

Conference report



53rd Annual Meeting of the
American Society for Clinical
Oncology (ASCO)

Chicago, USA 2-6 June, 2017

AND

22nd Congress of the
European Haematology
Association (EHA)

Madrid, Spain, 22-25 June, 2017



JUNE 2-6, 2017
McCormick Place | Chicago, Illinois
#ASCO17

53RD ANNUAL MEETING OF THE AMERICAN
SOCIETY FOR CLINICAL ONCOLOGY (ASCO)

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22ND CONGRESS OF THE EUROPEAN
HAEMATOLOGY ASSOCIATION (EHA)

MADRID, SPAIN, 22-25 JUNE, 2017

Introduction

This supplement highlights the key developments in myeloma research presented at ASCO and EHA in 2017.

In this issue

1. Highlights

Noted experts Professor Jesús F. San-Miguel and Dr Anna Sureda review trends in myeloma treatment in 2017 and explain how these may benefit patients, inclu-

ding new and better tools for diagnosing and monitoring treatment; the use of more effective triple and quadruple combinations of drugs to prolong progression-free

survival; and the emergence of new monoclonal antibodies and checkpointing inhibitors.

» Overview of new approaches to myeloma treatment in 2017



Caption: Professor Jesús F. San-Miguel, Director of Clinical & Translational Medicine at the University of Navarra (Spain).

The outcome for myeloma patients has significantly improved in the last 15 years, mainly due to the use of proteasome inhibitors (bortezomib, carfilzomib, ixazomib)

and immunomodulatory agents (thalidomide, lenalidomide, pomalidomide), and more recently, monoclonal antibodies (daratumumab, elotuzumab) and other novel drugs with a singular mechanism of action such as the HDAC inhibitor panobinostat, said **Jesús F. San-Miguel**, Professor of Haematology and Medical Director of the Clínica Universidad de Navarra, Spain. Moreover, the introduction of new criteria for early diagnosis of symptomatic myeloma and the possibility of early intervention are opening new therapeutic avenues, he said.

Dr Miguel presented an overview of new approaches to myeloma treatment on behalf of the Spanish Myeloma Group.

He listed three take-home messages:

- Better tools for diagnosis and monitoring treatment efficacy are being implemented;
- Early treatment and the use of more efficient drugs upfront prolong survival; and
- The treatment goal is to find the best possible balance between efficacy, toxicity and cost, particularly at the time of relapse.

In conclusion, he said:

“Myeloma should no longer be considered as a single entity. This, in conjunction with new monitoring tools, will contri-

tribute to treatment individualisation. The combination of a mononuclear antibody plus a triplet based on PI-IMiD-Dex may become the future upfront standard. Immunotherapy will play an important role in achieving our ultimate goal of curing myeloma.”

Other speakers in this session included **Hervé Avet-Lo-**

seau, from the University Cancer Centre of Toulouse, France, who reviewed the genetic classification of myeloma for prognostication and treatment selection; and **Nikhil Munshi** from Dana Farber Cancer Centre, Boston, USA, who reviewed the immunopathology of myeloma and explained how the targeting of the immune

system could provide new and very effective therapeutic strategies for myeloma.

References

New approaches to myeloma treatment in 2017.

» Overview of new approaches to myeloma treatment in 2017



Caption: Dr Anna Sureda, Head of the Haematology Department, Institut Català d'Oncologia (ICO), Spain during one of her sessions at the EHA Annual Meeting

Among the topics highlighted by Dr Sureda, Head of the Haematology Department, Institut Català d'Oncologia (ICO), Spain, as the most important developments in myeloma treatment presen-

ted during the European Haematology Association annual meeting (EHA 2017) was the impact of cytogenetic analysis in evaluating both the results of conventional protocols and also the impact of new drugs.

“New drugs improve the outcome of patients with adverse cytogenetic features but are not able to fully overcome the negative impact of these features,” commented Dr Sureda.

Second, Dr Sureda referred to the promising results of combinations of three and four drugs. She highlighted the long term and updated follow-up of various clinical trials including elotuzumab (ELOQUENT) and daratumumab (CASTOR and POLLUX). She explained that there is a possibility both to increase the rate of complete responses and to improve the rate of very good partial responses with the introduction of four drugs in front line setting.

Finally she drew attention to presentations on new monoclonal antibodies and checkpointing inhibitors including the presentation on the results with pembrolizumab by the Pamplona group.

2. New approaches

This is an overview of the most important new approaches presented at the two meetings.

Denosumab was compared to bisphosphonates such as zoledronic acid and was found to be equally effective in slowing down bone complications while reducing the renal problems associated with bisphosphonates;

Two triplet combinations of daratumumab in combination with bortezomib and dexamethasone (CASTOR) and lenalidomide and dexamethasone (POLLUX) had similar progression-free survival and treatment-related side effects in patients over 75 as in all age groups;

The monoclonal antibody elotuzumab in a triplet com-

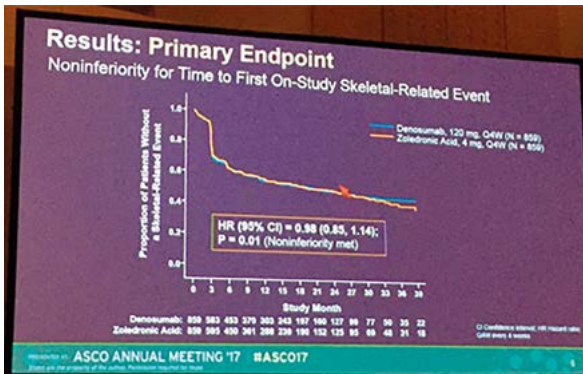
bination with lenalidomide and dexamethasone maintained its progression-free survival and overall response rate compared with lenalidomide and dexamethasone alone in a four-year update of the ELOQUENT study; and cytogenetics testing before treatment matters according to a new study from the Netherlands.

» Denosumab delays onset of first skeletal-related event in patients with myeloma

Bone lesions and renal dysfunction are frequent complications of myeloma. In the largest international myeloma trial ever conducted, the Phase 3 '482 study, patients who received denosumab had a significantly lower rate of renal adverse events

than those who received zoledronic acid. Denosumab also produced equivalent results to zoledronic acid in delaying the time to the first skeletal-related event. The results were presented during ASCO 2017.

The '482 study is an international, Phase 3, randomised, double-blind, multicentre trial of denosumab (XGEVA) compared with zoledronic acid in the prevention of fractures and other skeletal-related events in adult patients with newly diagnosed multiple myeloma and bone disease. Over 1,700 patients were randomised, 859 to each arm. Ten per cent of patients on denosumab experienced renal adverse events compared with 17 per cent of patients on zoledronic acid.



Caption: results show that denosumab is non-inferior to zoledronic acid in delaying the time to first on-study skeletal-related event in patients with myeloma

More than 90 per cent of myeloma patients develop osteolytic lesions during the course of the disease. Preventing bone complications is therefore a critical aspect of caring for patients with this disease. Current treatment options for these complications are limited

to bisphosphonates such as zoledronic acid, which are cleared by the kidneys and can be associated with increased renal toxicity. Although denosumab is already indicated for the prevention of fractures and other skeletal-related events in patients with bone metastases from solid tumours

it is not yet indicated for myeloma patients.

The manufacturer, Amgen, has applied to the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) to expand the currently approved denosumab indication to include myeloma patients.

“Renal impairment is a common complication in myeloma patients. Denosumab, which is not cleared by the kidneys, may offer a novel, safe and effective option,” explained **Noopur Raje, MD**, lead investigator and Director, Centre for Multiple Myeloma, Massachusetts General Hospital Cancer Centre, Boston.

References

- Noopur Raje et al. Impact of denosumab (DMB) compared with zoledronic acid (ZA) on renal function in the treatment of myeloma bone disease. *J Clin Oncol* 35, 2017 (suppl; abstr 8005)
- Press Release. Denosumab delays the time to first skeletal-related event in patients with myeloma. MPEurope. <http://www.mpeurope.org/news/denosumab-delays-the-time-to-first-skeletal-related-event-in-patients-with-myeloma/>
- Press Release. Amgen Presents New Data From Phase 3 XGEVA® (Denosumab) Study In Patients With Multiple Myeloma At ASCO 2017. Amgen. <http://www.prnewswire.com/news-releases/amgen-presents-new-data-from-phase-3-xgeva-denosumab-study-in-patients-with-multiple-myeloma-at-asco-2017-300468299.html>

» Daratumumab found to be safe and effective in older patients



Caption: Dr María-Victoria Mateos, PhD, Director of the Myeloma Unit, University Hospital of Salamanca-IB-SAL Salamanca, Spain

There is more news from the CASTOR and POLLUX phase 3 trials. This time, researchers looked at the effectiveness of daratumumab in combination with other drugs in patients aged 75 or older and assessed whether there was a difference in the side-effects.

Studies have already shown that daratumumab used in combination with bortezomib and dexamethasone (DvD; CASTOR) or lenalidomide and dexamethasone

(DRd; POLLUX) significantly prolongs progression-free survival with a manageable safety profile in patients with relapsed refractory myeloma compared with either Vd or Rd alone.

Researchers found that daratumumab in combination with these regimens was well-tolerated in most patients aged 75 or older and that the rates of treatment-related side-effects were similar to those found in all age groups. Infusion-re-

lated reactions were manageable and did not result in treatment having to be discontinued. The data were presented by **María-Victoria Mateos, MD, PhD**, Director of the Myeloma Unit of the University Hospital of Salamanca/IBSAL, Spain.

In CASTOR, 23 of the 251 patients in the DVd group and 35 of the 247 patients in the Vd group were over 75 years old. After 13 months, discontinuation rates due to treatment-related side effects were similar for patients in both the DVd and Vd arms.

Progression-free survival was significantly prolonged with DVd versus Vd, consistent with the overall progression-free survival observed in all age groups combined in the CASTOR trial.

In POLLUX, 29 of the 286

patients in the DRd group and 35 of the 283 patients in the Rd group were over 75 years old. After 17 months, 10 per cent of patients in the DRd group and 11 per cent in the Rd group discontinued the treatment due to treatment-related side-effects.

Progression-free survival was significantly prolonged with DRd compared with Rd in the elderly subgroup, consistent with the overall progression-free survival in all age groups combined seen in POLLUX.

Daratumumab is a monoclonal antibody that has been designed to recognise and bind to the CD38 protein, which is found in high amounts on myeloma cells. By attaching to CD38, daratumumab activates the immune system to kill the cancer cells. It is the first monoclonal antibody treatment approved

for treating myeloma.

The FDA in July 2016 granted breakthrough status for daratumumab in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy. And in February 2017, daratumumab was approved for that indication in Europe.

References

- María-Victoria Mateos et al. Daratumumab-based combination regimens in elderly (≥ 75 years) patients with relapsed or refractory multiple myeloma (RRMM): subgroup analysis of the phase 3 CASTOR and POLLUX studies. AHA 2017 (abstract P335)



» Triplet combination ELd continues to show good results after four years



Caption: Dr Meletios A Dimopoulos, Professor and Chairman of the Department of Clinical Therapeutics at the National and Kapodistrian University of Athens School of Medicine, Athens, Greece

Elotuzumab plus lenalidomide and dexamethasone (ELd) continues to show clinically relevant progression-free survival and overall response rate compared with lenalidomide and dexamethasone (Ld).

Professor Dr Meletios A Dimopoulos (Athens, Greece) presented the results of an extended four-year follow-up to evaluate the long-term efficacy and safety of elotuzumab plus lenalidomide and dexamethasone (ELd) at the EHA annual congress. This triple combination now has the longest follow-up of an immuno-oncology agent in myeloma.

The results presented at the EHA congress extend the results of the Phase 3 ELOQUENT-2 trial to evaluate the efficacy and safety of elotuzumab in combination with lenalidomide and dexamethasone, as compared with lenalidomide and dexamethasone alone, in patients with relapsed or refractory myeloma. In this study, 646 patients with relapsed or refractory myeloma were randomised to ELd or Ld. The two-year results were reported in the *New England Journal of Medicine* in 2015.

After four years, ELd demonstrated a sustained relative improvement compared with Ld.

ELd showed an improvement of 50 per cent (21 per cent versus 14 per cent in progression-free survival rates compared to Ld. The overall response rate was greater with ELd vs Ld (79 per cent vs 66 per cent) and the duration of response benefit was maintained over time.

Elotuzumab is an immunostimulatory monoclonal antibody that targets SLAMF7, a glycoprotein highly expressed on myeloma cells and natural killer cells but not on normal tissues that enables selective killing of myeloma cells with minimal effects on healthy tissue. It exerts a dual effect, directly activa-

ting natural killer cells and mediating myeloma cell death via antibody-dependent cell-mediated cytotoxicity.

“Overall, these data continue to support the durable efficacy of ELd,” commented Professor Dimopoulos. “Updated safety and tolerability was consistent with previous findings despite longer exposure, with minimal incremental adverse effects compared with Ld therapy.”

References

- Sagar Lonial et al. Elotuzumab Therapy for Relapsed or Refractory Multiple Myeloma. *New England Journal of Medicine* 2015
- Meletios A Dimopoulos et al. Phase 3 ELOQUENT-2 study: extended 4-year follow-up of elotuzumab plus lenalidomide/dexamethasone vs lenalidomide/dexamethasone in relapsed/refractory multiple myeloma. EHA, 2017 (abstract S456) <https://learningcenter.ehaweb.org/eha/2017/22nd/181743/meletios.a.dimopoulos.phase.3.eloquent-2.study.extended.4-year.follow-up.of.html?f=m3e1181>



» Cytogenetics testing matters

Myeloma patients who were diagnosed under the age of 66 and were treated with induction chemotherapy had a worse prognosis if they had not undergone cytogenetics testing beforehand, say Dutch scientists. Their results were presented as a poster at the EHA annual congress.

Researchers looked at the records of 731 myeloma patients in the Dutch Cancer Registry who were diagnosed in 2014-2015 and treated with induction chemotherapy.

The 'unperformed cytogenetics' (UPC) group of patients had worse outcomes than both the standard risk and high risk patients who had undergone cytogenetics testing. The progression-free

survival for patients in the standard risk group was highest, as compared to patients in the high-risk or UPC groups after one year of follow-up (88 per cent vs. 81 per cent vs. 74 per cent).

In total, 77 patients had progression of disease within three years after diagnosis.

Patients with UPC were more likely to progress than high risk and standard

risk patients who had been tested (16 per cent versus 13 per cent versus 9 per cent).

Cytogenetic testing was performed in almost 70 per cent of patients and was performed more frequently in 2015 than in 2014. One possible explanation for not performing cytogenetics

might be the patients' worse clinical condition when diagnosed which requires immediate treatment, say the authors.

References

- Mirian Brink et al. When performance of cytogenetics matters: a population-based study in the Netherlands on newly diagnosed multiple myeloma patients. EHA 2017. Abstract P686
<https://learningcenter.ehaweb.org/eha/2017/22nd/181973/mirian.brink.when.performance.of.cytogenetics.matters.a.population-based.study.html?f=m3>
- Press Release. Poster presentations IKNL-onderzoekers European Hematology Congress. 22 April 2017.

3. Novel treatments

Several presentations at ASCO described early-stage new treatments which hold promise for the future. Early results from a clinical trial in China using BCMA CAR T-cell therapy which is customised to individual patients with relapsed or refractory

myeloma has shown highly promising results. Results from a US multicentre trial were also reported during ASCO.

Two Phase 1 trials - pembrolizumab with lenalidomide and low-dose dexamethasone,

and isatuximab in a triplet combination with pomalidomide and dexamethasone - both show an acceptable safety profile. A new Phase 3 trial of isatuximab plus Pom/Dex started recruiting in January.

» CAR T-cell therapy shows promising results



Caption: Dr Wanhong Zhao, MD, PhD presenting the results of the Chinese CAR T-cell clinical trial during the ASCO Annual Meeting

Early results from a clinical trial in China using a new type of immunotherapy to treat patients with relapsed or refractory myeloma has shown highly promising results. Thirty-three (94 per cent) out of 35 patients experienced lasting clinical remission after being treated with chimeric antigen receptor (CAR) T-cells targeting B-cell maturation protein (BCMA). The results were presented during the ASCO 2017 annual meeting.

BCMA CAR T-cell therapy is

tailor-made for each patient. The patient's own T-cells are collected, genetically reprogrammed in the laboratory, and injected back into the patient. The reprogramming involves inserting an artificially designed gene into the T-cell genome, which helps the genetically reprogrammed cells find and destroy cancer cells throughout the body.

All patients were monitored for cytokine release syndrome (CRS), a common and potentially dangerous side

effect of CAR T-cell therapy. This occurred in 85 per cent of patients, but it was only transient. Most patients had only mild and manageable side-effects.

CAR T-cell therapy targeting a B-cell biomarker called CD19 has already proved effective in initial trials for acute lymphoblastic leukaemia (ALL) and some types of lymphoma, but this is one of the first clinical trials of CAR T-cells targeting BCMA.

Lead author **Wanhong Zhao, MD, PhD**, an associate director of haematology at The Second Affiliated Hospital of Xi'an Jiaotong University in Xi'an, China, explained: *"It appears that with this novel immunotherapy there may be a chance for cure in myeloma, but we will need to follow patients much longer to confirm that."*

The researchers plan to enroll 100 patients in this clinical trial, at four participating hospitals in China. They also

plan to launch a similar trial in the US in early 2018. “Looking ahead, we would also like to explore whether this therapy benefits patients who are newly diagnosed with myeloma,” said Dr Zhao.

Results from a US multicentre trial were also reported during ASCO. **James Kochenderfer MD** and his colleagues at the Experimental Transplantation and Immunology Branch of the

National Cancer Institute, Bethesda, developed the first BCMA-targeted CAR T-cells and in 2014 conducted the first human trial with bb2121. Jesus G. Berdeja, MD, of the Sarah Cannon Research Institute in Tennessee, presented an additional six months of follow-up on previously reported results with bb2121 at ASCO. *“These data support the potential of CAR T-cell therapy with bb2121 as a new treatment*

paradigm in myeloma,” said Dr Kochenderfer.

“The science behind [CAR T cells] is getting to be quite revolutionary,” said **Michael Sabel, MD**, of the University of Michigan Comprehensive Cancer Centre, during a press briefing on the results of the Chinese trial. *“But more research is needed to validate these findings and to see if we can make this type of therapy accessible to more patients.”*

References

- Frank (Xiaohu) Fan et al. Durable remissions with BCMA-specific chimeric antigen receptor (CAR)-modified T cells in patients with refractory/relapsed multiple myeloma. *J Clin Oncol* 35, 2017 (suppl; abstr LBA3001)
- Jesus G. Berdeja et al. First-in-human multicenter study of bb2121 anti-BCMA CAR T-cell therapy for relapsed/refractory multiple myeloma: Updated results. *J Clin Oncol* 35, 2017 (suppl; abstr 3010)
- Press Release. CAR T-Cell Therapy Sends Multiple Myeloma Into Lasting Remission. ASCO 5 June 2017 <https://www.asco.org/about-asco/press-center/news-releases/car-t-cell-therapy-sends-multiple-myeloma-lasting-remission>
- CART Cells: Expanding into Multiple Myeloma. National Cancer Institute. June 12, 2017 <https://www.cancer.gov/news-events/cancer-currents-blog/2017/car-t-cell-multiple-myeloma>
- Press Release. Promising results of CAR T-Cell therapy in myeloma patients. MPEurope. <http://www.mpeurope.org/news/promising-results-of-car-t-cell-therapy-in-myeloma-patients/>

» Triple combination with pembrolizumab has an acceptable safety profile and antitumour activity, say Phase 1 KEYNOTE 023 researchers

Dr Paula Rodriguez-Otero of the Clinical University of Navarra, Pamplona, Spain presented the results of an open label Phase 1 study to determine the maximum tolerated dose and safety and tolerability of a triple combination of pembrolizu-

mab plus lenalidomide and low-dose dexamethasone at the EHA.

The 40 patients in the trial were aged 46-77 years old and had between one and ten previous lines of therapy. About 75 per cent of patients

were lenalidomide-refractory, and 53 per cent were double refractory.

The researchers reported that this triple combination has an acceptable safety profile and antitumour activity in patients with

heavily pretreated relapsed or refractory myeloma, including both lenalidomide-refractory and double-refractory patients.

The maximum tolerated dose was determined as pembrolizumab 200 mg IV Q2W plus lenalidomide 25 mg and dexamethasone 40 mg. Two patients died because of treatment-related adverse events (hepatic failure, ischemic stroke). The most common grade ≥ 3 treatment-related side effects were neutropaenia (33 per

cent), thrombocytopenia (18 per cent), and anaemia (12 per cent). Immune-related adverse events occurred in five patients.

Pembrolizumab is a humanised monoclonal antibody first used in treating metastatic melanoma and is now used in the treatment of other metastatic solid tumours. It blocks a protective mechanism on cancer cells, and allows the immune system to destroy those cancer cells, targeting the programmed cell death 1 (PD-1) receptor.

References

- Paula Rodriguez-Otero et al. Pembrolizumab plus lenalidomide and low-dose dexamethasone for relapsed/refractory multiple myeloma: efficacy and biomarker results from the Phase 1 KEYNOTE 023 study. EHA (abstract S783) <https://learningcenter.ehaweb.org/eha/2017/22nd/182070/paula.rodriguez-otero.pembrolizumab.plus.lenalidomide.and.low-dose.html?f=m3>



» Isatuximab with pomalidomide and dexamethasone has manageable safety profile

The triplet combination of isatuximab with pomalidomide and dexamethasone had an acceptable and manageable safety profile in patients with relapsed or refractory multiple myeloma, according to the preliminary results of a Phase Ib study presented at ASCO.

Joseph R Mikhael, MD, of the Mayo Clinic, Scottsdale, Arizona, presented the results of the first 26 patients, of whom 50 per cent are still undergoing treatment. All patients had relapsed or refractory myeloma and had been treated with two or more previous therapies including lenalidomide and a proteasome inhibitor. Seventy-five per cent of patients had undergone a prior autologous

stem cell transplant.

Patients received isatuximab at 5 mg/kg, 10 mg/kg, or 20 mg/kg with pomalidomide 4 mg and dexamethasone 40 mg in 28-day cycles.

“Adverse events with this combination are generally consistent with the known safety profiles of the individual agents with perhaps a slight increase in grade 3/4 neutropenia [an abnormally low concentration of neutrophils in the blood] that was quite manageable,” said Dr. Mikhael.

The researchers concluded that this triplet combination was manageable and clinically active in heavily pretreated

relapsed or refractory myeloma.

A Phase 3 trial of this combination is ongoing. This multicentre, randomised, open-label study is being conducted to evaluate the clinical benefit of isatuximab in combination with pomalidomide and low-dose dexamethasone (Pom/Dex) versus Pom/Dex alone. It is being conducted in adult patients with relapsed and refractory myeloma and demonstrated disease progression within 60 days of the last therapy, and who have received at least two prior lines of therapy. The first patient was recruited in January 2017.

References

- Joseph Mikhael et al. A phase Ib study of isatuximab in combination with pomalidomide (Pom) and dexamethasone (Dex) in relapsed/refractory multiple myeloma (RRMM). *J Clin Oncol* 35, 2017 (suppl; abstr 8007). http://abstracts.asco.org/199/AbstView_199_181792.html
- Paul G. Richardson et al. A phase III, randomized, open-label study of isatuximab (SAR650984) plus pomalidomide (Pom) and dexamethasone (Dex) versus Pom and Dex in relapsed/refractory multiple myeloma. *J Clin Oncol* 35, 2017 (suppl; abstr TPS8057). http://abstracts.asco.org/199/AbstView_199_189890.html
- Press Release. Isatuximab Combination Safe, Active for Relapsed, Refractory Myeloma. Cancer Network. 9 June 2017. <http://www.cancernetwork.com/asco-multiple-myeloma/isatuximab-combination-safe-active-relapsed-refractory-myeloma>

4. Fertility and pregnancy during and after treatment

The outcome for cancer patients has significantly improved in the last years, but the longer survival and the better treatments open the door to the need of improvements in quality of life and solutions for the consequences that cancer may have such as infertility. Haematologists and oncologists usually are focused on clinical aspects and frequently forget these kinds of issues that can have a great impact in the patients' quality of life.

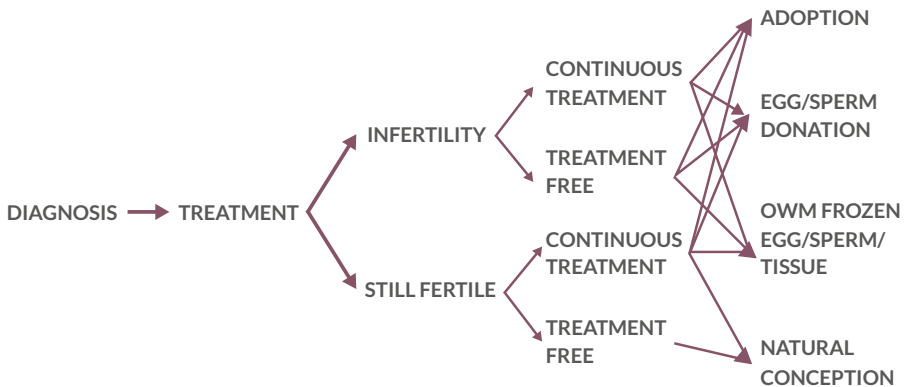
For most myeloma patients, fertility preservation and pregnancy during and after treatment is not a priority topic, mainly because most

patients are elderly at the time of diagnosis. So this topic, which is very relevant in other areas of haematology, affects only a small percentage of myeloma patients.

“When someone tells you that you have cancer, of course, the last thing you think about is having babies - your priority is surviving and so is the priority of your doctor. But at some point, normality returns to the lives of many patients, at least for a while, and with it also might come the desire of younger patients to plan a family. Unfortunately, at the time of diagnosis, few specialists explain to patients that they might become

infertile due to treatment and that fertility preservation can only be taken care of before treatment starts”, explained Ananda Plate, CEO of Myeloma Patients Europe (MPE) during the sessions “Fertility preservation in patients with haematological malignancies” and “Myths, reality, ethics and country borders in fertility treatment” at EHA 2017.

Own frozen egg or sperm tissue is the only way to preserve fertility. If fertility preservation was not successful, the only options currently available for having children are sperm donation or egg donation and adoption.



There are many barriers to fertility preservation and infertility treatment, in addition to the huge emotional and physical burden:

- **Informational hurdles:** the lack of information and misinformation about fertility preservation at diagnosis is the most important problem. Usually, patients get this information when they are on treatment or in remission. Also, they hardly ever receive information about the possibilities that exist in other countries.
- **Ethical and legal hurdles:** the legal landscape across Europe is very heterogenous. EU legislation only applies to use (procurement, storage, transport and traceability) of tissues and cells (eggs and sperm), and to their screening. The rest is national competence. In addition, procedures such as egg donation and freezing are not allowed in some countries and also patient eligibility criteria may change (e.g. sexual orientation, age, marital status...)
- **Clinical hurdles:** potential multiple cycles of hormone therapy, success rates of IVF vary enormously across Europe and between clinics and also there are clinical risks of a potential pregnancy during treatment (the difficult trade-off of risk of relapse, risk for the baby or the possibility of abortion).
- **Financial hurdles:** the untenable waiting times in public healthcare force patients to find solutions in the private healthcare system. That means a high financial burden (although prices vary between countries, every attempt could cost around 10,000 euros), and a limited number of attempts if the procedure is done under public healthcare.



“The information on fertility preservation should become part of the routine when a young patient is diagnosed. Doctors should be honest about the options patients have regarding pregnancy and try to find the best benefit-risk ratio for the patient’s future, not just the effectiveness of the cancer treatment”, said Plate.

5. Psychological issues

The distress of a cancer diagnosis not only erodes quality of life, but can also negatively affect the patient's ability to tolerate treatment and may impact the course of the disease. Two studies demonstrate how psychological intervention can help patients to cope.

» Conquering fears when patients are just diagnosed and after treatment – two interventional studies

Hearing those words “I’m sorry, you have cancer” can be devastating to patients. The distress not only erodes quality of life, but can also negatively affect the patient’s ability to tolerate

treatment and may impact the course of the disease. Yet few patients with cancer receive psychological support either at the time of diagnosis or after treatment.

Two novel studies assessed interventions in patients who had just been diagnosed, and in patients who had finished treatment.

The STREAM intervention

In the first of these, a new prospective study using an innovative intervention developed by oncologists and psychologists demonstrates that a web-based stress management programme can relieve distress and markedly improve quality of life for patients who have just been diagnosed. The STREAM intervention is an eight-week programme based on well-established cognitive behaviour approaches used in face-to-face psychotherapy. It covers eight different topics, such as, bodily reaction to stress, cognitive stress reduction, feelings, and social interactions. For each weekly topic, participants receive written and audio information and then complete exercises and questionnaires.

“Delivery of psychological support to patients at this early time in the course of their cancer care is hampered with lack of accessibility, time, and resources on both the patient’s and the provider’s side,” said lead study author **Viviane Hess, MD**, a medical oncologist at the University Hospital of Basel in Switzerland, who presented the study results during ASCO. *“We aim to close this gap with this online intervention.”*

Patients were assigned to either the STREAM intervention group or a control group within 12 weeks of starting cancer treatment. The majority of the 129 participants were women with early-stage breast cancer, although the study also included patients with

lung, ovarian, and gastrointestinal cancers, as well as those with lymphoma and melanoma.

Psychologists reviewed patients’ progress weekly and provided personalised, written guidance and support through a secure online portal. The psychologists were all based in Basel, but patients were located in Germany, Switzerland, and Austria. The patients also had the opportunity to write to the psychologists directly through the online programme.

At two months, patients in the intervention group had a greater improvement in quality of life than patients in the control group. The mean FACIT-F score increased by a mean of 8.59

points more in the intervention group than in the control group. The distress score decreased from 6 to 4 points in the intervention

group but stayed the same (6 points) in the control group. There were no significant differences in anxiety or depression between

the two groups. There are now plans to translate the programme into other languages.

The Conquer Fear study

In the second study, a Phase 2 randomised trial, a psychological intervention called Conquer Fear substantially lowered fear of recurrence immediately after the intervention, and three and six months later. About 50 per cent of all cancer survivors and 70 per cent of young breast cancer survivors report a moderate to high fear of recurrence, say the researchers. General anxiety, cancer-specific distress, and quality of life were better in the psychological intervention group immediately after therapy.

The Conquer Fear psychological intervention is based on a novel theoretical framework developed by the authors. Trained study therapists delivered the intervention in five 60- to 90-minute individual, face-to-face sessions over 10 weeks, to 222 individuals who were randomly assigned to an intervention or control group. All survivors had completed cancer treatment two months to five years before enrolling in this study and were cancer free at the time.

Conquer Fear focuses on: accepting the inherent uncertainty of whether the cancer would come back; teaching strategies to control worry; giving survivors more control over where they place their attention; helping them focus on what they want to get out of life; and choosing a sensible level of cancer screening and sticking to it.

Researchers used a measure called the Fear of Cancer Recurrence Inventory or FCRI. The average FCRI score at baseline was 82.7 in the intervention arm and 85.7 in the control arm. FCRI scores continued to decrease over time, with significant difference between groups at 6 months, decreasing by 27.2 points on average in the intervention group and 17.8 points on average in the control group which was considered to be clinically relevant.

“The reduction in fear of recurrence in the psychological intervention group was large enough to improve survivors’ psychological

and emotional wellbeing,” said lead study author Jane Beith, MD, PhD, a Medical Oncologist at the University of Sydney in Australia, who developed the Conquer Fear intervention with colleagues, including psycho-oncologist Phyllis Butow, BA(Hons) Dip Ed, MCLinPsych, MPH, PhD. “The majority of participants were young women with breast cancer, but we expect the intervention may be appropriate for other patients who have moderate to high fear of recurrence.”

References

- Viviane Hess et al. Web-based stress management for newly diagnosed cancer patients (STREAM): A randomized, wait-list controlled intervention study. *J Clin Oncol* 35, 2017 (suppl); abstr LBA10002. http://abstracts.asco.org/199/AbstractView_199_187932.html
- Press Release. Remote Therapy Program Improves Quality of Life, Lowers Distress After Cancer Diagnosis. ASCO. 2

June 2017. <https://www.asco.org/about-asco/press-center/news-releases/remote-therapy-program-improves-quality-life-lowers-distress>

- Jane Beith et al. Long-term results of a phase II randomized controlled trial (RCT) of a psychological intervention (Conquer Fear) to reduce clinical levels of fear of cancer recurrence in breast, colorectal, and melanoma cancer survivors. *J Clin Oncol* 35, 2017 (suppl; abstr LBA10000) http://abstracts.asco.org/199/AbstractView_199_186249.html
- Press Release. Psychological Intervention Lowers Survivors' Fear of Cancer Recurrence. ASCO. 2 June 2017. <https://www.asco.org/about-asco/press-center/news-releases/psychological-intervention-lowers-survivors-fear-cancer>



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