

# EMN

**The European Myeloma Network**

## Brief history of the network

Multiple myeloma is a rare and highly heterogeneous hematologic malignancy, and clinical research plays a fundamental role in the management of patients with this disease. To deal with such a complex scenario, in 2005, a group of European hematologists pulled together to increase their understanding of multiple myeloma and to produce effective research projects and clinical trials. These efforts resulted in the creation of the European Myeloma Network (EMN) foundation.

Over the years, the EMN has developed into a truly international co-operative network for all relevant aspects of research, diagnosis and treatment of multiple myeloma and related conditions. Besides myeloma, also other rarer hematologic diseases are covered by the network. Here follow the main areas of interest and the important objectives of the EMN:

- Organize international trials in rare plasma cell diseases, i.e. plasma cell leukemia, smoldering multiple myeloma, amyloidosis, POEMS syndrome
- Perform large phase 3 trials in newly diagnosed and relapsed/refractory multiple myeloma testing innovative molecules
- Provide uniform standards for correlative studies, such as genetics, imaging, minimal residual disease
- Coordinate consensus, guidelines and recommendations to harmonize treatment approaches in Europe
- Develop workshops and assure quality control
- Realize large data platform(s) for combined analyses and meta-analyses
- Spread knowledge through the organization of meetings and events for researchers, doctors and other persons interested in multiple myeloma and related conditions

The EMN has evolved since 2005, yet its scientific objectives and the deep commitment of its members have remained unchanged.

In 2017, the internal structure of the network has been modified and a new bylaw was adopted – further revised in 2019. Recently, more countries have started collaborating with the network, thus making the EMN a wide

organization for collaborative groups. This is a distinguishing feature of the EMN: as an open, scientific society, the EMN does not want to be exclusive; on the contrary, it aims to be as inclusive as possible, and to support the collaboration between the different national branches of the network.



## Organization

As reported in the revised 2019 bylaw, the EMN has a lean organization. This is to avoid a too complex internal structure and to allow an easier communication within the network itself.

The board is the main body of the network and it closely collaborates with participants/ members of the EMN foundation coming from various countries.

As for the administrative organization, the legal headquarters of the EMN is in Rotterdam – the Netherlands; whereas, the Italian branch – the EMN Research Italy in Turin – acts as the data center of the European network. The Dutch and Italian staff closely collaborate to successfully conduct projects and clinical trials under the EMN guidance.

In addition, the EMN can count on central facilities to perform essential trial activities. Minimal residual disease evaluations (NG-flow, NGS) are

centralized in Torino, Rotterdam, Brno, Aarhus sites; genetics analyses are conducted in Rotterdam and Bologna; and imaging is performed in Bologna and Amsterdam facilities.

## The Board

The EMN board oversees the management of the foundation and determines the policies and regulations of the network. The board is composed of a Chairman, a Secretary, and different Members, who are all experts in the hematologic field:

- *Pieter Sonneveld* from the Netherlands (Chairman);
- *Mario Boccardo* from Italy (Secretary);
- *Jesus Fernando San Miguel Izquierdo* from Spain (Member);
- *Herman Cristoph Einsele* from Germany (Member);
- *Meletios Athanasios Dimopoulos* from Greece (Member);
- *Heinz Ludwig* from Austria (Member).

The board is going to expand in 2019, and new members from other countries are being included:

- *Philippe Moreau* from France (Member);
- *Roman Hajek* from Czech Republic (Member);
- *Annette Vangsted* from Denmark (Member);
- *Gordon Cook* from the United Kingdom (Member).

## Members or participants

The EMN network has different members or participants from various countries, all actively involved and interested in the research on multiple myeloma and related conditions.

Becoming a member is simple, it just requires a notification to the foundation. Membership requests can now be done through the EMN website: [www.myeloma-europe.org](http://www.myeloma-europe.org).

When registering online, participants will also be asked to specify their main areas of interest/ expertise. This is to better organize the user's profile and to allow members to participate in projects and manuscripts relevant to their profile.

## Headquarters and data center

The headquarters of the EMN is in Rotterdam, where highly dedicated and experienced staff manages legal aspects, activates and coordinates international projects and trials. The Dutch team is supported by the Italian branch - the data center of the EMN Research Italy – in the organization and appropriate conduction of trials.

Below is a brief summary of the tasks and areas covered by the Dutch and Italian teams:



The EMN and the Italian branch have produced some policies that can be of interest to anyone who wishes to collaborate with the EMN. Of note, a specific form to propose studies has been created and is available online to members after registration (under “Policies & Templates”).

A Protocol Review Committee has been established to speed up the evaluation process. This committee is composed of physicians (Dr van de Donk, Dr Gay and Dr Terpos) and EMN administrative staff (Sarah Lonergan, Felicia Barbieri, Chiara Pautasso and Rossella Troia), and it performs both a scientific and technical evaluation of the proposals.

## Trials

Different trials have been coordinated by the EMN, and a complete list, with related details, can be found in the website.

The contribution of pharmaceutical industry is fundamental in this area: the EMN can collaborate with pharmaceutical companies in the design of innovative and useful clinical trials, where new and active molecules can be appropriately assessed, allowing patients to benefit from last-generation, effective treatments.

EMN studies are identified by sequential numbers, and the network has recently activated the EMN17 study assessing the combination daratumumab plus bortezomib, lenalidomide, dexamethasone in the myeloma transplant setting. The study looks promising and has been very well received by the scientific community.

Besides multiple myeloma, also other rarer conditions are covered by the EMN. The group is actively involved in the research on AL amyloidosis and plasma cell leukemia. For instance, the EMN12 is a very important study evaluating novel-agent carfilzomib and lenalidomide-based treatment for transplant eligible and non-transplant eligible patients with newly diagnosed primary plasma cell leukemia. Its results will be of great help to the patients and the scientific community.

Smoldering myeloma, extramedullary disease, Waldenstrom are other relevant fields. Indeed, the EMN has designed the EMN15 randomized, phase 2 trial to assess the role of carfilzomib plus lenalidomide and dexamethasone for the treatment of high-risk smoldering myeloma patients. In addition, the EMN19 will investigate the role of the monoclonal antibody daratumumab for the treatment of patients with extramedullary disease.

Here we have briefly summarized the studies available under the EMN:

EMN study code	Main study drug/s	Setting
EMN01	Lenalidomide	Newly diagnosed transplant-ineligible myeloma
EMN02	Bortezomib, Lenalidomide	Newly diagnosed transplant-eligible myeloma

EMN04	Reduced-intensity allogeneic	Relapsed myeloma
EMN07	Carfilzomib, Pomalidomide	Relapsed/Refractory myeloma
EMN09	Carfilzomib, Bendamustine	Relapsed/Refractory myeloma
EMN10	Ixazomib, Bendamustine	Newly diagnosed transplant-ineligible myeloma
EMN11	Carfilzomib, Pomalidomide	Relapsed/Refractory myeloma
EMN12	Carfilzomib, Lenalidomide	Newly diagnosed primary plasma cell leukemia
EMN13	Ixazomib	Relapsed/Refractory myeloma
EMN14	Pomalidomide, Daratumumab	Relapsed/Refractory myeloma
EMN15	Carfilzomib, Lenalidomide	Smoldering myeloma
EMN17	Daratumumab, Bortezomib, Lenalidomide	Newly diagnosed transplant-eligible myeloma
EMN18	Daratumumab, Bortezomib	Newly diagnosed transplant-eligible myeloma
EMN19	Daratumumab, Bortezomib	Extramedullary disease
EMN20	Carfilzomib, Lenalidomide	Newly diagnosed transplant-ineligible myeloma
EMN 22	Daratumumab	Newly diagnosed patients with stage 3B light chain AL amyloidosis
EMN23	Retrospective, observational	Patients with systemic AL amyloidosis in Europe

Other important EMN trials are being defined, and they will be available soon.

To propose a study to the Protocol Review Committee, investigators should register online first and then download the proposal form and protocol template.

## Meetings

Good ideas and projects need to be shared. This is the reason why the EMN is highly committed to organizing important events for physicians working in the myeloma field.



One of the major events is certainly the EMN Trialist Forum, a long-standing tradition in the history of the EMN, held in September in Baveno – Italy. Here, the core EMN trialist group discusses important aspects related to the network and practical issues in EMN clinical trials.

New proposals, recently activated or under activation, are addressed as well, and pharmaceutical companies participate in trial-specific meetings to solve open questions and define possible amendments together with investigators.

The EMN biannual meeting is a more recent event, open not only to the core EMN investigators but also to anyone working in the hematologic field and willing to participate. The biannual meeting is organized by the Dutch and Italian teams, with the collaboration of the



scientific secretariat. This event seeks to go beyond national boundaries by including research groups from all over Europe. Meet the expert sessions, relevant educational sessions, abstract submission, patient association talks and sponsored symposia are planned, and they contribute to make this biannual event a unique and highly formative experience for all attendees. The first edition was held in Turin in 2018 and it proved to be very successful, reaching approximately 800 participants. The EMN team is now organizing the new edition in 2020, in Amsterdam, and about 1000 participants are expected.

## Collaborative projects



**HARMONY**

Among the major works, the collaborative groups under the EMN – Prof. Sonneveld for the Netherlands, Prof. Boccadoro for Italy and Prof. San Miguel for Spain as key opinion leaders in myeloma – are actively involved in a major, international project, called HARMONY. What is HARMONY? “The HARMONY Alliance is a public-private European Network of Excellence, established in January 2017.” Its aim is to spread valuable knowledge on hematologic malignancies, with the goal to harness and mine Big Data to speed up the development of improved treatments. Clinical and translational data are merged together in a big database, and the EMN contribution through collaborative groups is fundamental. To date, HARMONY has 53 partners and 32 associated members from 22 countries, including 8 pharmaceutical companies from the European Federation of Pharmaceutical Industries and Associations (EFPIA). The EMN is proud to participate in such an important and wide, collaborative project.



The collaborative groups of the EMN have also participated in another innovative project under the HORIZON 2020 European Commission framework, together with SkylineDX company: MMpredict project.

The aim is to clinically validate a personalized medicine tool that predicts the most effective treatment option in myeloma patients. Currently, there are a range of single/combination novel agents and chemotherapy drugs available and in development for myeloma. Because multiple myeloma is a very heterogeneous disease, one treatment does not fit all. Consequently, the MMpredict project aims to investigate and produce a diagnostic tool that supports treatment decision-making process. To achieve this goal, SkylineDX is developing a microarray-test that can be used for genetic subtyping of myeloma patients. This tool should be able to determine the most suitable treatment for patients by predicting their response based on gene expression profiling. This will allow European health care systems to better allocate their resources and reduce costs, since patients will be able to receive the right and more appropriate treatment for them. Of course, this will lead to a considerable improvement in the quality of life of myeloma patients.

## Publications

EMN investigators produce relevant guidelines and recommendation papers, as well as EMN trial reports, to be submitted to peer reviewed journals. During the Baveno forum, the core team discusses burning, controversial topics that deserve the EMN attention and that need further discussion in a manuscript by the EMN. Lead authors and timelines for publications are also established during the annual forum in Baveno.

Here is a list of some of the major reviews and consensus papers published by the EMN group in 2018. These are valuable resources to hematologists and physicians working in this field:

- Patient-centered practice in elderly myeloma patients: an overview and consensus from the European Myeloma Network (EMN) – *Leukemia*
- Prevention and management of adverse events of novel agents in multiple myeloma: a consensus of the European Myeloma Network – *Leukemia*
- From transplant to novel cellular therapies in multiple myeloma: European Myeloma Network guidelines and future perspectives – *Haematologica*
- European myeloma network recommendations on diagnosis and management of patients with rare plasma cell dyscrasias – *Leukemia*
- Cardiovascular adverse events in modern myeloma therapy - Incidence and risks. A review from the European Myeloma Network (EMN) and Italian Society of Arterial Hypertension (SIIA) – *Haematologica*
- European Myeloma Network recommendations on tools for the diagnosis and monitoring of multiple myeloma: what to use and when – *Haematologica*
- Maintenance Treatment and Survival in Patients with Myeloma: A Systematic Review and Network Meta-analysis - *JAMA*

A complete list of EMN publications can be found in the website. The EMN is a very active group, highly committed to sharing knowledge with the scientific community. Due to the great advances in myeloma treatment and the rise of new clinical issues, many more EMN manuscripts and consensus are expected to come in the next future to address unanswered questions.

## To sum up

The EMN is the reference organization for studies on multiple myeloma and other rarer hemtologic conditions in Europe, bringing advantages to all the actors involved in the clinical research. EMN physicians can have the opportunity to participate in cooperative projects to increase and share their experiences, as well as to standardize and harmonize clinical practices; pharmaceutical companies can refer to the EMN as general interlocutor in Europe to plan and manage clinical trials with new effective molecules; finally – and most importantly – patients can be enrolled in well-designed clinical studies evaluating last-generation and promising drugs, with the ultimate goal of improving their survival and quality of life.

In the last few years, many steps forward have been made in the research on myeloma and related conditions, and the EMN is proud to have contributed to the development of successful clinical studies. Big objectives can be achieved only through big collaborations, and the EMN is a very active network that makes innovative projects come true in Europe.

## Contacts

The EMN staff is pleased to receive any comment, suggestion or proposal.

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