

Criteria defined by the Network for Myeloid malignancies

The following information defines the specific criteria for our proposal for a European Reference Network (ERN) for Rare Hematological Diseases, EuroBloodNet. Each health care provider willing to be member of our ERN has to fulfil these criteria. These evidence based criteria intend to be realistic while ensuring a high level patient care.

The following information corresponds to the following points in the HCP application form:

1) Point 7_Table in Page 6 Diseases, conditions and highly specialized interventions: it includes not only diseases but also highly specialized interventions, treatments eg bone marrow transplantation

2) Point 11_Table in Page 9 10 of the 16 “Diseases, conditions and highly specialized interventions” defined in point 7 needs to be quantified

3) Point 12_Table in page 11 “Multidisciplinary team” Up to 16 Health care professionals have to be defined: position, training and number of patients/procedures by year (for assure expertise)

4) Point 13_Table in page 12 “Specialised equipment, infrastructure and IT” Up to 16 Specialised equipment, infrastructure and IT used by the HCP to support diagnosis, care and treatment

5) Point 21_Table in page 18 “Clinical outcome data” Up to 22 relevant clinical outcomes related to the Rare or complex disease, condition or highly specialized interventions defined

- Subthematic area of expertise:
 - Rare red blood cell defects
 - Bone marrow (BM) failure and rare haematopoietic disorders
 - Hemochromatosis and other rare genetic disorders of iron metabolism and heme synthesis
 - Rare bleeding-coagulation disorders
 - X Myeloid malignancies**
 - Lymphoid malignancies

1) Point 7_Table in Page 6 Diseases, conditions and highly specialized interventions: it includes not only diseases but also highly specialized interventions, treatments eg bone marrow transplantation

Subthematic area of expertise	Rare or complex disease, condition or highly specialized interventions	ICD / Orphanet Code
Myeloid malignancies	Myelodysplastic syndrome (MDS)	ICD 10 D46/ORPHA 52688
Myeloid malignancies	Acute myeloid leukemia (AML)	ICD 10 D92.0/ORPHA 519
Myeloid malignancies	Chronic myelomonocytic leukemia (CMML)	ICD 10 D93.1/ORPHA 98823
Myeloid malignancies	Chronic Myeloid Leukemia (CML)	ICD 10 C92.1 C92.2/ORPHA 521
Myeloid malignancies	Myeloproliferative neoplasm (MPN)	ORPHA 98274
Myeloid malignancies	Myelofibrosis	ORPHA 824
Myeloid malignancies	Systemic mastocytosis	ICD10 Q82.2/ORPHA 2467
Myeloid malignancies	Access to MDS diagnostic services preferable present within the expert center Morphology, Immunophenotyping, Molecular diagnostics, Cytogenetics	
Myeloid malignancies	Access to MPN diagnostic services preferable present within the expert center Morphology, Immunophenotyping, Molecular diagnostics, Cytogenetics, molecular diagnostics (at minimum, driver mutations for MPN – JAK2V617F, JAK2exon 12, MPL, CALR, KIT, FIP1L1/PDGFRalpha, BCR/ABL, BCR/ABL mutations)	
Myeloid malignancies	Stem cell transplantation service in myeloid malignancies	
Myeloid malignancies	Acute care	
Myeloid malignancies	Phase I/II studies open	

	for inclusion on MDS	
Myeloid malignancies	Phase I/II studies open for inclusion on AML	
Myeloid malignancies	Phase I/II studies open for inclusion on MPN in the last 3 years	
Myeloid malignancies	Phase III/IV studies open for inclusion on MPN in the last three years	

2) Point 11_Table in Page 9 10 of the 16 “Diseases, conditions and highly specialized interventions” defined in point 7 needs to be quantified

Specific diseases, conditions and highly specialized interventions	Measure	Evidence
Stem cell transplantation service in myeloid malignancies	Number of procedures per year	20
Myelodysplastic syndrome (MDS) and Chronic myelomonocytic leukemia (CMML)	Number of new cases per year	30
Phase I/II studies open for inclusion on MDS	Number of procedures per year	3
Acute myeloid leukemia (AML)	Number of patients per year	30
Phase I/II studies open for inclusion on AML	Number of procedures per year	3
Myeloproliferative neoplasm (MPN) (including at least 4 new cases of myelofibrosis and 4 cases of CML)	Number of new patients per year	40
Phase I/II studies open for inclusion on MPN in the last three years	Number of procedures per year	2
Phase III/IV studies open for inclusion in the last three years	Number of procedures per year	2
Systemic mastocytosis	Number of new patients per year	2

3) Point 12_Table in page 11 “Multidisciplinary team Up to 16 Health care professionals have to be defined: position, training and number of patients/procedures by year (for assure expertise)

Healthcare professional	Training and qualifications	Nº procedures/patients per year
Haematologist	Experience in myeloid malignancies	100
Nurses	Experience with the type of treatments that are used in trials for myeloid malignancies. They are able to recognize and respond to known complications of chemotherapy and hypomethylating agents, and follow the trial specific nursing guidelines. They should also have an experience in hypomethylating agent treatment and transfusion therapy. At least 50% of the nurses have completed a specialized training in hematological care at an accredited institution.	100

4) Point 13_Table in page 12 “Specialised equipment, infrastructure and IT” Up to 16 Specialised equipment, infrastructure and IT used by the HCP to support diagnosis, care and treatment

Specific diseases, conditions and highly specialized interventions	Specific equipment, infrastructure and information technology (IT)
Myelodysplastic syndrome	
Medical care organization	Access to radiotherapy facilities for Stem cell transplantation JACIE accreditation for Allogeneic stem cell transplants Availability of transfusion care 24 hours a day, seven days a week. Availability of an Intensive Care unit. Adequate facilities for immune-incompetent patients: separated rooms or ward, active infection prevention protocol with involvement of a hospital hygiene specialist. Availability of in-house consultants for neurology and pneumology. Intensive in-house support of medical-microbiologists with

	<p>experience in problems caused by disrupted immune response: weekly consultations with the physicians, able to perform weekly cultures for infection surveillance with results available within 72 hours.</p> <p>Availability of a day care facility for hypomethylating agents and RBC and platelet transfusions</p>
Pharmacy	<p>In-house KNMP registered hospital pharmacist available. Pharmacy staff is aware of GCP requirements regarding study drug handling and drug accountability.</p> <p>Pharmacy has facilities to adequately store study drug: no unauthorized access, separate from regular medication, refrigerated with temperature log if necessary.</p> <p>Access to facilities for pharmacological assays (drug blood levels)</p> <p>Availability of pharmacy 24 hours a day, seven days a week for preparation and dispensing of medication.</p>
Diagnostic facilities	<p>Availability of in-house CKL accredited facilities for hematology and blood chemistry with the ability to provide test results within 24 hours.</p> <p>Access to facilities for cytogenetics and FISH, participating in review rounds (at least 80% of samples reviewed) and with the ability to provide test results within 72 hours.</p> <p>Access to facilities for molecular biology (mutational analysis by NGS)</p> <p>Access to facilities for pathology, participating in review rounds (at least 80% of samples reviewed) and with the ability to provide test results within 72 hours.</p> <p>Availability of in-house imaging facilities (x-ray and CT) for surveillance of infections and complications with the ability to provide imaging results and interpretation of those results within 24 hours.</p>
Myeloproliferative neoplasm	
Medical care organization	<p>Access to radiotherapy facilities for Stem cell transplantation</p> <p>Access to JACIE accreditation for Allogeneic stem cell transplants</p> <p>Availability of transfusion care 24 hours a day, seven days a week.</p> <p>Availability of an Intensive Care unit.</p> <p>Availability of a Service for management of anticoagulant therapy</p> <p>Availability of a Surgery Unit with experience in splenectomy for MPN patients.</p> <p>Availability of a day care facility for chemotherapeutic agents and RBC and platelet transfusions</p> <p>Multidisciplinary meetings between physicians and persons responsible for the execution and interpretation of diagnostic tests.</p> <p>Meetings for clinical cases discussion and procedures update must be regularly held.</p> <p>Standard operative procedures in written format according to Quality procedures as by Institutional practice must be available.</p> <p>Educational activities in the field of MPN are offered to physicians from other institutions under the form of Course/Preceptorships</p> <p>Educational activities for MPN patients are offered either as informative booklets and as structured meetings with physicians</p>
Pharmacy	<p>In-house K registered hospital pharmacist available. Pharmacy staff is aware of GCP requirements regarding study drug handling and drug</p>

	<p>accountability.</p> <p>Pharmacy has facilities to adequately store study drug: no unauthorized access, separate from regular medication, refrigerated with temperature log if necessary.</p> <p>Access to facilities for pharmacological assays (drug blood levels)</p> <p>Availability of pharmacy 24 hours a day, seven days a week for preparation and dispensing of medication.</p>
Diagnostic facilities	<p>Availability of in-house accredited facilities for hematology and blood chemistry with the ability to provide test results within 24 hours.</p> <p>Access to facilities for cytogenetics and FISH, participating in review rounds (at least 80% of samples reviewed) and with the ability to provide test results within 96 hours.</p> <p>Access to facilities for molecular biology (see above; mutational analysis by NGS is not strictly required but preferable)</p> <p>Access to facilities for pathology, participating in review rounds (at least 80% of samples reviewed) and with the ability to provide test results within 96 hours.</p> <p>Availability of in-house imaging facilities (x-ray and CT) for monitoring disease and disease-associated complications including thrombotic events, hemorrhage, extramedullary hematopoiesis; also for surveillance of infections and complications with the ability to provide imaging results and interpretation of those results within 24 hours.</p>
Acute myeloid leukemia	
Medical care organization	<p>Access to radiotherapy facilities.</p> <p>JACIE accreditation for Allogeneic/Autologous stem cell transplants</p> <p>Availability of transfusion care 24 hours a day, seven days a week.</p> <p>Availability of an Intensive Care unit.</p> <p>Adequate facilities for immune-incompetent patients: separated rooms or ward, active infection prevention protocol with involvement of a hospital hygiene specialist.</p> <p>Availability of in-house consultants for neurology and pneumology.</p> <p>Intensive in-house support of medical-microbiologists with experience in problems caused by disrupted immune response: weekly consultations with the physicians, able to perform weekly cultures for infection surveillance with results available within 72 hours.</p> <p>Multidisciplinary meetings between physicians and persons responsible for the execution and interpretation of diagnostic tests.</p>
Pharmacy	<p>In-house KNMP registered hospital pharmacist available. Pharmacy staff is aware of GCP requirements regarding study drug handling and drug accountability.</p> <p>Pharmacy has facilities to adequately store study drug: no unauthorized access, separate from regular medication, refrigerated with temperature log if necessary.</p> <p>Access to facilities for pharmacological assays (drug blood levels)</p> <p>Availability of pharmacy 24 hours a day, seven days a week for preparation and dispensing of medication.</p>
Diagnostic facilities	<p>Availability of in-house CKL accredited facilities for hematology and blood chemistry with the ability to provide test results within 24</p>

	<p>hours.</p> <p>Access to facilities for cytogenetics and FISH, participating in review rounds (at least 80% of samples reviewed) and with the ability to provide test results within 72 hours.</p> <p>Access to facilities for molecular biology (mutational analysis by NGS)</p> <p>Access to facilities for pathology, participating in review rounds (at least 80% of samples reviewed) and with the ability to provide test results within 72 hours.</p> <p>Availability of in-house imaging facilities (x-ray and CT) for surveillance of infections and complications with the ability to provide imaging results and interpretation of those results within 24 hours.</p>
--	--

5) Point 21_Table in page 18 “Clinical outcome data” Up to 22 relevant clinical outcomes related to the Rare or complex disease, condition or highly specialized interventions defined

Rare or complex disease, condition or highly specialized interventions	Clinical outcome	Evidence (quantifier)
Acute myeloid leukemia (AML)	CR rate, response duration, survival	
Myelodysplastic syndrome (MDS)	Survival, response to treatment	
Chronic Myeloid Leukemia (CML)	Molecular response and relapse, AML progression, survival	
Acute myeloid leukemia (AML)/ Myelodysplastic syndrome (MDS)	ET,MF,PV: response to treatment progression to MDS/AML, survival	
Systemic mastocytosis	Response to treatment, survival	