MPE MYELOMA PATIENTS EUROPE

CONFERENCE REPORT

The American Society of Clinical Oncology (ASCO) and European Hematology Association (EHA) 2021 Annual Congresses conference report
The American Society of Clinical Oncology (ASCO) and European Hematology Association (EHA) Annual Congresses conference report, 2021

The American Society of Clinical Oncology (ASCO) Annual Meeting and the European Hematology Association (EHA) annual meeting are the most important haematology scientific congresses worldwide. This year, both were held virtually in June due to the COVID-19 pandemic limitations. ASCO 2021 was held between the 4th and the 8th of June 2021 while EHA 2021 was held from the 9th of June to the 17th of June 2021. This report summarises the most important updates presented in both congresses around myeloma, AL amyloidosis and patient advocacy.

Please refer to the end of this document, as it contains a glossary of useful terms to help you understand some of the words used to explain each study.
MYELOMA UPDATES

Treatment of Newly Diagnosed Myeloma Patients

Carfilzomib 1

The aim of the study “Carfilzomib-based induction/consolidation with or without autologous transplant (ASCT) followed by lenalidomide (R) or carfilzomib-lenalidomide (KR) maintenance: efficacy in high-risk patients was to evaluate the impact of carfilzomib-based treatments for the use of induction and consolidation and as maintenance treatment after transplant in newly diagnosed high risk myeloma patients (NDMM) based on cytogenetics. In this trial patients were randomised to receive one of the following:

- 4 cycles of carfilzomib, cyclophosphamide, dexamethasone (KCd) - then autologous stem cell transplant - then another 4 cycles of KCd
- 4 cycles of carfilzomib, lenalidomide, dexamethasone (KRd) - then autologous stem cell transplant - then another 4 cycles of KRd
- 12 cycles of carfilzomib, lenalidomide, dexamethasone (KRd)

Then patients were again randomised to receive maintenance treatment with either carfilzomib and lenalidomide (KR) or with lenalidomide alone (R). Updated results of progression-free survival data were presented at ASCO2021. Data showed that the use of KRd with ASCT resulted in 62% of high-risk patients showing no worsening of their myeloma after 4 years, versus only 45% of patients that received 12 cycles of KRd.

Daratumumab 2

CASSIOPEIA Part 2 is a two-part, randomised, phase III study in 1085 patients with transplant eligible, newly diagnosed multiple myeloma. The first part of the CASSIOPEIA study evaluated daratumumab with bortezomib and thalidomide (dara+VTd) as an initial treatment before and after stem cell transplant. The CASSIOPEIA study led to the European regulatory approval of the combination in this patient population. Data from the second part of CASSIOPEIA were presented at ASCO2021, which evaluated the use of daratumumab as a maintenance treatment.

In the second part of the CASSIOPEIA study, 886 patients were randomised to receive maintenance treatment with either daratumumab or no treatment and observation. After 34.5 months follow-up, the median progression-free survival was not reached in the daratumumab group and was 46.7 months in the observation group. This study will continue to evaluate participants’ overall survival and progression-free survival in the study.

UK optimum/MUKnine trial 3

Results from the OPTIMUM clinical trial were presented at ASCO2021. This trial aimed to address the unmet needs of high-risk myeloma patients that often have worse outcomes and shorter overall survival. This trial took 128 primary plasma cell leukemia (pPCL) patients and high risk newly diagnosed myeloma patients (NDMM) and
were treated with induction therapy including daratumumab, bortezomib, lenalidomide, cyclophosphamide, and dexamethasone (dara-CVRd) and then received an autologous stem cell transplant (ASCT).

After transplant all patients were given consolidation treatment - 6 cycles of daratumumab, lenalidomide, bortezomib, and dexamethasone (dara-VRd) then 12 cycles of daratumumab, lenalidomide, and bortezomib (dara-VR), and then daratumumab and lenalidomide (dara-R) until disease progression. Patients were then tested at various intervals for minimal residual disease. 94% of patients responded to induction therapy with 41% achieving minimal residual disease and 83% had a response to ASCT with 64% achieving minimal residual disease. Side-effects were mostly haematologic, but with 12.1% of patients experiencing moderately severe infections requiring hospitalisation.

**GMGG-concept trial**

The aim of the GMGG-concept trial was to determine the benefit of isatuximab, carfilzomib, lenalidomide, and dexamethasone (isa-KRd) for the initial treatment of high-risk myeloma patients (HRMM). This is a phase II clinical trial conducted in Germany where 117 transplant eligible patients received 6 cycles of KRd then autologous stem cell transplant (ASCT) with isa-KRd as consolidation treatment post-transplant and isa-KR as maintenance treatment. In the other cohort of the study, 36 transplant non-eligible NDM patients received a total of 12 cycles of isa-KRd with subsequent isa-KR as maintenance treatment.

Results presented at EHA2021 showed that of the 50 patients that are currently evaluable for treatment response, 100% of patients in the study had partial response or better in their myeloma with 41/46 achieving very good partial response or better in the transplant cohort and 4/4 in the non-transplant eligible cohort. Overall, 40/50 patients had seen no worsening of their myeloma after one year. There have been no new safety concerns discovered within the trial, with most high-grade side-effects being haematologic but did have some high grade of high blood pressure. Two patients had high-grade heart failure and four patients died from infections.

**TOURMALINE-MM3 and MM45**

The TOURMALINE-MM3 was a phase III study that compared outcomes when newly diagnosed myeloma (NDMM) patients were treated with ixazomib versus placebo for maintenance after autologous stem cell transplant (ASCT) or after available standard of care treatments (for patients that are not transplant eligible). Data presented at EHA2021 showed that of the 1,280 patients evaluated for measurable residual disease (MRD), 262 were MRD negative and 1,018 were MRD positive.

Patients that were MRD negative went about 38.6 months without worsening of their myeloma and patients who were MRD positive went 15.6 months. Patients that were MRD positive and received ixazomib maintenance went longer without worsening of their myeloma (18.8 months) versus those who received placebo (11.6 months), but there was no difference in patients that were MRD negative before receiving maintenance treatment.
MAIA study

The MAIA study is a comparative phase III study investigating the benefits of lenalidomide and dexamethasone with or without daratumumab (D-Rd versus Rd) in newly diagnosed stem-cell transplant-ineligible patients. Results were presented at EHA2021. Patients were randomly assigned to the D-Rd or Rd groups and treated with their assigned regimen until disease progression or inability to tolerate treatment.

The updated data with 28 months follow-up shows that 90% of patients saw improvement in their myeloma in the D-Rd arm versus 82% in the Rd arm. At 60 months post-treatment, 52.5% of patients in the D-Rd arm had seen no worsening of their myeloma, and 66.3% of patients were still alive versus 28.7 in the Rd arm with 53.1% patients still alive. The most common adverse events were haematologic and pneumonia.

KCd consolidation with K maintenance

This research was conducted to determine the utility of consolidation treatment (post-transplant treatment) using carfilzomib, cyclophosphamide, and dexamethasone (KCd) versus autologous stem cell transplant (ASCT). The results were presented at ASCO2021. In this study all patients received induction, or initial treatment, with four cycles of KCd. Then patients were randomly assigned to receive treatment with either ASCT or another four cycles of KCd. All patients then received 18 cycles of carfilzomib maintenance.

Out of the 281 patients treated with KCd induction 58.5% showed very good partial response or better (VGPR). Of the 109 patients who received KCd consolidation, 77.3% showed >VGPR and of the 109 that received ASCT 80% showed >VGPR. The percentage of patients that showed no worsening of their myeloma after two years was 76% in the ASCT cohort and 70% in the KCd cohort. The researchers claim that this data shows that the use of KCd is no worse than the use of ASCT for initial treatment of myeloma, although more patients that received ASCT upfront showed high rates of minimal residual disease negativity.

Treatment of Relapsed and Refractory Myeloma Patients

ICARIA-MM

Updated results from the ICARIA-MM study were presented at ASCO2021 and EHA congresses. The combination of isatuximab, pomalidomide, and dexamethasone is currently approved by European regulators to treat RRMM patients. The ICARIA study compared the use of isatuximab with pomalidomide/dexamethasone (Pd) versus Pd alone. After prolonged follow-up, patients who received isatuximab with Pd went 11.1 months without worsening their myeloma. Patients with Pd alone went 5.8 months.

Patients who received isatuximab lived about 24.57 months, versus those who received only pom/dex, who lived 17.71 months. Furthermore, 63% of patients who received isatuximab had improved myeloma paraprotein levels, versus 33.3% in the group of patients who only received Pd. One analysis did show that subsequent treatment
with daratumumab alone after isatuximab shows that treatment with daratumumab may be less effective.

**CT103A**

This study was conducted in China and the results were summarised in a poster presentation at EHA2021. In this study, 35 patients were enrolled to receive treatment with CT103A autologous CAR-T that targets the BCMA proteins on myeloma cells. During the trial, 42.8% of patients experienced prolonged cytopenia (low cell levels), 13.3% of patients experienced grade 3 and 4 cytokine release syndrome (overall, 91.4% of patients developed cytokine release syndrome) and 2.9% of patients also developed neurotoxicity. 97.1% of patients saw improvement in their myeloma and went 20 months without worsening of their myeloma. CTA103A is being investigated in an ongoing phase 2 study.

**CARTITUDE-1 & 2**

During ASCO2021, two updates on trials of ciltacabtagene autoleucel (cilta-cel or JNJ-4528), a BCMA-targeting CAR-T therapy, were presented. One was focused on CARTITUDE-1 (NCT03548207), a phase 1b/2 study, the second update concerned CARTITUDE-2 (NCT04133636), a phase 2 study of cilta-cel.

In CARTITUDE-1, 97 patients were treated with a single cilta-cel infusion 5–7 days after receiving cyclophosphamide chemotherapy treatment. 97% of patients saw improvement in their myeloma. 66% of patients in the study saw no worsening of their myeloma, and 81% of patients were still alive 18 months after treatment with cilta-cel. Over two-thirds of patient-reported side-effects were cytokine release syndrome, neutropenia, anaemia, and thrombocytopenia. Cilta-cel-related neurotoxicity was reported in approximately 20% of patients. On longer follow-up, no new safety signals were detected.

At ASCO2021 and EHA, a subgroup analysis of the CARTITUDE 2 study was also presented. This sub-analysis evaluated the effects of cilta-cel in patients who had myeloma that was no longer responsive to 1-3 lines of treatment, including lenalidomide. The outcomes in this subgroup analysis showed that 95% of these patients saw an improvement in their myeloma disease.

**Elranatamab**

Elranatamab is a bispecific antibody that binds to the BCMA receptor on the surface of myeloma cells and to the CD3 receptor on the surface of immune cells called T-cells to stimulate the killing of cancerous cells. The safety and efficacy of intravenous (IV) and subcutaneous (SC) elranatamab were evaluated in a phase 1 study called MagnetisMM-1, and updates to the outcomes of the subcutaneous formulation were presented at ASCO2021.

SC elranatamab was given to 30 patients weekly with initial dosing done as step-up dosing. Overall, 73.3% of patients experienced grade 1 or 2 cytokine release syndrome. 70% of patients experienced a reduction in their paraprotein levels, and the duration of response and progression-free survival data were not yet available as the study is still ongoing.
Iberdomide\textsuperscript{12}

Iberdomide is a CELMoD agent, which is a new class of drugs being investigated to treat myeloma. CELMoDs work by degrading the proteins required for myeloma cell growth, leading to myeloma cancer cells’ death. In this ongoing phase 1/2 study, iberdomide was studied in several combinations, and the results of iberdomide in combination with the following were presented at EHA:

- iberdomide with daratumumab and dexamethasone (IberDd)
- iberdomide with bortezomib and dexamethasone (IberVd)
- iberdomide with carfilzomib and dexamethasone (IberKd)

In the IberDd cohort, 45.9% of patients saw improvement in their myeloma with 56% in the IberVd and 50% in the IberKd. The most common side-effects in all combinations were haematologic, and 32% of patients in the bortezomib cohort had grade 1 or 2 peripheral neuropathy (painful numbness or tingling in hands and feet). Several other ongoing studies investigate iberdomide in various combinations and doses, and further efficacy data is being collected.

Teclistamab\textsuperscript{13}

Teclistamab is a bispecific antibody that binds to the BCMA receptor on the surface of myeloma cells and to the CD3 receptor on the surface of immune cells called T-cells to stimulate the killing of cancerous cells. Updated results were presented at ASCO2021 for the recommended subcutaneous dosing of teclistamab. Findings showed that 70% of patients experienced grade 1 or 2 cytokine release syndrome (none experienced grade 3 or 4), and other common side-effects were related to low blood cell counts. 65% of patients receiving subcutaneous teclistamab in the recommended subcutaneous dose saw improvement in their myeloma. The investigators are studying teclistamab in later phase studies at the recommended dose, earlier lines of treatment, and in combination with other drugs.

Talquetamab\textsuperscript{14}

Talquetamab is a bispecific antibody that binds to the GPRC5D receptor on the surface of myeloma cells and to the CD3 receptor on the surface of immune cells called T-cells to stimulate the killing of cancerous cells. Updated results were presented at ASCO2021 for the recommended subcutaneous dosing of talquetamab. Findings showed that 73% of patients experienced grade 1 or 2 cytokine release syndrome and 2% with grade 3 or 4. Other common side-effects were related to low blood cell counts, and 60% of patients experienced dysgeusia, which is defined as an alteration of taste. 70% of patients receiving subcutaneous talquetamab in the recommended dose saw improvement in their myeloma. The investigators are studying talquetamab in later phase studies at the recommended dose.

DIAGNOSTICS AND BIOMARKERS

Circulating tumour cells (CTC)\textsuperscript{15}

The most common way of assessing disease prognosis and risk of disease progression in multiple myeloma patients is through the measure of tumour burden in the bone marrow...
(BM). Hence, patients usually undergo several BM aspirates for analysis. This procedure, however, is painful and may not be fully representative of myeloma as myeloma is considered a patchy disease, and some patients have myeloma that exists outside of the bone marrow (known as plasmacytomas). A novel, alternative method for predicting disease prognosis is by analysing circulating tumour cells (CTC) found circulating in a patient’s blood.

This can be done using a complex testing method known as next-generation flow cytometry. In their study, the results of which were shared during EHA2021, Garces and colleagues measured circulating tumour cells in blood samples taken from 375 patients enrolled in the GEM2012MENOS65 clinical trial. The investigators found that burden was a prognostic factor for progression-free survival, and notably, it significantly outperformed the measures of tumour burden measured with a bone marrow biopsy. This suggests that CTC measures using blood samples could become a superior method for evaluating response to therapies and assessing disease prognosis.

PATIENT-REPORTED OUTCOMES AND QUALITY OF LIFE

Patient-reported outcome surveys (PROs) are used to capture patient experience while enrolled in a clinical trial or receiving treatment. The use of PROs has become a topic of importance in regulatory and drug development decisions. In addition to PROs, patient preference studies are sometimes conducted to capture patient perspectives on trade-offs that patients are willing (or not) to accept when choosing a specific treatment. The following studies were presented as poster presentations at EHA this year.

Outcomes in myeloma clinical trials

The European Hematology Association (EHA) is working to develop guidelines for using PRO tools in adult patients with blood cancers and examined the literature to determine the use and frequency of PRO tools in current randomised controlled trials conducted in MM. The researchers searched databases to determine what PRO tools were used in trials conducted between 2018 and 2020.

The researchers identified 118 studies with 63 studies ongoing and with no PRO outcomes identified, with most studies measuring PRO outcomes in 2nd line patients. The most common PRO tools used were the EORTC, EORTC-MY20, and the EQ-5D. The authors concluded that there is inconsistency in collecting and reporting PRO data, and a need exists for further standardisation.

Developing treatment attributes for a patient preference survey

Myeloma Patients Europe (MPE) partnered with KU Leuven as part of the Innovative Medicines Initiative (IMI) PREFER. The study aimed to understand which characteristics of treatment myeloma patients find most important. This study was conducted in two parts. The first part was a qualitative phase looking at what characteristics of treatment patients find most important. The data collected from the interviews were then used to develop a quantitative survey which was widely distributed throughout Europe.
Twenty four patients took part in the qualitative study across Europe. The results of the interviews were presented at EHA and suggested that patients value the following characteristics of treatment:

- Life expectancy
- Risk of life-threatening side-effects
- Expected treatment response
- Duration and severity of nerve of bone problems affecting movement
- Duration and severity of thinking problems
- Duration and severity of increased susceptibility to infections
- Duration and severity of emotional problems
- Duration and severity of eating and digestive problems
- Duration and severity of vision problems

The second part of the study ranking specific treatment attributes and further quantitative evaluation of each characteristic is pending publication.

The results of this research have recently been published in the scientific journal Frontiers in Medicine. Read the complete article here.

REGN5458

REGN5458 is a bispecific antibody drug that targets the BCMA protein on the surface of myeloma cells that is being investigated to treat relapsed/refractory myeloma patients (RRMM). Data presented at EHA2021 discussed patient reported outcome (PRO) or quality of life data collected from patients involved in the first-in-human phase 1/2 clinical trial at baseline and during weeks 4, 8, 12, and 24 of treatment.

Patients were given the EORTC QLQ-C30 and the EORTC QLQ-MY20 questionnaires. The data collected showed that patients had statistically significant improvement (from baseline) in their future perspectives, global health status/ quality of life, emotional and social functioning, and pain symptoms. Findings suggest there were no meaningful improvements in physical, role, emotional, and cognitive functioning, or body image. As part of the study patients experienced worsening fatigue, appetite loss, and overall side-effects of treatment.

MPE welcomes the use of PRO surveys examining patient experience of treatment and side-effects. However, more research is needed to understand more about the impacts of treatment and the best ways of measuring patient experience.

THE COVID-19 PANDEMIC

COVID-19 and autologous stem cell transplantation (ASCT) in NDMM

Most fit and newly diagnosed myeloma patients (NDMM) undergo autologous stem cell transplantation. In the wake of the COVID-19 pandemic, some patients found themselves unable to receive transplantation to preserve hospital capacity and equipment. In this study, conducted in the UK, researchers collected data to provide
a snapshot of the impact of the COVID-19 lockdown and patients’ response to therapy changes. Data were collected from 115 newly diagnosed myeloma patients between December 2019 and January 2021, with three lockdowns taking place during this time, resulting in a temporary halt of stem cell transplants.

In the results shared during EHA2021, 28/73 patients did not see a delay in transplant, with 45 having a delay ranging from 5-17 months (median 11 months), and 31 were put on bridging chemotherapy. Despite these changes, the overall response rates to induction were comparable at 97.3% in the stem cell group and 95.2% in the non-stem cell group. Furthermore, using a qualitative thematic analysis after interviews with patients, researchers identified six significant themes related to patients’ reactions to treatment changes:

- Psychological response to diagnosis and initial therapy
- Beliefs and opinions about the benefits of autologous stem cell transplant
- Perceptions of information provided about multiple myeloma and autologous stem cell transplant
- High levels of fear and anxiety due to COVID-19
- Feelings about disruption or delay of stem cell transplant due to COVID-19
- Perceptions of care

AL AMYLOIDOSIS UPDATES

ANDROMEDA Study

An update of the results from the phase 3 ANDROMEDA study with longer follow-up was presented during ASCO2021. In this study, 388 adult patients with newly diagnosed AL amyloidosis were randomly assigned into two groups. The control group was treated for six 28-day cycles with weekly bortezomib, cyclophosphamide, and dexamethasone (VCd). The intervention group received the same treatment as the control but with the addition of subcutaneous daratumumab (dara+VCd). After six cycles, patients in the intervention group continued to receive daratumumab once every four weeks for up to 24 cycles.

Results from the study (at a median follow-up of 20.3 months) showed that 59% of patients showed a complete haematologic response in the dara+VCd group versus only 19% in the VCd group. Furthermore, 57% of patients in the dara+VCd group had improved heart function versus 28% in the VCd group. Similar findings were seen in patients with improvement in kidney failure. These findings led to the approval of dara+VCd as the first therapy for the treatment of AL amyloidosis by the United States Food and Drug Administration (FDA) as well as the European Medicines Agency (EMA). The safety and side-effect profiles were similar to the first results published in the 2020 conference report.
Erectile dysfunction (ED)

Erectile dysfunction (ED), while common, is often underreported in association with AL amyloidosis. This study was done to assess the presence and possibility of causes of ED in male patients with AL amyloidosis. Between July and November 2020, 13 patients older than 70 were recruited and screened to ensure they had no underlying causes of ED.

This study was conducted at the Haematology Department of Federico II University in Naples, Italy. The researchers found that 92.3% (12/13) of patients had a reduction in penile arterial inflow and ED. 9/13 patients had severe ED, 1 with moderate ED, and 2 with mild ED, and 1 patient with no ED and localised AL amyloidosis. The researchers therefore concluded that "a possible indication from our study may provide us that any patient seeking medical advice for unexplained ED (with common secondary causes ruled out) should undergo AL screening."

EHA 2021 Advocacy and Patient Sessions

At EHA 2021, five patient joint symposiums were held on various clinical trial and regulatory topics. MPE attended these sessions and has presented a summary of each below.

Session I: Diagnostic regulations – threat or opportunity for innovative diagnostics?

During the first patient symposium, the novel in vitro medical devices regulations (IVDRs) were discussed. Olga Tkakencho from the European Commission gave a comprehensive summary of the novel regulations, the implementation of which is still in progress with a deadline of May 2022. Nicholas Baker, IVDR certification manager on notified bodies, has also given his perspective, pointing out that “the number of products [medical devices and drugs] to be assessed by notified bodies went up from 10-15% to 85-90%", which raises concerns as there are currently not enough notified bodies (organisations that assess the conformity of products before being placed on the EU market), which leads to certification capacity issues.

Oliver Bisazza, director general of industrial policies at MedTech Europe, also highlighted this challenge, referring to the May 2022 one as "a looming deadline".

Monica Brüggemann, from the UKSH in Kiel, voiced her concerns about in-house diagnostic tests. She pointed out that the new system of evaluating and classifying new IVDs sets a high standard for quality and safety. It could, however, lead to labs not daring to develop in-house diagnostic devices. The lack of development of in-house diagnostics could lead to reduced access to innovative and specialised diagnostics, gaps for rare diseases and some patient groups and loss of academic expertise for optimised specialised diagnostics.

All speakers stressed the importance of all stakeholders, including patients and patient advocates, as well as advocacy organisations collaborating to solve the bureaucratic issues complicating regulation of IVDs.
**Session II: Fair pricing of orphan medicines**

The second panel discussion was centred around the fair pricing of orphan medicinal products (OMPs). Maria Piggin, chair at PNH UK, represented the patient perspective. She pointed out that there is a "lack of transparency regarding the process and decision making" in OMP pricing. Furthermore, she voiced her concerns about quality of life tools not capturing important data to determine the cost/benefit - for example, how patient quality of life is affected by mode of medicine administration and ability to work during/after treatment.

She said she believed that patient organisations should provide data relevant to the cost/benefit of OMP not captured by HTA and drug development process.

Furthermore, patient organisations could collect real world evidence to support OMP fair pricing and reimbursement and put pressure on governments and the pharmaceutical industry to provide OMP access and establish/facilitate access to clinical trials, as well as support alternative ways to reduce pricing.

Isabelle Durand-Zalenski represented the health economics perspective. She outlined the complexity of taking the often conflicting interests of all stakeholders into account. Furthermore, outlining the perspective of the pharmaceutical industry was Alexander Natz from EUCOPE, an organisation representing mid-sized innovative companies in the EU. He argued that OMPs are very specific products, and investing in OMP development is very risky, especially for smaller companies. Hence, a more modern approach to the value of these medicinal products is necessary. Innovative approaches to payment, based on outcome, are becoming more common and the need for these is apparent.

Dr. Aldo Golja shared his point of view from the payer perspective. He also stressed that there is a lack of transparency in the pricing process of OMPs. In the discussion that followed, the speakers agreed that more multi-stakeholder negotiations would be necessary and patients should be more extensively involved in these discussions.

**Session III: COVID-19 pandemic**

The session discussed the effects of the COVID-19 pandemic on which lessons from the pandemic can help to improve research, approvals, evidence generation and clinical practice and research. Main themes included the real-world experience of patients, including the psychosocial and emotional impact of the pandemic, treatment and research implications, and effects on the diagnosis of patients.

The nurse perspective was represented by Mairéad Ní Chonghaile, who made the point that the presence of carers (made more difficult by the pandemic) had been underestimated before COVID-19. She also reiterated that in-person meetings with patients are not always necessary and virtual interactions and telemedicine encounters often put less strain on the patients, as well as clinicians and carers. Outlining the regulatory view was Dr. Ralf Herold, who acknowledged the great strides that have been made towards the acceleration of healthcare processes and procedures in general as a result.
of the COVID-19 pandemic

The clinical perspective was represented by Dr. Jose Maria Moradeo, who stressed that the pandemic has shown the necessity for improvement and renewal in the healthcare system within Europe. Dr. Peter Loffelhardt was representing the patient perspective, pointing out that the psychological pressure on patients has been and still remains significant, and it is further aggravated by a lack of information and misinformation around the pandemic. He highlighted the importance of educating patients to approach some information sources with scepticism.

Session IV: Personalised medicine trials

The fourth session was a discussion around creating a framework for bringing personalised medicines to patients. Dr. Ulrich Jäger and Jean-Pierre Bourquin, explaining the perspective of clinicians and PIs, focused on the need for new ways to monitor patient response and for a unique regulatory system for personalised medicine to allow an evidence-based approach. The regulatory framework was represented by Francesco Pignatti. Monika Frenzel from ICPeRMed (The International Consortium for Personalised Medicine) pointed out the necessity of bringing all stakeholders together to advance personalised medicine.

The patient perspective was represented by the CEO of Myeloma Patients Europe (MPE), Ananda Plate, who stated: “New therapeutic approaches, tailored to individual biology and patients' preferences are essential for cancer patients, but trials should meet not only clinical needs but also patients’ needs, preferences and patient-relevant outcomes. When developing these novel therapeutic approaches, considering access to trials and to clinical practice is essential. What if patients cannot access a potentially effective treatment just because ‘personalised medicine’ is not accessible? Personalised medicine will only work if patients are able to access it within the common treatment pathway. Equally important is to ensure clinical trials are running also in Central and Eastern European countries. which is currently unlikely.”

Session V: Reducing bureaucracy in clinical trials

The development of personalised medicine and patient-centric clinical trials requires improving the complex regulatory frameworks to optimise treatments and patient safety. Therefore, this session provided a perspective on ways to successfully design patient-centric and less bureaucratic clinical trials. Steven Le Gouill spoke from the point of view of clinicians. In his opinion, clinical trials are made less safe by the overwhelming amount of bureaucracy, which leads to important safety signals often being overlooked. Natacha Bolanos, from the Lymphoma Coalition, spoke for the patient community, also pointing out that the extensive paperwork involved in clinical trials, for example lengthy, complex informed consent forms (ICFs), tend to “obscure the information most relevant to the potential research participant”.

She considered improving the readability of ICFs to be a very important goal. Fergus Sweeney from the EMA talked about the revision of good clinical practice (GCP), the EMA has already collected input from stakeholders in order to modernise
GCP in the most beneficial way for all. Dr. Susan Bhatti represented the industry/sponsor perspective, suggesting a greater use of digital tools to improve the efficiency of the bureaucratic process and the design of a global harmonised clinical trial platform to avoid having to post the same information in several platforms.
Glossary

- Adverse event (AE): any unfavourable event and unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of medical treatment or procedure; in the context of clinical trials, adverse events are given a specific grade in severity based on specific criteria
  - Grade 1: mild
  - Grade 2: moderate
  - Grade 3: severe
  - Grade 4: life-threatening
  - Grade 5: death

- Allogenic stem cell transplant: a type of stem cell transplant where cells that are genetically different are taken from someone other than the patient (usually a close relative or match)

- Anaemia: low levels of red blood cells in the body

- Antibodies: proteins that the body creates to fight infection

- Autologous stem cell transplant: a type of stem cell transplant where a patient’s own stem cells are taken out of their body, processed, and reinfused after a patient receives chemo with the goal to replace damaged cells

- Bone marrow: spongy material in the centre of large bones in the body. This is where many cells are produced, including white blood cells (also called plasma cells) and red blood cells

- Clinical trial phases: the development of new treatments and diagnostics is done using several stages of research
  - Phase 1: this is a small study that tests the drug in various doses to determine the safest and most efficacious dose for patients
  - Phase 2: this study is a bit larger than phase I, and the primary purpose is to determine the efficacy of the previously selected dose
  - Phase 3: these are large multinational studies that are done to determine the efficacy of the studied drug in comparison to currently available treatments

- Complete response (CR): a treatment response type where less than 5% of plasma cells can be found in the bone marrow and no paraproteins are detectable in blood or urine
■ Consolidation therapy: treatment given following a stem cell transplant or initial therapy once cancer can’t be detected. This works to kill any remaining cancer cells that may be left in the body.

■ Cytokines: proteins released by cells throughout the body to stimulate cell growth, kill target cells and microbes, which is part of the immune response

■ Cytokine release syndrome (CRS): a side-effect characterised as a systemic inflammatory response causing flu-like symptoms such as fever, body aches and fatigue, which, in severe cases, can be life-threatening

■ Dose-limiting toxicity (DLT): side-effects of a therapy that are serious enough to prevent a further increase in the dose of the given treatment

■ Graft-versus-host-disease: a condition that can occur after bone marrow, stem cell, or other immune cell containing transplants where the graft (cells from the donor) recognise the host (recipient of the transplant) as foreign and attack the recipient’s body

■ Inclusion criteria: characteristics participants must have if they are to be included in a clinical trial

■ Lymphodepletion: therapy given before stem cell transplant, which is usually high dose chemotherapy to kill remaining cancer cells and get rid of blood-producing cells that are left in the bone marrow

■ Mean: average of data/numbers

■ Median: middle value in a list of data/numbers

■ Minimal residual disease: use of specialised testing to test for microscopic levels of plasma cells in a patient that has had a complete response to treatment

■ Minimal response: a treatment response type that shows a less than 50% decrease in paraproteins

■ Non-secretory myeloma: a rare type of myeloma that occurs in about 3 per cent of patients; occurs when very few (oligosecretory) or no (non-secretory) abnormal paraproteins are produced. It is very challenging to diagnose these patients

■ Overall response rate /objective response rate (ORR): the percentage of patients with partial response or better

■ Overall survival (OS): number of individuals in a group who are alive after a duration of time

■ Partial response (PR): a treatment response type that shows a greater than 50% reduction in paraproteins in the blood

■ Penta-drug refractory: patients who have been treated with a combination of
monoclonal antibody, and dexamethasone and are no longer responding to four drugs such as an immunomodulatory drug, a proteasome inhibitor, a type therapy

- Plasma cell: type of cell found in the bone marrow that produces antibodies
- Plasmacytoma: a condition where cancerous myeloma plasma cells are found outside of the bone marrow in the form of a tumour
- Progressive disease (PD): a treatment response type that shows an increase by 25% of urine or blood paraprotein levels
- Proteasomes: protein complex in the body which degrades and gets rid of damaged proteins
- Randomisation: the process of assigning study participants into treatment versus placebo arm (a dummy treatment) of study at random (done using computer programs, random numbers, etc.)
- Recommended phase 2 dose (RP2D): the dose chosen for administration in a phase 2 trial, based on the results of the phase 1 portion of the trial
- Refractory: when the number of myeloma cells and paraproteins continues to increase despite someone receiving treatment
- Relapse: myeloma that initially responded to therapy but after some time, myeloma plasma cell levels continue to increase
- Remission: classified as partial (some cancer cells or symptoms are present but at lower levels) or complete (cancer cells or symptoms are undetectable)
- Stable disease: no worsening or improvement of myeloma after treatment; also, disease that has previously responded to therapy and paraproteins levels have not increased
- Step up dosing: a method used in clinical trials where patients are initially given a drug at low doses with the dose then gradually increased step by step
- Stringent complete response (sCR): a treatment response type that shows no detectable presence of paraproteins in blood or urine; absence of abnormal myeloma plasma cells in the bone marrow
- Triple class refractory: patients who have previously been treated with a combination of three drugs, such as an immunomodulatory drug, proteasome inhibitor, and a monoclonal antibody, and are no longer responding to therapy
- Very good partial response (VGPR): a treatment response type that shows a greater than 90% decrease in paraproteins in blood and a paraprotein level in urine of <100 mg/24 h
REFERENCES


MPE is a network of European myeloma patient organisations. It supports national patient organisations to improve treatment and access for patients in their countries and helps inform and raise awareness on a European level through its educational programmes. Please note, this information does not replace the information provided by your doctor. If there is anything that is not clear to you, please always ask your clinical team.