ASCO 2012 Multiple Myeloma Highlights

Summaries of Multiple Myeloma Presentations from the American Society of Clinical Oncology (ASCO) annual meeting held in Chicago, Illinois June 2–5, 2012



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ASCO 2012 Summaries of Multiple Myeloma Presentations

The American Society of Clinical Oncology (ASCO) 2012 conference brought together more than 25,000 experts and professionals in the field of oncology. At this event, nearly 66 myeloma-related abstracts were published to expand our knowledge around characteristics, risks, diagnostics, and treatment of multiple myeloma. The conference brought to light important work on efficacy and acceptability of new combination therapies, use of novel agents, and oral treatment options. This year's presentations and discussions particularly focused on therapy options for those with refractory and/or relapsed multiple myeloma, with encouraging data on the use of antibodies and proteasome inhibitors in that setting. Summarized here are the highlights from these presentations, following The International Myeloma Foundation's 10 STEPS TO BETTER CARE[™] framework.

Step 1: Know what you're dealing with. Get the correct diagnosis.

Several noteworthy abstracts that fell into this category looked at clinical and psychosocial characteristics of multiple myeloma. One was a presentation from the Asian Myeloma Network (AMN) to increase the body of knowledge on general clinical characteristics of patients treated for multiple myeloma, and the other was a study on the differences of quality of life indicators among various racial groups. Also relevant to this category was a poster on the apparent need for more accurate models to determine risks in progression from smoldering myeloma to multiple myeloma.

8097: Clinical profile of multiple myeloma in Asia: An Asian Myeloma Network (AMN) study.

This abstract by lead author Jae Hoon Lee (Gachon University Medical School, Incheon, Republic of Korea) on behalf of the AMN presented findings of a retrospective analysis of multiple myeloma patients from 21 health centers in seven Asian countries. Clinical characteristics of 2,969 patients were described and overall survival and prognostics were analyzed for 2,273 patients. OS observed was 54 months (patients diagnosed before the year 2000 had a lower OS rate). For the 513 patients who

underwent a transplant, longer survival of 84 months was observed; OS was nearly half (45 months) for those who had not received a transplant. First-line treatment of 2,339 patients was analyzed; response rate was 71%, with 30% VGPR or better, defined as a reduction in monoclonal protein of at least 90%. Bortezomib (Velcade[®]), thalidomide or lenalidomide (Revlimid[®]), combined for 32.5% of all 2,339 patients without difference in response rate according to combination.

E18556: Race- and health-related quality of life among patients newly diagnosed with multiple myeloma.

Chris Pashos (Cedars-Sinai Medical Center, Los Angeles, USA) presented findings of a study which took a closer look at the association of race and multiple myeloma by evaluating whether health-related quality of life indicators, of patients initiating treatment for myeloma varied by race. Of the 1,144 patients from the Connect MM (a prospective U.S. observational registry initiated in September 2009) who completed a Brief Pain Inventory, EQ-5D, and Functional Assessment of Cancer Therapy-Multiple Myeloma, 82% were white, 13% were black, and 6% were of another race (multiple myeloma stage did not differ widely between cohorts). African American patients reported less anxiety and depression and better emotional well-being than non-African Americans. Baseline health-related quality of life, prior to initiation of treatment, may vary by patient race with respect to emotional well-being, and specifically anxiety/depression.

8088: A prospective clinical study evaluating current models for risk of progression from smoldering multiple myeloma (SMM) to multiple myeloma (MM).

Benjamin Cherry (NCI, Bethesda, Maryland, USA) presented his work on a prospective natural history study evaluating two widely used models, the Mayo Clinic's and the Spanish PETHEMA's, to assess risk of progression from SMM to MM. He determined risk classifications for 70 patients using each model and realized significant disagreement in classifications between the two (e.g., among the 31 SMM patients determined as "high risk" by Spanish criteria, only two were classified as high risk by Mayo). Cherry's findings underscore the need for biologically-derived models to predict progression, which are critical for counseling individual patients and for the development of early treatment to prevent or delay progression to MM.

Step 2: Tests you really need [N/A]

Step 3: Initial treatment options

Encouraging outcomes of phase I-II trials assessing carfilzomib in various combination regimens to treat newly diagnosed multiple myeloma patients were reported at this year's conference. One oral presentation illustrated promising findings of a phase I-II trial combining carfilzomib with melphalan-prednisone to treat elderly myeloma patients. A new four-drug regimen called CYCLONE (including cyclophosphamide, carfilzomib, thalidomide, and dexamethasone) showed success among patients hoping to effectively collect stem cells. Additionally, there was one study reporting positive findings of long-term use of the combination of carfilzomib, lenalidomide, and dexamethasone.

Another important study is the first to look at the oral proteasome inhibitor, MLN9708, in combination with lenalidomide and dexamethasone in treatment of newly diagnosed patients. A maximum tolerated dose and positive patient response outcomes were reported.

8009: Phase I/II study of carfilzomib plus melphalan-prednisone (CMP) in elderly patients with de novo multiple myeloma.

Brigitte Kolb (Institute for Myeloma and Bone Cancer Research, West Hollywood, California, USA) looked at combining melphalan-prednisone with carfilzomib and evaluated toxicity and effectiveness in an elderly population – a group that cannot engage in high-dose treatment. Twenty-four patients enrolled in phase I were given varying levels of carfilzomib to assess maximum tolerated dose (MTD). To determine MTD, dosage level of carfilzomib was increased over three cohorts and toxicities/response rates evaluated. An additional 16 patients were included in phase II, assessing effectiveness of level 3 carfilzomib (which was given at 36mg/m² per dose). Altogether, 43 patients have been enrolled in the phase I/II studies; overall response rate was 89% including 40% at least VGPR. Event-free survival was estimated at 80%, with toxicity levels estimated at 6%. Efficacy in high-risk patients and longer follow-up data will be reported in the next year.

8010: A phase I/II trial of cyclophosphamide, carfilzomib, thalidomide, and dexamethasone (CYCLONE) in patients with newly diagnosed multiple myeloma.

Joseph Mikhael (Mayo Clinic, Scottsdale, Arizona, USA) presented his work on including carfilzomib in a fourdrug regimen designed for patients progressing to a stem cell transplant (to ensure effective collection of cells). In phase I, three patients were treated with CYCLONE (carfilzomib is given intravenously; the other three orally) and all responded well. Data from 27 enrollees from phase II have been collected; a 96% overall response rate (ORR) was reported, with 75% having a VGPR. Grade 3 toxicities were reported in 50% of patients; grade 4 toxicities were reported in 20% (these included arrhythmia, fatigue, muscle weakness, neutropenia, lymphopenia and thrombocytopenia). Twenty-six out of 27 patients are still alive. All patients advancing to stem cell harvest successfully collected stem cells (14 total). Seven cases of grade 1 peripheral neuropathy (PN) were reported. An even further depth of response was seen in patients posttransplant. In future work, the carfilzomib dose will be increased, as MTD was not reached in this trial.

8011: Stringent complete response in patients with newly diagnosed multiple myeloma treated with carfilzomib, lenalidomide, and dexamethasone.

Andrzej J. Jakubowiak (University of Iowa, Iowa City, Iowa, USA) examined long follow-up responses to the combination treatment carfilzomib, lenalidomide, and dexamethasone. Fifty-three newly diagnosed patients were treated in a 28-day cycle with carfilzomib (20–36 mg/m² intravenously on days 1, 2, 8, 9, 15, 16), lenalidomide (25 mg orally, days 1 through 21) and dexamethasone (40/20mg orally, weekly). After four cycles of this treatment patients achieving a positive result could collect stem cells (and 35 patients did). After 8 cycles patients received 16 maintenance therapy cycles (with modified carfilzomib). All 53 patients were evaluable; 81% were achieving VGPR or better, 62% were achieving complete response (CR), and 42% were achieving stringent complete response (sCR). The most common all-grade adverse events included lymphopenia (30%), leukopenia (26%), fatigue (25%), and PN (11%). Extended carfilzomib, lenalidomide, and dexamethasone is well tolerated and resulted in deep response.

8033: Oral weekly MLN9708, an investigational proteasome inhibitor, in combination with lenalidomide and dexamethasone in patients with previously untreated multiple myeloma: A phase I/II study.

Paul Richardson (Dana-Farber Cancer Institute, Boston, Massachusetts, USA) presented phase I/II results of a study on feasibility and effectiveness of MLN9708, an oral, reversible proteasome inhibitor, combined with lenalidomide and dexamethasone in treatment of newly diagnosed multiple myeloma patients. Phase I enrolled 15 patients and aimed to determine safety and MTD (determined to be 4.0 mg weekly). Phase II enrolled 50 patients and aimed to establish efficacy. Of the 65 study participants, one died due to pneumonia, 64 completed at least one cycle of treatment, and 46 received a median of 5 cycles of treatment. Of the 46 patients evaluated, the ORR was 98%, with 21% VGPR and 12% CR. The combination was well tolerated: a skin rash was observed in about 1/3 of patients, which proved to be manageable with ointment and steroids. Otherwise, side effects were typical of the lenalidomide and dexamethasone combination. This is an active and tolerable drug combination in newly diagnosed multiple myeloma patients.

Step 4: Supportive care and how to get it

In this category, there were several important findings that contribute to clinical knowledge around patient risks and preferences. Two studies highlighted here explored the development of second primary malignancy in a population of patients exposed to lenalidomide; one found more risk associated with demographics than with this drug; another found that myeloma is actually oftentimes itself the second malignancy. One study, supporting a patient-focused approach, took a closer look at intravenous (IV) versus subcutaneous (SQ) administration of bortezomib, and found that patients preferred SQ administration despite some associated adverse side effects.

8038: Risk factors for development of second primary malignancies (SPM) after autologous stem cell transplant (ASCT) for multiple myeloma.

Amrita Krishnan (City of Hope Cancer Center, Duarte, California, USA) evaluated the potential treatment risk of second primary malignancy post-stem cell transplant in patients on lenalidomide maintenance. Studies have suggested an increased incidence of second primary malignancy post-stem cell transplant in patients on lenalidomide maintenance. From 1989 to 2009 a retrospective cohort study of 841 multiple myeloma patients who underwent at least one stem cell transplant at City of Hope were assessed; 60 cases with second primary malignancies were identified and compared to 60 patients who underwent transplantation and did not develop second malignancies. Factors examined included age, race, sex, therapeutic exposures, and disease status at transplantation. Analyses revealed non-Hispanic whites and older age (>55) at diagnosis are associated with an increased risk of developing second primary malignancies. Only cumulative thalidomide exposure demonstrated a trend toward second malignancies. Six patients (3 cases and 3 controls) were exposed to lenalidomide prior to development of malignancies. Krishnan's study found that second primary malignancies are more associated with demographics (which may be associated with the fact that patients are living longer on treatment than before) than with lenalidomide maintenance treatment. She recommends the potential use of thalidomide in shorter doses to prevent risk of malignancy with prolonged thalidomide exposure.

8090: Retrospective analysis of second malignancies in patients with multiple myeloma.

Giampaolo Talamo (Penn State Hershey Cancer Institute, Philadelphia, Pennsylvania, USA) followed up on the previous reports of second malignancies with lenalidomide in multiple myeloma patients. Talamo's study retrospectively analyzed medical records of 320 multiple myeloma patients followed at Penn State Hershey Cancer Institute (2006 to 2010), 43 of whom were found to have second malignancies, 5 a third cancer, and one with 4 cancers. Second malignancies included prostate, breast, leukemia, colorectal, melanoma, lung, uterine, bladder, kidney, pancreatic, testicular, myeloproliferative disorders, and sarcoma. Of 50 cancers, 36 (72%) developed before multiple myeloma diagnosis and 14 after. Findings suggest that multiple myeloma was oftentimes the second malignancy, and the use of lenalidomide in this patient population could not be indicated as a possible carcinogenic factor for the majority of patients with second malignancies.

E18553: An evaluation of efficiency, safety, tolerability, patient satisfaction, and preference of subcutaneous (SQ) versus intravenous (IV) bortezomib administration in patients with multiple myeloma.

Meagan Barbee (Emory University Clinic, Atlanta, Georgia) assessed clinic practice and patient preference of those who are treated with bortezomib by SQ injection. Barbee also looked at PN in treatment-naïve patients. This was a retrospective efficiency study that assessed 92 patients over 1,458 clinic visits who had received six or more doses of bortezomib either SQ or IV in 2011. Chair and overall visit time were assessed, patients in each group were surveyed for satisfaction, and patient charts were reviewed to identify neuropathy. Average chair time was 54 minutes less and overall clinic visit was 46 minutes less with SQ than with IV bortezomib. Twenty-eight patients who had had at least one dose of both IV and SQ botezomib completed the survey, of which 19 preferred SQ, 11 experienced injection site reactions, and 14 agreed they would feel comfortable with self-administration. One of the 14 treatment-naïve patients had PN and 3 had worsened neuropathy from baseline. SQ administration of bortezomib could provide a preferable experience for patients, although side effects should be carefully monitored.

Step 5: Transplant
[N/A]

Step 6: Response Assessment

Two poster presentations increased knowledge around this category. One was an assessment of how patients with the chromosomal abnormality t(11;14) fare on treatment versus those without. Another provided longer follow-up data of patients treated with lenalidomide and dexamethasone; this study further proved the effective-ness of this regimen.

8040: Impact of t (11;14) on the outcome of autologous hematopoietic cell transplantation (Auto-HCT) in multiple myeloma.

Koji Sasaki (Beth Israel Medical Center, New York, New York, USA) reported findings on a retrospective chart review of multiple myeloma patients who underwent high-dose chemotherapy followed by cytogenetic or florescent in situ hybridization (FISH) analysis before transplant from 2000 to 2010. Sakaki compared progression-free survival (PFS) and OS of patients with t(11;14) to those without chromosomal abnormalities. Median PFS in patients with t(11;14) and normal karyotype was 15.7 months and 35.9 months, respectively, and median OS was 51.4 months and 88.4 months, respectively. These results will lead us to reconsider the previously held view that t(11;14) was a genetic mutation that conferred low or standard risk.

8096: Long-term outcome with lenalidomide and dexamethasone therapy for newly diagnosed multiple myeloma.

Geetika Srivastava (Mayo Clinic, Rochester, Minnesota, USA) presented findings from a study on long-term outcomes of the drug combination lenalidomide and dexamethasone. Newly diagnosed multiple myeloma patients at Mayo who received the combination as initial therapy were followed for a median of 4 years. Of the 286 patients, 203 were alive at the time of last follow-up. Overall response was 72% and 26% had VGPR or better to this combined treatment. The median OS for the entire cohort from diagnosis was 7.4 years, and the estimated 5-year survival was 67%. This study further supports the efficacy of lenalidomide and dexamethasone at diagnosis and relapse and confirms the survival improvements seen in multiple myeloma patients in the last decade.

Step 7: Consolidation and/or Maintenance

One study that particularly focused on maintenance therapy is highlighted here. This study looked at a lenalidomide, bortezomib, and dexamethasone combination maintenance regimen in a high-risk population and found that it was most effective if given following an early transplant.

8100: Survival outcomes of early autologous stem cell transplant (ASCT) followed by lenalidomide, bortezomib, and dexamethasone (RVD) maintenance in patients with high-risk multiple myeloma.

Jonathan Kaufman (Emory University Clinic, Atlanta, Georgia, USA) reported on his trial, which examined the possibility of improving treatment response rates for multiple myeloma patients with high-risk genetic profiles. Thirty-seven patients with high-risk features (e.g., del(17p), t(4;14), t(14;16), hypodiploidy, del(13), complex karyotype, plasma cell leukemia [PCL]) were assessed after completing induction therapy, a stem cell transplant, and lenalidomide, bortezomib, and dexamethasone maintenance. Seven out of 36 patients progressed while on this maintenance. Some grade 1 and 2 toxicities during maintenance schedule were recorded (40% PN, 10% rash, 78% fatigue). Early transplant followed by the maintenance regimen delivered a strong response in this high-risk group, preventing early relapse and showing few adverse events. The median PFS and OS have not yet been reached. This maintenance regimen is well tolerated and shows promise.

Step 8: Monitoring without mystery [N/A]

Step 9: Relapse – Do you need a change in treatment?

Research in this area is advancing by leaps and bounds. Effective treatment options described in detail here include second autologous stem cell transplantation, metronomic therapy, and a few others.

8092: Second autologous stem cell transplantation as a strategy for management of relapsed multiple myeloma.

Wilson Gonsalvez (Mayo Clinic, Rochester, Minnesota, USA) presented findings on an acceptability study of second autologous stem cell transplant in relapsed and/ or refractory multiple myeloma patients. PFS and OS of 98 patients who underwent a second transplant were assessed. Median patient age of those enrolled was 60, and median number of years between first and second transplant was 4. The study group followed participants

for about 5 years after second transplant. A partial response (PR is defined as >/= 50% reduction in m-protein) or better was seen in 90%; 60% exhibited VGPR. OS was estimated at 33 months. Shorter survival was linked to shorter duration of response to first transplant, higher plasma cell labeling index, and more regimens used prior to the second transplant. A second autologous stem cell transplant may be used as an effective therapy for patients relapsing, as it provides a meaningful duration of response and appears to be well tolerated.

8041: Metronomic therapy for heavily pretreated relapsed/refractory multiple myeloma.

Xenofon Papanikolaou (Univerity of Arkansas Myeloma Institute for Research and Therapy, Little Rock, Arkansas, USA) presented findings on an analysis of metronomicallyscheduled therapy to manage disease in refractory and/or relapsed multiple myeloma patients. Of 187 patients who were treated with metronomic therapy between 2004 and 2011, 79% had previously undergone transplantation, 99% had prior exposure to bortezomib, 98% to an IMiD. The median number of complete therapy cycles was 1 (range 1–5). The ORR was 65%, VGPR was 7%, and CR was 6%. Hematological toxicities were practically universal (grade 4 leukopenia, anemia, and thrombocytopenia) and grade 3-4 non-hematological toxicities included hypophosphatemia, hypocalcemia, fatigue/malaise. With careful management of such toxicities, metronomic therapy is a promising treatment in heavily pretreated relapsed/refractory multiple myeloma patients.

Steps 9/10: Relapse – Do you need a change in treatment? / New Trials – How to find them?

At this year's ASCO meeting, there were quite a few presentations on responses of patients with relapsed and/ or refractory multiple myeloma in ongoing clinical trials. Several treatment regimens are showing promise among relapsed and/or refractory patients. These include the pomalidomide and low-dexamathosone combination; panobinostat with bortezomib and dexamethasone; pomalidomide and low-dexamathosone; MLN9708; carfilzomib; clarithromycin, pomalidomide, and dexamethasone; and the monoclonal antibodies elotuzumab, siltuximab and daratumumab. Novel agents and a focus on oral administration were of particular interest here, telling us, as Ola Landgren of the National Cancer Institute said, "how we will be treating this cancer in the coming years."

TPS8112: ELOQUENT-2: A phase III, randomized, open-label trial of lenalidomide/ dexamethasone with or without elotuzumab in relapsed or refractory multiple myeloma (CA204-004).

Sagar Lonial (Emory University Clinic, Atlanta, Georgia, USA) gave a brief update on his randomized, open-label phase III trial to determine if the addition of elotuzumab, a humanized monoclonal IgG1 antibody, to lenalidomide/ dexamethasone will improve survival in patients with relapsed or refractory multiple myeloma. Results will be compared to outcomes of lenalidomide/dexamethasone alone. ORR and OS, safety, response time, quality of life indicators, and pharmacokinetics and immunogenicity of Elo will be assessed. To date, 107 patients have enrolled and 68 patients were treated.

E18572: Phase III study of panobinostat with bortezomib and dexamethasone in patients with relapsed multiple myeloma (PANORAMA 1).

Jesús San-Miguel (University of Salamanca, Salamanca, Spain) updated attendees on progress of a blinded safety analysis from PANORAMA 1, an international, randomized, double-blind, phase III study of pan-deacetylase inhibitor panobinostat (or placebo) with bortezomib and dexamethasone in patients with relapsed or refractory myeloma. Preliminary demographic and blinded safety data from 536 patients (median age 63), who had 1-3 prior therapies (not including bortezomib-refractory patients), were assessed. Treatment is ongoing in 257. Adverse events include high-grade (3/4) thrombocytopenia (36.2%), diarrhea (14.5%), anemia (13.0%), fatigue (12.2%), neutropenia (11.4%), and hypokalemia (11.0%). Peripheral neuropathy was observed in about 25% of patients at any grade. Preliminary results for 525 treated patients indicate a comparable safety profile to the bortezomib and dexamethasone. The data monitoring committee recommended the study continue as planned.

8016: Pomalidomide with or without low-dose dexamethasone in patients with relapsed/ refractory multiple myeloma: Outcomes in patients refractory to lenalidomide and/or bortezomib.

Ravi Vij (Washington University School of Medicine, St. Louis, Missouri, USA) presented an analysis evaluating pomalidomide and low-dose dexamathosone regimen outcomes among patients who had relapsed following and/or were refractory to bortezomib, lenalidomide, or both, as well those who had relapsed following an autologous transplant. In this phase II randomized, balanced trial, 108 patients were given pomalidomide (4 mg/day orally on days 1-21 of a 28-day cycle) alone and 113 were given a combination of pomalidomide with lowdose dexamethasone (40 mg/week). A slightly longer PFS and OS was apparent in those on the combination regimen (3.8 versus 2.5, and 14.4 versus 13.6 months). ORR among the group of patients receiving the combination therapy was 30%, and response rates were similar regardless of type of prior refractoriness, suggesting lack of cross-resistance between pomalidomide and lenalidomide. Toxicities of the combination were mostly hematologic (neutropenia, thrombocytopenia and anemia). A phase III trial is underway.

8018: Phase II, randomized, double-blind, placebo-controlled study comparing siltuximab plus bortezomib versus bortezomib alone in patients with relapsed/refractory multiple myeloma.

Robert Orlowski (University of Texas MD Anderson Cancer Center, Houston, Texas, USA) presented findings on his study looking at the effectiveness of siltuximab in combination with bortezomib in refractory and/or relapsed multiple myeloma patients. Orlowski reported on 286 randomized patients receiving either siltuximab with bortezomib or placebo with bortezomib (both intravenously). PFS in the combination group was 8.1 months (placebo was 7.6). Response rates were 55% in patients on siltuximab with bortezomib and 47% on placebo/bortezomib; CR rates were 11% and 7%, respectively. Adverse events were higher in the combination group, and included grade 3 or higher neutropenia (49%) and thrombocytopenia (48%). However, it is important to note that less anemia was observed in the combination group.

8019: Daratumumab, a CD38 MAb, for the treatment of relapsed/refractory multiple myeloma patients: Preliminary efficacy data from a multicenter phase I/II study.

Torben Plesner (Vejle Hospital, Vejle, Denmark) presented on an ongoing first-in-human dose-escalation study of daratumumab in relapsed and/or refractory myeloma (after at least two different prior lines of therapy). Among 18 of 29 heavily pre-treated multiple myeloma patients receiving eight weeks of daratumumab (in doses up to 16mg/kg), a marked reduction in M-component has been observed. Daratumab's MTD was not established; 7 patients achieved PR. Grade 3/4 adverse events included anemia, thrombocytopenia, and bronchospasm. Continuous studies to determine an MTD, safety profile, and efficacy are planned.

8020: A randomized phase II study of elotuzumab with lenalidomide and low-dose dexamethasone in patients with relapsed/ refractory multiple myeloma.

Philippe Moreau (University of Nantes, Nantes, France) presented efficacy findings from a phase II study of the combination of elotuzumab (intravenously administered) with lenalidomide and low-dose dexamethasone in relapsed and/or refractory multiple myeloma. Among 72 patients enrolled, ORR was 82%, including 48% or better VGPR. This combination showed encouraging activity in patients with high-risk cytogenetics (response rate in this group was 80%) and/or Stage 2–3 myeloma (response rate was 81%). The most common grade 3/4 toxicities were neutropenia (16%), lymphopenia (16%), and thrombocytopenia (16%). This drug combination demonstrates promising results in relapsed and/or refractory patients, with moderate toxicity. Phase III trials are forthcoming.

8034: Weekly dosing of the investigational oral proteasome inhibitor MLN9708 in patients with relapsed/refractory multiple myeloma: phase I study.

Shaji Kumar (Mayo Clinic, Rochester, Minnesota, USA) expanded on the study he presented at ASH 2011 on weekly dosing of the reversible proteasome inhibitor

MLN9708. At this year's ASCO, he reported on the safety, pharmacokinetics, and preliminary responses with weekly oral MLN9708 in patients with relapsed and/or refractory (to either bortezomib, thalidomide/lenalidomide, and corticosteroids) multiple myeloma patients. The MTD among 36 patients enrolled was determined at 2.97 mg/m². Overall, 69% of patients had drug-related adverse effects; 28% had grade 3 and above thrombocy-topenia (17%), diarrhea (11%), nausea, neutropenia, and fatigue (each 8%). Peripheral neuropathy was low (8%). Current data suggest weekly oral MLN9708 is generally well tolerated, and shows signs of antitumor activity.

8035: Response rates to single-agent carfilzomib in patients refractory or intolerant to both bortezomib and immunomodulators in trial PX-171-003-A1.

David Siegel (Hackensack University Medical Center, Hackensack, New Jersey, USA) presented an analysis of responses to carfilzomib in so-called "double refractory" patients including those intolerant of or refractory to all 5 approved classes of myeloma treatments. Carfilzomib was given on days 1, 2, 8, 9, 15, 16 of 28-day cycles at 20 mg/m² in the first cycle and 27 mg/m² in cycles 2-12. Patients with double-refractory/intolerant disease were analyzed, as were patients with disease refractory to all approved treatments. The ORR to single-agent carfilzomib among these patients was 22.9%, with median duration of response of 7.8 months (these indicators were similar among those with double-refractory and intolerant disease). Carfilzomib demonstrated effective and durable responses in patients with double-refractory/ intolerant multiple myeloma or disease refractory to all five approved classes of treatments.

8036: Clarithromycin, pomalidomide, and dexamethasone (ClaPD) in relapsed or refractory multiple myeloma.

Adrianna Rossi (Weill Cornell Medical College/Presbyterian Hospital, New York, New York, USA) presented her findings on clarithromycin's enhancement of pomalidomide and dexamethasone in relapsed and/or refractory multiple myeloma patients. This is an updated single-arm, phase II study that enrolled 80 patients with relapsed and/or refractory multiple myeloma who had at least three prior treatments, one of which was lenalidomide. This presentation reported on 66 patients. Clarithromycin was given at 500mg twice daily, dexamethasone at 40mg weekly; and pomalidomide at 4mg for days 1–21 of a 28-day cycle. Bone marrow biopsy with skeletal imaging was used to assess patient response to treatment. Of the 66 patients who completed 1 cycle or more, 33% exhibited a PR and 5% had a sCR. The ORR was 60%. Rossi reported that the toxicities were mostly hematologic (fatigue was most often reported). These are encouraging results for a high-risk population.

8014: Bendamustine, bortezomib, and dexamethasone (BVD) in elderly patients with relapsed/refractory multiple myeloma (RRMM): The Intergroupe Francophone du Myélome (IFM) 2009-01 protocol.

Philippe Rodon (Centre Hospitalier, Blois, France) conducted a phase II trial combining bendamustine, bortezomib, and dexamethasone in elderly relapsed and/ or refractory multiple myeloma patients. Of 73 patients enrolled, ORR was 67.1%, with 8% experiencing CR, 12% VGPR, and 34% PR. PN occurred in close to 40% of the study population. Other adverse events included grade 3–4 neutropenia (among 16 patients), sepsis (among 12), and gastrointestinal side effects (among 8). Treatment was stopped in 23 patients.

Conclusion

Although the annual meeting of the American Society of Clinical Oncology (ASCO) did not have the number or scope of abstracts presented at the meeting of the American Society of Hematology (ASH) in December 2011, there were nonetheless several important presentations, some of which will undoubtedly give rise to further research.

New data are moving the field forward and helping to identify the best approaches to diagnosis and therapy for myeloma patients worldwide. To keep abreast of the latest information, visit the IMF website myeloma.org, subscribe to the quarterly newsletter *Myeloma Today* and the weekly e-newsletter *Myeloma Minute*, download the IMF's Myeloma Post iPad app free of charge from the iTunes Store, and contact the IMF Hotline at 800-452-CURE (2873).

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