Practice-changing abstracts selected by the Multiple Myeloma Hub Steering Committee

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The world-leading experts in multiple myeloma (MM) shared the top abstracts from ASH 2019 that they believe could have the greatest impact on clinical practice.

In this document, you will find comments from the MM Hub Steering Committee members on treating newly diagnosed patients with MM non-eligible for transplant, treating newly diagnosed patients with MM eligible for transplant, treating newly diagnosed patients with relapsed or refractory MM, autologous stem cell transplantation, treating patients with smoldering myeloma, CAR T-cell therapy and BiTEs, prognostic factors, and novel targets.

ASH, American Society of Hematology; BiTEs, bi-specific T-cell engagers; CAR, chimeric antigen receptor.
Treating newly diagnosed patients with MM non-eligible for transplant

**#694 Randomized Trial of Lenalidomide and Dexamethasone Versus Clarythromycin, Lenalidomide and Dexamethasone As First Line Treatment in Patients with Multiple Myeloma Not Candidates for Autologous Stem Cell Transplantation: Results of the GEM-Claridex Clinical Trial**

Professor Maria Victoria Mateos

“Although some physicians use clarythromycin as part of their immunomodulatory-based regimens to improve the efficacy, they have to take care because clarythromycin increases the area under the curve for dexamethasone and the higher dexamethasone levels can result into a deleterious effect because more infectious processes and dexamethasone-related events can happen. The benefit in higher efficacy with clarythromycin plus Rd vs Rd alone in this phase 3 trial was overcome by the higher incidence of toxic deaths, especially in the population older than 75 years. Is it recommended to add clarythromycin to an IMiD-based combination as a strategy to improve the efficacy? I don’t think so.”

**#859 Daratumumab Plus Bortezomib, Melphalan, and Prednisone Versus Bortezomib, Melphalan, and Prednisone in Patients with Transplant-Ineligible Newly Diagnosed Multiple Myeloma: Overall Survival in Alcyone**

Professor Philippe Moreau

“With a longer follow-up, VMP + dara is now associated with an overall survival benefit (vs VMP alone). This is the first time that a combination including daratumumab as part of frontline therapy is showing an OS advantage. VMP-dara is approved and may become one of the standard of care for the future. VMP is not widely used in the US, but remains commonly used in EU and South America. The addition of daratumumab to VMP is an important step forward, and safe.”

Professor Mohamad Mohty

“In frontline therapy, the ALCYONE trial showed mature data to suggest survival advantage with daratumumab + VMP which can be used in a wide range of patients.”

Updated results from the ALCYONE study demonstrate overall survival benefit with D-VMP versus VMP in patients with transplant-ineligible newly diagnosed MM

Sub-analysis of East Asian patients from the ALCYONE trial

Subcutaneous daratumumab receives positive opinion from EMA CHMP and approval from the FDA

Subcutaneous formulation of daratumumab approved by the European Commission

IMiD, Immunomodulatory imide drug; OS, overall survival; VMP, bortezomib + melphalan + prednisolone.
Treating newly diagnosed patients with MM eligible for transplant

**#860 Daratumumab, Carfilzomib, Lenalidomide and Dexamethasone (Dara-KRd) Induction, Autologous Transplantation and Post-Transplant, Response-Adapted, Measurable Residual Disease (MRD)-Based Dara-Krd Consolidation in Patients with Newly Diagnosed Multiple Myeloma (NDMM)**

Professor Hermann Einsele

“This is an important trial studying patients with newly diagnosed multiple myeloma. Increasingly, four drug regimens including a monoclonal antibody, especially directed against CD38, are now used in the frontline setting. In addition, response adapted consolidation is added to improve outcome in this patient population. Thus, this trial really describes one of the most innovative concepts in the treatment of newly diagnosed multiple myeloma.”

**#864 Phase 2 Trial of Daratumumab, Ixazomib, Lenalidomide and Modified Dose Dexamethasone in Patients with Newly Diagnosed Multiple Myeloma**

Professor Morie Gertz

“This study has really changed practice for me. It indicates to me that the addition of daratumumab for the induction of newly diagnosed multiple myeloma will become the standard of care moving forward.”

**MASTER trial | Monoclonal antibody-based quadruplet regimen (Dara-KRd) with MRD-based response-adapted therapy in patients with NDMM**

High MRD-negativity rates observed with wKRd-D for patients with newly diagnosed multiple myeloma.

How do MRD negativity rates with Dara-KRd compare to other treatment options in patients with NDMM?
#782 Breaking the Glass Ceiling of Age in Transplant in Multiple Myeloma

Professor Hermann Einsele

“This study addresses the question about the age limit of high-dose chemotherapy and autologous stem cell transplantation performed for patients with multiple myeloma. Probably the chronological age is no more the best parameter to decide about transplant in a patient with newly diagnosed multiple myeloma. We need to consider new indices assessing the frailty of the potential candidate for high-dose chemotherapy and autologous stem cell transplantation. On the other hand, the alternative treatment options are continuously increasing and are becoming more effective.”

Efficacy of autologous stem cell transplantation in patients aged ≥70 years with multiple myeloma
Treating patients with relapsed or refractory MM

#LBA-6 Carfilzomib, Dexamethasone, and Daratumumab Versus Carfilzomib and Dexamethasone for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma (RRMM): Primary Analysis Results from the Randomized, Open-Label, Phase 3 Study Candor (NCT03158688)

Professor Maria Victoria Mateos

“Kd plus daratumumab will be a new standard of care for patients with relapsed/refractory myeloma after 1–3 prior lines of therapy and a choice for patients daratumumab-naïve but treated with bortezomib and lenalidomide as part of the prior lines of therapy. The only question is: would it be possible to use K weekly instead of twice a week? This would significantly optimize this combination.”

Professor Philippe Moreau

“Kd-dara was prospectively compared to Kd for patients with relapsed/refractory MM. The primary endpoint was PFS. Overall, K (twice weekly) + dex and dara significantly reduced the risk of progression or death. Survival data are immature. This regimen will probably be approved by EMA and FDA based on these important findings. The most important message is the high efficacy of Kd-dara in patients refractory to lenalidomide. The number of patients progressing on frontline lenalidomide is highly increasing (len maintenance after ASCT or len-dex until progression in elderly patients); therefore, Kd-dara may become one of the best options at the time of progression after frontline len.”

ASCT, autologous stem cell transplant; EMA, European Medicines Agency; FDA, U.S. Food and Drug Administration; K, carfilzomib; Kd, carfilzomib + dexamethasone.
#143 First Clinical Study of the B-Cell Maturation Antigen (BCMA) 2+1 T Cell Engager (TCE) CC-93269 in Patients (Pts) with Relapsed/Refractory Multiple Myeloma (RRMM): Interim Results of a Phase 1 Multicenter Trial

Professor Mohamad Mohty

“Studies involving bispecific antibodies (BiTEs), such as CC-93269, show an amazing rate of response in heavily treated populations. BiTEs are easy to use and appear to have a good safety profile. CAR T cells and BiTEs are likely to become key players in the next couple of years, especially in patients who have had multiple lines of therapy.”

Is CC-93269, a novel BCMA T-cell engager, safe and efficacious for patients with RRMM?

Interim results from the first study of CC-93269 in patients with relapsed/refractory multiple myeloma

#577 Results from CARTITUDE-1: A Phase 1b/2 Study of JNJ-4528, a CAR-T Cell Therapy Directed Against B-Cell Maturation Antigen (BCMA), in Patients with Relapsed and/or Refractory Multiple Myeloma (R/R MM)

Professor Mohamad Mohty

“The immunotherapy of myeloma is moving in the right direction; there are some nice CAR T-cell data, including CARTITUDE-1 phase I data with high response rates, a good safety profile with low incidence of CRS, and — most importantly — 1/3 of patients achieving deep MRD responses.”

CARTITUDE-1 trial: Is JNJ-4528 safe and efficacious for patients with RRMM?

LEGEND-2 and CARTITUDE-1: CAR T for relapsed/refractory multiple myeloma

BiTEs, bi-specific T-cell engagers; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; MRD, measurable residual disease.
CAR T-cell therapy and BiTEs

#579 Long-Term Follow-up of a Phase 1, First-in-Human Open-Label Study of LCAR-B38M, a Structurally Differentiated Chimeric Antigen Receptor T (CAR-T) Cell Therapy Targeting B-Cell Maturation Antigen (BCMA), in Patients (pts) with Relapsed/Refractory Multiple Myeloma (RRMM)

Professor Philippe Moreau
“This important presentation described the update analysis of the LEGEND-2 study looking at the efficacy and safety of a CAR-T targeting BCMA. The median PFS in advanced patients is impressive — 19.9 months (best results ever reported with CAR-Ts in multiple myeloma). Nevertheless, the patients enrolled into the study were not all refractory to IMiDs, PIs, and daratumumab. These very good results need to be confirmed in a more advanced patient population.”

Professor Hermann Einsele
“This is the first long-term follow-up report on a phase I, first-in-human, open-label study with CAR T cells in multiple myeloma. Some long-term disease controls are reported. It will be important to learn more about the patients with the long-term control to optimize CAR T-cell therapy in multiple myeloma.”

LEGEND-2 and CARTITUDE-1: CAR T for relapsed/refractory multiple myeloma

BCMA, B-cell maturation antigen; BiTEs, bi-specific T-cell engagers; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; IMiDs, immunomodulatory imide drugs; PIs, protease inhibitors; PFS, progression-free survival.
Professor Mohamad Mohty

“In terms of antibodies, TAK-079 is a novel anti-CD38 antibody with an excellent safety profile and impressive response rate in RRMM. This is a welcome addition to the treatment arena of MM.”

Novel targets

**#140 Preliminary Results from a Phase 1b Study of TAK-079, an Investigational Anti-CD38 Monoclonal Antibody (mAb) in Patients with Relapsed/ Refractory Multiple Myeloma (RRMM)**

Novel approaches in multiple myeloma: TAK-079

Sequencing treatments for relapsed/refractory multiple myeloma
#693 Evaluation of the Prognostic Value of Positron Emission Tomography-Computed Tomography (PET-CT) at Diagnosis and Follow-up in Transplant-Eligible Newly Diagnosed Multiple Myeloma (TE NDMM) Patients Treated in the Phase 3 Cassiopeia Study: Results of the Cassiopet Companion Study

Professor Heinz Ludwig

“PET/CT is a powerful imaging tool for detection and follow-up of myeloma bone lesions, paramedullary, and extramedullary myeloma manifestations. PET/CT may be positive in patients with MRD negative disease status and provides information about response and prognosis. Twenty percent of patients enrolled in the Cassiopeia trial were PET/CT negative at baseline and showed significantly better PFS compared to patients with positive results. Furthermore, outcome was superior in patients achieving both a PET/CT and MRD negative status, compared to those with only one of both tests being negative. Multivariate analysis revealed presence of paramedullary lesions as the only factor associated with poor PFS, with no statistical impact of diffuse infiltrations, focal lesions, and extramedullary disease.”

CASSIOPET study: Is PET-CT a surrogate prognostic marker in transplant eligible patients with NDMM?

MRD, measurable residual disease; PET/CT, positron emission tomography–computed tomography; PFS, progression-free survival.
#781 Curative Strategy (GEM-CESAR) for High-Risk Smoldering Myeloma (SMM): Carfilzomib, Lenalidomide and Dexamethasone (KRd) As Induction Followed By HDT-ASCT, Consolidation with Krd and Maintenance with Rd

Professor Mohamad Mohty

“In SMM, GEM-CESAR update showed an impressive survival rate.”

EHA 2019 | GEM-CESAR shows promise for smoldering MM: KRd + HDT-ASCT therapy

Has the GEM-CESAR study demonstrated that early intervention in SMM should be a new SOC?

Towards ASH 2020: Highlights on smoldering multiple myeloma