53B), Sun, 8:00 AM-11:45 AM

Measures of immune recovery following autologous stem cell transplantation for multiple myeloma and outcome.

Livia Hegerova, Morie Gertz, Martha Lacy, Angela Dispenzieri, Francis Buadi, Suzanne R. Hayman, David Dingli, Luis F. Porrata, Shaji Kumar; Mayo Clinic, Rochester, MN; Division of Hematology, Mayo Clinic, Rochester, MN

Background: Autologous stem cell transplant (ASCT) improves survival in patients with multiple myeloma (MM). Recent studies have elucidated the relationship in ASCT between absolute lymphocyte count (ALC) recovery and improved survival, highlighting the importance of immune recovery. We conducted a retrospective analysis of patients with multiple myeloma to observe the impact of different measures of immune recovery at day 100 post-ASCT on outcome. **Methods:** Retrospective analysis of data from the existing clinical databases identified 1184 patients with multiple myeloma that underwent ASCT at Mayo Clinic between 1987-2011. Markers of immune recovery analyzed on day 100 status-post ASCT included ALC, monocyte count, and immunoglobulin levels. Kaplan Meier analysis was performed to determine progression free survival (PFS) and overall survival (OS). **Results:** Among the 1184 patients, median age at diagnosis of multiple myeloma was 57 (range, 23-75 yr), and median age at time of transplantation was 59 (range, 24-75 yr); 59% were male. The median OS and PFS post-transplant were 80 months and 34 months respectively. 62% of patients were alive 5-years post-transplant. The median OS was not improved with normal vs. abnormal IgG levels at day 100 ($p=.298$). In contrast, monocyte recovery was a significant predictor of OS. Patients with normal monocyte counts of greater than 0.3×10^9 cells/L at day 100 showed superior survival (65 vs. 37 months, $p= .001$). Similarly, patients with normal monocyte recovery at day 15 post-transplant showed a significant survival benefit (68 vs. 50 months, $p=.007$). Early ALC recovery, which has been shown to be a positive prognostic indicator at day 15 post-transplant, was not prognostic at day 100 ($p= .960$). **Conclusions:** The present study further elucidates prognostic indicators after ASCT for MM highlighting the importance of various markers of immune recovery. Immunoglobulin recovery was not associated with superior survival, while monocyte recovery at day 15 and day 100 post-transplant translated to an improved survival and requires further study. It may be hypothesized that early immune system reconstitution may have a positive effect against disease post-transplant.

8582 General Poster Session (Board #53C), Sun, 8:00 AM-11:45 AM

Effect of a novel agent, SL-401, targeting interleukin-3 (IL-3)-receptor on plasmacytoid dendritic cell (pDC)-induced myeloma cell growth and drug resistance.

Dharminder Chauhan, Arghya Ray, Christopher Brooks, Eric K. Rowinsky, Kenneth Carl Anderson; Dana-Farber Cancer Institute, Boston, MA; Stemline Therapeutics, Inc., New York, NY

Background: Multiple myeloma (MM) remains incurable despite novel therapies, highlighting the need for further identification of factors mediating disease progression and drug resistance. The bone marrow (BM) microenvironment confers growth, survival, and drug resistance in MM cells. Our recent study utilized in vitro and in vivo MM xenograft models to show that plasmacytoid dendritic cells (pDCs) were significantly increased in MM BM and promote MM growth (Chauhan et al., *Cancer Cell 2009, 16:309*). Importantly, we found increased IL-3 levels upon pDC-MM interaction, which in turn, trigger MM cell growth and pDCs survival. IL-3R is highly expressed on pDCs. We utilized SL-401, a novel biologic conjugate that targets IL-3R, to examine whether abrogation of IL-3–IL-3R signaling axis affects pDC-MM interaction and its tumor promoting sequelae. **Methods**: MM cell lines, patient MM cells, and pDCs from healthy donors or MM patients were utilized to study the anti-MM activity of SL-401. MM cells and pDCs were cultured alone or together in the presence or absence of SL-401, followed by analysis of cell growth or viability. **Results**: SL-401 significantly decreased the viability of pDCs at low concentrations (IC_{50}: 0.83 ng/ml; $P < 0.005$, $n = 3$). SL-401 also decreased the viability of MM cells at clinically achievable doses. Co-culture of pDCs with MM cells induced growth of MM cell lines; and importantly, low doses (0.8 ng/ml) of SL-401 blocked MM cell growth-promoting activity of pDCs. MM patient-derived pDCs induced growth of MM cell lines and primary MM cells as well; conversely, SL-401 inhibited pDC-triggered MM cell growth ($P < 0.005$, $n= 5$). Tumor cells from 3 of the 5 patients were from patients whose disease was progressing while on bortezomib, dexamethasone, and lenalidomide therapies. In agreement with these results, SL-401 blocked pDC-induced growth of dexamethasone-resistant MM cell lines. **Conclusions**: Our study therefore provides the basis for directly targeting pDCs or blocking the pDC-MM interaction, as well as targeting MM, in novel therapeutic strategies with SL-401 to enhance MM cytotoxicity, overcome drug-resistance, and improve patient outcome.

8583 General Poster Session (Board #53D), Sun, 8:00 AM-11:45 AM

Quality of life (QOL) improvements for pomalidomide plus low-dose dexamethasone (POM + LoDEX) in relapsed and refractory multiple myeloma (RRMM) patients (pts) enrolled in MM-003.

Kevin W. Song, Meletios A. Dimopoulos, Katja C. Weisel, Philippe Moreau, Martha Lacy, Michel Delforge, Lionel Karlin, Hartmut Goldschmidt, Anne Banos, Albert Oriol Rocafiguera, Stacie Hudgens, Zhinuan Yu, Lars Sternas, Christian Jacques, Mohamed H. Zaki, Jesùs F. San-Miguel; Vancouver General Hospital, Vancouver, BC, Canada; Alexandra Hospital, Athens, Greece; Hematology & Oncology, Department of Medicine, University Hospital Tuebingen, Tuebingen, Germany; Hematology, University Hospital Hotel-Dieu, Nantes, France; Mayo Clinic, Rochester, MN; Department of Hematology, University Hospital Leuven, Leuven, Belgium; Centre Hospitalier Lyon Sud/Hospices Civils de Lyon, Pierre-Bénite, France; Universitätsklinikum Heidelberg, Heidelberg, Germany; Hematology, Centre Hospital de la Côte Basque, Bayonne, France; Institut Catala d'Oncologia, HGTiP, Barcelona, Spain; Adelphi Values, Boston, MA; Celgene Corporation, Summit, NJ; Hematology, Hospital Universitario de Salamanca, Salamanca, Spain

Background: Poor prognosis and therapy exhaustion have been associated with reduced QOL in RRMM. In MM-003, a randomized, multicenter, open-label phase 3 trial, POM + LoDEX (n = 302) significantly improved progression-free and overall survival vs. high-dose dexamethasone (HiDEX; n = 153) in pts who failed lenalidomide (LEN) and bortezomib (BORT) and progressed on their last therapy. This analysis evaluated QOL changes in these pts. **Methods:** To assess pt-reported outcomes, cross-sectional and longitudinal analyses were performed. Minimal important differences for 5 clinically relevant EORTC QLQ-C30 domains (Global Health Status, Physical Functioning, Fatigue, Emotional Functioning, and Pain) were calculated as meaningful change thresholds (1 standard error of measurement) from baseline through cycle (C) 5. Time to QOL worsening was compared between arms using the Kaplan-Meier method. **Results:** Favorable trends were observed for POM + LoDEX vs. HiDEX in each of the 5 relevant domains. The cross-sectional analysis indicated statistically or marginally significant ($P < .10$) differences favoring POM + LoDEX in Global Health Status (C2, 4), Physical Function (C2, 3, 4), Emotional Function (C2, 3, 4), and Fatigue (C2) scores. Longitudinal comparisons between arms confirmed the significance of score changes for Global Health Status (C2; $P = .01$), Physical Functioning (C3 and 4; $P = .018$ and .028, respectively), Emotional Functioning (C3; $P = .018$), and Fatigue (C5; $P = .008$) for POM + LoDEX vs. HiDEX. HiDEX pts exhibited clinically meaningful worsening in Global Health Status and Physical Functioning scores vs. POM + LoDEX by C2 ($P = .04$) and C3 ($P = .02$), respectively. POM + LoDEX extended median time to meaningful worsening vs. HiDEX for Global Health Status (114 vs. 85 days, $P = .05$), Physical Functioning (174 vs. 106 days; $P = .09$), Fatigue (113 vs. 60 days; $P = .02$), Emotional Functioning (190 vs. 124 days; $P = .04$), and Pain (147 vs. 113 days; $P = .2$). **Conclusions:** In heavily pretreated pts who failed LEN and BORT, POM + LoDEX resulted in better clinical outcomes as well as improvement in clinically relevant QOL measurements over the course of treatment. Clinical trial information: NCT01311687.

8584 General Poster Session (Board #53E), Sun, 8:00 AM-11:45 AM

MM-005: A phase I trial of pomalidomide, bortezomib, and low-dose dexamethasone (PVD) in relapsed and/or refractory multiple myeloma (RRMM).

Paul Gerard Guy Richardson, Craig C. Hofmeister, David Samuel DiCapua Siegel, Sagar Lonial, Jacob Laubach, Yvonne Adeduni Efebera, David H. Vesole, Ajay K. Nooka, Jacalyn Rosenblatt, Noopur S. Raje, Mohamed H. Zaki, Ye Hua, Sheetal Shah, Jianming Wang, Kenneth Carl Anderson; Dana-Farber Cancer Institute, Boston, MA; Department of Internal Medicine, Division of Hematology, The Ohio State University, Columbus, OH; John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; Emory University School of Medicine, Atlanta, GA; Jerome Lipper Multiple Myeloma Center, Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA; Division of BMT, Emory University, Winship Cancer Institute - Hematology and Medical Oncology, Atlanta, GA; Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA; Massachusetts General Hospital, Boston, MA; Celgene Corporation, Summit, NJ

Background: Combinations of lenalidomide (LEN), bortezomib (BORT), and dexamethasone (DEX) have demonstrated preclinical and clinical activity in patients (pts) with multiple myeloma. Pomalidomide with low-dose DEX (LoDEX) has demonstrated efficacy in RRMM pts treated with prior LEN and BORT. MM-005 was designed to identify the optimal PVD dose for a phase 3 trial comparing PVD vs BORT + LoDEX (VD) in RRMM (MM-007). **Methods:** Eligible pts had RRMM with 1-4 prior therapies including $\geq$ 2 consecutive cycles of LEN and a proteasome inhibitor. Pts must have been refractory to LEN (progressive disease [PD] during or within 60 days of LEN treatment), but not refractory to BORT (at 1.3 mg/m^2 twice-weekly). The maximum tolerated dose (MTD) was determined using a 3 + 3 design in 5 cohorts. Each cohort received 21-day cycles of POM 1-4mg/day on D1-14; BORT 1-1.3mg/m^{2}on D1, 4, 8, 11; and LoDEX 20mg/day on D1-2, 4-5, 8-9, 11-12. An expansion cohort was enrolled at the MTD. Treatment was continued until PD or unacceptable toxicity. Dose-limiting toxicities (DLTs) were assessed during cycle 1. The primary endpoint was MTD; secondary endpoints were safety, overall response rate (ORR; $\geq$ partial response), duration of response, and time to response (TTR). **Results:** As of Dec 31, 2012, 21 pts were enrolled (3 pts per escalating dose cohort; 6 in the expansion cohort). Median age was 57 years (36-75). All were LEN-refractory and had prior BORT. No DLTs were observed at any dose level. The most common grade 3/4 adverse events (AEs) were neutropenia (32%) and thrombocytopenia (21%). With thromboprophylaxis, no deep vein thrombosis was observed. 17 pts remain on study and no pts have discontinued treatment due to AE. Thus far, the ORR was 72% (n = 18 evaluable) and responses were rapid (median TTR, 2 cycles). **Conclusions:** PVD was well-tolerated in RRMM with no DLTs and no discontinuations due to AE to date. PVD has promising activity with a current ORR of 72%. The maximum planned dose of POM 4mg/day on D1-14; BORT 1.3mg/m^2 on D1, 4, 8, and 11; and DEX 20mg on D1-2, 4-5, 8-9, 11-12 of a 21-day cycle has now been incorporated into the MM-007 phase III trial comparing PVD with VD in RRMM pts (N = 782 planned). Clinical trial information: NCT01497093.

8585^ General Poster Session (Board #53F), Sun, 8:00 AM-11:45 AM

MM-008 trial: Pharmacokinetics (PK) and tolerability of pomalidomide plus low-dose dexamethasone (POM plus LoDEX) in relapsed/refractory multiple myeloma (RRMM) patients with renal impairment (RI).

Jeffrey Matous, David Samuel DiCapua Siegel, Hien Kim Duong, Claudia Kasserra, Lars Sternas, Christian Jacques, Kenneth Klesczewski, Mohamed H. Zaki, Jatin J. Shah; Colorado Blood Cancer Institute, Denver, CO; John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; Department of Hematologic Oncology and Blood Disorders, Cleveland Clinic Taussig Cancer Institute, Cleveland, OH; Celgene Corpoation, Summit, NJ; Celgene Corporation, Summit, NJ; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: POM + LoDEX has shown significant clinical activity in RRMM pts including those refractory to lenalidomide and bortezomib. Renal impairment is a common comorbidity for MM pts, occurring in > 40%. POM is extensively metabolized with less than 5% renally eliminated as parent drug. Thus, renal function may not substantively affect parent drug exposure. Previous POM trials excluded pts with severe renal impairment. MM-008 is a phase 1, multicenter, open-label study designed to assess the PK and safety of POM + LoDEX in RRMM pts and normal or impaired renal function. **Methods:** RRMM pts (≥ 1 prior therapy [Tx]) with creatinine clearance (CrCl) ≥ 60 ml/min (cohort A) or severe renal impairment (CrCl < 30 ml/min [cohort B]) not requiring dialysis were included. Cohort A received POM 4 mg and cohort B received POM 2 mg or 4 mg D1-21/28-day cycle following a standard 3 + 3 dose-escalation design. Both cohorts received DEX 40 mg (20 mg for pts aged > 75 y) D1, 8, 15, and 22. Cohort C will assess pts with severe renal impairment (CrCl < 30 ml/min) requiring dialysis (up to 14 pts planned). Pts were not permitted to enroll in more than 1 cohort. G-CSF was not permitted in cycle 1. Tx continued until progressive disease or unacceptable toxicity. **Results:** As of Feb 5, 2013, 11 pts have been treated (8 pts in cohort A; 3 pts in cohort B at 2 mg). Age ranged from 46-71 y (cohort A) and 57-64 (cohort B). 5 pts were aged > 65 y in cohort A (aged 66, 69 [n = 3], and 71 y); none in cohort B. 7 pts in cohort A have received > 1 cycle of Tx; 5 pts have received ≥ 3 cycles. One pt in cohort B has received > 3 cycles. All 3 pts in cohort B have completed 1 full cycle of Tx with no dose-limiting toxicities reported. Dose escalation is planned. The most common grade 3/4 adverse events (AEs) in cohort A were neutropenia (n = 3) and pneumonia (n = 2). No grade 3/4 AEs have been observed for pts in cohort B to date. POM dose reduction due to AE occurred in 2 pts (both in cohort A), all pts remain on study. PK and updated AE data will be presented at the meeting. **Conclusions:** MM-008 is an ongoing trial evaluating PK and safety in pts with renal impairment. Early tolerability data are encouraging. Clinical trial information: NCT01575925.

8586 General Poster Session (Board #53G), Sun, 8:00 AM-11:45 AM

Changes in patient-reported outcomes in patients diagnosed with and treated for multiple myeloma in the Connect MM registry.

Chris L. Pashos, Jatin J. Shah, Howard R. Terebelo, Brian G. Durie, Rafat Abonour, Cristina Gasparetto, Jayesh Mehta, Mohit Narang, Sachdev Thomas, Kathleen Toomey, Arlene S. Swern, Kristen A. Sullivan, Thomas K. Street, Zeba M. Khan, Ali Nourbakhsh, James Hardin, Tanya Marya Wildes, Robert M. Rifkin; United BioSource Corporation, Lexington, MA; The University of Texas MD Anderson Cancer Center, Houston, TX; Providence Cancer Institute, Southfield, MI; International Myeloma Foundation and Cedars-Sinai Comprehensive Cancer Center, Los Angeles, CA; Indiana University Simon Cancer Center, Indianapolis, IN; Duke University Medical Center, Durham, NC; Northwestern University, Chicago, IL; Maryland Oncology Hematology, Columbia, MD; Illinois Cancer Center, Peoria, IL; Steeplechase Cancer Center, Somerville, NJ; Celgene Corporation, Summit, NJ; University of South Carolina, Columbia, SC; Washington University School of Medicine in St. Louis, St. Louis, MO; US Oncology, Denver, CO

Background: Little is known about the impact of treatment on patient-reported outcomes (PROs) and health-related quality of life (HRQoL) in multiple myeloma (MM) patients (pts). The change in PROs of MM pts between baseline and 1 year was assessed relative to their baseline International Staging System (ISS) stage and Eastern Cooperative Oncology Group (ECOG) performance status (PS) score. **Methods:** Connect MM is a prospective US registry of MM pts initiated in 2009. Clinicians reported pt demographics, ECOG PS score, and ISS stage. PROs were collected at baseline and at 1 year utilizing the Functional Assessment of Cancer Therapy (FACT)-MM, EQ-5D, and Brief Pain Inventory (BPI). Changes in FACT-MM, EQ-5D, and BPI scores were analyzed by ISS stage and ECOG PS score in 636 pts meeting CRAB criteria from 189 centers. **Results:** Most pts were male (58%) and white (84%). Mean age was 66 years ($\pm$ 11). Pts were treated in community (81%), academic (17%), or veterans/military (2%) settings. ISS stages of pts were: I (29%), II (35%), and III (35%). ECOG PS scores were 0 (37%), 1 (49%), 2 (11%), and 3 (3%). Improvements in overall HRQoL as shown by the FACT-MM and FACT-General (G) total scores, were observed across all ISS stages ($P = 0.03$ to < 0.0001) with no significant differences between stages. Improvements in FACT-MM and FACT-G total scores were observed with ECOG PS scores 1–3 ($P = 0.03$ to 0.005). Pts with poorer ECOG PS scores tended to have greater improvement in EQ-5D domains of mobility, self-care, and usual activities. HRQoL/functional ability improved in 4 of 5 FACT domains (except social/family; all others $P < 0.0001$), and in 4 of 5 EQ-5D domains (except pain/discomfort; all others, $P = 0.01$ to < 0.0001). BPI showed that overall average pain improved ($P < 0.0005$) over 1 year, but statistically significant differences by ISS stage or ECOG PS score were not observed. **Conclusions:** Connect MM data showed that overall HRQoL of MM pts improved between baseline and 1 year, with a consistent benefit observed across pts with different ISS stages and ECOG PS scores. Additional analysis should examine which disease- and treatment-related factors are associated with these HRQoL improvements.

8587 General Poster Session (Board #53H), Sun, 8:00 AM-11:45 AM

Continued monoclonal protein response beyond day 100 after auto-transplantation for multiple myeloma.

Wilson I. Gonsalves, Morie Gertz, Yi Lin, Martha Lacy, Angela Dispenzieri, Suzanne R. Hayman, Francis Buadi, David Dingli, Prashant Kapoor, Arleigh Robertson McCurdy, Preet Paul Singh, Vinay Gupta, Shaji Kumar; Mayo Clinic, Rochester, MN; Division of Hematology, Mayo Clinic, Rochester, MN; Division of Hematology. Mayo Clinic, Rochester, MN

Background: Patients (pts) undergoing an auto-transplant (ASCT) for multiple myeloma (MM) have disease assessment approximately 100 days later. This result may direct decisions of further therapy versus observation. However, some pts continue to experience a decline in their serum or urine monoclonal (M) - protein after day 100 without more therapy. Little is known about the prevalence and significance of this phenomenon. **Methods:** We identified 903 MM pts who underwent ASCT within 12 months (mos) of diagnosis (Dx) at our institution. Their day 100 post-ASCT M-protein from serum and urine electrophoresis with immunofixation as well as serum free light chains were compared to subsequent values during follow-up. The IMWG criteria were used to evaluate response. **Results:** Of the pts included, 510 (56%) were male and median age at ASCT was 59 (range 28-76). Median follow up from Dx and ASCT was 82 mos (95% CI; 75 - 86) and 74 mos (95% CI; 70 - 79) respectively. There were 453 (50%) pts seen in follow-up who had not achieved a CR at Day 100 nor initiated on maintenance therapy. Of these pts, 167 (37%) had a further decrease in their M-protein after day 100 at a median of 9.4 mos (95% CI; 8 – 10) post-ASCT. Given the time taken for maximal response, we assessed patients' clinical response at one year post-ASCT. Compared to patients who did not have further clinical response between day 100 and 1 year, pts experiencing further response had a longer time to next therapy (TTNT) (43 mos vs. 17 mos, $P < 0.001$) as well as overall survival (OS) (96 mos vs. 62 mos, $P < 0.001$). Positive predictors for continued response included having an IgG isotype, evolution from a pre-existing MGUS, smoldering myeloma or solitary plasmacytoma and a Day 100 bone marrow plasma cell $< 3\%$. In a multivariate analysis, elevated creatinine at Dx and lack of continued response predicted for shorter TTNT and OS post-ASCT. Older age and high-risk MM by FISH also predicted a shorter OS. **Conclusions:** In MM pts undergoing ASCT, continued M - protein response was seen in a third of the pts lacking a CR at day 100. This phenomenon appears prognostic and must be considered when interpreting studies evaluating post-ASCT response and the need for further therapy.

8588 General Poster Session (Board #54A), Sun, 8:00 AM-11:45 AM

Long-term safety and efficacy of pomalidomide (POM) with or without low-dose dexamethasone (LoDEX) in relapsed and refractory multiple myeloma (RRMM) patients enrolled in the MM-002 phase II trial.

David Samuel DiCapua Siegel, Paul Gerard Guy Richardson, Ravi Vij, Craig C. Hofmeister, Rachid C. Baz, Sundar Jagannath, Christine Chen, Sagar Lonial, Andrzej J. Jakubowiak, Nizar J. Bahlis, Kevin W. Song, Andrew Belch, Noopur S. Raje, Chaim Shustik, Suzanne Lentzsch, Min Chen, Mohamed H. Zaki, Kenneth Carl Anderson; John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; Dana-Farber Cancer Institute, Boston, MA; Washington University in St. Louis, St Louis, MO; Ohio State University Medical Center, Columbus, OH; H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; Mount Sinai Medical Center, New York, NY; Princess Margaret Hospital, Toronto, ON, Canada; Emory University School of Medicine, Atlanta, GA; University of Chicago Medical Center, Chicago, IL; University of Calgary, Calgary, AB, Canada; Vancouver General Hospital, Vancouver, BC, Canada; University of Alberta, Edmonton, AB, Canada; Massachusetts General Hospital, Boston, MA; Royal Victoria Hospital; McGill University Health Centre, Montreal, QC, Canada; College of Physicians and Surgeons of Columbia University, New York, NY; Celgene Corporation, Summit, NJ

Background: MM-002 is a randomized, open-label, multicenter phase II trial evaluating the safety and efficacy of POM with or without LoDEX in advanced RRMM pts. **Methods:** Pts who had received ≥ 2 prior therapies, including lenalidomide (LEN) and bortezomib (BORT), and were refractory to their last treatment were randomized to POM+LoDEX (POM 4 mg/day, days 1–21 of a 28-day cycle; LoDEX 40 mg/week) or POM alone. End points included progression-free survival (PFS), response rate (according to EBMT criteria and investigator assessment), response duration, overall survival (OS), and safety. The efficacy outcomes are based on the intent-to-treat population (POM+LoDEX, n = 113; POM, n = 108). **Results:** The median number of prior therapies in each group was 5 (range 1–13). In the POM+LoDEX arm, 30 (27%) pts had high-risk cytogenetics, including del(17p13) and/or t(4p16/14q32). The overall response rate (≥ partial response) was 34% and 15% with POM+LoDEX and POM, respectively, with a median duration of 8.3 (95% CI: 5.8–10.1) and 8.8 (95% CI: 5.5–11.4) mos, respectively. At least minimal response was observed in 45% and 31% of pts, respectively. Median PFS was 4.6 (95% CI: 3.6–5.5) and 2.6 (95% CI: 1.9–2.8) mos with POM+LoDEX and POM, respectively, with a median follow-up of 16.0 and 12.2 mos. Median OS was 16.5 (95% CI: 12.4–18.5) and 13.6 (95% CI: 9.6–18.1) mos, respectively. The most common treatment emergent Gr 3/4 adverse events (AEs) reported in the safety population (n = 219) were neutropenia (44%), anemia (23%), thrombocytopenia (21%), and pneumonia (18%); there were no reports of Gr 3/4 peripheral neuropathy. The incidence of deep-vein thrombosis was low (2%). AEs were managed through dose reductions or interruptions, and supportive care with G-CSF (52%), RBC transfusions (47%), and platelet transfusions (17%). Discontinuations due to AEs were 10%. **Conclusions:** POM with or without LoDEX is clinically effective and generally well tolerated in RRMM pts who have received multiple prior treatments, including LEN and BORT. AEs were predictable and manageable. Updated data will be presented at the meeting. Clinical trial information: NCT00833833.

8589 General Poster Session (Board #54B), Sun, 8:00 AM-11:45 AM

Evaluating results from the multiple myeloma subset of patients treated with denosumab or zoledronic acid (ZA) in a randomized phase III study.

Noopur S. Raje, Wolfgang Willenbacher, Vania Hungria, Andrew Spencer, Yulia Alexeeva, Thierry Facon, A. Keith Stewart, David Roodman, Evangelos Terpos, Amy Feng, Ada Braun, Arun Balakumaran; Center for Multiple Myeloma, Massachusetts General Hospital Cancer Center, Boston, MA; Medical University of Innsbruck, Innsbruck, Austria; Irmandade da Santa Casa de Misericordia de São Paulo, São Paulo, Brazil; The Alfred Hospital, Melbourne, Australia; City Hospital #31, Saint Petersburg, Russia; Hôpital Claude Huriez, Lille, France; Mayo Clinic, Scottsdale, AZ; Indiana University School of Medicine, Indianapolis, IN; University of Athens School of Medicine, Alexandra General Hospital, Athens, Greece; Amgen, Inc., Thousand Oaks, CA

Background: Denosumab (dmab) is a fully human monoclonal antibody against RANKL and is superior to ZA in preventing skeletal-related events (SREs) as shown in 3 identically designed phase 3 trials (N=5723). Overall survival (OS) was balanced between treatment groups in the overall study populations of these trials. In the trial of patients (pts) with solid tumors (excluding breast and prostate) and multiple myeloma (MM), OS was longer for dmab pts with lung cancer, shorter for pts with MM, and balanced for pts with other solid tumors. This analysis further characterizes the results from the MM subset of this trial. **Methods:** Pts with solid tumors or MM were randomized (1:1) to receive 120 mg of SC dmab or 4 mg of IV ZA Q4W. Daily calcium and vit D supplements were strongly recommended. The primary endpoint was the time to first on-study SRE; results from the primary endpoint and lung cancer subset were previously reported. **Results:** Of 1776 randomized pts, 10% had MM (93 ZA, 87 dmab). OS favored ZA (hazard ratio: 2.26; 10 subject difference in deaths). 1-year OS was 83% dmab, 97% ZA. Imbalances in baseline prognostic characteristics were observed. More pts in the dmab arm had low baseline renal function (CrCl $<$ 40 mL/min) (ZA 2 [2%], dmab 9 [10%]) and more ZA pts underwent stem cell transplant (ZA 23 [25%], dmab 15 [17%]). Additionally, more ZA pts had stage I tumors at diagnosis (ZA 13 [14%], dmab 9 [10%]) and better performance status (ECOG = 0; ZA 30 [32%], dmab 21 [24%]). Study discontinuations due to consent withdrawal or lost to follow-up were also higher in the ZA group (ZA 17 [18%], dmab 11 [13%]) and occurred earlier in the ZA arm (ZA 59%, dmab 45% within 9 months of randomization). **Conclusions:** In this SRE study of dmab vs ZA, pts were stratified by baseline characteristics known to affect SRE outcomes, but not by prognostic factors or concurrent anticancer therapy that may impact survival in MM. OS results in the MM cohort are difficult to interpret due to small sample size and imbalances in baseline disease characteristics, stem cell transplant therapy, and consent withdrawal or loss of follow-up that favored ZA. A phase 3 trial is currently underway, which controls for these factors in pts with MM. Clinical trial information: NCT00330759.

8590 General Poster Session (Board #54C), Sun, 8:00 AM-11:45 AM

Longitudinal whole body MRI (wbMRI) in monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma.

Maximilian Merz, Barbara Wagner-Gund, Kai Neben, Anthony D. Ho, Hartmut Goldschmidt, Jens Hillengass; Department of Hematology, Oncology and Rheumatology, University of Heidelberg, Heidelberg, Germany; Department of Hematology, Oncology, and Rheumatology, Heidelberg University Hospital, Heidelberg, Germany; Department of Hematology, Oncology, and Rheumatology, University of Heidelberg, Heidelberg, Germany

Background: The detection of bone marrow focal lesions (FLs) by MRI at the initial work up has prognostic significance in multiple myeloma (MM), smoldering MM as well as MGUS. Currently, there are no data available on the predictive relevance of new FLs or FLs increasing in size in longitudinally performed wbMRIs for the follow-up of sMM and MGUS. **Methods:** We retrospectively analyzed 87 patients (sMM n=65; MGUS n=22) that received at least 2 (up to 5) wbMRIs for follow-up. The date of progression into MM requiring systemic therapy was defined as event for the analysis of progression free survival (PFS). Radiological progressive disease (rPD) was defined as the appearance of novel FLs or increase in size of preexisting FLs. Kaplan-Meier plots of PFS for patients with rPD and patients without rPD were analyzed using the log-rank test for significant differences. **Results:** Median follow-up was 61 months (9.8-101) with a median time between follow-up wbMRIs of 15.8 months (1-73). Progression from sMM/MGUS into MM was found in 28 patients (sMM 40%; MGUS 9%). Using wbMRI, rPD was found in 21 patients (sMM 32%; MGUS 0%). Of all patients, 76% (n=16) with rPD and 16% (n= 9) without rPD progressed into MM during the observation period. Analysis of Kaplan Meyer plots for PFS revealed a highly significant shorter PFS for patients with rPD (32 months) compared to patients with radiological stable disease in wbMRI (PFS not reached; $p<0.0001$). New appearance or progression of diffuse bone marrow infiltration was not associated with a shorter PFS (not reached; $p>0.05$). **Conclusions:** In our study, the appearance of novel FLs or progression of preexisting FLs was highly predictive for progression from sMM into MM requiring systemic treatment. We conclude that wbMRI is effective for the longitudinal follow-up of patients with sMM and MGUS and identifies a group of patients at risk for progression into MM.

8591 General Poster Session (Board #54D), Sun, 8:00 AM-11:45 AM

Promotion of human multiple myeloma cell growth in vitro and bone marrow invasion in vivo by Notch receptors and the CXCR4/SDF1 axis.

Maurizio Chiriva-Internati, Leonardo Mirandola, Elisa Lazzari, Michela Colombo, Marialuigia Lancellotti, Everardo Cobos, Yuefei Yu, Jose A. Figueroa, Charles Saadeh, Raymond Wade, Kristopher Zepeda, Jesse Mer, Venu Konala, Saba Radhi, Amardeep Aulakh, Marjorie Jenkins, Cynthia A. Jumper, Raed Alalawi, Raffaella Chiaramonte; Texas Tech University Health Sciences Center, Lubbock, TX; Texas Tech University Health Sciences Center and the Southwest Cancer Treatment and Research Center, Lubbock, TX; University of Milano, Milano, Italy

Background: Multiple myeloma (MM) originates from post-germinal center B cells, and is caused by malignant plasma cells accumulating in the bone marrow. Interactions of MM cells with the bone marrow stroma promote tumor growth, migration and drug resistance. The chemokine receptor CXCR4 and its ligand SDF1 are critical regulators of this process. MM cells frequently hyper-express CXCR4 and respond to SDF1,2 enhancing MM cell infiltration, proliferation and osteolysis. Notch receptors similarly promote MM cell growth, drug resistance and the associated osteolytic process. We hypothesized that the CXCR4/SDF1 axis mediates the effects of Notch signals in MM. **Methods:** We used real-time PCR, flow-cytometry, E.L.I.S.A. and chemotaxis assay to explore the effects of CXCR4 in cultured human MM cell lines after Notch inhibition or over-stimulation. Additionally, we validated our findings in a NOD/SCID murine model xenografted with human MM cells. **Results:** Our results show that Notch blocking reduced CXCR4 and SDF1 expression by MM cells. Further, Notch activation was required for MM cell chemotactic and proliferative response to SDF1 in vitro. We then investigated the outcome of anti-Notch treatment on human MM cells bone invasion in NOD/SCID mice. Interfering with Notch activity dramatically reduced xenografted MM cell ability to infiltrate the bone marrow, ultimately resulting in diminished tumor burden. Notably, such effect was associated with a decrease of CXCR4 expression. **Conclusions:** This was the first time that Notch receptors were reported to regulate the CXCR4/SDF1 axis and bone marrow invasion in human MM. These findings indicate that specific Notch-tailored therapies may effectively hamper CXCR4-mediated bone infiltration and associated lesions, and are expected to significantly improve treatment outcome and survival.

8592 General Poster Session (Board #54E), Sun, 8:00 AM-11:45 AM

Strategies to overcome barriers to accrual (BtA) to NCI-sponsored clinical trials: A project of the NCI-Myeloma Steering Committee Accrual Working Group (NCI-MYSC AWG).

Matthias Weiss, Morie A. Gertz, Richard F. Little, Vincent Rajkumar, Susanna J. Jacobus, Rafat Abonour, Kenneth Carl Anderson, Bart Barlogie, Natalie Scott Callander, Edward J. Gorak, Jeffrey Matous, Glenn Morris Mills, Robert C. Kane, Michael S. Katz, LeeAnn Jensen, James Omel, Robert Z. Orlowski, Paul Gerard Guy Richardson, Nikhil C. Munshi; Marshfield Clinic, Marshfield, WI; Mayo Clinic, Rochester, MN; National Cancer Institute, Rockville, MD; Dana-Farber Cancer Institute, Boston, MA; Indiana University Simon Cancer Center, Indianapolis, IN; Myeloma Institute for Research and Therapy, Little Rock, AR; University of Wisconsin, Madison, WI; Geisinger Medical Center, Danville, PA; Rocky Mountain Cancer Centers, Denver, CO; LSU Health Sciences Center, Shreveport, LA; Food and Drug Administration, Silver Spring, MD; International Myeloma Foundation, North Hollywood, CA; National Cancer Institue, Rockville, MD; Patient Advocate, Rockville, MD; The University of Texas MD Anderson Cancer Center, Houston, TX; VA Boston Healthcare System; Dana-Farber Cancer Institute, Boston, MA

Background: Accrual to NCI clinical trials(CT)is often slower than planned at times mandating premature closure resulting in loss of valuable resources and delay of scientific progress. **Methods:** The NCI-MYSC AWG identified 10 potential BtA. SWOG, ECOG and Alliance investigators were queried and agreed that these barriers impede accrual (results stratified for academic and community sites). The MYSC AWG developed in collaboration with NCI and FDA strategies to overcome these barriers. **Results:** Strategies listed for the 3 most often cited BtA: 1. Reimbursement for CT related expenses:increase awareness of improved reimbursement for phase II CT; tailor reimbursement according to CT complexity; request funds from industry and other sources (http://biqsfp.cancer.gov) for qualifying ancillary CT components. 2. Spectrum of available treatment options influences CT participation: educate patients and providers about the significance of a new CT using social media, presentations at national meetings and by adding educational material to CT protocol; encourage opinion leaders and advocacy groups not to promote a new therapy as "standard" in the absence of phase III data. 3. Requirement of CT specific therapy at NCI designated sites only: "MYSC AWG Drug Administration Table" describes NCI/FDA approved rules for CT specific drug administration; CT protocol will outline which standard treatment components of a CT can be administered at any site as long as protocol specific guidelines are followed and conduct is supervised by enrolling investigator. Examples of additional strategies to overcome identified BtA: determine feasibility, indication and insurance coverage of CT specific tests during protocol development; discourage narrow eligibility criteria; avoid competing CT; allow up to 1 cycle of commercially available therapy prior to enrollment; CIRB support for phase II CT. **Conclusions:** The MYSC Accrual Working Group developed in collaboration with NCI and FDA strategies to overcome barriers to myeloma clinical trial accrual. These strategies may be applicable to NCI-sponsored clinical trials evaluating interventions in other diseases.

8593 General Poster Session (Board #54F), Sun, 8:00 AM-11:45 AM

Early versus late treatment for smoldering (asymptomatic) multiple myeloma: A systematic review.

Mubarak Salem Alahamdi, Jason Tay; University of Ottawa, Ottawa, ON, Canada

Background: Expectant management remains the current standard of care for patients with smoldering multiple myeloma (SMM). Recent appreciation of ″high risk″ smoldering myeloma and the advent of novel therapeutic agents may allow one to better tailor the timing of therapeutic interventions. Herein, we performed a systematic review of the literature, summarizing the available randomized controlled trial (RCT) evidence for treatment of SMM. **Methods:** Our systematic search strategy includes MEDLINE, EMBASE, Cochrane Database, and relevant bibliographies where the following search concepts were used: RCT, SMM as defined as per the IMW Criteria, and treatment. Two reviewers independently extracted data on study design, population, sample size, treatment, clinical outcomes, and trial quality, were any discrepancies were discussed and resolved. **Results:** We identified 7 RCTs (2 articles and 5 abstracts) representing 869 patients. Six articles compared early versus deferred treatment for SMM; 2 studies compared early Melphalan plus Prednisone (MP) versus deferred MP. 3 studies compared bisphosphonates versus abstention while one study compared lenalidomide with dexamethasone to therapeutic abstention. Further, one study compared thalidomide with zoledronate to zoledronate alone. The median age is 66. Four studies received a Jadad score of 3 while three studies received a score of 2. Allocation concealment was described in four studies. Risk of disease progression was lower in patients receiving therapy compared to abstention OR 0.5(0.38-0.68). The events that demonstrate disease progression were not clearly defined. Further, the use of combination therapy compared to a single intervention decreased the risk of progression OR 0.23(0.11-0.51). No difference in OS was noted in patients receiving therapy compared to abstention OR 0.95(0.57-1.57). **Conclusions:** Early treatment of SMM compared with abstention decreases the risk of disease progression. However, OS was not improved by earlier intervention. High risk SMM may benefit from early intervention. The optimal intervention(s) remains to be defined, and further studies are warranted in this understudied population.

8594 General Poster Session (Board #54G), Sun, 8:00 AM-11:45 AM

Profile of multiple myeloma in the inner city: Disease presentation and clinical course.

Adam Goldrich, Andriane Melanthiou, Anuja Kriplani, Elizabeth Helzner, Arvind Babu, Daniel Fein, Juhee Sidhu, Jason Parker Gonsky, Olcay Batuman; SUNY Downstate Medical Center, Brooklyn, NY; Wyckoff Heights Medical Center, Brooklyn, NY; Kings County Hospital Center, Brooklyn, NY

Background: Multiple myeloma (MM) is the most common hematologic neoplasm in blacks in the US. Based on SEER data of all Americans, the disease is more common in men, has a median diagnosis age of 70 and median survival of 3-6 years. The subclinical syndrome MGUS precedes MM, and blacks have a 2-3-fold higher risk of developing MGUS and MM. Further, recent improvements in survival observed for white patients are not observed in blacks. To gain new insight into pathogenesis and to optimize patient care, we characterized our inner city, largely Caribbean-African population in Brooklyn, NY, in terms of disease presentation and course. **Methods:** MM patients were identified by tumor registries based on histopathology. Data including survival were collected from records of patients diagnosed between 2001-2011 (n=242). Data analysis was performed using SPSS Advanced Statistics. **Results:** Median age was 64 (range 35-91), male: female ratio was 0.70. The most common presenting pathology was the presence of multiple skeletal lesions with fractures (67% of patients). Spinal cord compression and spinal compression fractures occurred in 33% and 32% of patients, respectively. Renal disease was present in 26%, indicated by serum creatinine >2 mg/dL. Consistent with advanced stage and renal failure, median serum beta-2 microglobulin was 4.25 (range 0.96-82.8). Chromosome banding and FISH was available on 133 patients and showed no cytogenetic abnormalities in 53%; hyperdiploidy (30.4%). Common trisomies included chr 1, 5, 15 and 19. Other abnormalities were del 13 (13%) and chr 14 translocations (11%). Comorbidities include hypertension (65%), diabetes (35%) and obesity (BMI over 30 in 24%). While recent improvements in acquiring health insurance have improved access, less than 10% of patients received HDCT and ASCT. As of October 1, 2012, 36% of all patients are living. Survival analyses are underway. **Conclusions:** MM presents at an advanced stage and affects younger AA's in the Downstate community. Strategies for identifying and treating patients with progressive MGUS and at earlier disease stages may enhance survival.

8595 General Poster Session (Board #54H), Sun, 8:00 AM-11:45 AM

Retrospective analysis of cardiovascular (CV) events following compassionate use of carfilzomib (CFZ) in patients (Pts) with relapsed and refractory multiple myeloma (RRMM).

Shebli Atrash, Amanda Tullos, Susan Panozzo, Sarah Waheed, Frits Van Rhee, Alejandro Restrepo, Jameel Muzaffar, Aziz Bakhous, Monica Grazziutti, Zainab Shahid, Senu Apewokin, Al-Ola A. Abdallah, Bart Barlogie, Saad Zafar Usmani; Myeloma Institute for Research and Therapy, Little Rock, AR

Background: Herein, we report CV events observed in late-stage, heavily pretreated pts who received salvage CFZ under a compassionate use protocol. **Methods:** Pts received IV single-agent CFZ (20-45 mg/m^2) over 2-30 min on days 1, 2, 8, 9, 15, and 16 of a 28-day cycle (C) or CFZ with weekly dexamethasone (4-40 mg) during C1, along with other agents (eg, lenalidomide, thalidomide, cyclophosphamide, doxorubicin, cisplatin, vorinostat) during C2 and beyond. CV events were grouped according to preferred terms. Serious CV events were defined as those that required hospitalization. B-type natriuretic peptide (BNP) values were measured at baseline; peak values were recorded during C1. **Results:** 143 pts (median age, 61 years old; 70% were male) received treatment. Prior to enrollment, pts received a median of 7 prior lines of therapy (range, 2-15), including doxorubicin (range, 0-360 mg/m^2). Most pts (92%) had prior autologous stem cell transplants (ASCT), with 74% receiving ≥2 ASCT (range, 0-5). Pts received CFZ for a median of 2C (range, 1-36). Of pts with available BNP values at baseline and during C1 (n=69; 48.3%), the median peak BNP increase from baseline was 407 pg/ml ($P<0.001$). 27 pts (18.9%) experienced a serious CV event, 21 (77.7%) of which had preexisting CV risk factors. Of these 27 pts, 11 pts (7.7%) developed CHF or worsening of existing CHF (confirmed by echocardiogram [ECHO] ≤1 month from diagnosis), and 13 (9.1%) required hospitalization for hypotension (n=6), arrhythmia (n=2), hypertension (n=2), pulmonary edema (n=1), pulmonary embolism (n=1), or pulmonary hypertension (n=1). Additionally, 3 pts (2.1%) experienced cardiopulmonary arrest. Of the 11 CHF pts, 10 had a baseline ECHO (recorded ≤6 months before study); left ventricular ejection fraction decreased from a median of 55% (pretreatment) to 33% (posttreatment). **Conclusions:** Late-line, heavily pretreated pts with RRMM occasionally experienced CV events following administration of CFZ with or without other antimyeloma agents. Given the number of confounding factors and the uncontrolled nature of these data, causality for these CV events could not be definitively determined.

8596 General Poster Session (Board #55A), Sun, 8:00 AM-11:45 AM

Early mortality (EM) for newly diagnosed multiple myeloma (NDMM) in the Connect MM U.S. registry.

Howard R. Terebelo, Jatin J. Shah, Brian G. Durie, Rafat Abonour, Cristina Gasparetto, Jayesh Mehta, Mohit Narang, Sachdev P. Thomas, Kathleen Toomey, Chris L. Pashos, Arlene S. Swern, Kristen A. Sullivan, Thomas K. Street, Shankar Srinivasan, Ali Nourbakhsh, James W. Hardin, Robert M. Rifkin; Providence Cancer Institute, Southfield, MI; The University of Texas MD Anderson Cancer Center, Houston, TX; International Myeloma Foundation and Cedars-Sinai Comprehensive Cancer Center, Los Angeles, CA; Indiana University Simon Cancer Center, Indianapolis, IN; Duke University Medical Center, Durham, NC; Northwestern University, Chicago, IL; Maryland Oncology Hematology, Columbia, MD; Illinois Cancer Care, Peoria, IL; Steeplechase Cancer Center, Somerville, NJ; United BioSource Corporation, Lexington, MA; Celgene Corporation, Summit, NJ; University of South Carolina, Columbia, SC; US Oncology Research, Denver, CO

Background: EM occurring $\leq$ 6 mos from diagnosis of MM has been reported in several NDMM studies. Incidence of EM in the pre-novel-therapy era was 10–14% of patients (pts); causes included infection/pneumonia, renal failure, refractory disease, and cardiac events. Identifying risk factors and improving response rates (RR) could lower EM. Established risk factors only have a sensitivity of 61% and specificity of 74%. Introduction of novel therapies is improving RRs and changing the profile of morbidity risk factors. Fewer indwelling catheters, better antibiotics, and bisphosphonates have reduced morbidity and mortality in MM. This analysis aims to better understand the causes of EM in this new era. **Methods:** Connect MM is a prospective observational registry of NDMM pts. Since 2009, 1494 pts in 228 US centers have been enrolled. Baseline characteristics were compared for pts who died $\leq$ 6 mos after enrollment vs pts who survived $>$ 6 mos. Multivariate logistic analyses identified significant associations between baseline characteristics and EM. **Results:** Most pts received novel therapies (91%). In the entire cohort, EM occurred in 103 pts (7%), of which 93 were treated (6.5%). EM associated characteristics by multivariate analyses ($P< 0.05$) were: age, ISS disease stage, PS, history of hypertension, hypercalcemia, lower clonal bone marrow cells (subject to further study), and platelet count. Venous thromboembolism and cytogenetics were not risk factors. Causes of the 103 early deaths were: MM progression (38%), cardiac failure (13%), infection (7%), pneumonia (6%), renal failure (4%), sudden death (3%), vascular event, bleeding, pulmonary embolism (1% each), other (15%) and unknown (13%). **Conclusions:** It is important to recognize EM as a distinct entity in MM. Better understanding of the biology and pt characteristics is required to further reduce its incidence. This is the first assessment of EM in a registry where almost all pts received novel agents. Of the 103 early deaths, 38% were due to MM, representing a 2.6% incidence in the total cohort (under further review). Although the 7% EM in Connect MM is encouraging, there is still room for improvement. Additional analyses on improvements and causes of death should be performed.

8597 General Poster Session (Board #55B), Sun, 8:00 AM-11:45 AM

Altered cytokine profiles in multiple myeloma (MM) and precursor disease: Predictors of progression and potential targets for treatment.

Nishant Tageja, Weixin Wang, Ryan Plyler, Meghan Corrigan-Cummins, Neha Korde, Elisabet E. Manasanch, Manisha Bhutani, Mary Kwok, Aaron W. Flanders, Diamond Zuchlinski, Marcia Mulquin, Rene Costello, Mark J. Roschewski, Ola Landgren, Katherine R. Calvo, Adriana Zingone; Metabolism Branch, NCI, NIH, Bethesda, MD; Hematology Service, DLM, CCR, NCI, NIH, Bethesda, MD; Hematology Service, DLM, CCR, NIH, Bethesda, MD; Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD

Background: Presently, there is no reliable biomarker for predicting clinical progression from smoldering (SMM) to symptomatic MM for individual patients. To improve our understanding on the pathogenesis from SMM to MM, we conducted a screening study of circulating cytokines using peripheral blood (PB) and bone marrow supernatant (BM) collected from treatment naïve SMM and MM patients as well as healthy donors as controls. **Methods:** PB samples from 14 SMM and 38 MM patients and 7 controls and BM obtained from 17 MM patients and 9 controls were assayed in duplicates using ultra-sensitive Human TH1/TH2 10-plex multi-spot plate and multi-array plate for interleukin-(IL)-6. Two-tailed Mann-Whitney test was used for statistical analysis. **Results:** PB of SMM patients (vs controls) had increased levels of several cytokines, including IL-8 ($p=0.008$) and IFN-gamma ($p=0.002$). In PB, MM patients (compared to SMM patient and controls) had increased levels of IL-6 ($p=0.006$ and 0.001, respectively), IL-8 ($p=0.0001$ and 0.008), IL-10 ($p=0.02$ and 0.02), TNF-alpha ($p=0.01$ and 0.009), and IFN-gamma ($p=0.01$ and 0.02). Analysis of BM revealed a similar profile with increased levels of IL-2, IL-6, IL-8, and TNF-alpha in MM patients compared with controls ($p=0.007$, $p=0.0003$, $p=0.0001$ and $p=0.0008$). **Conclusions:** We found significantly increased levels of key cytokines associated with progressive disease state (controls→SMM→MM). Patterns of cytokines were similar in BM and PB, suggesting that serum based cytokines may have a future role as biomarkers for disease progression, and could potentially be assessed as novel targets for treatment.

8598 General Poster Session (Board #55C), Sun, 8:00 AM-11:45 AM

A phase I/II study (NCT01541332) of pomalidomide (POM), dexamethasone (DEX), and pegylated liposomal doxorubicin (PLD) for patients with relapsed/refractory (R/R) multiple myeloma (MM).

James D. Hilger, James R. Berenson, Leonard M. Klein, Alberto Bessudo, Peter J. Rosen, Shahrooz Eshaghian, Hilda Chamras, Youram Nassir, Regina A. Swift, Robert A. Vescio; Oncotherapeutics, West Hollywood, CA; Institute for Myeloma and Bone Cancer Research, West Hollywood, CA; Illinois Cancer Specialists, Niles, IL; California Cancer Associates for Research and Excellence, Encinitas, CA; Providence Saint Joseph Medical Center, Burbank, CA; Cedars-Sinai Medical Center, Los Angeles, CA; Cancer Care Institute, Los Angeles, CA; James R. Berenson, MD, Inc., West Hollywood, CA

Background: POM is a newer IMiD immunomodulatory compound with high in vitro potency that has shown promise in combination with DEX as an effective treatment option for R/R MM patients (pts), even those refractory to bortezomib and lenalidomide (LEN). We conducted a phase I/II trial investigating the safety and efficacy of POM in combination with IV DEX and PLD using a modified dose and longer 28-day schedule in R/R MM pts. **Methods:** Phase I pts had progressive MM at the time of enrollment that was R/R to at least one anti-MM regimen. Phase II pts had to be refractory to LEN (singe-agent or in combination) demonstrated by progressive disease while receiving LEN or relapse within 8 weeks of its last dose. During phase I, POM was administered orally at 2, 3, or 4 mg daily in 3 successive cohorts of 3 pts each on days 1-21 of each 28-day cycle. DEX was administered IV at 40 mg over 30 min and PLD was administered at 5 mg/m^{2}as an IV infusion over 30-90 min on days 1, 4, 8, and 11 of each cycle. POM doses were escalated until maximum tolerated dose (MTD) was reached. Once MTD was reached, all subsequent pts were enrolled at that dose. **Results:** To date, 27 pts have been enrolled, with 18 evaluable for efficacy and 19 for safety. Pts received a median of 5 prior treatments (range, 1-18) with a median of 1 prior PLD regimens (range, 0-2). Pts have completed a median of 1 cycle (range: 0-8) with a median of 1.4 months of follow up (range: 0-7.1). No DLTs were seen during phase I, which established the MTD at 4 mg. Phase II has enrolled 16 pts at 4 mg so far. Clinical benefit was seen in 7 (39%) of evaluable pts (partial response = 22%; minor response = 17%) with another 44% showing stable disease. Common $\geq$ G3 adverse events included leukopenia (32% of pts), neutropenia (32%), lymphopenia (26%), and hyponatremia (16%). Neutropenia at $\geq$ G3 occurred in more than half of patients on the phase II trial (4 mg POM). **Conclusions:** The combination of pomalidomide with dexamethasone and PLD on a 28-day cycle shows efficacy for R/R MM pts. However, because of excessive $\geq$ G3 neutropenia, POM is being reduced to 3 mg for newly enrolled patients. Clinical trial information: NCT01541332.

8599 General Poster Session (Board #55D), Sun, 8:00 AM-11:45 AM

Results of a phase I/II study (NCT01365559) of carfilzomib (CFZ) replacing bortezomib (BTZ) in BTZ-containing regimens for BTZ-treated patients (pts) with relapsed and refractory multiple myeloma (MM).

James R. Berenson, James D. Hilger, Robert Dichmann, Dipti Patel-Donnelly, Ralph V. Boccia, Alberto Bessudo, Laura Stampleman, Donald Gravenor, Shahrooz Eshaghian, Hilda Chamras, Youram Nassir, Regina A. Swift, Robert A. Vescio; Institute for Myeloma and Bone Cancer Research, West Hollywood, CA; Oncotherapeutics, West Hollywood, CA; Central Coast Medical Oncology, Santa Maria, CA; Fairfax Northern Virginia Hematology Oncology, Fairfax, VA; Center for Cancer and Blood Disorders, Bethesda, MD; California Cancer Associates for Research and Excellence, Encinitas, CA; Pacific Cancer Care, Monterey, CA; Family Cancer Center Foundation, Memphis, TN; Cedars-Sinai Medical Center, Los Angeles, CA; Cancer Care Institute, Los Angeles, CA; James R. Berenson, MD, Inc., West Hollywood, CA

Background: Recent data has shown that single-agent CFZ can produce responses among MM pts refractory to previous treatment regimens including those containing BTZ. We conducted an intrapatient phase I/II trial investigating the safety and efficacy of CFZ as a replacement for BTZ in BTZEcontaining regimens to which pts have progressed. **Methods:** Eligible pts progressed while receiving their most recent BTZEcontaining regimen after at least 4 doses of BTZ at $\geq$1.0 mg/m^2 in $\leq$4 weeks per cycle. CFZ replaced BTZ in each regimen via intravenous administration over 30 min on days 1, 2, 8, 9, 15, and 16 of each cycle. Treatment continued using the same dose(s) and schedule(s) of each drug administered in the BTZEcontaining regimen. CFZ doses were escalated on each of the first 4 cycles from 20 to 27, 36, and 45 mg/m^2 or until a maximum tolerated dose (MTD) was reached for that regimen. **Results:** Of 37 enrolled pts, 33 were evaluable for efficacy and 37 for safety. Pts received a median of 4 prior treatments (range, 1-23) and 2 different BTZ-containing regimens (range, 1-13). Pts were treated with CFZ and a variety of different combinations of agents, including: bendamustine, clarithromycin, cyclophosphamide, dexamethasone, melphalan, methylprednisolone, pegylated liposomal doxorubicin, thalidomide, lenalidomide, and ascorbic acid. Pts have completed a median of 3 cycles with 12 pts going on to maintenance. One of 14 combinations, CFZ + ascorbic acid + cyclophosphamide, has reached a MTD at 45 mg/m^2. Clinical benefit was seen in 23 (70%) evaluable pts (complete response = 6%; very good partial response = 18%; partial response = 21%; minor response = 24%) with another 18% showing stable disease. The median time to progression is 8.8 mo. (95% CI: 6.4-11.1 mo.) with 21 pts progressing overall and 9 progressing on study treatment. The most common $\geq$ G3 adverse events were lymphopenia (35% of pts), thrombocytopenia (19%), neutropenia (11%), and anemia (8%). **Conclusions:** These results suggest that replacement of BTZ with CFZ in a BTZ-containing combination regimen to which a MM patient is failing often leads to responses and is well-tolerated. Clinical trial information: NCT01365559.

8600 General Poster Session (Board #55E), Sun, 8:00 AM-11:45 AM

Clinical outcomes after intensive VDT-PACE therapy for relapsed multiple myeloma.

Preet Paul Singh, Wilson I. Gonsalves, Vinay Gupta, Francis Buadi, Martha Lacy, Angela Dispenzieri, Morie Gertz, Suzanne R. Hayman, David Dingli, Stephen J. Russell, John Anthony Lust, Steven R. Zeldenrust, Prashant Kapoor, Arleigh Robertson McCurdy, S. Vincent Rajkumar, Shaji Kumar; Mayo Clinic, Rochester, MN

Background: The combination of bortezomib, dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide and etoposide (VDTPACE) was developed as an intense regimen for disease control prior to tandem transplantation for multiple myeloma (MM) in total therapy protocols. The regimen is very effective in this setting, and since has also been used in the relapsed setting. We examined the outcomes of a set of patients undergoing VDTPACE therapy for relapsed MM at our institution. **Methods:** We identified 71 patients who received VDTPACE for relapsed MM, at Mayo Clinic from 7/2006 to 7/2012. Plasma cell leukemia was excluded. All data was extracted from clinical records. **Results:** The median age of patients was 59 years (range, 39-80); 48 (67.6%) were male. The median time from diagnosis to initiation of VDTPACE was 38.2 months (range, 2-125). The median number of cycles given was 1 (range, 1-9). The overall response rate after one cycle was 57.1% (14.3% VGPR, 22.2% PR and 20.6% MR) in the 63 patients in whom the response was evaluable. The median overall survival (OS) post-VDTPACE was 8.2 months (95% CI, 5.7-10.9). Eighteen (25.4%) patients went on to autologous stem cell transplantation (SCT), and 7 (9.9%) received matched allogeneic SCT following VDTPACE, and the median OS post-VDTPACE was significantly longer for these groups compared to those who were not transplanted (15.3 and 20.5 months, respectively vs 5 months, p-value <0.001). Thirty eight of 66 (57.6%) patients were rehospitalized after initial admission for infusion therapy for a median duration of 6 days (range, 1-26). The median platelet and red cell transfusions were 4 (range, 0-21) and 5 (range, 0-22) units, respectively. Renal toxicity was seen in 13/62 (21%) patients and 27/65 (41.5%) patients developed neutropenic fever. The median duration to absolute neutrophil and platelet count recovery was 18 (range 12-42) and 27 (range, 12-42) days, respectively. Three (4.2%) patients died within 30 days and 11 (15.5%) within 8 weeks of initiating VDTPACE. **Conclusions:** VDTPACE is an effective therapy in relapsed MM but is associated with significant morbidity and short-term mortality. It appears to be more effective when followed by an autologous or allogeneic SCT.

8601 General Poster Session (Board #55F), Sun, 8:00 AM-11:45 AM

A comparison between next-generation sequencing and ASO-qPCR for minimal residual disease detection in multiple myeloma.

Hiroyuki Takamatsu, Ryoichi Murata, Jianbiao Zheng, Martin Moorhead, Yasushi Terasaki, Takashi Yoshida, Malek Faham, Shinji Nakao; Kanazawa University, Graduate School of Medical Science, Kanazawa, Japan; NTT West Kanazawa Hospital, Kanazawa, Japan; Sequenta, Inc., South San Francisco, CA; Toyama City Hospital, Toyama, Japan; Toyama Red Cross Blood Center, Toyama, Japan

Background: Although molecular CR in multiple myeloma (MM) can be assessed by allele-specific oligonucleotide (ASO)-PCR, this technique requires preparation of clonotype-specific primers for each individual which is laborious and time-consuming. The usage of the LymphoSIGHT method, a next-generation sequencing (NGS)-based platform, may overcome these challenges and increase sensitivity and specificity. We compared the LymphoSIGHT approach with ASO-qPCR for minimal residual disease (MRD) detection in autografts in the autologous peripheral blood stem cell transplantation (ASCT) setting. **Methods:** Seventeen Japanese patients with newly diagnosed MM who received various induction regimens prior to ASCT were retrospectively analyzed. All patients had achieved a PR or CR after ASCT. Bone marrow (BM) slides from 13 MM patients and fresh BM cells from 4 MM patients at diagnosis as well as autografts were obtained for DNA extraction. Using universal primer sets, we amplified *IGH* variable (V), diversity (D), and joining (J) gene segments, *IGH-DJ*, and *IGK* from genomic DNA. Amplified products were subjected to deep sequencing using NGS. Reads were analyzed using standardized algorithms for clonotype determination. Myeloma-specific clonotypes were identified for each patient based on their high frequency in BM samples. The presence of the myeloma clonotype was then assessed in follow-up samples. **Results:** MRD in autografts was detected in 6 of 17 (35%) by ASO-qPCR and 13 of 17 (76%) by NGS. When MRD was assessed by NGS, 6 MRD (+) cases received post-ASCT therapy while 4 MRD (-) cases and 7 MRD (+) cases were followed without post-ASCT therapy. The MRD (-) cases tended to show a better PFS than the MRD (+) cases with post-ASCT therapy ($P = 0.26$) and those without post-ASCT therapy ($P = 0.09$) although overall survival rates were comparable among the three groups. There was no difference in PFS between MRD (-) and MRD (+) cases when MRD was assessed by ASO-qPCR ($P = 0.6$). These studies will be extended in 30 additional MM patients, and results will be presented. **Conclusions:** MRD-negativity in autografts revealed by NGS may be more closely associated with durable remission of MM than that revealed by ASO-qPCR.

8602 General Poster Session (Board #55G), Sun, 8:00 AM-11:45 AM

Phase I study of TH-302, an investigational hypoxia-targeted drug, and dexamethasone in patients with relapsed/refractory multiple myeloma.

Irene M. Ghobrial, Jacob Laubach, Philippe Armand, Erica Boswell, Courtney Hanlon, Stacey Chuma, Esther Dawn Chu, Damian Handisides, Stew Kroll, Barbara Hickingbottom, Kenneth Carl Anderson, Paul Gerard Guy Richardson; Dana-Farber Cancer Institute, Boston, MA; Jerome Lipper Multiple Myeloma Center, Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA; Threshold Pharmaceuticals, Inc., South San Francisco, CA; Threshold Pharmaceuticals, South San Francisco, CA

Background: TH-302 is an investigational 2-nitroimidazole prodrug of the DNA alkylator Br-IPM designed to be selectively activated in hypoxia. In multiple myeloma (MM) mouse models, diseased animals demonstrate a marked expansion of areas of hypoxia in the bone marrow. TH-302 exhibited anti-tumor activity against MM in vitro and in vivo and synergism was seen when combined with bortezomib (Hu et al, *Blood* 2010; Chesi et al, *Blood* 2012). Based on these findings, a phase I/II study of TH-302 plus dexamethasone (dex) was initiated for patients (pts) with relapsed/refractory MM. **Methods:** Eligible pts in the study (NCT01522872) had ECOG PS $\leq$ 2, receipt of at least two prior therapies, and acceptable hepatorenal function and hematologic status. A standard 3+3 dose escalation design was used with a fixed oral 40 mg dose of dex and 40% dose increments of TH-302. TH-302 was administered IV with dex on days 1, 4, 8, and 11 of a 21-day cycle. The objectives were to determine DLTs and the MTD; assess the safety, tolerability and preliminary clinical activity of TH-302 plus dex; and study the relationship between hypoxia within the bone marrow and response to TH-302. **Results:** Eleven pts have been treated: 7M/4F with a median age 61 years (range: 53 – 86) and 6 prior therapies (range: 3 – 10). All received both bortezomib and lenalidomide/thalidomide containing regimens. TH-302 was dosed at 240 (n=5), 340 (n=4), and 480 (n=2) mg/m^2 for a median of 5 cycles. No DLTs were reported at 240 or 340 mg/m^2. Two pts treated at 480 mg/m^2 had DLTs of grade 3 mucositis, exceeding the definition of MTD. A dose expansion is thus ongoing at 340 mg/m^2. Two patients had SAEs related to TH-302 (pneumonia). Five pts continue on study after a median of 7 cycles (range: 2–11). Nine pts have had efficacy evaluations: 2 pts with partial responses, 2 pts with minimal responses, and 5 pts with stable disease, for an overall response rate (of MR or better) of 44%. **Conclusions:** TH-302 can be administered at 340 mg/m^2 biweekly + dex, with dose limiting mucositis seen at higher doses. Initial clinical activity has been noted with an ORR of 44% in heavily pretreated MM pts who are relapsed/refractory to both bortezomib and lenalidomide. Clinical trial information: NCT01522872.

8603 General Poster Session (Board #55H), Sun, 8:00 AM-11:45 AM

Cure candidates: Characteristics of >10yr progression-free survivors (PFS-10) and continuous CR (CCR-10) after total therapy 1 and 2 (TT1, TT2) for multiple myeloma (MM).

Sarah Waheed, Frits Van Rhee, Adam Rosenthal, Saad Zafar Usmani, Mian Adnan Waheed, Antje Hoering, Bart Barlogie; Myeloma Institute for Research and Therapy, Little Rock, AR; Cancer Research and Biostatistics, Seattle, WA; Texas Tech University, Odessa, TX

Background: Our TT studies demonstrate that long term progression free survival is achievable in MM pointing to the possible curability of MM. We report here on the base line characteristics of 33/231 TT1 patients and 109/475 TT2 patients qualifying for PFS-10, including 45/245 randomized to the control arm and 64/230 randomized to thalidomide. **Methods:** Baseline and response levels were compared between <10yr and >=10yr survivors and logistic regression applied to identify the critical features linked to PFS-10 status. **Results:** Compared to the remainder, PFS>=10yr and CCR>=10yr were characterized by lower frequencies of cytogenetic abnormalities (CA), B2M>=3.5mg/L and age >=65yr. More females and more patients with platelets >150.000/uL qualified for the >=10yr category. Finally, timely administration of 2 transplants was also over-represented in these patients. **Conclusions:** Long-term survival PFS-10 and CCR-10 were adversely affected by by CA and elevated B2M levels. Females more frequently attained PFS-10. Assessment of MRD by 8-color flow cytometry in these patients is in progress and will be presented at the meeting. Clinical trial information: NCT00580372, NCT 00083551.

Patient characteristics by PFS10 and CCR 10 categorization, TT1+2 patients.

Factor	PFS<10 years	PFS>10 years	P value	Not CCR at 10 years	CCR at 10 years	P value
Age >= 65 yr	107/601 (18%)	16/160 (10%)	0.017	111/646(17%)	12/15(10%)	0.070
Female	218/601 (36%)	74/160 (46%)	0.021	237/646(37%)	55/115(48%)	0.024
B2M >= 3.5 mg/L	232/601 (39%)	39/160 (24%)	<.001	244/646(38%)	27/115(23%)	0.003
B2M > 5.5 mg/L	118/601 (20%)	18/160 (11%)	0.014	123/646(19%	13/115(11%)	0.046
Prestudy CA	210/589 (36%)	28/157 (18%)	<.001	219/632(35%)	19/114(17%)	<0.001
Received transplant 1	490/601(82%)	148/60(93%)	<.001	526/646(91%	114/115(99%)	<0.001
Received transplant 2	383/601(64%)	123/160(77%)	0.002	406/646(63%)	100/115(87%)	<0.001

Logistic regression

			10-year PFS			
	Variable	N	With factor	Without factor	OR (95% CI)	P value
Multivariate	Female	743	73/286 (26%)	82/457 (18%)	1.57 (1.09, 2.26)	0.0152
	B2M >= 3.5 mg/L	743	37/261 (14%)	118/482 (24%)	0.58 (0.38, 0.88)	0.0107
	Prestudy CA	743	28/238 (12%)	127/505 (25%)	0.44 (0.28, 0.70)	0.0004

8604 General Poster Session (Board #56A), Sun, 8:00 AM-11:45 AM

HM1.24/CD317-directed immunotoxin to eliminate malignant plasma cells in vitro and in vivo.

Martin Gramatzki, Matthias Staudinger, Pia Glorius, Katja Klausz, Christian Kellner, Andreas Günther, Roland Repp, Renate Burger, Matthias Peipp; Division of Stem Cell Transplantation and Immunotherapy, 2nd Department of Medicine, University of Kiel, Kiel, Germany; Klinikum am Bruderwald, Bamberg, Germany

Background: Targeted immunotherapy, based on antibodies against tumor-associated antigens, is a promising approach for the treatment of multiple myeloma (MM). Recently, antibody-based strategies delivering a toxic payload have documented impressive clinical activity in hematological malignancies. In particular, surface molecules overexpressed on malignant plasma cells and efficiently internalized represent promising targets for developing myeloma-directed immunoconstructs. Here, the identification of CD317 (HM1.24) as a potent target structure and the characterization of a novel CD317-directed single-chain immunotoxin, HM1.24-ETA', is described. **Methods:** Using a novel screening tool, a panel of antibodies against MM-associated antigens was evaluated for their ability to mediate antigen-dependent delivery of a truncated version of Pseudomonas exotoxin A (ETA') to MM cells. HM1.24-ETA' was generated by genetic fusion of a CD317-specific single-chain Fv antibody and ETA'. The anti-myeloma activity of the E. coli-expressed immunotoxin was evaluated in vitro and in a xenograft mouse model. **Results:** By screening a panel of antibodies including CD38, CS1, IL-6R, CD138 and CD317, CD317 was identified as a suitable receptor to deliver ETA' to MM cells. The subsequently designed recombinant HM1.24-ETA' immunotoxin efficiently inhibited growth of MM cell lines with halfmaximal growth inhibition at concentrations of less than 1 nM. Antigen-specific MM cell killing occurred via induction of apoptosis. The proliferation of IL-6 dependent INA-6 cells was completely inhibited by HM1.24-ETA' even in the presence of bone marrow stromal cells that otherwise strongly support tumor cell growth. Importantly, HM1.24-ETA' strongly triggered apoptosis (up to 80%) in freshly isolated tumor cells from 7 out of 7 MM patients. In a xenograft SCID mouse model, establishment of INA-6 plasma cell tumors was efficiently abrogated by treatment with HM1.24-ETA' immunotoxin ($p < 0.04$). **Conclusions:** The HM1.24-ETA' immunotoxin in vitro and in the preclinical xenograft model in vivo demonstrates that the CD317 antigen may represent a promising target structure for immunotherapy of MM using immunoconjugates with toxic payloads.

8605 General Poster Session (Board #56B), Sun, 8:00 AM-11:45 AM

Minimal residual disease (MRD) status pre- and post- high-dose therapy/autologous stem (HDC/ASCT) cell transplantation for multiple myeloma (MM) in the era of novel agents.

Adetola Kassim, Jeremy Scott McDuffie, Claudio A Mosse, Bipin N. Savani, John P. Greer, Olalekan O. Oluwole, Stacey Goodman, Brian G. Engelhardt, Wichai Chinratanalab, Annette S Kim, Madan H. Jagasia; Vanderbilt University Medical Center, Nashville, TN; School of Medicine, Vanderbilt University, Nashville, TN; VA Medical Center, Nashville, TN

Background: MRD assayed by multi-parameter flow cytometer (MFC), has prognostic significance after HDT/ASCT for MM (Paiva et. al. 2008). The frequency of MRD negativity (-) after induction therapy using novel agents such as immunomodulatory drugs like lenalidomide (IMiDs), and proteasome inhibitors like bortezomib, is unknown. The impact of HDT/ASCT on MRD status in this patient group has not been studied. **Methods:** We performed a retrospective study of all MM patients undergoing HDT/ASCT (January 2010 - December 2012) in our institution. No restrictions on inclusion were made based on the International Myeloma Working Group response criteria. All patients had novel agents as part of their initial induction regimen. Statistical analysis was by SPSS software (V 12.0). MRD status was determined by MFC on bone marrow samples pre- HDC/ASCT [M1] and post- HDC/ASCT (D100 [M2] and I year [M3]). MFC was done with antibodies against CD45, CD19, CD138, CD38, CD20, CD56, and anti-k and l cytoplasmic antibodies. **Results**: MRD status was available on 91 patients pre-transplant. Of these patients, 80 had MFC recorded at M2 and 17 patients had MFC recorded at M3. Fifty-eight percent were male and 76% were Caucasian. Forty percent received IMiDs, while 60% got proteasome based therapies. Of the 91 patients with MRD pre-HDC/ASCT, 58% (53/91) were MRD (-), and of these patients 89% (41/46) remained MRD (-) at M2. 48 patients were MRD positive (+) pre-HDC/ASCT, 58% (20/34) became MRD (-) at M2. Age, cytogenetic risk, disease stage, number of chemotherapy cycles or immunofixation status had no impact on MRD status. There were only 6 relapses in the cohort, thus the impact of MRD status on progression-free survival could not be studied. **Conclusions:** Novel agents improve depth of response pre-transplant. HDC/ASCT increases MRD negativity post-transplant. MRD status could aid better timing of HDC/ASCT or adoption of a risk-adapted strategy for high-risk patients. MRD status validation in a prospective cohort is underway at our center (NCT01215344). With future follow-up, the impact of MRD on progression-free survival in the era of novel agents will be determined.

8606 General Poster Session (Board #56C), Sun, 8:00 AM-11:45 AM

Implications of rapidity of response to initial therapy in multiple myeloma.

Krishna Bilas Ghimire, Vincent Rajkumar, Angela Dispenzieri, Martha Lacy, Morie Gertz, Francis Buadi, David Dingli, Suzanne R. Hayman, Nelson Leung, Stephen Russell, John Anthony Lust, Steven R. Zeldenrust, Yi Lin, Prashant Kapoor, Arleigh Robertson McCurdy, Robert A. Kyle, Shaji Kumar; Mayo Clinic, Rochester, MN; Division of Hematology, Mayo Clinic, Rochester, MN

Background: The rapidity of response to initial therapy in multiple myeloma (MM) depends on a variety of factors. There is limited data on its implications on long term outcomes in patients (pts) with newly diagnosed MM. **Methods:** We retrospectively examined the outcomes in a cohort of 454 pts with newly diagnosed MM between Jan 2000- Dec 2011 undergoing induction therapy. **Results:** The median age at diagnosis was 66 yrs (29-92). Pts had measurable serum M-spike (>= 1 g/dL), dFLC (>=10 mg/dl) or 24 hour urinary M protein excretion (UrM; >=200 mg) in 70, 63 and 39% respectively. We first examined the relationship between the response to first cycle of therapy and overall survival (OS). We divided pts into quartiles based on their % reduction in the serum M spike, dFLC or UrM. The median OS (Table) was poorest for pts with the least reduction of serum M protein (P<0.001) and of dFLC. The cutoffs for Q1 was 25, 40and 40% decrease for serum M spike, dFLC and 24 hr UrM respectively. Among various baseline characteristics only higher age was predictive of a poor (Q1) response. Given the trend toward worse OS among the Q 4 group (maximum decrease in serum M spike), we examined the relationship to cytogenetic risk. Among 232 pts with FISH data available, proportion of pts with high-risk disease was 27, 12, 22 and 31% respectively in quartiles 1 - 4). In a multivariate analysis, quartile 1 and 4 of serum M-protein response and the high-risk FISH were independent risk factors associated inferior OS. **Conclusions:** Both shallow and very deep response to therapy in cycle 1 is a strong indicator of eventual disease outcome and should be considered as marker of high-risk disease, likely through different mechanisms. For the shallow responders, prospective trials should assess if a change in therapeutic management will alter the outcome of these pts. The rapid deep responders also appear represent a different high-risk biology, emphasizing the fact that pts with high-risk disease often have excellent initial responses, but poor long term outcomes.

Median overall survival from diagnosis (mo).

Quartile (based on protein reduction)	Serum M-spike		dFLC		24-hour urinary M protein	
1 Lowest	40		51		40	
2	91	88	61	65	74	67
3	89		69		61	
4 Greatest	65		81		88	
P value	< 0.001	<0.001*	0.16	0.04*	0.5	0.13*

* Quartile 1 vs. Q2-4.

8607 General Poster Session (Board #56D), Sun, 8:00 AM-11:45 AM

Risk-adapted maintenance therapy (MaintRx) after ASCT in first-line therapy for multiple myeloma (MM).

Jonathan L. Kaufman, Joanne Willey, Michael E. Williams, Brynn Tiscione, Arden Buettner, Douglas Neely, Mark R. Green; Emory University, Atlanta, GA; Xcenda, Palm Harbor, FL; University of Virginia Medical Center, Charlottesville, VA

Background: Maintenance lenalidomide improves survival in patients who have undergone induction therapy and then autologous stem cell transplant (ASCT) as first line management for MM. We studied how the extent of cytoreduction after induction therapy à ASCT (as measured by CR, VGPR, or PR as best response) influences MAINTRX prescribing preferences among American Hematology-Oncology physicians (AHOP). **Methods:** We studied 284 individual AHOPs using a proprietary, live, case-based market research tool to assess prescribing preferences. A core case scenario and variations based on extent of response to induction à ASCT was constructed. Preference data were acquired using blinded audience response technology. All responses for each scenario were obtained contemporaneously prior to any display of respondent selections. All sources of research support were double blinded. The core scenario involved a 59-year-old patient (42% plasma cells in BM, no cytogenetic abnormalities, CrCl 65ml/min, B2M 5.8, PS 1) treated with induction therapy of choice à ASCT. The same query was then posed in each of 3 settings: Following CR (or following VGPR or following PR) as best response, what, if any, further therapy would you recommend now? **Results:** See Table. **Conclusions:** Among patients with myeloma getting first-line therapy, MaintRx is almost uniformly preferred by AHOPs. Specific single or doublet therapy preferences are dependent upon best response to induction à ASCT treatment. Compared to the CR setting, preferences for 2 drug MaintRx are significantly increased in patients with VGPR ($p < .0.001$) or with PR ($p < 0.001$)] as best overall response. The potential for benefit from intensified MaintRx in these response subsets needs prospective phase III testing.

	Best response after induction à ASCT		
Post ASCT options	CR N=282	VGPR N=281	PR N=284
Bortezomib fixed interval [FI]	6%	1%	1%
Bortezomib to progression [PD]	4%	10%	10%
Lenalidomide FI	25%	8%	3%
Lenalidomide PD	48%	63%	45%
Daily lenalidomide and intermittent bortezomib both for FI	2%	2%	5%
Daily lenalidomide and intermittent bortezomib both to PD	1%	10%	31%
Total with plans to use a maintenance strategy	86%	94%	95%
Observe post ASCT	12%	4%	1%
Other	2%	2%	4%

8608 General Poster Session (Board #56E), Sun, 8:00 AM-11:45 AM

Outcomes of patients with solitary plasmacytomas (SP) in the era of PET imaging and serum-free light chain (sFLC) testing: A single institution experience.

Abby L. Koch, Kenneth H. Shain, Melissa Alsina, Daniel Sullivan, Taiga Nishihori, Jose L. Ochoa-Bayona, Rachid C. Baz; University of South Florida, Morsani College of Medicine, Tampa, FL; H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL

Background: SP can occur in bone (SPB) or in extramedullary sites (EMP) and generally accounts for ~ 3-5% of plasma cell dyscrasias. Up to 50% of SPB and 15% of EMP will progress to multiple myeloma (MM). We evaluated the utility and prognostic significance of positron emission tomography (PET) imaging and SFLC ratio (sFLCr). **Methods:** We retrospectively reviewed electronic medical records of patients with SP evaluated at Moffitt Cancer Center between 1990-2012. The diagnosis of SP was per IMWG criteria (BJH 2003, 121:749) (biopsy proven single site, negative skeletal survey, bone marrow biopsy with no more than 10% plasma cells). Initial and post therapy sFLCr as well as PET findings were correlated with progression to symptomatic MM (PFS). Radiation therapy (XRT) was at the discretion of the treating physician. **Results:** 135 patients were identified and 91 (67%) were males. The median age was 58 years (range 20-82). Consistent with prior reports, the PFS of the entire cohort was 43 months (95% CI 17.8-70). 23 patients had PET prior to progression. All patients had uptake in the primary lesion (except 4 who had resection of the primary). 8 patients had additional PET findings in other bony structure (PET+), and 15 did not (PET-). 2 and 6 of the PET- and PET+ patients progressed (median PFS Not reached (NR) vs. 8.1 months, $p=0.021$) respectively. Of the 49 patients with available sFLC data, 32 had an abnormal ratio (17 progressed) and 17 patients had a normal ratio (2 progressed). Abnormal baseline sFLCr was associated with progression (median PFS 19 months vs NR, $p=0.012$). Post XRT, 44 patients had an available sFLCr, of which 23 had an abnormal ratio and 21 a normal ratio. A persistent serum/urine m spike after XRT was associated with progression to MM (median PFS 20.8 months vs NR, $p<0.0001$). However, the association between Post XRT sFLCr and progression to MM was not statistically significant (median PFS 19 vs 43 months (abnormal vs normal ratio) $p=0.2$). **Conclusions:** PET imaging and sFLC are predictors of outcomes in SP and their routine inclusion in the diagnostic work up of patients with SP will result in a stage migration where patients outcomes are improved compared to historical controls.

8609 General Poster Session (Board #56F), Sun, 8:00 AM-11:45 AM

Survival outcomes of plasma cell leukemia (PCL) in the United States: A SEER analysis.

Hari Prasad Ravipati, Jonathan L. Kaufman, Amelia A. Langston, Lawrence Boise, Christopher Flowers, Sagar Lonial, Ajay K. Nooka; Morehouse School of Medicine, Atlanta, GA; Emory University, Atlanta, GA; The Winship Cancer Institute of Emory University, Atlanta, GA; Department of Medical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA; Emory University School of Medicine, Atlanta, GA; Division of BMT, Emory University, Winship Cancer Institute - Hematology and Medical Oncology, Atlanta, GA

Background: Plasma cell leukemia (PCL) is an aggressive plasma cell disorder that is associated with poor outcomes. Previous studies have shown improved survival with bortezomib-based regimens in this subset of patients undergoing stem cell transplant (SCT), but this may reflect referral bias. Current knowledge evaluating outcomes of PCL is limited in the era of novel agents. **Methods:** We analyzed the Surveillance, Epidemiology, and End Results (SEER) database from 18 registries for survival characteristics in PCL stratified by age, sex, race and the era of diagnosis. International Classification of Diseases for Oncology 3rd edition histology code 9733 was used to identify cases. **Results:** From 1973 to 2009, 74826 cases of myeloma and 479 cases of PCL were recorded. Survival data was available for 397 PCL patients. The median overall survival (OS) was 6 months (95% Confidence Interval (CI): 4.8 months – 7.2 months); and 1-year, 2-year, and 4-year OS rates were 34%, 20%, and 9% compared to corresponding myeloma survival rates of 66%, 52%, and 32%, respectively. Median overall survival differences were observed for women vs. men (7 months vs. 5 months, $p=0.026$); black vs. white patients (7 months vs. 5 months, $p=0.01$); and patients aged <60 years vs. ≥ 60 years (9 months vs. 4 months; $P=0.01$), respectively. In addition, patients diagnosed after 2005 had superior median OS compared with patients diagnosed prior to 2005 (7 months vs. 3 months; $P=0.005$). **Conclusions:** Black patients, women and patients aged <60 years have improved OS compared to white patients, males and patients aged ≥ 60 years. The survival benefit seen in patients diagnosed after 2005 may be attributed to the benefit conferred by access to new agents, but OS remains poor. Newer treatment approaches for managing PCL are clearly needed.

8610 General Poster Session (Board #56G), Sun, 8:00 AM-11:45 AM

Factors that predict successful remobilization after autologous hematopoietic progenitor cell transplant (aHCT) for multiple myeloma.

Xenofon Dimitrios Papanikolaou, Eric Rosenbaum, Lisa Tyler, Bart Barlogie, Michele Cottler-Fox; Myeloma Institute for Research and Therapy, Little Rock, AR; Department of Pathology, University of Arkansas for Medical Sciences, Little Rock, AR

Background: aHCT is a proven therapeutic modality in treating relapsed multiple myeloma (MM). However, previously transplanted patients may have no hematopoietic progenitor cells (HPC) left in storage. **Methods:** Collection of HPC after aHCT was studied in 221 MM patients who underwent 333 mobilization attempts between 10/2000 and 06/2012. **Results:** The median number of CD34+ collected was 4.7 $\times 10^6$/kg, with 74% of collections yielding at least 2.5×10^6/kg. Mobilization with chemotherapy and G-CSF was most efficient, yielding a median of 6.84×10^6/kg ($p<0.001$). Growth factor-only mobilization was least effective, with a median of 3.01×10^6/kg ($p<0.001$). The addition of plerixafor yielded a significant increase if there was a previous "poor" ($<2.5\times 10^6$/kg) collection (1.83 vs. 3.43×10^6/kg, $p<0.001$). In univariate statistical analysis female sex ($p=0.048$), platelets (PLT) $\leq 100\times 10^6$/L ($p<0.001$), hemoglobin $\leq$11g/dL ($p=0.032$), and albumin $\leq$3.5 g/dL ($p=0.003$) prior to mobilization correlated with a "poor" collection. In multivariate analysis only PLT $\leq 100\times 10^6$/L was significant ($p<0.001$). Of the 221 patients collected, 154 underwent subsequent aHCT. Infusion of HPC procured after previous aHCT did not yield a difference in treatment-related mortality ($p=0.766$). Use of only cells collected after aHCT was related to a delayed platelet engraftment $\geq 50\times 10^6$/L ($p<0.001$). **Conclusions:** Remobilization and collection of an adequate number of HPC after previous aHCT is feasible. PLT $\leq 100\times 10^6$/L suggest the need for plerixafor for a successful collection. Infusion of the graft procured is safe and effective, but use of only cells collected after aHCT is associated with delayed platelet engraftment $>50\times 10^6$/L.

TPS8611 General Poster Session (Board #56H), Sun, 8:00 AM-11:45 AM

Phase III trial of brentuximab vedotin and CHP versus CHOP in the frontline treatment of patients (pts) with CD30+ mature T-cell lymphomas (MTCL).

Owen A. O'Connor, Barbara Pro, Tim Illidge, Lorenz H. Trumper, Emily K. Larsen, Dana A. Kennedy; Columbia University Medical Center / New York Presbyterian Hospital, New York, NY; Kimmel Cancer Center of Thomas Jefferson University, Philadelphia, PA; Christie Hospital NHS Foundation Trust, Manchester, United Kingdom; Georg-August-University, Göttingen, Germany; Seattle Genetics, Inc., Bothell, WA

Background: MTCL including systemic anaplastic large cell lymphoma (sALCL) are aggressive neoplasms. Anthracycline-based multiagent chemotherapy regimens have demonstrated response rates ranging from 76 to 88%. Five-year overall survival rates range from 12 to 49% depending on the histologic subtype. Brentuximab vedotin is an antibody drug conjugate that has shown efficacy in a pivotal phase 2 study as a single agent in relapsed sALCL (Pro et al., J Clin Oncol, 2012) and evidence of clinical activity in combination with CHP in the frontline treatment of MTCL including sALCL in a phase 1 study (Fanale et al., ASH 2012). **Methods:** This randomized, double-blind, placebo-controlled, multicenter, phase 3 study (NCT01777152) is evaluating the safety and efficacy of 1.8 mg/kg brentuximab vedotin with CHP (A+CHP) vs CHOP for frontline treatment of CD30+ MTCL. Pts must have FDG-avid disease by PET and measureable disease of at least 1.5 cm by CT. Approximately 300 pts will be randomized 1:1 to receive A+CHP or CHOP for 6–8 cycles (q3wk). Randomization will be stratified by ALK+ sALCL vs other histologic subtypes and IPI score (0–1, 2–3, or 4–5). The target proportion of pts with a diagnosis of sALCL will be 75%. The primary objective is to compare progression-free survival (PFS) between the 2 treatment arms as determined by an independent review facility (IRF). Secondary objectives include comparisons of PFS per IRF in sALCL patients, safety, overall survival, and complete remission rate between the 2 arms. After completion of treatment, pts will be followed for disease progression, medical resource utilization, quality of life, and survival. Post-treatment stem cell transplant is permitted. Efficacy assessments will use the Revised Response Criteria for Malignant Lymphoma (Cheson 2007). CT and PET scans will be performed at baseline, after Cycle 4, and after the completion of treatment. CT scans will also be performed at regular intervals during follow-up until disease progression, death, or analysis of the primary endpoint. Safety assessments will occur throughout the study until 30 days after last dose of study treatment. Enrollment for this global trial began in early 2013. Clinical trial information: NCT01777152.

TPS8612 General Poster Session (Board #57A), Sun, 8:00 AM-11:45 AM

Phase III study of brentuximab vedotin plus doxorubicin, vinblastine, and dacarbazine (A+AVD) versus doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) as front-line treatment for advanced classical Hodgkin lymphoma (HL).

Anas Younes, John Radford, Stephen Maxted Ansell, Andrea Gallamini, Won Seog Kim, Tatyana A. Feldman, Mehdi Hamadani, Jeanenne Chung, Jingyuan Wang, Dirk Huebner, Joseph M. Connors; The University of Texas MD Anderson Cancer Center, Houston, TX; The Christie Hospital NHS Foundation Trust, Manchester, United Kingdom; Mayo Clinic, Rochester, MN; Nice University, Nice, France; Samsung Medical Center, Seoul, South Korea; John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; West Virginia University, Morgantown, WV; Millennium Pharmaceuticals, Inc., Cambridge, MA; British Columbia Cancer Agency/University of British Columbia, Vancouver, BC, Canada

Background: Brentuximab vedotin, a CD30-targeted antibody-drug conjugate, has conditional approval in Europe for relapsed/refractory (RR) CD30-positive HL following autologous stem cell transplant (ASCT) or following ≥2 prior therapies when ASCT or multi-agent chemotherapy is not a treatment option. ABVD, a common front-line regimen for advanced HL, achieves complete response (CR) rates of 70–80%. However, 10–20% of patients (pts) are refractory to front-line treatment and up to 35% relapse after front-line multi-modality therapy. In pts with relapsed HL post-ASCT, single-agent brentuximab vedotin yields an objective response rate of 75% (CR, 33%; Chen ASH 2012). In a phase 1 study in treatment-naïve HL pts, A+AVD was associated with manageable toxicity and a CR rate of 96%; brentuximab vedotin + ABVD was contraindicated due to pulmonary toxicity (Ansell ASH 2012). We hypothesized that substituting bleomycin with brentuximab vedotin would eliminate bleomycin-associated pulmonary toxicity and improve progression-free survival (PFS) compared to a standard ABVD regimen. **Methods:** This ongoing, open-label, randomized, multicenter study (NCT01712490) will compare A+AVD vs ABVD in 1040 pts with stage III/IV classical HL. Primary endpoint: modified (m) PFS (death, progression, and receipt of chemotherapy or radiotherapy by pts not in CR after completing A+AVD or ABVD will count as progression event). Key secondary endpoint: overall survival. Key inclusion criteria: histologically-confirmed previously untreated stage III/IV classical HL. Pts will be stratified by region and International Prognostic Score, and will be randomized 1:1 to receive A+AVD (brentuximab vedotin 1.2 mg/kg with each dose of AVD) or ABVD administered intravenously on Days 1 and 15 of 28-day cycles, for up to 6 cycles. Disease status and survival will be evaluated regularly until study closure. Safety assessments: incidence and severity of adverse events, changes to physical and laboratory tests. Clinical trial information: NCT01712490.

TPS8613^ General Poster Session (Board #57B), Sun, 8:00 AM-11:45 AM

A phase III study of ibrutinib in combination with bendamustine and rituximab (BR) in elderly patients with newly diagnosed mantle cell lymphoma (MCL).

Michael Wang, Leo I. Gordon, Simon Rule, Andre Goy, Olivier Hermine, Aleksandra Rizo, Sen Hong Zhuang, Martin H. Dreyling; The University of Texas MD Anderson Cancer Center, Houston, TX; Northwestern Memorial Hospital, Chicago, IL; Department of Haematology, Derriford Hospital, Plymouth, United Kingdom; John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; Hematology Department, Necker Hospital, Paris, France; Janssen Research & Development, LLC, Beerse, Belgium; Janssen Research & Development, LLC, Raritan, NJ; Department of Internal Medicine III, University of Munich, Munich, Germany

Background: MCL is a distinct subtype of B-cell non-Hodgkin lymphoma (NHL) accounting for approximately 6% of NHL diagnoses. Current immunochemotherapy followed by rituximab maintenance results in a prolonged duration of remission, but a constant relapse pattern is still observed. Ibrutinib, an oral Bruton's tyrosine kinase(BTK) inhibitor, demonstrated promising single-agent activity in 115 patients with relapsed or refractory MCL who were enrolled in the phase II study PCYC-1104. The overall response rate (ORR) was 68%, with 46% of patients achieving partial response (PR) and 22% achieving complete remission (CR) (Wang ASH 2012). Blum et al (ASH 2012) demonstrated that ibrutinib can be safely combined with BR in a phase I combination study in relapsed or refractory NHL and that it enhanced BR's clinical activity with an ORR in 5 evaluable MCL patients of 100% (80% CR, 20% PR). These data suggest that combining ibrutinib with BR will improve the outcome of these patients. **Methods:** The SHINE study, PCI-32765MCL3002, is a phase III double-blind study of ibrutinib in combination with BR versus BR for the treatment of patients with newly diagnosed MCL. The study aims to enroll 520 patients (approximately 260 patients per arm). All patients will receive BR therapy for 6 cycles; those patients achieving a CR or PR will receive R maintenance for 2 years. In addition to BR and R, all patients will receive an oral daily dose of 560 mg ibrutinib or placebo concomitant with the chemotherapy and ongoing as a single agent until disease progression or unacceptable toxicity. The primary objective is to evaluate if the addition of ibrutinib to BR will result in prolongation of progression-free survival, with secondary objectives of ORR (CR+PR), CR rate, duration of response, safety, and overall survival. The study will enroll patients aged 65 years or older who are not suitable for high-dose chemotherapy. Key exclusion criteria include diagnosis or treatment for malignancy other than MCL, requirement for treatment with warfarin or equivalent vitamin K antagonists, and treatment with strong CYP3A4/5 inhibitors. Approximately 200 sites globally will enroll patients. Enrollment began in Q1 of 2013. Clinical trial information: NCT01776840.

TPS8614^ General Poster Session (Board #57C), Sun, 8:00 AM-11:45 AM

An open-label phase II study of ibrutinib in patients with refractory follicular lymphoma.

Gilles A. Salles, Ajay K. Gopal, Peter Martin, Robert Marcus, Georg Hess, Pier Luigi Zinzani, Tahamtan Ahmadi, Sen Hong Zhuang, Ronald Levy; Centre Hospitalier Lyon Sud, Oullins, France; University of Washington/Seattle Cancer Care Alliance, Seattle, WA; Weill Cornell Medical College, New York, NY; King's College Hospital, London, United Kingdom; Johannes Gutenberg University, Mainz, Germany; University of Bologna, Bologna, Italy; Janssen Research & Development, LLC, Spring House, PA; Janssen Research & Development, LLC, Raritan, NJ; Stanford University, School of Medicine, Stanford, CA

Background: Follicular lymphoma (FL) is the second most common non-Hodgkin lymphoma (NHL) and comprises approximately 22% of all NHL cases. Most patients treated eventually relapse and subsequent responses and duration of responses become shorter. Patients ultimately become resistant to chemoimmunotherapy and repeated treatment-related toxicity commonly outweighs the benefit of treatment. Ibrutinib is a potent inhibitor of BTK (downstream of the B-cell receptor, BCR) that binds covalently to Cys-481 in the active site, abrogating intrinsic survival pathways (eg, ERK1/2, NF-kB, AKT) as well as survival signals from the microenvironment (eg, TNF family members: BAFF, CD40L; cytokines from T-cells: IL4, IL6, IL10, TNFα). Irish et al (2010) have also shown that up to 60% of FL patients display BCR signaling addiction. Early indications from study PCYC-04753 suggest activity of the BTK inhibitor ibrutinib in FL. Three CR and 3 PR were observed in 11 patients at a dose of 2.5 mg/kg or higher that achieved full BTK occupancy (Fowler, ASH 2012). **Methods:** The DAWN study, PCI-32765FLR2002, is a phase II, single-arm study of ibrutinib in refractory FL. The study aims to enroll 110 patients with chemoimmunotherapy-resistant FL. Patients will receive an oral daily dose of 560 mg ibrutinib. Patients must have been treated with at least 2 prior lines of therapy, at least 1 rituximab-containing combination chemotherapy regimen, and the last prior line of therapy included an anti-CD20 monoclonal antibody-containing chemotherapy regimen. The primary objective of the study is to evaluate the ORR (CR + PR), with secondary objectives of duration of response, progression-free survival, overall survival, and safety. To better understand the mechanism of action of ibrutinib, blood and tumor samples will be collected and, where feasible, characterized by GEP, SMA, IHC, or other technology as applicable. These evaluations aim to identify biomarkers associated with response or resistance to ibrutinib in subjects with FL and results may assist in the development of this drug in this and potentially other indications. Approximately 64 sites in the US and Europe will enroll patients. Enrollment began in 1Q of 2013. Clinical trial information: NCT01779791.

TPS8615 General Poster Session (Board #57D), Sun, 8:00 AM-11:45 AM

AHL 2011: A Lysa randomized phase III study of a treatment driven by early PET response compared to a standard treatment in patients with Ann Arbor stage III-IV or high-risk IIB Hodgkin lymphoma.

Rene-Olivier Casasnovas, Michel Meignan, Oumedaly Reman, Isabelle Gaillard, Aspasia Stamatoullas, Pauline Brice, Gilles A. Salles, Reda Bouabdallah, Serge Bologna, Emmanuelle Nicolas-Virelizier, Franck Morschhauser, Maud Janvier, Marc Andre, Alina Berriolo-Riedinger, Alexandra Traverse-Glehen, Veronique Edeline, Peggy Dartigues, Marie Parrens, Nicolas Mounier, Christophe Ferme; Hôpital Le Bocage, Dijon, France; Hôpital Henri Mondor, Créteil, France; Centre Hospitalier Universitaire Caen, Caen, France; Centre Henri Becquerel, Rouen, France; Hospital Saint-Louis, Paris, France; Centre Hospitalier Lyon Sud, Oullins, France; Institut Paoli Calmettes, Marseille, France; Centre Hospitalier Universitaire, Nancy, France; Centre Léon Bérard, Lyon, France; Hôpital Claude Huriez, Lille, France; Institut Curie, Paris, France; Centre Hospitalier Universitaire Mont-Godinne, Dinant, Belgium; Centre Georges François Leclerc, Dijon, France; Hospices Civils de Lyon - Hopital Lyon Sud, Pierre-Benite, France; Institut Gustave Roussy, Villejuif, France; Centre Hospitalier Universitaire, Bordeaux, Bordeaux, France; Centre Hospitalier Universitaire l'Archet, Nice, France

Background: ABVD is the most widely chemotherapy regimen used as standard treatment of advanced Hodgkin lymphoma (HL). The escalated BEACOPP (BEAesc) regimen which delivers more drugs at higher dose intensity was shown to improve patient's PFS but not OS when compared to ABVD (Federico M, 2009; Viviani S, 2011; Carde P, 2012). The better efficiency of BEAesc is associated to a marked immediate hematologic toxicity and a higher risk of secondary myelodysplasia/leukemia. Also, the gonadal toxicity which is a real concern in young women, is quite higher when using BEAesc. So, to better manage HL treatment we need to identify early responding patients able to benefit from a strategy of dose intensity decrease after upfront BEAesc, without impairing the disease control. PET performed after 2 cycles of chemotherapy (PET2) might identify such a population suitable for receiving ABVD after 2 cycles of upfront BEAesc, and was implemented in the present study. **Methods:** The AHL 2011 trial (NCT01358747) was designed to test in 16 to 60 years old HL patients with Ann Arbor stage III, IV or high risk IIB, a treatment strategy driven by PET after 2 cycles of BEACOPPesc, delivering 4 cycles of ABVD for PET2 negative patients and 4 cycles of BEAesc for PET2 positive patients, compared to a treatment not monitored by PET, delivering the best BEAesc schedule consisting in 6 cycles of this regimen (Engert A, 2012). A baseline PET is mandatory before treatment and PET2 are centrally reviewed within 48 hours and interpreted according to Deauville criteria. The allocation of treatment in the experimental arm is based on the PET2 central review result. PFS is the primary endpoint of the study with an hypothesis of non-inferiority of the experimental arm with a margin of 10% (85% 5y-PFS in the control arm vs $>$75% in the experimental arm). With a 6-year of accrual period, inclusion of 405 patients in each arm would have 80% power to detect a HR of 1.77 using a one-sided log rank test with significance level of 0.025. The trial started in May 2011 and to date, 385 patients have been enrolled. The DSMC reviewed the trial in November 2012 and suggested that the trial continue as planned. Clinical trial information: NCT01358747.

TPS8616 **General Poster Session (Board #57E), Sun, 8:00 AM-11:45 AM**

ROCHOP study: A phase III randomized study of CHOP compared to romidepsin-CHOP in untreated peripheral T-cell lymphoma.

Richard Delarue, Pier Luigi Zinzani, Mark S. Hertzberg, Won Seog Kim, Dolores Caballero, Antonio Pezzutto, Marc Andre, Maria Gomes Da Silva, Philippe Gaulard, Bertrand Coiffier; Hopital Necker, Paris, France; Institute of Hematology and Clinical Oncology, Bologna, Italy; Westmead Hospital, Sydney, Australia; Samsung Medical Center, Seoul, South Korea; Hospital Clinico Universitario de Salamanca, Salamanca, Spain; Department of Hematology, Oncology, and Tumor Immunology, Charité University Medicine, Campus Benjamin Franklin, Berlin, Germany; Centre Hospitalier Universitaire Mont-Godinne, Dinant, Belgium; Instituto Portuges de Oncologia, Lisboa, Portugal; Hôpital Henri Mondor, Créteil, France; Hospices Civils de Lyon Sud, Pierre-Bénite, France

Background: Peripheral T-cell lymphomas (PTCL) account for 10-15% of lymphomas. They share an aggressive clinical behaviour and a poor prognosis when treated by CHOP-like regimen which is nevertheless consider as a standard because others regimens failed to demonstrate survival advantage. Romidepsin is a histone deacetylase inhibitor with promising results in PTCL. First trials showed a response rate of 38% in heavily pre-treated PTCL patients. These results were confirmed with 15% of patients reaching a CR/CRu, 89% of them without disease progression at 13 months. Adverse events include gastrointestinal, hematologic and asthenic conditions. A phase I study of romidepsin combined with CHOP was conducted by LYSA. A total of 18 patients were included. The recommended dose was 12 mg/m^2 administered at day 1 and day 8 of each cycle. **Methods:** Ro-CHOP study is an international phase III study comparing 6 cycles of CHOP21 with 6 cycles of romidepsin-CHOP21 (EUDRACT 2012-001580-68). Primary endpoint is Progression-Free Survival assessed independently. Secondary objectives include overall survival, other efficacy parameters, analysis of response rate according to ^{18}FDG-PET, safety, quality of life and biological ancillary studies. A total of 420 subjects aged from 18 to 80 years will be enrolled in the study. Main inclusion criteria are untreated PTCL whatever Ann Arbor stage and a performance status of 0-2. Main exclusion criteria are other subtypes of lymphoma, HTLV1 positivity, any cardiac abnormality, poor renal, hepatic and marrow functions unless related to lymphoma. Patients are randomized 1:1 between the two regimens. A stratification is performed with IPI score, age and histology. The first patient has been included in January 2013. A recruitment of 10.5 patients per month is anticipated, with a total duration of the study of 60 months. An update on enrolment will be presented at the meeting. Clinical trial information: 2012-001580-68.

TPS8617 General Poster Session (Board #58A), Sun, 8:00 AM-11:45 AM

A phase III, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of idelalisib (GS-1101) in combination with rituximab for previously treated indolent non-Hodgkin lymphomas (iNHL).

John Leonard, Pier Luigi Zinzani, Wojciech Jurczak, Mathias J. Rummel, Gilles A. Salles, Eva Kimby, Hendrik-Tobias Arkenau, Andrew John Davies, David Michael Johnson, Shelley Evans, Roger D. Dansey, Wayne R. Godfrey, Brad S. Kahl; Weill Cornell Medical College, New York, NY; Dipartimento di Ematologia e Scienze Oncologiche, Bologna, Italy; Department of Hematology, Collegium Medicum at the Jagiellonian University, Krakow, Poland; Universitaetsklinik, Giessen, Germany; Centre Hospitalier Lyon Sud, Oullins, France; Karolinska Institute at Huddinge University Hospital, Stockholm, Sweden; Sarah Cannon Research UK, London, United Kingdom; University of Southampton, Southampton, United Kingdom; Gilead Sciences, Inc., Seattle, WA; University of Wisconsin Carbone Cancer Center, Madison, WI

Background: PI3K-delta is critical for activation, proliferation and survival of B cells and plays a role in homing and retention in lymphoid tissues. PI3Kδ signaling is hyperactive in many B-cell malignancies. Idelalisib is a first-in-class, targeted, highly selective, oral inhibitor of PI3Kδ that reduces proliferation, enhances apoptosis, and inhibits homing and retention of malignant B cells in lymphoid tissues (Lannutti et al, 2011). Phase 1 trials demonstrated that idelalisib is highly active in pts with heavily pretreated iNHL: pts experienced reductions in disease-associated chemokines, profound and rapid reductions in lymphadenopathy, and durable clinical benefit with acceptable safety profile (de Vos et al, 2011). **Methods:** 375 pts with previously treated iNHL, who have measurable lymphadenopathy, have received prior anti-CD20-antibody-containing therapy, and who have iNHL that is not refractory to rituximab (R) are randomized in a 2:1 ratio into Arm A or Arm B. In Arm A, pts receive idelalisib at 150 mg BID continuously + R at 375 mg/m^2 (weekly x 4 then every 8 weeks x 4). In Arm B, pts receive placebo BID instead of idelalisib. Stratification factors include tumor type (follicular lymphoma vs others), tumor burden (high vs low), and time since completion of last prior therapy for iNHL ($<$18 months vs $\geq$18 months). The primary endpoint is PFS and key secondary endpoints include ORR, lymph node response rate, CR rate, and OS. This is an event-driven trial and primary endpoint evaluation will be based on independent central review. For the primary efficacy analysis, the difference in PFS between the treatment arms will be assessed in the ITT analysis set using Kaplan-Meier methods and the stratified log-rank test. The study opened for enrollment in Dec 2012 (NCT01732913). Clinical trial information: NCT01732913.

TPS8618 General Poster Session (Board #58B), Sun, 8:00 AM-11:45 AM

A phase III, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of idelalisib (GS-1101) in combination with bendamustine and rituximab for previously treated indolent non-Hodgkin lymphomas (iNHL).

Sven De Vos, Laurie Helen Sehn, Stephen P. Mulligan, Martin H. Dreyling, Mathias J. Rummel, Pier Luigi Zinzani, David Michael Johnson, Shelley Evans, Roger D. Dansey, Wayne R. Godfrey, Myron Stefan Czuczman; University of California, Los Angeles Medical Center, Los Angeles, CA; British Columbia Cancer Agency, Vancouver, BC, Canada; University of Sydney, Sydney, Australia; Department of Internal Medicine III, University of Munich, Munich, Germany; Universitaetsklinik, Giessen, Germany; University of Bologna, Bologna, Italy; Gilead Sciences, Inc., Seattle, WA; Roswell Park Cancer Institute, Buffalo, NY

Background: PI3K-delta is critical for activation, proliferation and survival of B cells and plays a role in homing and retention in lymphoid tissues. PI3Kδ signaling is hyperactive in many B-cell malignancies. Idelalisib is a first-in-class, selective, oral inhibitor of PI3Kδ that reduces proliferation, enhances apoptosis, and inhibits homing and retention of malignant B cells in lymphoid tissues (Lannutti et al, 2011). Phase I trials demonstrated that idelalisib is highly active in pts with heavily pretreated iNHL: pts experienced reductions in disease-associated chemokines, profound and rapid reductions in lymphadenopathy, and durable clinical benefit with an acceptable safety profile (de Vos et al, 2011). **Methods:** 450 pts with previously treated iNHL, who have measurable lymphadenopathy, require therapy for iNHL, have received prior anti-CD20-antibody-containing therapy and chemotherapy, and who have iNHL that is not refractory to bendamustine (B) are randomized in a 2:1 ratio into Arm A or B. In Arm A, pts receive idelalisib at 150 mg BID continuously + rituximab (R) at 375 mg/m^2 every 28 days for 6 cycles + B at 90 mg/m^2 on days 1 and 2 of each 28-d cycle. In Arm B, pts receive placebo BID instead of idelalisib. Stratification factors include tumor type (follicular lymphoma vs others), tumor burden (high vs low), and time since completion of last prior therapy for iNHL ($<$18 months vs $\geq$18 months). The primary endpoint is PFS, and key secondary endpoints include CR rate, ORR, lymph node response rate, and OS. This is an event-driven trial and primary endpoint evaluation will be based on independent central review. For the primary efficacy analysis, the difference in PFS between the treatment arms will be assessed in the ITT analysis set using Kaplan-Meier methods and the stratified log-rank test. The study opened for enrollment in Dec 2012 (NCT01732926). Clinical trial information: NCT01732926.

TPS8619 General Poster Session (Board #58C), Sun, 8:00 AM-11:45 AM

A randomized, multicenter, open-label, phase III study of the Bruton tyrosine kinase (BTK) inhibitor ibrutinib (PCI-32765) versus ofatumumab in patients (pts) with relapsed or refractory (RR) chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL): RESONATE.

John C. Byrd, Jacqueline Claudia Barrientos, Stephen Devereux, Jennifer R. Brown, Neil E. Kay, Nishitha M. Reddy, Susan Mary O'Brien, Thomas J. Kipps, Richard R. Furman, Stephen J. Schuster, Adrian Bloor, Devinder Singh Gill, Patrick Thornton, Claire E. Dearden, Ulrich Jäger, Christine Barker, Jennifer Lin, Lori A. Kunkel, Danelle Frances James, Peter Hillmen; The Ohio State University, Columbus, OH; Long Island Jewish Medical Center, Hyde Park, NY; King's College, London, United Kingdom; Dana-Farber Cancer Institute, Boston, MA; Mayo Clinic, Rochester, MN; Vanderbilt University Medical Center, Nashville, TN; Department of Leukemia, MD Anderson Cancer Center, Houston, TX; UC San Diego Moores Cancer Center, La Jolla, CA; Weill Cornell Medical College, New York, NY; Hospital of the University of Pennsylvania, Philadelphia, PA; The Christie Hospital NHS Foundation Trust, Manchester, United Kingdom; Princess Alexandra Hosptial, Woodville, Australia; Hermitage Medical Clinic, Dublin, Ireland; The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom; Medical University of Vienna, Vienna, Austria; Pharmacyclics, Inc., Sunnyvale, CA; Pharmacyclics, Sunnyvale, CA; St James's University Hospital, Leeds, United Kingdom

Background: Chemoimmunotherapy (CIT) treatment approaches such as FCR have markedly improved outcomes for CLL pts when administered as initial or second-line therapy. Despite this progress, virtually all pts relapse and effective salvage regimens that induce durable remissions or can be administered safely to elderly pts or those with comorbidities are lacking. BTK, an essential mediator of B-cell receptor signaling, is a novel target in CLL. Ibrutinib, a first-in class inhibitor of BTK, promotes apoptosis and inhibits proliferation, migration and adhesion in CLL cells. Phase II data of ibrutinib monotherapy in RR CLL demonstrated an estimated PFS and OS of 75% and 83% respectively at 26 months (Byrd Abst #189 ASH 2012). These findings confirmed BTK as an important target in CLL and supported initiation of a pivotal phase III study in pts with RR CLL/SLL. **Methods:** PCYC-1112-CA is an ongoing international Phase 3 randomized controlled study of ibrutinib versus ofatumumab for treatment of pts with RR CLL/SLL. The study is enrolling 350 planned pts in 9 countries. Pts are randomized 1:1 to receive ibrutinib 420 mg orally once daily or ofatumumab per the package insert at 300 mg for the first dose, then 2000 mg for a total of 12 doses over 24 weeks. Pts are stratified based on del 17p and disease refractory to purine analogs. Key inclusion criteria include RR CLL/SLL with $>=$ 1 prior line of therapy including pts who experienced a short remission duration to purine analog based CIT, pts who are older or have comorbidities, and pts with del 17p. Pts must have active disease meeting criterion for requiring therapy and measurable nodal disease by CT. Key exclusion criteria include Richter's transformation, stem cell transplantation within 6 months, GVHD or immunosuppression, platelet count $<$30,000 cells/ul or use of warfarin The primary objective of the study is PFS evaluated by an IRC. Other outcomes include ORR, OS, hematologic improvement, and safety. An independent DMC is monitoring the study. Clinical trial information: NCT01744691.