ERN-EuroBloodNet

Pierre Fenaux – pierre.fenaux@aphp.fr
Béatrice Gulbis - beatrice.gulbis@erasme.ulb.ac.be
María del Mar Mañú Pereira – mar.manu@vhir.org
Victoria Gutiérrez Valle – victoria.gutierrez@vhir.org
Mariangela Pellegrini - mariangela.pellegrini@aphp.fr

European Reference Networks (ERNs) involve healthcare providers across Europe. They aim to facilitate discussion on complex or rare diseases and conditions that require highly specialized treatment, concentrated knowledge and resources.

The first **24 ERNs** covering 24 different medical specialities were officially approved by the EC in December 2016 and started their activity in March 2017.

European Commission

Co-funded by the Health Programme of the European Union

ERN-EuroBloodNet

results from a joint effort of many pieces

ERN-EuroBloodNet is a collaborative network of **66 healthcare providers (HCPs) in 15 MS** that brings together individuals and institutions committed to improving healthcare services in **Rare Hematological Diseases**

Member Sate	nº HCP
Belgium	5
Bulgaria	2
Cyprus	1
Czech Republic	1
Germany	4
Spain	1
France	12
Ireland	1
Italy	21
Lithuania	1
The Netherlands	6
Poland	1
Portugal	3
Sweden	1
United Kingdom	6
Members	**66**

ERN-EuroBloodNet – Disease coverage and coordinators

EuroBloodNet

Oncological diseases Hub
Coordinated by Prof P. Fenaux
AP-HP, Hôpital St Louis, Paris

- Myeloid malignancies
- Lymphoid malignancies

Non -oncological diseases Hub
Coordinated by Prof B. Gulbis
CUB-Hôpital Erasme, Brussels

- Rare red blood cell defects
- Bone marrow failures and rare haematopoietic disorders
- Rare bleeding-coagulation disorders and related diseases
- Haemochromatosis and rare hereditary iron metabolism disorders

Oncological diseases coordinators:

- Myeloid malignancies
  23 HCPs from 9 MS
  P. Fenaux (France)
  U. Platzbecker (Germany)
  S. Wintrich (UK) - ePAG
- Lymphoid malignancies
  22 HCPs from 10 MS
  A. Engert (Germany)
  C. Thieblemont (France)
  P. Aumont (France) -ePAG

Non-Oncological diseases:

- Rare Red blood cell defects
  36 HCPs from 12 MS
  B. Gulbis (Belgium)
  N. Cappellini (Italy)
  L. Brunetta (Italy) - ePAG
- Bone marrow failure
  20 HCPs from 8 MS
  A. Iolascon (Italy)
  R. Peffault (France)
  M. Piggin (UK)
- Rare bleeding-coagulation disorders
  35 HCPs from 10 MS
  M. Makris (UK)
  F. Peyvandi (Italy)
  A. Bok (UK) - ePAG
- Hemochromatosis and hereditary iron disorders
  15 HCPs from 6 MS
  G. Porto (Portugal)
  D. Swinkels (The Netherlands)

ERN-EuroBloodNet

results from a joint effort of many pieces

European Commission

Co-funded by the Health Programme of the European Union

EUROPEAN HEMATOLOGY ASSOCIATION

- Promotes excellence in patient care, research, and education in hematology
- EHA's annual congress is the largest European event for hematology.
- Haematologica is the primary general hematology journal

enerca

- Pilot ERN in rare and congenital anaemias since 2002
- eHealth solutions: e-Registry, e-Learning, Telemedicine platforms
- WhiteBook : ENERCA recommendations for Centres of Expertise in Rare Anaemias

EURORDIS RARE DISEASES EUROPE

- Patient-driven alliance of organisations and individuals active in the field of RD in Europe
- Represents 724 RD organisations in 64 MS, covering more than 4000 RD
- ePAGs - European Patient Advocacy Groups, are the patients representatives for ERNs

And many more…

EUHANET

- Pilot ERN for the Haemophilia and other inherited bleeding disorders

European Iron Club

- Network for patient care and research for inherited disorders of iron metabolism and heme synthesis

ELN European LeukemiaNet

- Publicly funded research network of excellence for the cure of leukemia.

Objectives and Transversal Fields of Action (TFAs)

ERN-EuroBloodNet objective is to promote **excellence for best health care** in rare hematological diseases based on cutting-edge diagnosis procedures and therapies while **removing barriers** for making them available at the European level

Objective 1: Improve **equal access to highly specialized healthcare** delivery for RHD across Europe.

Objective 2: Promote **the best practices** in prevention, diagnosis and safe clinical care across Europe

Objective 3: Disseminate cutting-edge knowledge and facilitate **continuing medical education** in the field of RHD

Objective 4: Provide **inter-professional consultation** by sharing of expertise and safe exchange of clinical information

Objective 5: Foster **European cooperation** in highly specialized procedures for diagnosis, innovative treatments and research

Cross-border health

Best practices

Continuing medical education

Telemedicine

Clinical trials and research

Cross border health

Linked to Objective 1: Improve equal access to highly specialized healthcare delivery for RHD across Europe.

Coordinated by: J.Apperley (oncological hub), R. Colombatti (non-oncological hub) and A. Plate (ePAG representative)

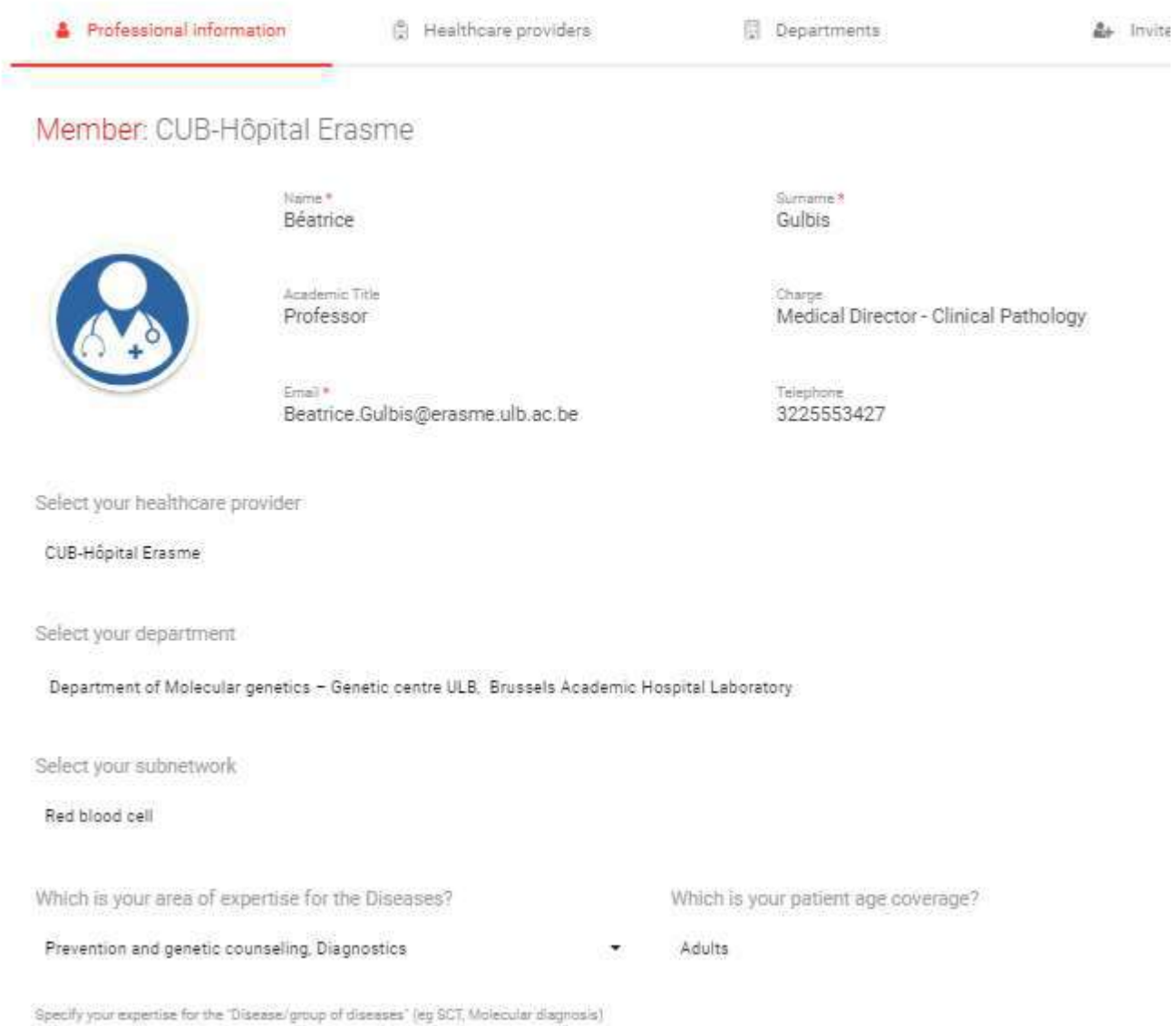
Challenge: Reduce inequalities in the access to specialized healthcare delivery for RHD among EU Member States.

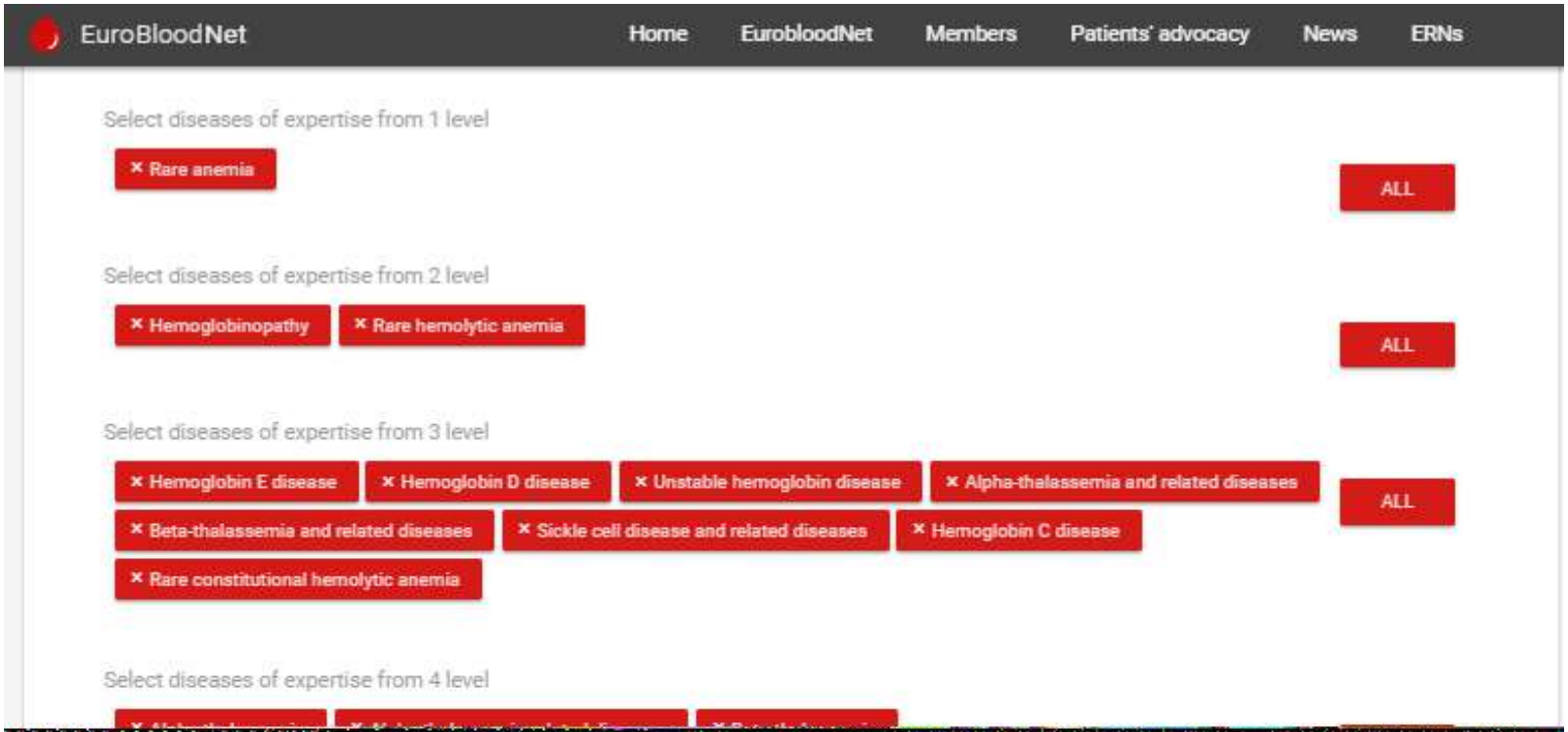
Action: Mapping of services available in EU

Outcome: **Creation of the dynamic inventory of ERN-EuroBloodNet members including ORPHA classification for RHDs**

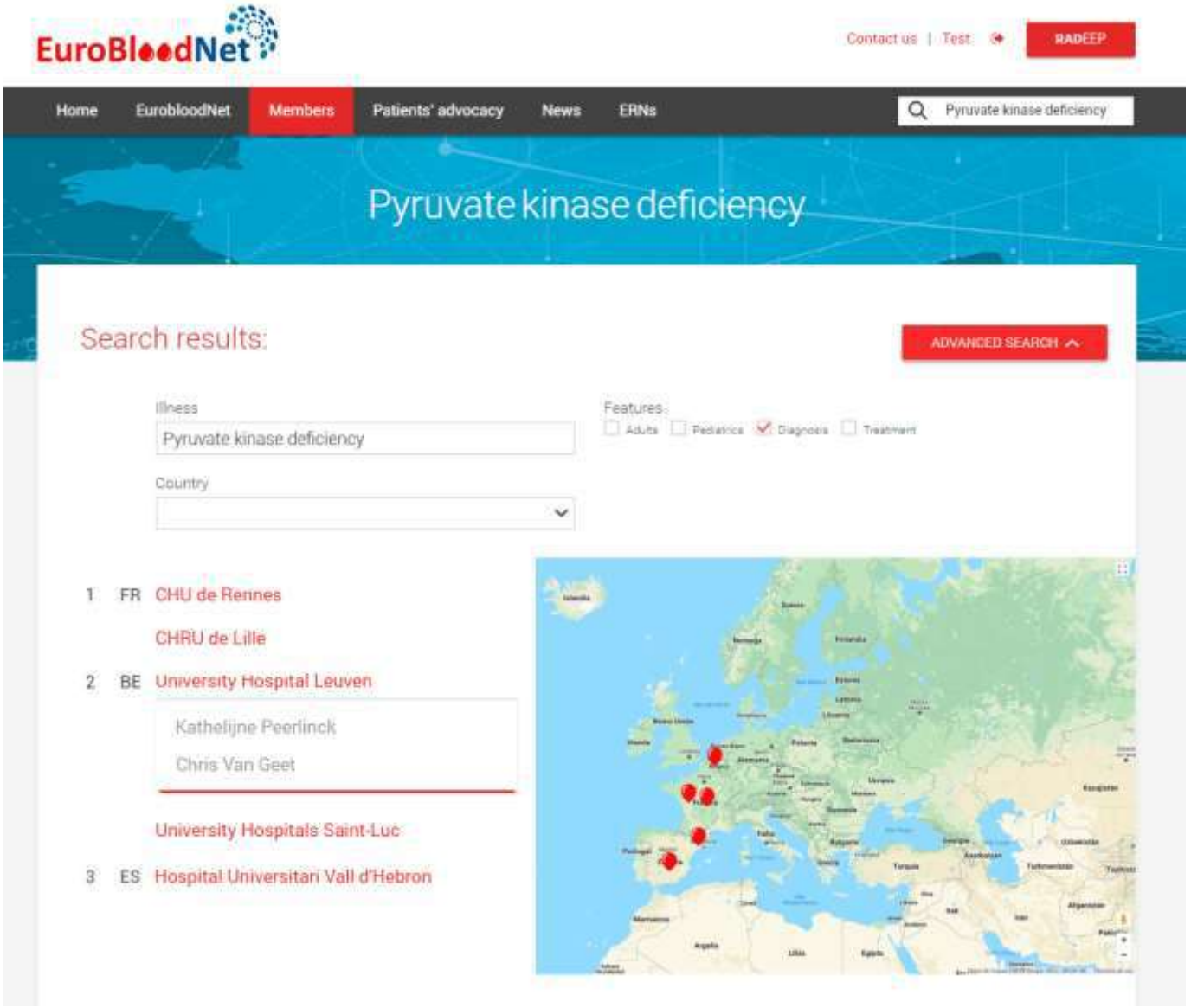
Deliverable 3 Report on ERN-EuroBloodNet members activity/facilities for RHD health provision

"If you haven't completed your profile login to private area and invite colleagues from your Hospital to join"





"Orpha classification has been implemented in order to be chosen in your personal and departments profiles"



Search by:

- Disease/group of diseases – ORPHA
- Subnetwork

Filters:

- Country
- Patient age coverage (Pediatrics, adults, ageing)
- Area of expertise (Prevention and genetic counseling, diagnostics, treatment and care)

Objective: Directive 2011/24/EU

Patient access to

- Correct diagnosis
- Highly specialized procedures
- Clinical trials - New therapies

Challenges:

- Lack of **awareness** on the procedure to follow for application on Crossborder Health directive
  - Are NCPs for cross border health really in place?
- **Reimbursement** process
  - payment in advance
  - WHAT is REIMBURSED in ONE COUNTRY MIGHT NOT BE THE SAME IN ANOTHER
  - Other costs not covered...the patient is not at home

PILOT PROJECT of cross border for BMT in Sickle Cell Disorders

IRELAND (Dublin) – ITALY (Padova)

June 2017: decision to work on this project based on Ireland's need a cooperation in the field of SCD

June-December 2017: obtain "in theory"approval by both institution with letter of Intent from both institutions

December 2017:

beginning of draft of Clinical/Medical Protocol;

beginning of Financial review of all previous BMT for SCD by Italian Hospital

June 2018: Ireland's Team visit to Padova; final review of Medical and Logistic Protocol

June-November 2018: review and draft of financial and aministrative aspects`

November 6 th 2018:

Approval by both institution of the financial/administrative aspects

Agreement to be signed by the end of November

Create a comprehensive public database of reliable guidelines

Database: 96 international guidelines and recommendations

- **Level A: Evidence- and consensus-based guidelines / recommendations** involving assessment of the quality of scientific evidence (e.g. GRADE, SIGN) and formal consensus development techniques (e.g. Delphi method)

- **Level B: Consensus-based guidelines / recommendations** – Adopting formal consensus development techniques (e.g. Delphi method) without assessment of the quality of scientific evidence.

- **Level C: Expert opinion** only includes consensus among experts

Collaboration with UKNEQAS: Development of a new Scheme (Pyruvate Kinase Deficiency)

UK NEQAS
International Quality Expertise

Challenges:

- **Guidelines Lacking** for some groups of diseases – especially non malignant disorders
- Guidelines need to be reviewed and **updated**
- +++ are they really **implemented**?

Objective: Fill the existing gaps on the dissemination of cutting-edge knowledge in hematology in EU

Identification of educational GAPs in collaboration with EHA and ESH

A survey for the identification of educational gaps has been conducted:

Challenges:

- A lot of education courses and material due to EHA and ESH in malignant hematology
- Gaps in education
  - for non-malignant hematology
  - For nurses, laboratory staff, patients
  - Material in different EU languages
- **Importance of pharmaceutical companies in education**

Short fellowships of health professionals in ERN-EuroBloodNet members with very specific expertise

Paroxysmal nocturnal hemoglobinuria (PNH) was identified during the first year of implementation as one of the areas that will benefit from organizing short stays.

Sessions include:

- Interactive lectures on diagnosis, treatment and long term management
- Tutorials on clinical cases
- Attendance to ward round
- Attendance to diagnostic lab

Telemedicine

Linked to Objective 4: Provide inter-professional consultation by sharing of expertise and safe exchange of clinical information

Coordinated by: A. Engert (oncological hub) B. Gulbis (non-oncological hub) and S.Wintrich (ePAG represenetative)

Challenge: Facilitate interprofessional consultation of RHD complex cases.

Clinical Patients Management System

Action: Promotion of the use of the Clinical Patient Management System (CPMS) as the platform provided by the EC for the secure sharing of clinical data.

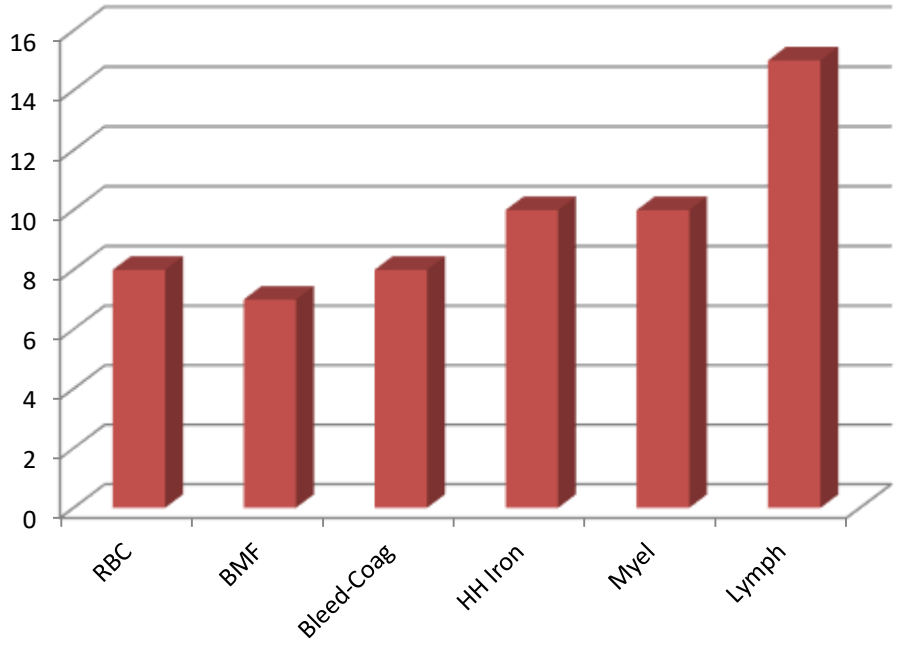
Outcomes:

1) **Participation in the CPMS pilot phase**
2) **Identification of a Board of 58 Experts** for each area of expertise for their involvement in the related panels created
3) **Legal analysis of the CPMS in the context of the General Data Protection Regulation** addressing key legal aspects that may affect the interprofessional consultation

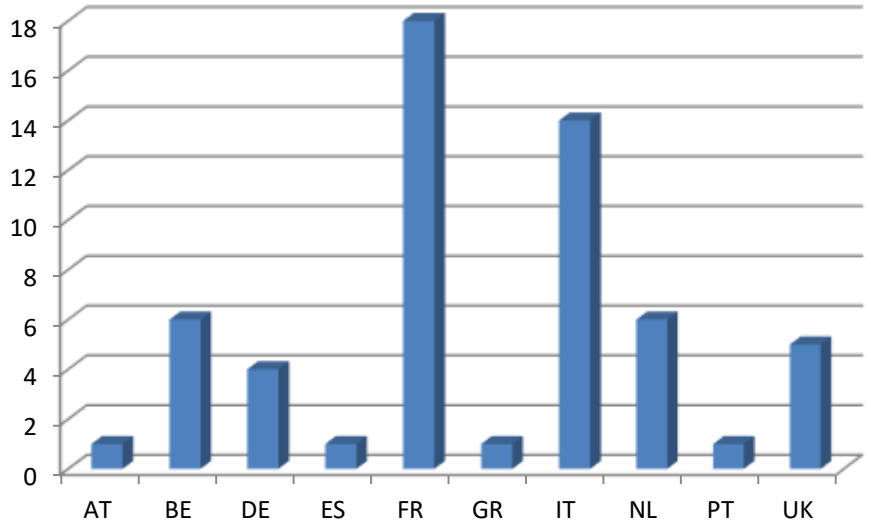
Deliverable 6 Report on legal issues on inter-professional consultation of complex cases.

❖ 58 Experts already identified.

❖ Number of experts of the Board by Subnetwork



❖ Number of experts of the of the Board by MS



Experts identified will be officially contacted during the second period for their involvement at the CPMS.

	ERN-EuroBloodNet Board of Experts for the CPMS		
	Rare Red blood cell defects		
BE	Béatrice Gulbis	CUB-Hôpital Erasme	Hemoglobinophaties
IT	Domenica Cappellini	Foundation IRCCS CA'Granda Ospedale Maggiore polyclinic - Milan	Hemoglobinophaties
IT	Wilma Barcellini	Foundation IRCCS CA'Granda Ospedale Maggiore polyclinic - Milan	Haemolytic anaemia
NL	Richard van Wijk	University Medical Center Utrecht	Rare enzymophaties
GR	Antonis Kattamis	Aghia Sophia Children's Hospital - (Greece) NO ERN	Hemoglobinophaties
IT	Antonio Piga	AOU S.Luigi Gonzaga	Hemoglobinophaties
NL	Eduard van Beers	University Medical Center Utrecht	Rare enzymophaties
IT	Raffaella Colombatti	AO Padua	Hemoglobinophaties
	Bone marrow failure (BMF) and hematopoietic disorders		
IT	Achille Iolascon	AOU Federico II - Naples	Dyserythropoietic anemias and DBA
FR	Régis Peffault de Latour	Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis	Inherited aplastic anemia, Acquired aplastic anemia and PNH
IT	Antonio Risitano	AOU Federico II - Naples	Inherited aplastic anemia, Acquired aplastic anemia and PNH
IT	Carlo Dufour	IRCCS Institute Giannina Gaslini - Genoa	Inherited aplastic anemia, Acquired aplastic anemia and PNH
FR	Lydie da Costa	CHU Paris - Hôpital Robert Debré	Dyserythropoietic anemias and DBA
UK	Noemi Roy	Oxford University Hospitals NHS Foundation Trust	Dyserythropoietic anemias and DBA
GR	Antonis Kattamis	Aghia Sophia Children's Hospital - (Greece) NO ERN	Dyserythropoietic anemias and DBA
	Rare bleeding-coagulation disorders and related diseases		
UK	Michael Markis	Sheffield Teaching Hospitals NHS Foundation Trust	Haemophilia congenital and acquired
IT	Flora Peyvandi	Foundation IRCCS CA'Granda Ospedale Maggiore polyclinic - Milan	Haemophilia, Rare bleeding disorders
BE	Cedric Hermans	University Hospitals Saint-Luc	Haemophilia congenital and acquired
IT	Giancarlo Castaman	AOU Careggi, Florence	Haemophilia and von Willendand disease
NL	Karin Fijn van Draat	Academic Medical Center Amsterdam	Paediatric haemophilia, mild haemophilia
NL	Roger Schutgens	University Medical Center Utrecht	Haemophilia of older age
UK	Steve Kitchen	Sheffield Teaching Hospitals NHS Foundation Trust	Laboratory issues
BE	Kathelijn Peerlinck	University Hospital Leuven	Haemophilia congenital and acquired
	Hemochromatosis and other rare genetic disorders of iron metabolism and heme synthesis		
PT	Graça Porto	Centro Hospitalar do Porto, EPE	Hemochromatosis
NL	Dorine Swinkels	Radboud University Medical Center Nijmegen	Hemochromatosis, Rare anemias
FR	Patricia Aguillar-Martinez	CHU de Montpellier	Hemochromatosis, Rare anemias
FR	Edouard Bardou-Jacquet	CHU rennes	Hemochromatosis
IT	Domenico Girelli	AOUI Verona	Hemochromatosis, Rare anemias
IT	Antonello Pietrangelo	University Hospital of Modena	Hemochromatosis
IT	Alberto Piperno	S. Gerardo Hospital - Monza	Hemochromatosis, Rare anemias
UK	Noemi Roy	Oxford University Hospitals NHS Foundation Trust	Hemochromatosis, Rare anemias
ES	Mayka Sanchez	Hospital Universitari Germans Trias i Pujol (HGTiP) and IJC (NO ERN)	Hemochromatosis, Rare anemias
AT	Heinz Zoller	Medizinische Universität Innsbruck (NO ERN)	Hemochromatosis

	Myeloid malignancies		
FR	Pierre Fenaux	Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis	AML, APL, MDS, CMML
GE	Uwe Platzbecker	Universitätsklinikum Carl Gustav Carus	AML, APL, MDS
NL	Bob Lowenberg	Erasmus MC: University Medical Center Rotterdam	AML
FR	Raphaël Itzykson	Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis	CMML, Atypical CML
FR	Delphine Réa	Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis	CML, Atypical CML
UK	Jane Apperley	Imperial college Healthcare NHS Trust	CML, Atypical CML
FR	Olivier Hermine	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	Mast cell disorders
FR	Jean Jacques Kiladjian	Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis	MPN
IT	Alessandro Vannucchi	AOU Careggi, Florence	MPN
BE	Florence Roufosse	CUB-Hôpital Erasme	Hypereosinophilia and hypereosinophilic syndrome
	Lymphoid malignancies		
GE	Andreas Engert	Universitätsklinikum Köln	Large cell lymphoma
FR	Catherine Thieblemont	Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis	Marginal zone lymphoma, Large cell lymphoma, Follicular lymphoma, Hairy cell leukemia
FR	Martine Bagot	Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis	Cutaneous lymphoma
BE	Dominique Bron	Jules Bordet Institute	CLL
GE	Michael Hallek	Universitätsklinikum Köln	CLL
BE	Pieter Sonneveld	Erasmus MC: University Medical Center Rotterdam	Myeloma
FR	Bertrand Arnulf	Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis	Myeloma
FR	Arnaud Jaccard	CHU de Limoges	Amyloidosis
GE	Stefan Schönland	Universitätsklinikum Heidelberg	Amyloidosis
FR	Veronique Leblond	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpêtrière (NO ERN)	Waldenstrom's disease
FR	Sylvain Choquet	Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpêtrière (NO ERN)	CNS lymphoma
FR	Carole Soussain	Institut Curie	CNS lymphoma
FR	Olivier Hermine	Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades	Mantle cell lymphoma
IT	Roberto Foà	AOU Policlinico Umberto I - Rome	ALL
FR	Corinne Haioun	Assistance Publique-Hôpitaux de Paris, Hôpital Henri-Mondor	Large cell lymphoma, Follicular lymphoma

Challenges for the Clinical Patient Management System (CPMS):

- **Reimbursement** of professionals/ Institutions at the HCP level ?
- How to avoid **simple cases**? - Filter for Rare Diseases
- **++ Cumbersome/ time consuming** procedure in daily practice for cases coming from centers outside of the ERN

Clinical Trials and Research

Linked to Objective 5: Foster European cooperation in highly specialized procedures for diagnosis, innovative treatments and research

Coordinated by: M. della Porta (oncolgical hub), A. Piga (non-oncological hub) and A.L. Brunetta (ePAG representative)

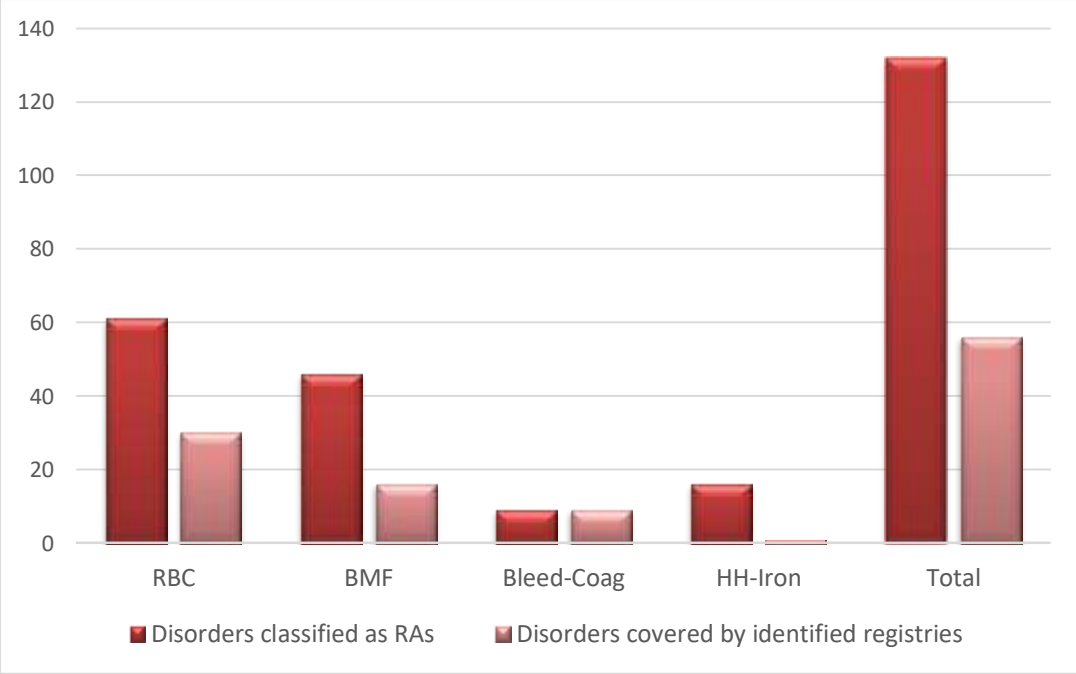
Challenge: Promote European cooperation for epidemiological surveillance, development of highly specialized procedures for diagnosis, innovative treatments and research.

Action: Facilitate European epidemiological surveillance of RHD by supporting the implementation of Rare Anaemia Disorders European Epidemiological Platform (RADeep)

Outcomes:

State of the art existing registries for RAs with the creation of the list of National/European and international registries on RAs gathering 55 registries from 15 European countries

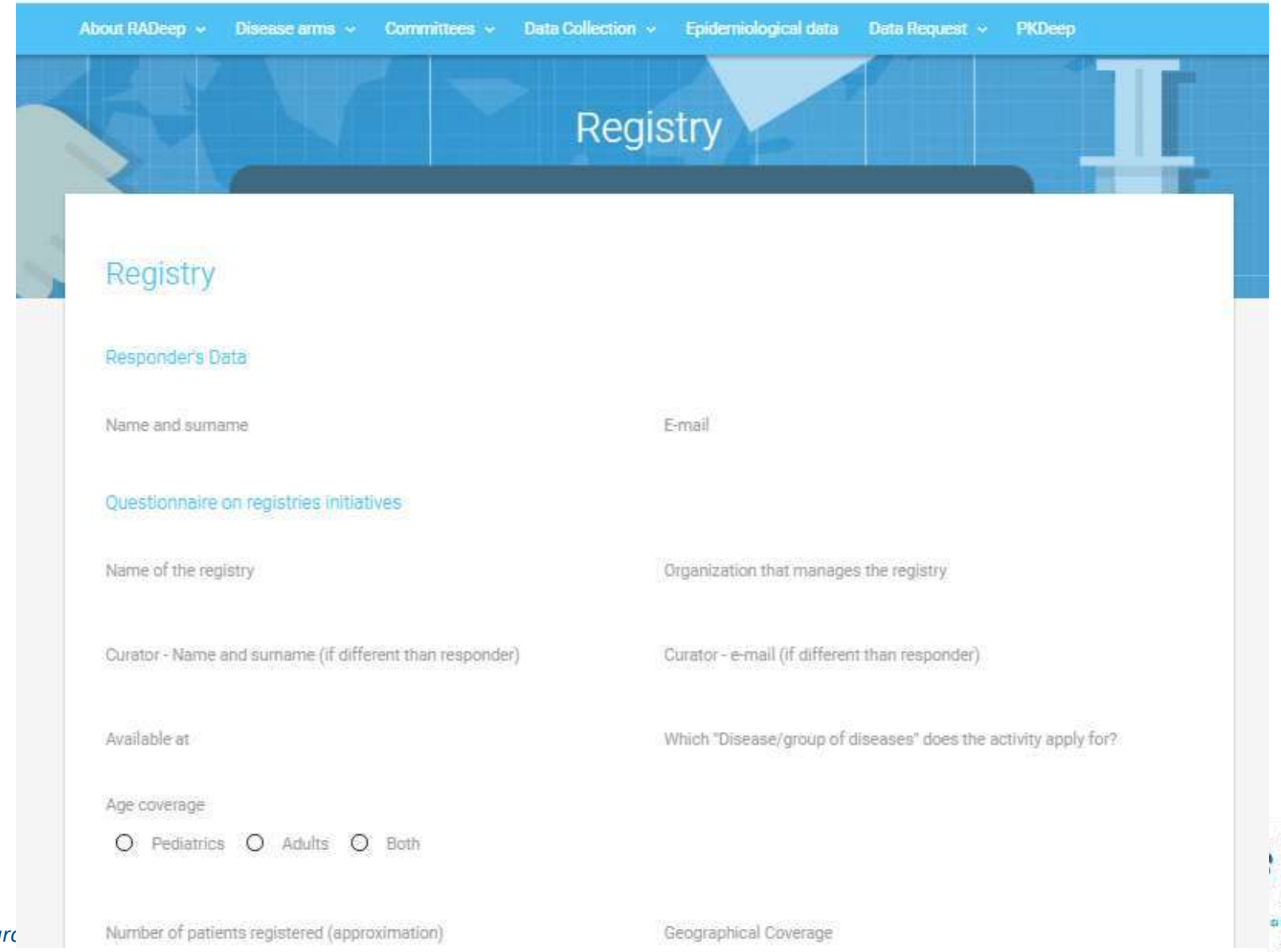
Deliverable 7 Report on existing registries for RAs



RADEEP

https://eurobloodnet.eu/radeep/registry

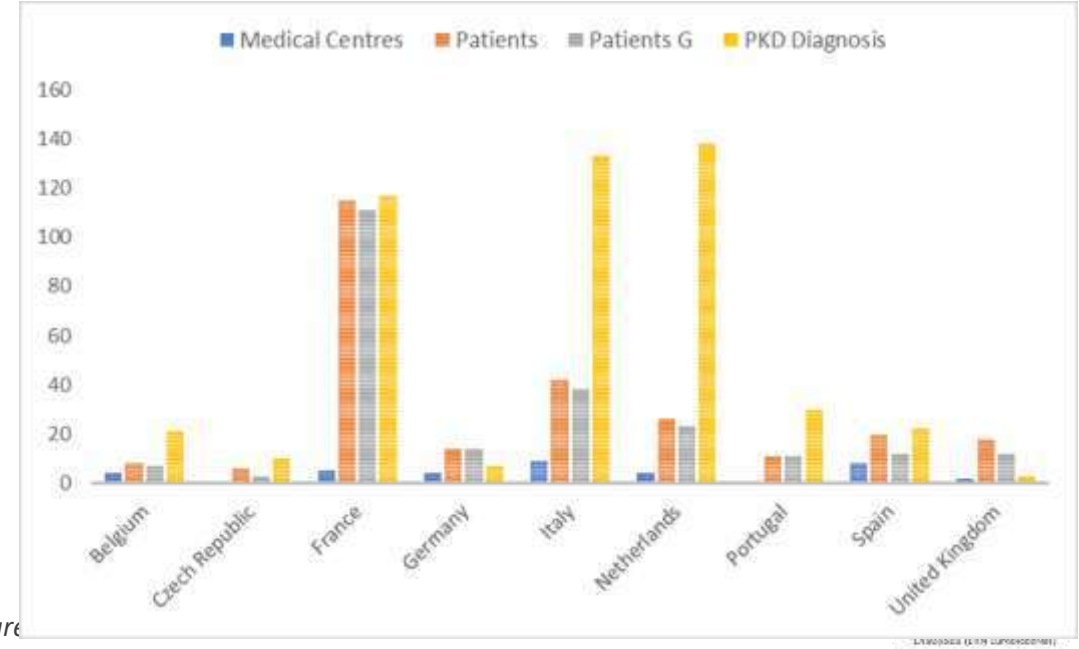
EUROBLOODNET



European Reference Network

A total of 41 medical centres from 10 countries showed interest to join PKDeep initiative

Distribution Patients and diagnosis	Medical Centres	Patients in follow up	Patients Genotyped	% Patients Genotyped	PKD Diagnosis
Belgium	4	8	7	88%	21
Czech Republic	1	6	3	50%	10
France	5	115	111	97%	117
Germany	4	14	14	100%	7
Italy	9	42	38	90%	133
Netherlands	4	26	23	88%	138
Portugal	1	11	11	100%	30
Spain	8	20	12	60%	22
United Kingdom	2	18	12	67%	3
Total	**38**	**260**	**231**	**89%**	**481**



Diagnostics facilities	Medical Centres	PK_Act	HK_Act	PK_Act Ext	HK_Act Ext	PKLR Gene	PKLR Gene Ext	Counselling	Prenatal
Belgium	4	3	3	1	1	0	4	3	3
Czech Republic	2	2	0	0	0	1	1	1	1
France	5	2	2	3	4	2	4	5	4
Germany	4	1	0	4	3	0	4	4	1
Italy	10	5	1	5	4	4	6	10	6
Lithuania	1	0	0	0	0	1	0	1	1
Netherlands	4	4	2	2	0	3	2	4	3
Portugal	1	1	0	0	0	1	0	1	1
Spain	8	0	0	8	7	2	5	5	2
United Kingdom	2	2	1	1	1	0	2	1	1
Total	**41**	**20**	**9**	**24**	**20**	**14**	**28**	**35**	**23**

1) Survey conducted through ERN-EuroBloodNet website - 33 registries gathered

✓ 25 for RBC subnetwork, 4 for BMF subnetwork, 3 for RAs and 1 for RHDs

2) Orphanet database: "Rare Disease Registries in Europe" - 30 registries addressing RAs, including 56 different entities

Subnetwork	Disorders classified as RAs	Disorders covered by identified registries
Rare Red Blood Cell (RBC) defects	61	30
Bone marrow failure (BMF) and hematopoietic disorders	46	16
Rare bleeding-coagulation disorders and related diseases	9	9
Hemochromatosis and other rare genetic disorders of iron metabolism and heme synthesis	16	1
	132	56

3) Analysis of the coverage of the registries involved in the epidemiological surveillance of RAs classified by subnetworks

4) List of National/European and international registries on RAs - Total list of **55 registries** (after removing duplications) including information from **15 European countries:**

- 33 from the online survey,
- 21 registries from the ORPHA report
- 1 from desk research

Objective:

Registries
Clinical research

Mapping of Clinical Trials

Mapping of existing CTs with focusing on:

- *Diseases where there are no or very few clinical trials available*
- *Breakthrough new drugs available in only few member states*

Challenges:

- How to organize clinical research (sponsorship…) and how to fund it?
  - Official sponsor
  - funding

✓ **Project 15 linked to the coordination – Repertoire of existing patient support groups in hematology across EU MS**

Implementation of Patients associations profiles and publication at the ERN-EuroBloodNet website

✓ **Project 16 linked to the coordination – Creation of an European Sickle Cell Disease patients association**

- Identify a small group of SCD patients interested in collaborating with the ERN.
- Create a SCD patient network and try to federate the existing patients associations.

Thank You!!!

ERN-EuroBloodNet coordination team – Contact us!

Prof Pierre Fenaux
Coordinator
Oncological Hub Chair
Ht. Saint Louis, Paris
pierre.fenaux@aphp.fr

Prof Béatrice Gulbis
Co-Coordinator
Non-Oncological Hub Chair
CUB-Ht. ERASME
Beatrice.Gulbis@erasme.ulb.ac.be

Dr. Maria del Mar Mañú Pereira
Scientific Director
Ht. Saint Louis, Paris
University Hospital Vall d'Hebron, Barcelona
Vall d'Hebron Research Institute
Mar.manu@vhir.org

Victoria Gutiérrez Valle
IT and Dissemination manager
Ht. Saint Louis, Paris
University Hospital Vall d'Hebron, Barcelona
Vall d'Hebron Research Institute
Victoria.gutierrez@vhir.org

Mariangela Pellegrini
ERN manager
Ht. Saint Louis, Paris
mariangela.pellegrini@aphp.fr