ERN-EuroBloodNet
6th Progress meeting

21st November 2024, online

ERN | EuroBloodNet

European Reference Network | Hematological Diseases (ERN EuroBloodNet)

Co-funded by the European Union

Funded by the European Union.
Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or European Health and Digital Executive Agency (HaDEA). Neither the European Union nor the granting authority can be held responsible for them.

ERN-EuroBloodNet 6th Progress meeting was held 21st November 2024 online. **170 participants from 64 ERN-EuroBloodNet Healthcare providers and 14 EU Member States** registered to the meeting. 73% of participants were members representatives or part of the multidisciplinary teams, while 10% were ePAGs and patients representatives (Fig 1). The most represented areas of expertise were red blood cell disorders and bone marrow failures (Fig 2).

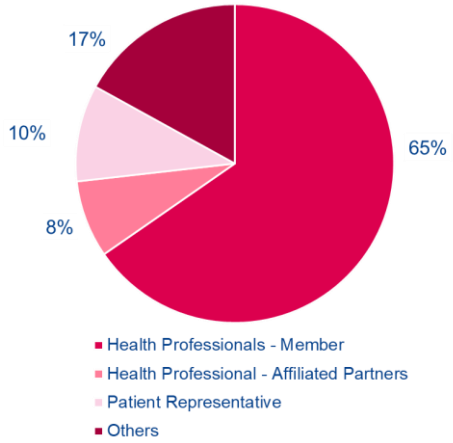

Fig 1. Role of participants of the meeting

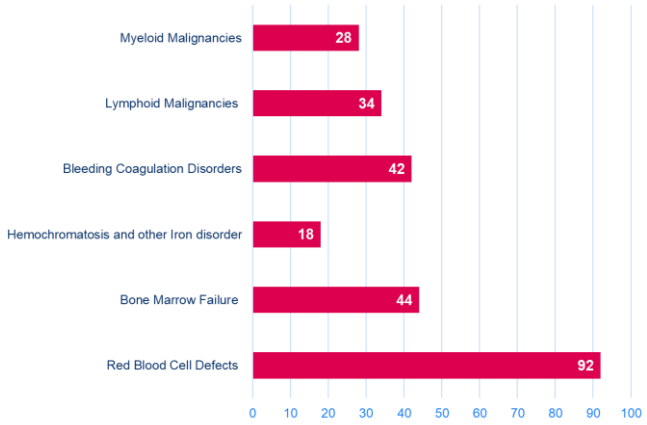

Fig 2. Area of expertise of participants

The event kicked off with a welcome message provided by the ERN co-coordinators who presented the current overview of the ERN relevant stakeholders and agenda for the day.

Luca Sangiorgi, Coordinator of the ERN on rare bone diseases (ERN-BOND) and current Coordinator of the ERNs Coordinators group, presented the European Reference Networks state of play. He highlighted relevant transversal activities ongoing for all ERNs, including a position paper on ERNs under drafting, the creation of new ERNs working groups and the CPMS 2.0 transition. Importantly, the general frame for the upcoming ERNs and Members Evaluation was presented.

Till Voigtländer, Coordinator of the Joint Action on Integration of ERNs into National Healthcare Systems (JARDIN) and representative of the Board of Member States in Austria, presented the JARDIN action general aims and how will improve the accessibility of the ERNs for people living with rare diseases (RD) or complex conditions in EU Member States. JARDIN will pave the way for ERNs integration in the national healthcare systems and increase their sustainability.

Ana Rath, ORPHANET director and pillar leader on the European Rare Disease Research Alliance (ERDERA), presented the data services developed for RD research in the European Joint Programme on Rare Diseases (EJP-RD) and their expansion and consolidation under ERDERA.

Clinical Practice Guidelines & Access to Highly Specialized Care

ERN-EuroBloodNet is developing Clinical Practice Guidelines (CPGs) and other Clinical Decision Support Tools (CDSTs) in the field of rare hematological diseases (RHD) in collaboration with the EC and the main hematologic networks and associations. Over 2024 the status of ERN-EuroBloodNet CPGs and CDSTs was shown to the audience:

- CPG on Diagnosis and management of Pyruvate Kinase Deficiency and on diagnosis and treatment on Burkitt lymphoma (in press) have been published. CPG on diagnosis and treatment on Vexas Syndrome is in submission stage.
- Recommendations for diagnosis on rare haemolytic anaemias has been recently launched as a joint collaboration between European Hematology Association (EHA) and ERN-EuroBloodNet.
- Recommendations on sickle cell disease are also being produced as a European consensus based on the analysis performed with the national or local recommendations available. These EU recommendations will highlight disparities in practice and identify unanswered questions that can be the focus of future research.
- CDSTs are pivotal in delivering safer, more personalized, and effective healthcare experiences. ERN-EuroBloodNet, in collaboration with ePAGs, is developing these tools to enhance patient therapeutic education (PTE) and improve health outcomes in disease management. As example, the method developed for creating patient journeys through PTE programs was also presented. This method addresses two critical needs of the RD patient community: the lack of education and the sharing of best practices. A pilot study on Von Willebrand Disease, in collaboration with the European Haemophilia Consortium is currently being conducted.

ERN-EuroBloodNet supports the conduction of EU Mapping exercises to assess the availability and accessibility of Highly Specialized Procedures (HSP) and treatments, as standards of core elements for CPGs and CDSTs that may not be available in all EU Member States. Two successful mappings were presented:

- Mapping for management of venous thrombosis and arterial thrombosis in paediatric patients has allowed to better know the state the art of paediatric thrombosis in Europe, a rare condition in children. Also, as a result, the ERN-EuroBloodNet Pediatric Thrombosis Working Group has been created to develop the “European Principles of Care for Pediatric Thrombosis” and to arrange regular meetings for discussing of complex cases.
- The Mapping on phlebotomy practice for sickle cell disease has demonstrated that despite not being a highly complex procedure, there are disparity of practices across EU and variety of indications.

Education & Collaborative programs

Main results from the ERN-EuroBloodNet educational actions ongoing were presented into two main targets:

- Health professionals including expert training, case discussions, and access to cutting-edge guidelines to improve rare hematological care.
- Patients developing tools and programs that empower them through education, enabling better disease understanding and management. Kind of programs are advocacy training, PTE and Public Patient involvement in research.These efforts bridge the gap between expertise and patient needs.

EHA&ERN-EuroBloodNet partnership fosters a commitment to education and knowledge sharing across rare hematological diseases. A clear example is the EHA & ERN-EuroBloodNet Spotlight webinar programs devoted to castleman disease or hypereosinophilich syndrome, that have consolidated a collaboration for coming years on different areas on need. The collaboration with the EHA has been reiforced and a mutual agreement of havin a common annual plan on CME has been reached (for a maximum of 8 webinars sessions). For the upcoming year two new Spotlight programs are foreesen starting in April 2025.

The ongoing collaborative programs for education on research were also introduced to the audience, including the concrete collaborations with:

- Genomics and Personalized Medicine for all though Artificial Intelligence in Haematological Diseases (GenoMed4ALL) and Synthetic generation of hematological data over federated computing frameworks (Synthema) for the Educational program on Artificial Intelligence in hematology.
- Assessing efficacy and safety of genome EDITing approaches for Sickle Cell Disease (EDITSCD) including the e-workshop on gene editing will be organized to disseminate knowledge on gene therapies for patients advocates on sickle cell disease, gene editing tools and their efficacy and safety profiles. A method for training researchers in delivery knowledge in lay language will be explored.
- Haemoglobinopathies in European Liaison of Medicine and Science (HELIOS) offering an educational program for patient advocates focused on hemoglobinopathies.

Artificial intelligence tools like Translated Captions in Zoom are being tested to provide live, automatic translations of educational content. This aims to reach a wider audience and reduce the language barrier.

CPMS & Cross border health

Clinical Patient Management System (CPMS) 2.0 has been designed to improve both functionality and user experience in assisting ERNs to enhance the diagnosis and treatment of rare or low-prevalence complex diseases across Member States.

- ERN-EuroBloodNet will transition to CPMS 2.0 first week of December, with a mobile version expected to follow soon.
- Additionally, this updated version will enable clinicians in Ukraine to submit cases for advice. ERN-EuroBloodNet is eager to engage in this significant advancement.

ERN-EuroBloodNet website includes two engines implemented at the website to increase the searchability of ERN-EuroBloodNet healthcare providers and health professionals expertise and activity

- Disease Cards, pooling reference centres and experts, materials (as CPG and CDST, webinars, etc.) and actions by 72 RHD disease groups.
- Repository of RHD experts and facilities and PDF generator to allow the download of reports by the search criteria

ERN-EuroBlooNet Patients Assistance Infopoint helps patients navigate healthcare systems, facilitating access to specialized treatment across EU member states. It connects patients with healthcare providers, offers expert-led resources, and advocates for patient-centered care, ensuring equitable access to high-quality services. During the Progress Meeting we heard about testimonies and expectations on paroxysmal nocturnal hemoglobinuria, thalassemia and von Willebrand disease from 3 ERN ePAGs advocates, in the areas of Access to treatment, search for expertise abroad and access to diagnosis.

Data driven research & Innovative therapies

Real World Data and Evidence in the evaluation of new drugs

The formation of ERN registries, along with national and patient-driven RD registries, offer significant potential for therapeutic innovation. However, there are substantial obstacles in collecting and using real-world data (RWD) across the value chain, from data capture to clinical trial readiness.

European Rare Disease Research Alliance (ERDERA) aims to create a Clinical Research Network to:

- Leverage facilities and expertise to address these challenges by creating, integrating, and processing real-world RD cohort data for clinical trials.
- Develop a platform for the development and validation of regulatory-grade patient-reported as well as indirect Clinical outcome assessment for RD
- Develop digital tools allowing efficient and broad collection of patient self-reported data in RD and integration with patient databases

The role of Real World Evidence (RWE) in enriching benefit-risk evaluations, underscoring its capacity to augment traditional trial findings and inform healthcare decisions was also discussed with the audience:

- The results of the European Medicine Agency (EMA) – European Hematology Association (EHA) survey on RWE in regulatory and clinical decisions was presented including the beliefs about real-world evidence and how this impact assessment of scenarios with single arm trials.
- The Stichting Hemato-Oncologie voor Volwassenen Nederland (HOVON) and Dutch Cancer registry experience in building quality sources for RWE highlights significant flaws in medical literature related to RWD used as external control cohorts for prospective studies in patients with hematological cancers. To increase RWD utility, suggested improvements include: prospective RWD collection; incorporation of co-morbidity-data; use of matching; inclusion of safety data; optimized predefined statistical analysis; and adherence to similar endpoints and follow-up and inclusion criteria as in the prospective phase II/III study.
- Patients perspective highlight the key role of registries and patients advocates in supporting the use of RWE in the evaluation of new drugs. RWE can enhance regulatory decision-making by addressing data quality, standardization, and governance challenges, enabling patient-centric approaches and empowered advocacy through early patient involvement, and improved understanding of patient perspectives and outcomes. An approach possible via FAIR-aligned registries.
- Ensemble Leucémie Lymphomes Espoir (ELLyE) contribution to the evaluation of medicines with the High Authority of Health and to research through the patient associations participation in research and clinical trials were also presented to the audience, together with the key results from the global surveys that provide valuable real-world insights into unmet needs and experiences of chronic lymphocytic leukemia patients globally conducted by the Chronic Lymphocytic Leukemia Advocates Network (CLLAN)

ENROL contribution to Epidemiology surveillance

The European Rare Blood Disorders Platform (ENROL) Registry Module for the Collection of annual counts of RHDs patients (EpiBlood) aims to systematically collect standardized information on the annual counts of patients with RHDs through a secured REDCap system.

- Contribution from each HCP is mandatory for the subnetworks where the institution is recognized as ERN Member. The opportunity to contribute is also extended to other subnetworks.
- Next data collection exercise for year 2024 will start 1st February 2025 until 28th February 2025.
- ERN-EuroBloodNet Members and Affiliated Partners will be contacted during January with the Handbook and PDF template with the information that will be requested for this year campaign.

Fair pricing in hematology

The session on fair pricing in hematology allowed the discussion on the meaning of fair from the clinicians and patients perspective as well as the tools needed to improve the decision making on pricing and reimbursement.

- In countries where drug reimbursement is shared, health technology agencies play a critical role in informing public decision-makers. Clinical benefit and efficiency cannot be measured without evidences and transparency.
- Paroxysmal nocturnal hemoglobinuria access to treatment has allowed the identification of a gap between market access and effective patient access to drugs across EU Member States, highlighting discrepancy between regulatory aims and the reality. Reimbursements pathways affect more effective patient's access to treatments than market authorization.
- The case of interferons in myeloproliferative neoplasms is a clear example of discrepancies on pricing and accessibility across countries. A reasonable price could cover research and development costs while being affordable for healthcare systems and patients.

Clinical trials

ERN-EuroBloodNet is sponsoring two clinical trials:

- The SATISFY study (Mitapivat in red blood cell membranopathies) is the first ERN-EuroBloodNet sponsored clinical trial. The trial is now open in Denmark and the Netherlands, providing targeted treatments to patients with hereditary spherocytosis, hereditary stomatocytosis, and congenital dyserythropoietic anemia II. Expansion to other rare hereditary anaemias is foreseen.
- The LUSPARA trial (Luspatercept in rare inherited anemias) is a Phase II clinical trial evaluating Luspatercept in patients affected with rare inherited anemias. 45 patients are expected to be enrolled in 3 different centers (France, Spain and Italy)

New methodological approaches on Clinical Trials in RD were also presented through RealiseD, an IHI project starting in January 2025 enhancing clinical trials for RD through a collaborative, patient-centered approach.

- RealiseD focuses on efficient drug development by refining statistical methods and certifying clinical sites, using European case studies.
- By involving regulators and reducing uncertainties, RealiseD aims to motivate pharmaceutical investment and streamline the regulatory pathway for new treatments.

Thank you all for your participation!

Presentations are available on the ERNs Collaborative Platform and on demand by contacting giulio.sannasardo@aphp.fr