Highlights of Multiple Myeloma at the Annual Meeting of American Society of Hematology, 2016

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Abstract This review discusses the landmark studies in the field of multiple myeloma (MM) which were presented at American society of hematology annual meeting, 2016. There were contrary results from two large phase III trials (one from US and one from Europe) that evaluated the role of additional interventions like tandem autologous transplant (ASCT) and consolidation after induction therapy followed by ASCT in newly diagnosed MM (NDMM) patients, but there were critical differences between the two studies. Novel agents like carfilzomib and ixazomib proved to be of benefit when used as induction and post ASCT consolidation and maintenance in NDMM. The early data on subcutaneous administration of daratumumab (DARA) looked promising. The high rate of minimal residual disease negativity after using DARA even in relapsed/refractory MM (RRMM) setting reinforces the benefit of targeting CD38. The responses seen with venetoclax in RRMM with t(11;14)(high BCL-2, low BCL-XL and MCL-1) and selinexor in penta-refractory myeloma which fulfills the FDA category of unmet need, opens up newer options for these patients. BCMA CAR-T infusion shows encouraging results in advanced refractory myeloma patients.

Hematologists, oncologists, pathologists, scientists and trainees from all over the world attended the annual meeting of American Society of Hematology (ASH) at San Diego from 3rd to 6th December 2016. The meeting featured advances in clinical and translational research, evaluation of new diagnostic techniques and novel therapeutic approaches in patients with hematological disorders including malignancies. Various landmark studies were discussed in the field of multiple myeloma (MM) which are summarized in this review.

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Genetic and Molecular Characterization

An interesting German study addressed the sequential clonal evolution of asymptomatic MM. CD138-purified plasma cell samples of 2369 consecutive patients with monoclonal gammopathy of unknown significance (MGUS), smoldering and symptomatic MM were investigated by fluorescence-in situ-hybridization (FISH), 40% of whom also underwent gene expression profiling. Up-front tumor mass, plasma cell accumulation rate, alterations in gene expression and presence of chromosomal aberrations, i.e. t(4;14), deletions of 13q14, 17p13, 8p21, gains of 1q21, and hyperdiploidy, all drive and predict evolution of asymptomatic MM. It was also found that molecularly, all chromosomal aberrations, most chromosomal mutations and transcriptomic changes including NRAS, KRAS, DIS3, HIST1H1E are already present in MGUS or smoldering MM [1]. Hence, it can be inferred that the mechanisms (except hyperdiploidy) that drive progression after treatment also influence evolution from asymptomatic to symptomatic myeloma.

Treatment of Newly-Diagnosed Transplant Eligible Multiple Myeloma

The Myeloma XI study is the first randomized study to evaluate the impact of a response-adapted approach to induction for newly diagnosed MM (NDMM) patients. Patients who received an immunomodulator (IMiD) based triplet (cyclophosphamide, thalidomide and dexamethasone, CTD or lenalidomide, cyclophosphamide and dexamethasone, RCD)

for a minimum of 4 (transplant eligible) or 6 (transplant ineligible) cycles and to maximum response, were assessed for response to initial therapy. A total of 581 patients who achieved a suboptimal response (minimal or partial response) were randomized between further induction therapy with VCD (bortezomib, cyclophosphamide and dexamethasone) and no further induction therapy. Overall, the sequential use of VCD significantly improved median progression free survival (PFS) from 24 to 30 months (HR = 0.67, 95% CI 0.53–0.85, $P = 0.0005$), probably due to upgrading of response in 41% of the evaluable patients. The benefit in PFS was seen predominantly in transplant eligible patients and the improvement in response rates (RR) among these patients persisted after autologous stem cell transplant (ASCT) [2]. The study also randomized patients to receive lenalidomide versus no maintenance and found that lenalidomide maintenance leads to a 55% reduction in risk of progression or death. This PFS benefit was seen in both transplant eligible and ineligible patients and is independent of induction therapy and its response. Importantly, 72 s primary malignancies (SPM) were observed during follow-up; among which 48 occurred in lenalidomide arm [3]. Hence, it could be deduced that the use of a response-adapted therapy based on the use of anti-myeloma agent with a different mode of action and the use of lenalidomide in maintenance can help to delay progression in NDMM patients.

Two major studies evaluated the role of additional interventions including tandem ASCT and consolidation post ASCT in NDMM patients who underwent induction therapy followed by transplant.

The US StaMINA trial was a large phase III study of 758 patients who had already received induction followed by a single ASCT (with melphalan 200 mg/m²) and were randomized 1:1:1 to receive four cycles of VRD consolidation (lenalidomide, dexamethasone and bortezomib; ACM), versus tandem ASCT (with melphalan 200 mg/m²; TAM) versus no further intervention (AM). All arms went on receive lenalidomide maintenance (until progression) with dose modifications for toxicities. The results showed that there was no statistically significant difference in the estimated 38-months probabilities for PFS (ACM, 57%; TAM, 56%; AM, 52%; ACM vs. TAM $P = 0.75$; ACM vs. AM $P = 0.21$; TAM vs. AM $P = 0.37$) as well as overall survival (OS; ACM, 86%; TAM, 82%; AM, 83%) among the 3 arms. Also, it was noted that the cumulative incidence for first SPM was 6, 5.9 and 4% for the ACM, TAM, and AM arms, respectively [4].

The European Myeloma Network study (EMN02/HO95) was a phases III study of 1510 NDMM patients whose updated results were presented in the congress. The patients underwent induction with 3–4 cycles of VCD followed by the first randomization (R1) into standard-dose intensification with VMP (bortezomib, melphalan and

prednisone) versus high-dose intensification with melphalan at 200 mg/m² (HDM) followed by ASCT. In centers with a policy of double ASCT, patients were randomized in a 1:1:1 ratio to either VMP or single ASCT (ASCT-1) or two sequential courses of HDM and tandem ASCT (ASCT-2). This was followed by second randomization (R2) to consolidation with two cycles of VRD versus no consolidation. Lenalidomide maintenance was given until progression or toxicity in both arms. Among the 1192 patients eligible for R1, the median PFS was 44 months in the VMP arm and was not reached (NR) in the HDM arm (HR = 0.73, 95% CI 0.59–0.90, $P = 0.003$). The advantage in benefit with HDM was retained across predefined subgroups, including various revised international staging system (RISS) stages, standard-risk or high-risk cytogenetic profile [5]. Among the 614 eligible patients who received treatment in centers with a double intensification policy, the median PFS was 45 months in the ASCT-1 arm and was NR in the ASCT-2 arm (HR = 0.66, 95% CI 0.45–0.96, $P = 0.030$). The PFS benefit with tandem ASCT was retained across predefined subgroups, including patients with β_2 -microglobulin >3.5 mg/L, bone marrow plasma cells >60%, LDH values above the upper limits, RISS stage II and high-risk cytogenetics [6]. Of the 903 patients eligible for R2, the PFS from R2 with adjustment for R1 was prolonged in VRD consolidation arm (HR = 0.78; 95% CI 0.61–1.00; $P = 0.045$), a benefit retained across predefined subgroups with RISS stage III and low-risk cytogenetics, but not in patients with high-risk cytogenetics [7].

Hence, while the US trial showed that the addition of VRD consolidation or tandem ASCT was not superior to a single ASCT followed by lenalidomide maintenance in NDMM patients, the European trial showed contrary results. However, while the US trial utilized various induction therapies (majority being VRD), the European study used VCD in all patients. In addition, the non-compliance rate for tandem ASCT in StaMINA trial was 32%.

Another important study compared the outcomes of NDMM patients with normal/mild renal insufficiency (RI; $n = 1240$), moderate RI ($n = 185$) and severe RI ($n = 67$) who underwent ASCT between 2008 and 2013. Thirty-five patients were on dialysis prior to ASCT, among whom 85% achieved dialysis independence post ASCT. The probability of PFS ($P = 0.42$) and OS ($P = 0.69$) at 5 years was not statistically different in patients with normal/mild, moderate and severe RI. For patients with moderate RI, the probability of PFS at 5 years was higher for those receiving conditioning melphalan at 140 versus 200 mg/m² (18 vs. 46%, $P = 0.009$) while the probability of OS was similar (67 vs. 68%, $P = 0.52$). For patients with severe RI, the probability of PFS at 5 years as well as OS was similar for patients conditioned with melphalan at 140 and 200 mg/m²

(PFS 25% vs. 32%, $P = 0.37$; OS 63% vs. 55%, $P = 0.65$) [8].

An analysis of 5077 patients from the Center for International Blood and Marrow Transplant Research (CIBMTR) database evaluated the trends of upfront ASCT in the United States between 2004 and 2014. The outcomes have improved over the last decade. VRD is currently the most common induction regimen since 2010. Approximately half of patients are placed on maintenance treatment after ASCT, with lenalidomide as the most frequently used agent [9].

Treatment of Newly-Diagnosed Transplant Ineligible Multiple Myeloma

The final analysis of the pivotal FIRST trial evaluated the outcomes of initial treatment with continuous RD (lenalidomide and dexamethasone) as compared to RD for 18 cycles and MPT (melphalan, prednisone, and thalidomide) in 1623 transplant ineligible patients. After a median follow-up of 67 months, it was found that continuous RD significantly prolonged PFS and OS as compared to MPT (HR for PFS, 0.69; 95% CI 0.59–0.79; $P < 0.00001$; HR for OS, 0.78; 95% CI 0.67–0.92; $P = 0.00234$) as well as RD for 18 months (HR for PFS, 0.70; 95% CI 0.60–0.81, HR for OS, 1.02; 95% CI 0.86–1.20). It was also found that fewer hematologic malignancies occurred in the RD arms, and the incidence of SPMs was similar between RD continuous (6%) and RD for 18 months (6.9%) [10].

Novel Agents in Newly Diagnosed Multiple Myeloma

A phase II dose escalation study of carfilzomib in combination with thalidomide and dexamethasone (KTD) for induction and consolidation in 111 transplant-eligible NDMM patients showed an overall RR (ORR) of 95%. The rate of complete response (CR) and stringent CR (sCR) was 18% after induction which increased to 31% post ASCT and 64% after consolidation. The OS at 30 months was comparable between patients with standard risk (91%) and high risk cytogenetics (90%) [11]. In addition, the final results of the phase I/II study of using carfilzomib in combination with lenalidomide and dexamethasone (KRD) as induction, consolidation post ASCT and maintenance for ten cycles was also presented. The rate of sCR improved from 20% post-ASCT to 69% after consolidation and to 82% after KRD maintenance. Also, the rate of minimal residual disease (MRD) in patients was 82% by 10-color multiparameter flow cytometry (MFC) and 66% by next generation sequencing (NGS) after consolidation, and 90

and 71%, respectively, after maintenance. After a median follow-up of 17.5 months, the 2-years PFS was 97% and 2-years OS was 99% for all 76 patients [12].

A phase II study from the IFM analyzed the safety and efficacy of the ixazomib triplet with lenalidomide and dexamethasone (IRD) prior to, and after ASCT followed by ixazomib maintenance in 42 NDMM patients younger than 66 years. IRD induction was very well tolerated with 13 cases of non-hematologic grade 3–4 toxicities out of 120 administered cycles (infections—8, abdominal pain—2, atrial fibrillation—1, thrombosis—1 and DRESS syndrome—1). Following induction, the ORR was 81%, with CR rate of 12% which improved to 38% following ASCT, and 44% following consolidation [13].

Treatment of Relapsed/Refractory Multiple Myeloma

Daratumumab (DARA), is a human CD38 IgG1κ monoclonal antibody, that has demonstrated significant efficacy as a single agent and in combination with standard-of-care (SOC) regimens in patients with MM who have received ≥ 1 prior lines of therapy [14, 15]. PAVO was the first study to assess the safety, pharmacokinetics, and efficacy of subcutaneous (SC) administration of DARA in combination with the recombinant human hyaluronidase enzyme in patients with relapsed or refractory MM (RRMM). It was found that SC administration was well tolerated and achieved serum trough concentrations similar to or greater than intravenous (IV) administration. It was also noted that SC DARA had a significantly shorter infusion time (20–30 min) with a lower rate of infusion related reactions (22%) as compared to IV DARA [16]. This will greatly enhance patient's convenience without any associated increase in the adverse events.

The update of results of studies evaluating DARA combinations—Pollux trial (DARA RD vs. RD) and Castor trial (DARA VD vs. VD) were also discussed at the congress. As regards to Pollux trial, after a median follow-up of 13.5 months, the addition of DARA to RD resulted in significant improvement of median PFS (NR vs. 18.4 months, HR = 0.36, 95% CI 0.25–0.50, $P < 0.0001$), ORR (94 vs. 77%) and CR (44 vs. 20%). The benefit in ORR and PFS persisted in subgroup of patients with high-risk cytogenetics, those with treatment free interval of less than and more than 12 months as well as those who were refractory to their last line of therapy [17]. In addition, the PFS advantage was seen in patients who were lenalidomide-naïve prior to the start of study treatment (NR vs. 18.4 months, HR = 0.36, 95% CI 0.25–0.52, $P < 0.0001$), lenalidomide-exposed subgroup (NR in both arms, HR = 0.49, 95% CI 0.22–1.12, $P = 0.0826$), bortezomib-

naïve subgroup (NR vs. 15.8 months, HR = 0.34, 95% CI 0.13–0.86, $P = 0.0170$), bortezomib-exposed subgroup (NR vs. 18.4 months, HR = 0.35, 95% CI = 0.24–0.50, $P < 0.0001$) as well as bortezomib-refractory patients (NR vs. 10.3 months, HR = 0.46, 95% CI 0.25–0.85, $P = 0.0117$) [18]. As regards to Castor trial, the updated analysis after a median follow-up of 7.4 months showed that the addition of DARA to VD significantly prolonged the median PFS (NR vs. 7.3 months, HR = 0.39, 95% CI 0.28–0.55, $P < 0.0001$); improved the ORR (84 vs. 67%, $P < 0.0001$) and the rates of very good partial response (VGPR) or better (62 vs. 32%, $P < 0.0001$). The benefit in PFS was seen in patients with standard-risk cytogenetics as well as those with high-risk cytogenetics [19].

The meeting also demonstrated for the first time, the assessment of MRD in patients with RRMM in a phase III trial setting. The addition of DARA to the SOC regimens resulted in significantly higher MRD negative rates at all 3 sensitivity thresholds (10^{-4} , 10^{-5} , and 10^{-6}). Additionally, patients who achieved MRD negative status experienced fewer PFS events compared with MRD positive patients at a threshold of 10^{-5} . Regardless of the SOC component, DARA-containing regimens consistently demonstrated $\geq$ threefold increase in MRD negative rate compared with the control groups at all evaluated thresholds among patients who achieve CR or better [20].

Venetoclax (VEN) is a potent, selective, orally available small-molecule BCL-2 inhibitor that showed promising results in a phase I study in patients with RRMM. The ORR for all patients on VEN monotherapy was 21 with 15% achieving VGPR or better. Of particular interest was the high response seen in patients with t (11; 14) and a favorable BCL-2 family expression profile (high BCL-2, low BCL-XL, low MCL-1) by immunohistochemistry [21]. Another study showed that VEN in combination with bortezomib and dexamethasone has an acceptable safety profile with an ORR of 68% (94% in patients not refractory to bortezomib) in RRMM patients [22].

Selinexor is an oral selective XPO1 inhibitor that induces nuclear accumulation and activation of tumor suppressor proteins, inhibition of NF- κ B, and inhibition of translation of several oncoprotein mRNAs such as c-myc and cyclin D. It was studied in RRMM patients who were “quad refractory” to IMiDs (lenalidomide and pomalidomide) and PIs (bortezomib and carfilzomib), and “penta refractory” to anti-CD38 Abs (daratumumab and isatuximab) in the phase II STORM trial. Among the 78 evaluable patients, the ORR was 21% (21% in quad refractory and 20% in penta refractory) with a median OS of 9.3 months (NR in responders vs. 5.3 months in non-responders) [23]. STOMP trial was a phase Ib study of selinexor in combination with bortezomib and

dexamethasone which depicted an ORR of 77% with 27% of patients achieving VGPR or better [24].

Pembrolizumab is a PD-1-blocking antibody, which is hypothesized to enhance the immune modulatory properties of pomalidomide in RRMM pts. In a phase II study, pembrolizumab in combination with pomalidomide and dexamethasone resulted in an ORR of 56% (55% in double refractory patients) with 27% of patients achieving VGPR or better and the median duration of response was 8.8 months, among 48 patients with RRMM [25].

Chimeric antigen receptor T cells (CAR-T) is a new form of genetically engineered immunotherapy that utilizes the target specificity of monoclonal antibodies in combination with potent cytotoxicity of T cells. B cell Maturation Antigen (BCMA)-specific CAR-T cells were tested for safety and efficacy at 4 dose levels in the first in human phase I study of 14 patients with RRMM after ≥ 3 prior lines (≥ 2 prior lines if “dual-refractory” to PI and IMiD). The median number of previous lines of therapy was 9 (range 4–11) and 100% of these patients had high risk cytogenetics including TP53 mutations in 67% of the patients. Among 9 patients evaluable for safety, the main adverse events were cytokine release syndrome in 8 patients (89%, grade $\frac{3}{4}$ in 33.3%) and grade 4 posterior reversible encephalopathy syndrome in 1 patient. Other grade $\frac{3}{4}$ toxicities included hypophosphatemia ($n = 4$, 44%), infection ($n = 4$, 44%), thrombocytopenia ($n = 3$, 33%), anemia ($n = 2$, 22%), neutropenia ($n = 2$, 22%), hypocalcemia ($n = 2$, 22%), hypokalemia ($n = 2$, 22%) and encephalopathy ($n = 2$, 22%). Clinical activity was seen in 6 patients with minimal response in 2 patients, partial response in 1 patient, VGPR in 2 patients and sCR in 1 patient [26].

An interesting phase II study evaluated the combination of nelfinavir (an oral HIV protease inhibitor) with bortezomib and dexamethasone in PI refractory MM patients. Among 34 patients enrolled, 26 (76%) patients were also refractory to IMiD. The ORR was 65% (69% in double refractory) with 14.7% VGPRs. These results are exceptional as compared to what is expected in this patient population and warrants further development of nelfinavir as a sensitizing drug for PI based treatment [27].

Treatment of Systemic Light Chain Amyloidosis

The existing treatment of light chain (AL) amyloidosis is aimed at targeting the plasma cells that produce the misfolded proteins but do not address the amyloid protein that is already deposited in the organs. NEOD001 is an investigational antibody designed to specifically target AL amyloid in a phase I/II study of NEOD001 in 42 previously treated AL amyloidosis patients with persistent organ

(cardiac/renal/peripheral neuropathy) dysfunction. NEOD001 was safe and well tolerated and $\geq$ grade 3 toxicities included anemia ($n = 1$, 1.4%) and fatigue ($n = 1$, 1.4%). The cardiac ($n = 19$ among 36 patients, 53%) and renal ($n = 23$ among 36 patients, 64%) best response rates were found to be better than what is expected after plasma cell-directed therapies. Also, this was the first time that such patients showed an improvement in peripheral neuropathy ($n = 9$ among 11 patients, 82%) [28].

Take Home Message

In summary, there were various exciting studies discussed in the field of MM at ASH annual meeting, 2016, which may be practice changing. There were mixed results from 2 large phase III trials that evaluated the role of tandem ASCT and consolidation therapy after induction therapy followed by ASCT in NDMM patients, but there were various differences between the 2 studies. Novel agents like carfilzomib and ixazomib proved to be of benefit when used as induction and post ASCT consolidation and maintenance. The early data on SC administration of DARA looked promising. The high rate of MRD negativity after using DARA with SOC regimens reinforces the benefit of targeting CD38. The responses seen with VEN in t(11;14) myeloma (high BCL-2, low BCL-XL and MCL-1) and selinexor in penta-refractory myeloma which fulfills the FDA category of unmet need, opens up newer options for these patients. BCMA CAR-T infusion shows encouraging results in advanced refractory myeloma patients.

Compliance with Ethical Standards

Conflict of interest First Author—None. Corresponding Author—Celgene (Consultancy and Research Funding), Millennium (Consultancy and Research Funding), Novartis (Research Funding), Onyx (Consultancy and Research Funding), AbbVie (Research Funding), Janssen (Consultancy and Research Funding), BMS (Consultancy and Research Funding).

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References

1. Seckinger A et al (2016) Asymptomatic multiple myeloma—background of progression, evolution, and prognosis. *Blood* 128(22):235
2. Jackson GH et al (2016) Response adapted induction treatment improves outcomes for myeloma patients; results of the phase III myeloma XI study. *Blood* 128(22):244
3. Jackson GH et al (2016) Lenalidomide is a highly effective maintenance therapy in myeloma patients of all ages; results of the phase III myeloma XI study. *Blood* 128(22):1143
4. Stadtmauer EA et al (2016) Comparison of autologous hematopoietic cell transplant (autoHCT), bortezomib, lenalidomide (Len) and dexamethasone (RVD) consolidation with len maintenance (ACM), tandem autohct with len maintenance (TAM) and autohct with len maintenance (AM) for up-front treatment of patients with multiple myeloma (MM): primary results from the randomized phase III trial of the blood and marrow transplant clinical trials network (BMT CTN 0702-Stamina Trial). *Blood* 128(22):LBA-1
5. Cavo M et al (2016) Intensification therapy with bortezomib-melphalan-prednisone versus autologous stem cell transplantation for newly diagnosed multiple myeloma: an intergroup, multicenter, phase III Study of the European Myeloma Network (EMN02/HO95 MM Trial). *Blood* 128(22):673
6. Cavo M et al (2016) Upfront single versus double autologous stem cell transplantation for newly diagnosed multiple myeloma: an intergroup, multicenter, phase III Study of the European Myeloma Network (EMN02/HO95 MM Trial). *Blood* 128(22):991
7. Sonneveld P et al (2016) Consolidation followed by maintenance therapy versus maintenance alone in newly diagnosed, transplant eligible patients with multiple myeloma (MM): a randomized phase 3 Study of the European Myeloma Network (EMN02/HO95 MM Trial). *Blood* 128(22):242
8. Mahindra A et al (2016) Patients (pts) with renal insufficiency (RI) and multiple myeloma (MM) have similar outcomes after autologous hematopoietic cell transplantation (AHCT) as those without. *Blood* 128(22):994
9. D'Souza A et al (2016) Trends in pre- and post-transplant therapies prior to first autologous hematopoietic cell transplantation among patients with multiple myeloma in the United States, 2004–2014. *Blood* 128(22):677
10. Facon T et al (2016) Final Analysis of Overall Survival from the First Trial. *Blood* 128(22):241
11. Wester R et al (2016) Phase 2 study of carfilzomib, thalidomide, and low-dose dexamethasone as induction/consolidation in newly diagnosed, transplant eligible patients with multiple myeloma, the carthadex trial. *Blood* 128(22):1141
12. Zimmermann T et al (2016) Final results of a phase 2 trial of extended treatment (tx) with carfilzomib (CFZ), lenalidomide (LEN), and dexamethasone (KRd) plus autologous stem cell transplantation (ASCT) in newly diagnosed multiple myeloma (NDMM). *Blood* 128(22):675
13. Moreau P et al (2016) Ixazomib-lenalidomide-dexamethasone (IRd) combination before and after autologous stem cell transplantation (ASCT) followed by ixazomib maintenance in patients with newly diagnosed multiple myeloma (NDMM): a phase 2 study from the intergroupe francophone du myélome (IFM). *Blood* 128(22):674
14. Lokhorst HM et al (2015) Targeting CD38 with daratumumab monotherapy in multiple myeloma. *N Engl J Med* 373(13):1207–1219
15. Lonial S et al (2016) Daratumumab monotherapy in patients with treatment-refractory multiple myeloma (SIRIUS): an open-label, randomised, phase 2 trial. *Lancet* 387(10027):1551–1560
16. Usmani SZ et al (2016) Open-label, multicenter, dose escalation phase 1b study to assess the subcutaneous delivery of daratumumab in patients (pts) with relapsed or refractory multiple myeloma (PAVO). *Blood* 128(22):1149
17. Usmani SZ et al (2016) Efficacy of daratumumab, lenalidomide, and dexamethasone versus lenalidomide and dexamethasone in relapsed or refractory multiple myeloma patients with 1 to 3 prior lines of therapy: updated analysis of pollux. *Blood* 128(22):1151
18. Moreau P et al (2016) Efficacy of daratumumab, lenalidomide and dexamethasone versus lenalidomide and dexamethasone alone for relapsed or refractory multiple myeloma among patients

- with 1 to 3 prior lines of therapy based on previous treatment exposure: updated analysis of pollux. *Blood* 128(22):489
19. Mateos M-V et al (2016) Efficacy of daratumumab, bortezomib, and dexamethasone versus bortezomib and dexamethasone in relapsed or refractory myeloma based on prior lines of therapy: updated analysis of castor. *Blood* 128(22):1150
 20. Avet-Loiseau H et al (2016) Evaluation of minimal residual disease (MRD) in relapsed/refractory multiple myeloma (RRMM) patients treated with daratumumab in combination with lenalidomide plus dexamethasone or bortezomib plus dexamethasone. *Blood* 128(22):246
 21. Kumar S et al (2016) Venetoclax monotherapy for relapsed/refractory multiple myeloma: safety and efficacy results from a phase I study. *Blood* 128(22):488
 22. Moreau P et al (2016) Venetoclax combined with bortezomib and dexamethasone for patients with relapsed/refractory multiple myeloma. *Blood* 128(22):975
 23. Vogl DT et al (2016) Selinexor and low dose dexamethasone (Sd) in patients with lenalidomide, pomalidomide, bortezomib, carfilzomib and anti-CD38 Ab refractory multiple myeloma (MM): STORM study. *Blood* 128(22):491
 24. Bahlis NJ et al (2016) Selinexor in combination with bortezomib and dexamethasone (SdB) demonstrates significant activity in patients with refractory multiple myeloma (MM) including proteasome-inhibitor refractory patients: results of the phase I stomp trial. *Blood* 128(22):977
 25. Badros AZ et al (2016) Pembrolizumab in combination with pomalidomide and dexamethasone for relapsed/refractory multiple myeloma (RRMM). *Blood* 128(22):490
 26. Cohen AD et al (2016) B-cell maturation antigen (BCMA)-specific chimeric antigen receptor T cells (CART-BCMA) for multiple myeloma (MM): initial safety and efficacy from a phase I study. *Blood* 128(22):1147
 27. Driessen C et al (2016) The HIV protease inhibitor nelfinavir in combination with bortezomib and dexamethasone (NVd) has excellent activity in patients with advanced, proteasome inhibitor-refractory multiple myeloma: a multicenter phase II trial (SAKK 39/13). *Blood* 128(22):487
 28. Gertz MA et al (2016) NEOD001 demonstrates organ biomarker responses in patients with light chain amyloidosis and persistent organ dysfunction: results from the expansion cohort of a phase 1/2 study. *Blood* 128(22):644