



MP*e*
Myeloma
Patients
Europe

CONFERENCE REPORT

**23rd Congress of the
European Haematology
Association 2018**

STOCKHOLM, SWEDEN. 14-17 JUNE 2018

Contenido Myeloma Patients Europe Conference Report

23rd Congress of the European Haematology Association 2018

Stockholm, Sweden. 14-17 June 2018

CAR-T cell therapy	2
BB2121	3
SLAMF7 CAR-T cell therapy	3
Frailty in myeloma patients	3
Myeloma treatment updates	4
Elotuzumab, pomalidomide and dexamethasone	4
Daratumumab, bortezomib, melphalan and prednisolone (D-VMP).....	4
Subcutaneous daratumumab in patients with relapsed or refractory myeloma	5
Autologous stem cell transplantation (ASCT) for older myeloma patients	5
Patient advocacy sessions	5
Quality of life in cancer	6
Patient related endpoints and outcomes	7
Advocacy development programme	7
About the MPE Advocate Development Programme	8
AL amyloidosis	8

Myeloma Patients Europe Conference Report

23rd Congress of the European Haematology Association 2018

The most important scientific conference on haematological diseases in Europe, the Annual Congress of the European Haematology Association (EHA), took place in Stockholm from 14 to 17 June 2018. This Myeloma Patients Europe (MPE) Conference Report presents the myeloma and AL amyloidosis highlights from EHA 2018.

CAR-T cell therapy

CAR-T cell therapy is a very promising new treatment for haematological diseases. Data from clinical trials show that it can be effective against leukaemia and lymphoma and now researchers are looking at it in myeloma.

During EHA 2018, Myeloma Patients Europe (MPE) interviewed two leading myeloma doctors about CAR-T cell therapy: Dr Michael Hudecek (University of Würzburg, Germany) and Prof Sonja Zweegman (VU University Medical Centre, The Netherlands).

Dr Michael Hudecek explained:

“CAR-T cell therapy is a new form of immune-based treatment for cancer which is very attractive as it is free from chemotherapy and is very potent against advanced malignancies. The scientific term “CAR” comes from ‘chimeric antigen receptor’ which acts like a biosensor that instructs white blood cells to recognise a molecule that is expressed on the tumour cells.”

CAR-T cells go through a very complex procedure to be used in patients. He continued:

“The way this works is by obtaining blood cells from the patient, taking these blood cells to the lab and encrypting them with the CAR, amplifying the cells and then infusing them back to the patient. Once CAR-T cells are inside the patient, they start to find and destroy the tumour cells.”

As well as understanding the effectiveness of CAR-T cell therapy in myeloma, the complexity of the procedure is one of the biggest issues experts need to address, not only because of the time needed by scientists to prepare the CAR-T cells, but also because the complexity of the procedure makes it very expensive.

Prof Zweegman also provided her opinion on CAR-T cell therapy:

“We are of course very impressed with CAR-T cell therapy. We must wait longer but I hope CAR-T cells will really change the landscape of myeloma treatment. We have seen a high rate of response in myeloma patients who were heavily pre-treated. Data from ASCO showed an immediate progression free survival of approximately 11 months, which is impressive in heavily pre-treated patients. In my opinion, more information is needed because there are many issues to be resolved but I do think CAR-T cells will be implemented in the treatment of myeloma patients.”

Several early phase studies showing promising results of CAR-T cell therapy in myeloma were presented at EHA 2018. The two main studies are outlined below.

BB2121

Dr Jesús Berdeja (Sarah Cannon Research Institute, US) presented promising results on a CAR-T cell therapy known as bb2121. bb2121 targets the B-cell maturation antigen (BCMA), a molecule expressed on the surface of myeloma cells.

Initial data from the dose-escalation phase of the CRB-401 trial, a first-in-human clinical trial of bb2121 in 43 relapsed and/or refractory myeloma patients, highlighted promising safety and efficacy in patients alongside deep and durable responses and manageable side-effects.

In this ongoing trial, median progression free survival (PFS – the length of time following treatment before myeloma returns) among 18 patients treated with active doses in the dose escalation cohort was 11.8 months and a 96% overall response rate (ORR – the percentage of patients that responded to treatment) was reported in 22 patients treated. Additionally, an unprecedented rate of minimal residual disease (MRD – a sensitive measure of remaining myeloma cells) negativity was observed, with 100% of 16 evaluable responders achieving this parameter.

SLAMF7 CAR-T cell therapy

A separate presentation given at EHA 2018 outlined the role of SLAMF7 CAR-T in myeloma. This is now being further explored through “CARAMBA”, a project led by Dr Michael Hudecek and funded by the European Commission (EC) within the Horizon 2020 programme.

SLAMF7 is another molecule expressed on the surface of myeloma cells, which CAR-T cells are designed to target and destroy. In laboratory models run at the University of Wurzburg, researchers have seen a very potent anti-myeloma effect with SLAMF7 CAR-T, so researchers in CARAMBA are now developing a Phase I/II trial to explore how this works in patients.

The Phase I part of the trial is a dose escalation study and the experts will explore the effective dose of the CAR-T cell therapy. For the Phase II part, 25 patients will be treated with the maximum tolerated dose of SLAMF7 CAR-T to understand the safety and efficacy of the treatment. The trial is expected to open in the second half of 2019.

Frailty in myeloma patients

One of the challenges haematologists face in myeloma is how to treat frailer patients. Whilst the availability of proteasome inhibitors (PIs) (e.g. bortezomib [Velcade®], ixazomib [Ninlaro®] and carfilzomib [Kyprolis®]) and immunomodulatory agents (IMiDs) (e.g. thalidomide, lenalidomide [Revlimid®] and pomalidomide [Imnovid®]), have significantly improved the outcomes of myeloma patients in the last decade, frailer patients have shown a lesser improvement. This is mainly due to the toxicity some drugs can have in frailer patients, which may lead to subsequent early discontinuation of treatment. This is a topic that was addressed in an EHA “Meet-the-Experts” session led by Prof Sonja Zweegman on “The issue of frailty in multiple myeloma.”

MPE interviewed Prof Zweegman before the session. She commented:

“Frailty is a problem in myeloma treatment. We know that in elderly patients who are frail the negative impact on overall survival is even more pronounced than having high-risk cytogenetics or age. We don’t know exactly how to determine whether a patient is frail or not. We have the International Myeloma Working Group (IMWG) frailty index and that is a good starting point but still there are many questions to be answered.”

Prof Zweegman also outlined that for frailer myeloma patients it is useful to give less intensive versions of current treatment regimens:

“When we look at one of the standards of care in Europe - bortezomib, melphalan and prednisone - in the VISTA trial there were nine cycles, but you can just give six cycles and then continue with two or three years of maintenance therapy. This means your cumulative term of bortezomib will be similar and your outcome regarding progression-free survival will be better. Hopefully we will also have better tools to define frailty. We are now investigating the role of muscle mass and function because with sarcopenia [the loss of skeletal mass] you have less muscle mass and less function. Hopefully we will be able to present the data at the upcoming ASH and we are also looking for hand grip signs and walking speed to see which patients are really frail.”

Myeloma treatment updates

Elotuzumab, pomalidomide and dexamethasone

A “late-breaking” abstract published at EHA 2018 highlighted positive results from a Phase II clinical trial, known as ELOQUENT-3, which was looking at elotuzumab (Empliciti®) in combination with pomalidomide (Imnovid®) and low dose dexamethasone vs. pomalidomide and low dose dexamethasone.

Elotuzumab is a type of immunotherapy known as a monoclonal antibody and is currently approved by the European Medicines Agency (EMA) in combination with lenalidomide and dexamethasone.

117 patients with relapsed and/or refractory myeloma participated in the ELOQUENT-3 trial, all of whom had received prior treatment with both an IMiD and a PI. The results from the trial found that patients who received the elotuzumab combination achieved a significant improvement in PFS (10.3 months vs. 4.7 months), which is particularly important given the advanced stage of relapse patients were at. The PFS advantage was seen in all subgroups that were analysed, for instance in: older/frailer patients, patients with “high-risk” myeloma (e.g. patients with myeloma that is more difficult to treat), patients with four or more prior lines of therapy, and in patients who were refractory to bortezomib and lenalidomide.

Dr Meletios Dimopoulos (University of Athens, Greece) who presented the data as an EHA “late-breaking abstract” concluded:

“This combination demonstrated a favourable safety profile, with lower than expected rates of neutropenia and few infusion reactions. We believe that this study shows that elotuzumab, pomalidomide and low-dose dexamethasone is a new treatment option for patients with relapsed or refractory myeloma who have failed treatment with lenalidomide and a proteasome inhibitor.”

Daratumumab, bortezomib, melphalan and prednisolone (D-VMP)

Many myeloma patients who are older/frailer are ineligible to receive high-dose therapy and autologous stem cell transplantation (ASCT) – a recognised standard of care in myeloma. This is due to the intensive nature of ASCT.

Myeloma researchers are constantly looking for well-tolerated and effective treatment combinations for myeloma patients who are ineligible to undergo ASCT. An example is research presented at EHA 2018 by Dr Jesús San Miguel (Clínica Universidad de Navarra, Spain) on the Phase

III clinical trial ALCYONE. More than 700 newly diagnosed myeloma patients were randomised in this clinical trial to receive either daratumumab (Darzalex®), bortezomib, melphalan and prednisolone (D-VMP) or bortezomib, melphalan and prednisolone (VMP – a current standard of care for transplant ineligible patients). All of them were 65 years of age or older or otherwise ineligible for high-dose chemotherapy with ASCT.

The clinical trial showed that the D-VMP arm was well tolerated by patients and had favourable safety and efficacy results compared to VMP. After average follow-up of 16.5 months, PFS was prolonged with D-VMP vs. VMP (median not reached vs. 20.4 months). MRD-negative rates, overall and complete response rates were also consistently higher for D-VMP.

Subcutaneous daratumumab in patients with relapsed or refractory myeloma

Clinical trials involving daratumumab have shown very good efficacy in all stages of myeloma. However, one of the disadvantages of this intravenous (IV – through the vein) drug is that it has a long infusion time (the first infusion takes about 7 hours; future infusions last from 3-5 hours). This means time spent in the hospital for patients, including a potential overnight stay in hospital for the first infusion.

Daratumumab is also linked to something called an “infusion-related reaction” (IRR) in patients – usually in the first infusion, but it can also happen in subsequent infusions. Around half of patients experience this, leading to symptoms including fever, chills, cough, nausea, changes in blood pressure, flushing, rash and fatigue. Patients are monitored during the first infusion to ensure that they are given appropriate supportive care by healthcare professionals.

Finding a different route of administration for daratumumab could therefore make it easier for patients to receive this drug and reduce the cost to healthcare systems.

Research presented at EHA 2018 assessed the efficacy of subcutaneous (SC - injection, through the skin) daratumumab in patients with relapsed or refractory myeloma. This open-label, multi-centre, dose escalation Phase IB study involved 25 myeloma patients receiving daratumumab through SC injection. At a median follow-up of 4.6 months, no patients discontinued due to treatment-emergent adverse events.

The trial found that daratumumab SC, which enables patients to receive daratumumab in 3 - 5 minutes, was well tolerated with low IRR rates, had an acceptable side-effect profile, and demonstrated clinical response rates similar to IV daratumumab.

Autologous stem cell transplantation (ASCT) for older myeloma patients

ASCT remains the standard of care for all eligible myeloma patients. Typically, ASCT is used in myeloma patients who are less than 65 years old as they are considered fitter and more able to tolerate the treatment. However, a high percentage of patients aged 65 - 75 are physically able to receive this treatment.

A large Phase III clinical trial in the UK, the NCR1 Myeloma XI trial, enrolled most newly-diagnosed myeloma patients in the UK and evaluated the outcomes of older patients who received ASCT. Data presented by Dr Charlotte Pawlyn (Institute of Cancer Research, London) showed that ASCT improves outcomes for newly diagnosed myeloma patients and supported its use as standard of care for all patients considered able to tolerate the procedure, without strict age limits.

Patient advocacy sessions

A major highlight of EHA 2018 were the patient advocacy sessions.

Through membership of the EHA Working Group, MPE plays a pivotal role in the development of the patient advocacy sessions, ensuring that the agenda enables discussion of topics most relevant to the community. During EHA 2018, the patient advocacy sessions were well attended and included sessions on the following topics:

- Quality of life during and after treatment, which included a presentation from Ananda Plate, CEO of MPE
- Patient related endpoints and outcomes, chaired by Alfonso Aguaron, Project Manager at MPE

MPE also co-created the agenda of the EHA 2018 Capacity Building Programme, which is designed to help patient advocates attending the conference to navigate the scientific sessions. This year it was held in collaboration between EHA, the hematology European Reference Network (ERN) EuroBloodNet and the EHA Working Group. The session set the tone for the congress, starting discussions about topics such as PRO-tools and QoL instruments and promoting information sharing on ongoing projects relevant to the advocacy community, including the work of EuroBloodNet on setting up networks of haematology expertise across Europe.

Attendance at the Capacity Building Programme forms part of the EHA fellowship programme, which provides free entry into the EHA conference for identified patient advocates. MPE staff team was able to attend, alongside the five MPE member organisations involved in the first face-to-face meeting of the Advocate Development Programme.

Both the Capacity Building Programme and the patient advocacy track were very successful this year, with record numbers of attendance in the meetings – something the EHA Workgroup aims to develop in the coming years. The highlights of the advocacy sessions are summarised below.

Quality of life in cancer

Quality of life (QoL) is an issue that is very important to patients, particularly as the side-effects of cancer treatment and “late-effects” can impact significantly on their ability to continue with normal daily activities and to “live well” with and beyond cancer.

This session, chaired by Sophie Wintrich, MDS UK Patient Support Group and Loris Brunetta, TIF explored the issues through five presentations on QoL in cancer from a variety of different perspectives. The introductory presentation, given by patient Amanda Bok, European Haemophilia Consortium outlined considerations around the importance of QoL and how this is currently factored into treatment discussions and decision-making.

Dr Harpreet Kaur from Sheffield University, then discussed common side-effects and symptoms that impact on the QoL of patients such as fatigue and emotional impact of treatment. Whilst these are common issues, they are often poorly understood, under treated and inadequately measured. He advocated for the importance of these being addressed to improve QoL and outcomes from treatment.

A presentation from Lars Kjeldsen, Rigs Hospital outlined a model of treatment in the home for haematological patients can improve patient experience of their cancer. He shed light on his work on implementing a system in Denmark, navigating the complexities of local services, funding issues and shortages of trained personnel. In addition, he outlined the importance of such models for improving patient QoL, reducing burden on clinical staff and improving cost-savings for hospitals.

Ananda Plate, MPE then presented the impact that cancer and its treatment have on sex life, focusing on sexual dysfunction and the impact this can have emotionally, on self-esteem and relationships. Sexual dysfunction is a common consequence of cancer treatment. Problems are

usually linked to damage to nerves, blood vessels, and hormones that underlie normal sexual function.

Finally, Natacha Bolaños, Lymphoma Coalition addressed how pre-rehabilitation can help patients get through treatment better and the importance of rehabilitation to help cancer patients improve their quality of life and get back to “normality” faster.

Patient related endpoints and outcomes

An interesting discussion about patient-relevant endpoints (e.g. target outcomes measured in a clinical trial such as survival) and patient-reported outcomes (PRO) (e.g. health outcome reported directly by a patient) was moderated by Maria Piggini, from PNH Support, and Alfonso Aguarón, from MPE.

In the first talk, Jan Geissler (CML Advocates Network) reflected on whether study survival related endpoints such overall survival (OS – the length of time patients live following treatment) and PFS are most relevant to patients. Whilst agreeing that they are important, Geissler pointed out that patients have a variety of different preferences and, in this scenario, clinical efficacy may not be the only thing that is important.

Issues around the quality of life, psychosocial and financial impact of treatment, administration preferences and social and family planning were addressed during the talk. The conclusion was that endpoints preferred by patients may not be the same as the ones that researchers and regulators look for. An evidence-based collaborative model which supports patient preferences is required to change the current status quo.

During the second talk, Dr Guillermo García-Manero (MD Anderson Centre Houston, US), explored the ways in which PRO can be better captured in clinical research through real life clinical experience. Dr García-Manero advocated for the adoption of a systematic approach to capturing and analysing PRO that better reflects the insights of patients. Challenges such as the limited amount of time patients have at a doctor’s appointment, the changing nature of healthcare systems and the need to generate evidence that supports the use of PRO were raised during the discussion.

Finally, Dr Harpreet Kaur presented an overview on innovative electronic tools used to capture PRO. Based on the premise and evidence that, while validated health-related quality of life questionnaires, such as EORTC QLQ-C30 or EQ-5D, are likely to be accepted by the regulator, they do not generally reflect the reality of patient experience and can be a burden to complete. Dr Kaur emphasised two potentially beneficial aspects of new tools: first, the use of electronic tools with adapted QoL questionnaires that reduce the burden for the patients and provide more relevant data; secondly, the use of technologies such as wearables, able to capture QoL data, such as sleep quality, fatigue related markers etc. Dr Kaur ended her talk by highlighting the need to gain experience on the use of new techniques, as well as to keep a continuous dialogue with regulatory bodies, to allow their deployment in a systematic way.

Advocacy development programme

In the lead up to EHA 2018, MPE also held the first face-to-face meeting of the Advocate Development Programme (ADP) in Stockholm.

Chaired by leading patient advocate, Jan Geissler (Patvocates), the two-day session covered a wide-range of topics relating to clinical development of new medicines and pipeline drugs in myeloma and AL amyloidosis. Highlights included talks on the latest developments in myeloma and AL amyloidosis from three leading European haematologists; Dr Laurent Garderet from Saint Antoine Hospital Paris, Prof. Dr Sonia Zweegman from VU University Medical Centre Amsterdam and Dr

Anna Sureda, Dexeus University Hospital, Barcelona. Other talks covered topics critical to patient advocates such as the importance of patient data and evidence to decision-making.

Following the ADP sessions, participants went to the EHA Annual Congress, joining in the EHA Capacity Building Programme and attending scientific and patient advocacy sessions. The MPE ADP team provided daily debriefs on congress highlights and a “poster walk” introducing key poster presentations at the congress.

About the MPE Advocate Development Programme

The ADP face-to-face session is part of a year-long learning programme involving six myeloma and AL amyloidosis advocates from across Europe and further afield. This year, the ADP has six advocates participating from Armenia, Sweden, Israel, Macedonia and Spain.

Through tailored webinars and four face-to-face meetings, the aim is to help myeloma and AL amyloidosis advocates to understand the research and development process of drugs, from the preclinical stages through to post-marketing surveillance and national access. The programme also includes attendance and participation at the EHA Annual Congress, the European Society of Medical Oncology (ESMO) Annual Meeting and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Europe meeting.

AL amyloidosis

The main AL amyloidosis highlight was a plenary session at EHA from Prof Giampaolo Merlini, (University of Pavia, Italy) which looked at the current diagnostic and treatment options in AL amyloidosis. He outlined that the most important goals in AL amyloidosis treatment are:

- Improving the early diagnosis of AL amyloidosis using biomarkers and imaging techniques
- Selecting an appropriate upfront therapy based on risk assessment and establishing an effective follow-up aiming at haematologic and organ response
- Exploiting the latest therapeutic developments, particularly immunotherapy, towards improved cardiac response and extended survival

The prevalence of AL amyloidosis is approximately 9 cases per million inhabitants per year. Between 10 and 15% of myeloma patients also develop the disease. In this session entitled: ‘The rapidly changing face of diagnosis and therapy in AL amyloidosis’, Dr Merlini highlighted the importance of an early diagnosis in the disease and looked at it as a key goal to improving outcomes. During the session he commented:

“Early diagnosis is so important. It is also important to reduce as much as possible the concentration of the light chains to block the process. These are challenging tasks and unfortunately nowadays, 60% of our patients are diagnosed when they are symptomatic. This is translating into a very poor survival. We have to focus all efforts on at least identifying these patients while they are still asymptomatic. If we diagnose this disease earlier, we can preserve the renal function in almost all patients. If we diagnose these patients in time we save their lives.”

The use of biomarkers in combination with imaging techniques is improving the early diagnosis of AL amyloidosis patients. However, more than half of them are diagnosed when they are already symptomatic. He particularly highlighted advanced cardiac AL amyloidosis, and the need to understand the mechanism of cardiac damage and determine effective treatment options in this setting, as an area of unmet need.

According to Dr Merlini, effectively using drug combinations to treat AL amyloidosis is key to improving outcomes in the disease. He outlined:

“In the near future we will combine drugs and this will open new possibilities and new hopes. The treatment of systemic amyloidosis will include the combination of agents targeting critical steps of the amyloid cascade, increasing efficacy.”

He went on to discuss his concern about sustainability and access to AL amyloidosis drugs due to cost (particularly in combinations) and stated that novel collaborative models are necessary to tackle these challenges.

One of the treatment combinations in AL amyloidosis is being explored in the Andromeda clinical trial, led by Dr Merlini. The safety run-in of this ongoing Phase III clinical trial is looking at subcutaneous daratumumab, in combination with cyclophosphamide, bortezomib and dexamethasone (CyBorD) vs CyBorD alone in newly diagnosed AL amyloidosis patients. According to the results presented, DARA-CyBorD is tolerable in patients with AL amyloidosis, with a low rate of the IRR reaction (which some patients experience during their first infusion of daratumumab) and no new safety signals.



CONTACT US



Myeloma Patients Europe AISBL
Avenue Louise 149/24
1050 Brussels
Belgium



info@mpeurope.org



www.mpeurope.org



[@mpeurope](https://www.facebook.com/mpeurope)



[@MyelomaEurope](https://twitter.com/MyelomaEurope)