Perspectives on clinical trials in MDS in Europe

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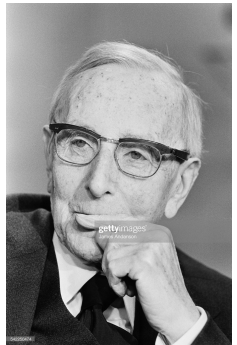
Groupe Francophone des Myélodysplasies

Firenze, Oct 2025

EMSCO MYELODYSPLASTIC SYNDROMES

Université Paris Cité

UNIVERSITÉ PARIS 13



Academic trials in the EU

- Complementary to industry sponsored trials
- Possible in one or several countries, thanks to (?)EU directives on clinical trials
- Several countries needed for rare entities, or when « lobbying » on companies is required to obtain a drug, or when rapid response is desired


EMSCO
MYELODYSPLASTIC
SYNDROMES


gfm
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Francophone des
Myélodysplasies


FISM
FONDAZIONE
ITALIANA
SINDROMI
MIELODISPLASTICHE


D·MDS
Deutsche MDS-Studiengruppe


GESMD

Perspectives on clinical trials in MDS in Europe

- Recently completed cooperative EMSCO studies
- Current studies
- How can we envisage the future ?

Perspectives on clinical trials in MDS in Europe

- Recently completed cooperative EMSCO studies

- Current studies

- How can we envisage the future ?

ARTICLE OPEN

Check for updates

MYELODYSPLASTIC NEOPLASMS

Prospective validation of a biomarker-driven response prediction model to romiplostim in lower-risk myelodysplastic neoplasms – results of the EUROPE trial by EMSCO

Anne Sophie Kubasch[1,2,3], Aristoteles Giagounidis[2,3,4], Georgia Metzgeroth[5], Anna Jonasova[6], Regina Herbst[7], Jose Miguel Torregrosa Diaz[8], Benoit De Renzis[9], Katharina S. Götze[2,3,10], Marie-Luise Huetter-Kroenke[11], Marie-Pierre Gourin[12], Borhane Slama[13], Sophie Dimicoli-Salazar[14], Pascale Cony-Makhoul[15], Kamel Laribi[16], Sophie Park[17], Katja Jersemann[18], Dorothea Schipp[19], Klaus H. Metzeler[1,2,3], Oliver Tiebel[20], Katja Sockel[2,3,21], Silke Gloaguen[1,2,3,18], Anna Mies[21], Fatiha Chermat[22], Christian Thiede[21], Rosa Sapena[22], Richard F. Schlenk[23,24], Pierre Fenaux[3,22,25], Uwe Platzbecker[1,2,3,26]✉ and Lionel Adès[3,22,25,26]

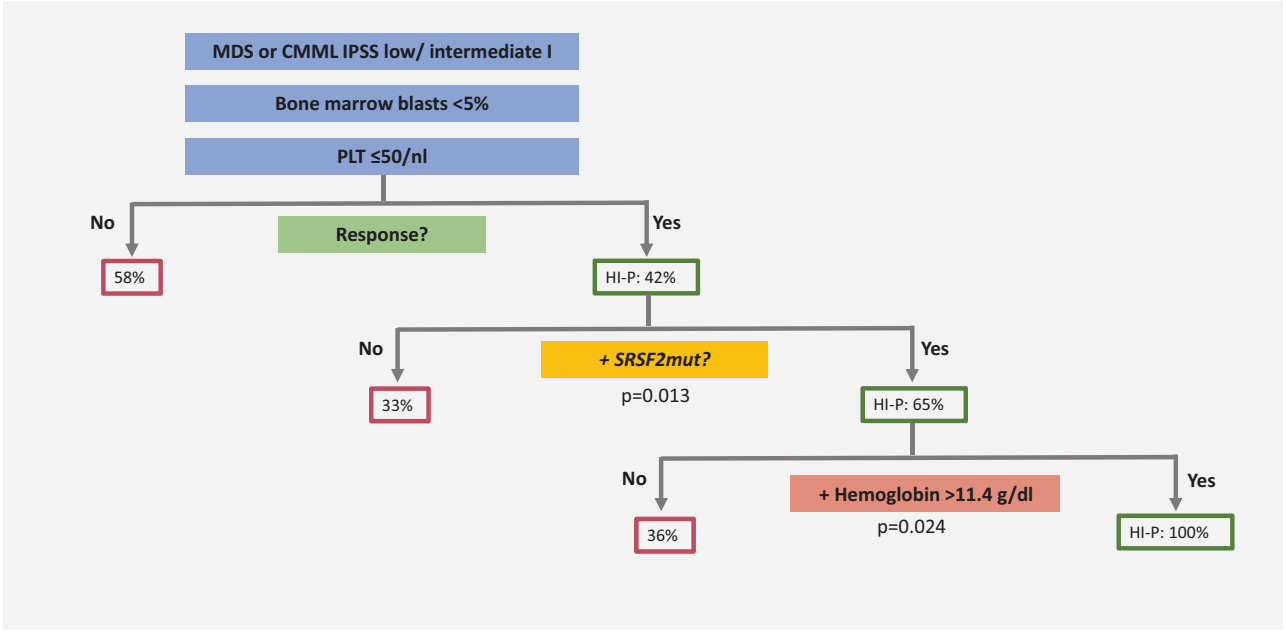


Fig. 3 Response prediction model to Romiplostim based on the results of the EUROPE trial. The newly developed response prediction model contains the SRSF2 mutation status in combination with platelet count and hemoglobin level (threshold 11.4 g/dl).

EMSCO MYELODYSPLASTIC SYNDROMES

Low dose lenalidomide versus placebo in non-transfusion dependent patients with low risk, del(5q) myelodysplastic syndromes (SintraREV): a randomised, double-blind, phase 3 trial

María Díez-Campelo, Félix López-Cadenas*, Blanca Xicoy, Eva Lumbreras, Teresa González, Mónica del Rey González, Joaquín Sánchez-García, Rosa Coll Jordà, Bohrane Slama, Jose-Ángel Hernández-Rivas, Sylvain Thepot, Teresa Bernal, Agnès Guerci-Bresler, Joan Bargay, María Luz Amigo, Claude Preudhomme, Laurene Fenwarth, Uwe Platzbecker, Katharina S Götze, Ali Arar, Sofía Toribio, Consuelo Del Cañizo, Jesús María Hernández-Rivas, Pierre Fenaux*

Summary

Background Lenalidomide is the standard of care for patients who are transfusion dependent with chromosome 5q *Lancet Haematol* 2024;

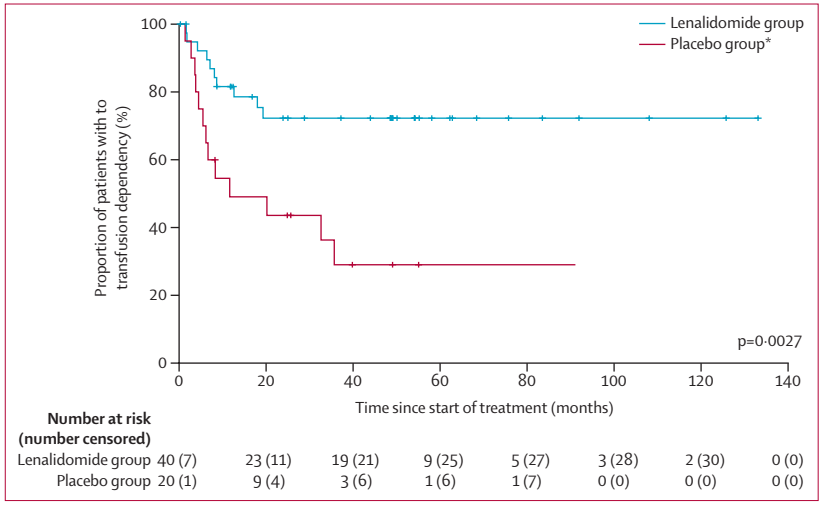
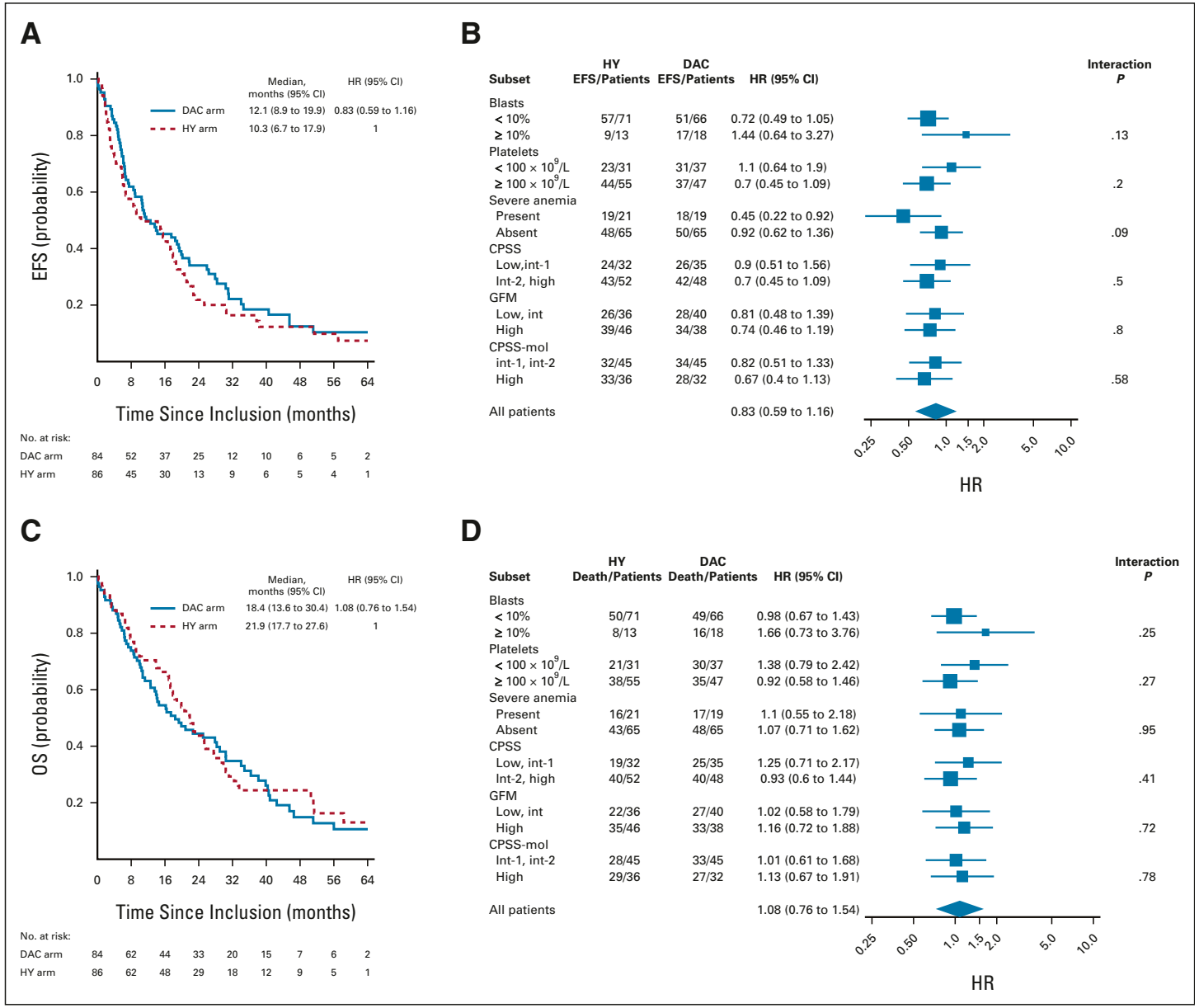


Figure 2: Time to transfusion dependency in the intention-to-treat population

Decitabine Versus Hydroxyurea for Advanced Proliferative Chronic Myelomonocytic Leukemia: Results of a Randomized Phase III Trial Within the EMSCO Network

Raphael Itzykson, MD, PhD[1,2,3]; Valeria Santini, MD[4,5]; Sylvain Thepot, MD[3,6]; Lionel Ades, MD, PhD[1,3,7]; Cendrine Chaffaut, MSc[8]; Aristoteles Giagounidis, MD[9,10]; Margot Morabito, BSc[11]; Nathalie Droin, PhD[11]; Michael Lübbert, MD[10,12]; Rosa Sapena, PhD[3]; Stanislas Nimubona, MD[3,13]; Jean Goasguen, MD[14]; Eric Wattel, MD, PhD[3,15]; Gina Zini, MD, PhD[16,17]; Jose Miguel Torregrosa Diaz, MD[3,18]; Ulrich Germing, MD[10,19]; Anna Maria Pelizzari, MD[5,20]; Sophie Park, MD, PhD[3,21]; Nadja Jaekel, MD[10,22]; Georgia Metzgeroth, MD[10,23]; Francesco Onida, MD[5,24]; Robert Navarro, MD[3,25]; Andrea Patriarca, MD[5,26]; Aspasia Stamatoullas, MD[3,27]; Katharina Götze, MD[10,28]; Martin Puttrich, MSc[10,29]; Sandra Mossuto, MSc[5]; Eric Solary, MD[3,11,30]; Silke Gloaguen, MSc[10,31]; Sylvie Chevret, MD, PhD[8]; Fatiha Chermat, DMD[3]; Uwe Platzbecker, MD[10,31]; and Pierre Fenaux, MD, PhD[1,3,7]

EMSCO
MYELODYSPLASTIC SYNDROMES



LETTER OPEN

MYELODYSPLASTIC NEOPLASM

Efficacy and safety of bemcentinib in patients with advanced myelodysplastic neoplasms or acute myeloid leukemia failing hypomethylating agents- the EMSCO phase II BERGAMO trial

A. S. Kubasch[1,2,3], P. Peterlin[3,4], T. Cluzeau[3,5], K. S. Götze[2,3,6], K. Sockel[2,7], R. Teipel[7], M. Jentzsch[1], H. Attalah[8], M. Sebert[8,9], F. Chermat[8], S. Gloaguen[2,3], M. Puttrich[10], M. Cross[1], M. Schneider[1], S. Kayser[11,12], D. Schipp[13], A. Giagounidis[2,3,14], I. Tirado-Gonzalez[15], A. Descot[15], A. van de Loosdrecht[3,16], A. Weigert[1], K. H. Metzeler[1], P. Fenaux[3,8,9], H. Medyouf[15,17,18,19], U. Platzbecker[1,2,3,19]✉ and L. Ades[3,8,9,19]

Leukemia (2020) 34:1182–1186
https://doi.org/10.1038/s41375-019-0645-z

LETTER

Immunotherapy

Single agent talacotuzumab demonstrates limited efficacy but considerable toxicity in elderly high-risk MDS or AML patients failing hypomethylating agents

Anne Sophie Kubasch[1,2,3] · Freya Schulze[2,3,4] · Aristoteles Giagounidis[2,3,5] · Katharina S. Götze[2,3,6] · Jan Krönke[2,3,7] · Katja Sockel[2,3,4] · Jan Moritz Middeke[2,3,4] · Fatiha Chermat[3,8] · Silke Gloaguen[2,3] · Martin Puttrich[3,9] · Carmen Weigt[3,9] · Doreen William[10,11] · Pierre Fenaux[3,8,12] · Richard F. Schlenk[3,11,13] · Christian Thiede[3,4] · Sebastian Stasik[3,4] · Anna Mies[3,4] · Lionel Adès[3,8,12] · Uta Oelschlägel[2,3,4] · Uwe Platzbecker[1,2,3]

Perspectives on clinical trials in MDS in Europe

- Recently completed cooperative EMSCO studies
- Current studies
- How can we envisage the future ?

CLINICAL TRIALS

& research projects

GESMD GRUPO ESPAÑOL DE SÍNDROMES MIELODISPLÁSICOS

- **SIMIDIS (Aza + EPOα in LR-MDS TD)**
- **SINTRA REV[1,2] [Len (limited & lower doses, 5mg x 2y) in non-TD MDS del(5q)]**
- **3 PROPOSALS ONGOING**

[1] Díez Campelo, Lancet Haematol 2024
[2] Toribio, submitted

GESMD GRUPO ESPAÑOL DE SÍNDROMES MIELODISPLÁSICOS

HOME TRANSFUSION VERSUS HOSPITAL TRANSFUSION IN PATIENTS DIAGNOSED WITH LOWER RISK MDS: A PHASE III CLINICAL TRIAL

Coord.: Fernando Ramos MD MPH PhD, Hospital Universitario de León (Spain)

Courtesy of Dr Ramos

MDS-TRANSF@HOME

6.1. SELECTION CRITERIA

6.1.1. Inclusion Criteria.

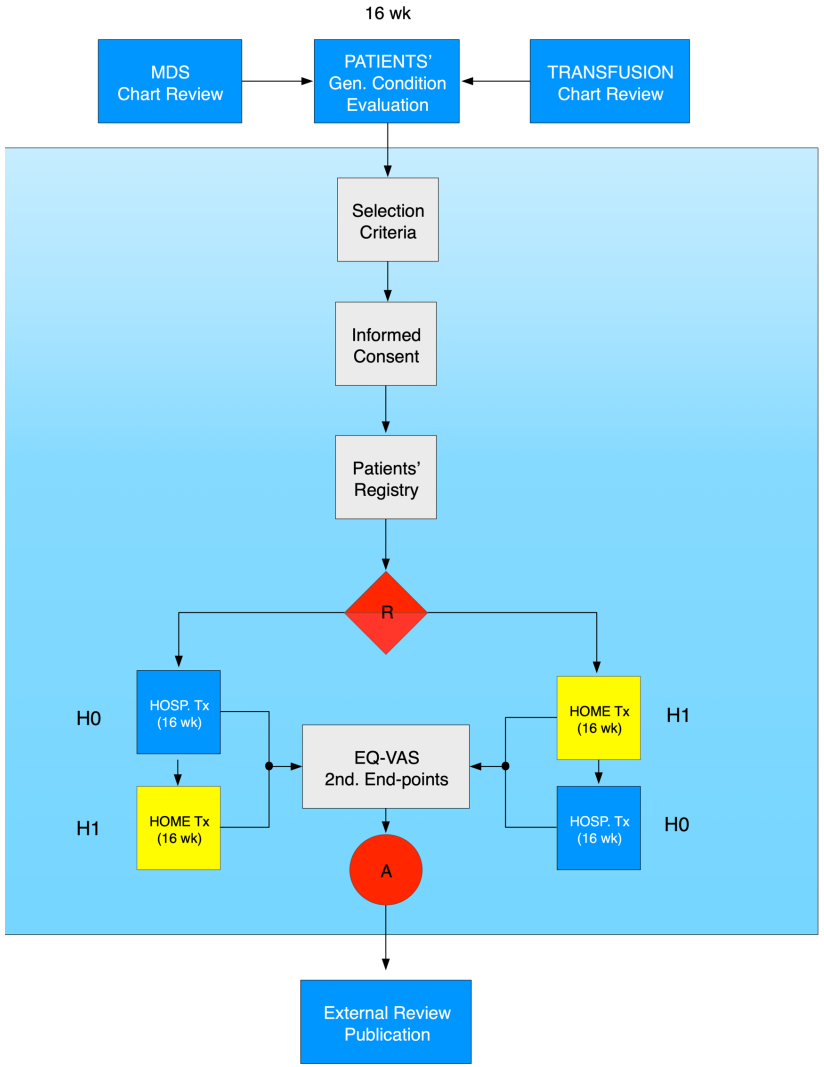
Eligible patients will have to fullfill ALL the following conditions:

1. MDS diagnosis (WHO 2017 criteria), no time limits.
2. BMA available in the last 12m (or willing to repeat before inclusion)
3. Age 65+ years, or 50-64 AND MDS-CI score >1
4. IPSS-R score up to 3.5, calculated (date of BMA) in the last 12m
5. Available transfusion and Hb records in the last 16 wk
6. Mean pre-Tx Hb <100 g/L in the last 16 wk (availability: 90% + episodes)
7. Informed consent

6.1.1. Exclusion Criteria.

Eligible patients MUST NOT incur in ANY of the following situations:

1. Prior severe transfusion reactions or alloinmunization.
2. MDS treatment (ESAs, lenalidomide, HMA) initiated in the last 16 wk.
3. Active neoplasm (on therapy/therapy in the last 3 months). See exceptions.
4. Major surgery in the last 4wk.
5. BMT in the last 2y or receiving immunosuppresive therapy
6. Concurrent participation in other clinical trial.



Courtesy of Dr Ramos

Allogeneic CD33 CAR-T

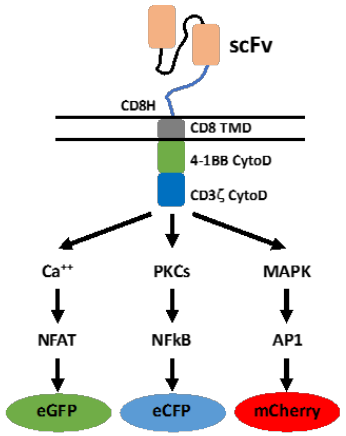
Ana Alfonso Piérola

Clínica Universidad de Navarra

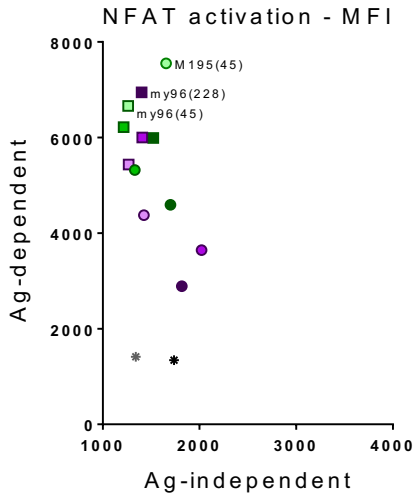
Courtesy of Dr Alfonso

CD33

Allogeneic CD33 CAR-T



Jurkat triple reporter system

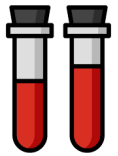


Selected CARs:

- M195(45)
- my96(45)
- my96(228)

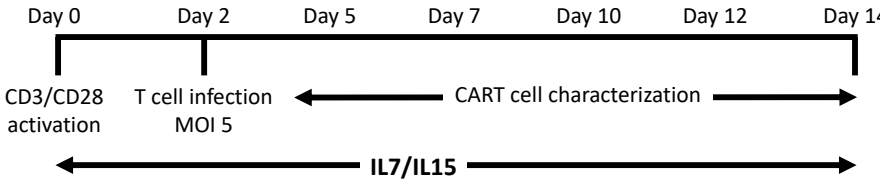
Functional studies

- *In vitro*
- *In vivo*

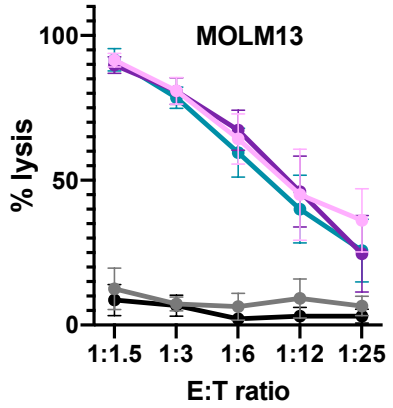


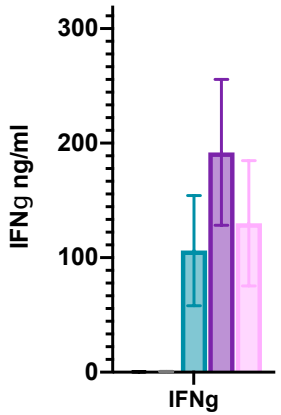
CD4/CD8 isolation

Healthy donors
AML patients

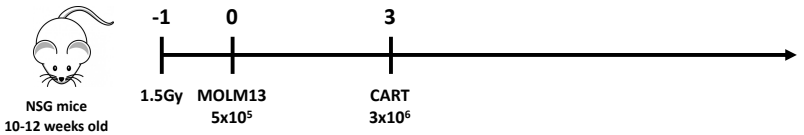


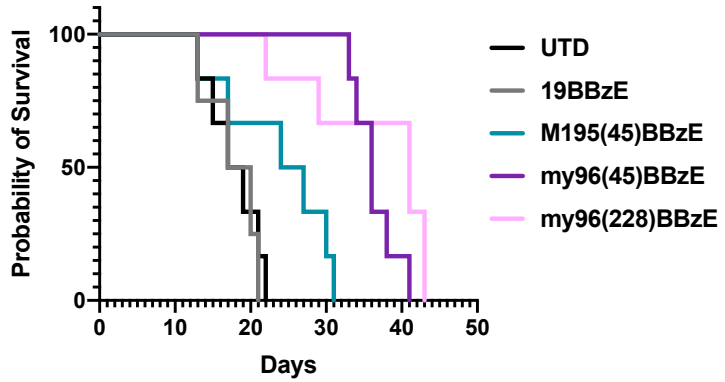
In vitro functionality

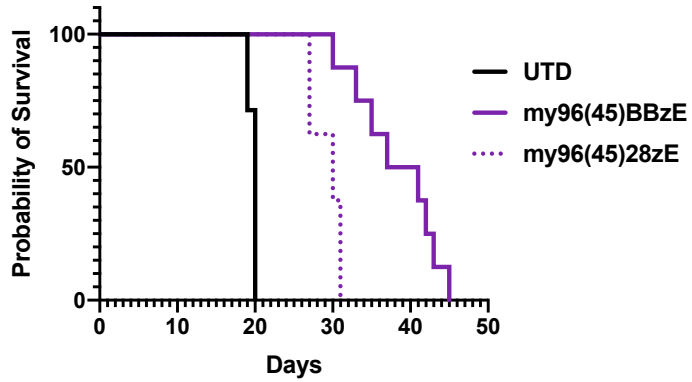




In vivo functionality







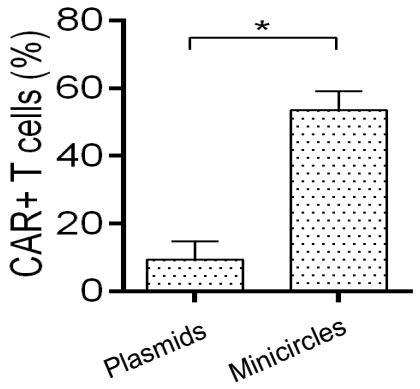
Courtesy of Dr Alfonso

Calviño C (2023). Front. Immunol. 14:1270843.

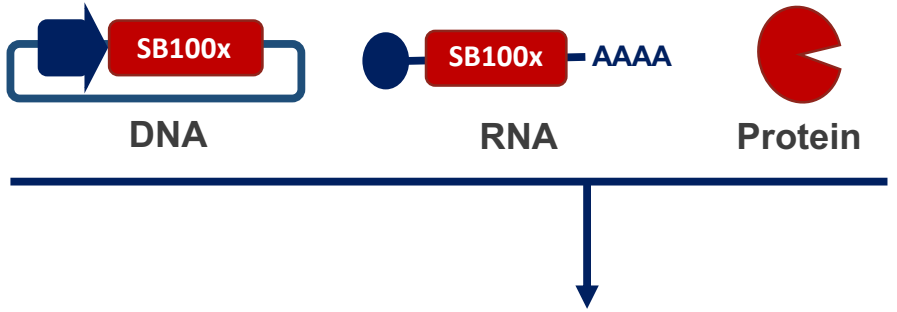
Cell selection & manufacturing

Advantages of transposon systems

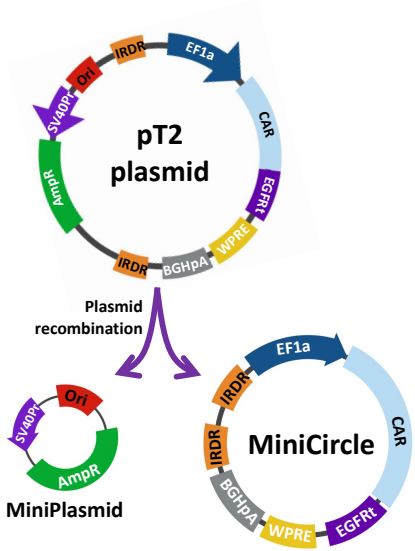
- High transduction efficacy
- Safer integration profile than LV
- Stable gene expression
- Simpler manufacturing
- Lower production costs



Sleeping Beauty transposon



Minicircle
DNA technology



Transposon vector

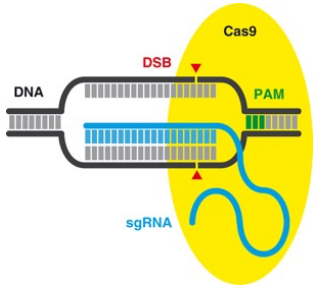
Transposase (SB100x)

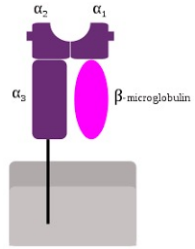
paste

cut

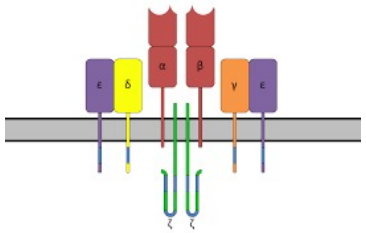
Courtesy of Dr Alfonso

CRISPR-Cas9 systems for TCR/HLA deletion



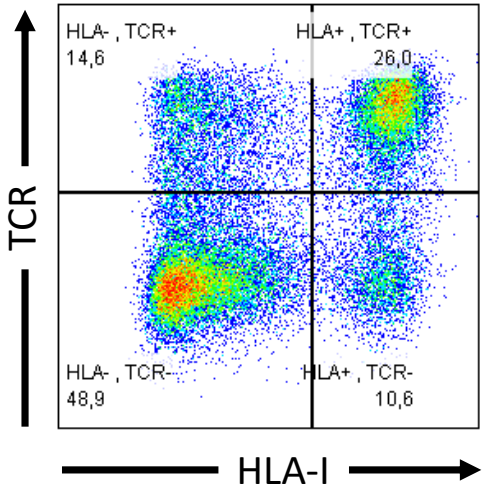


sgRNAs for b2M

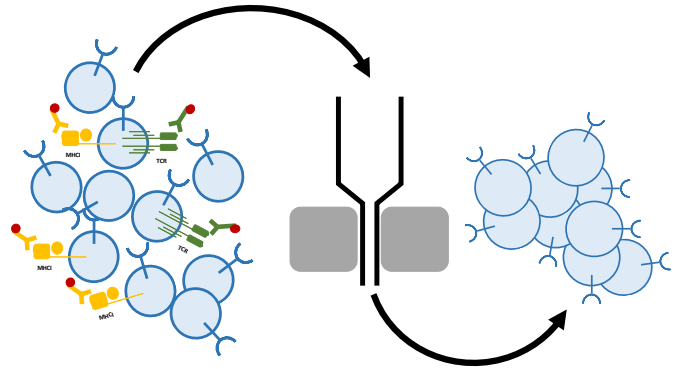


sgRNAs for TRAC

Nucleofection set-up

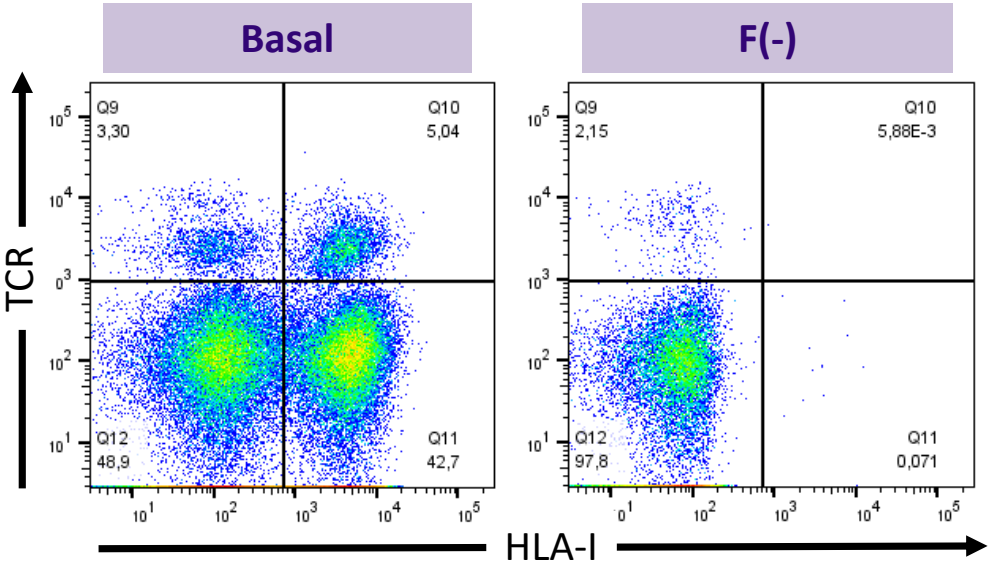


45-55% TCR/HLA KO cells
(up to 76% in some experiments)



αTCR/αHLA-I

AutoMACS system



>95%
TCR/HLA KO cells

60-80%
recuperation yield

Courtesy of Dr Alfonso

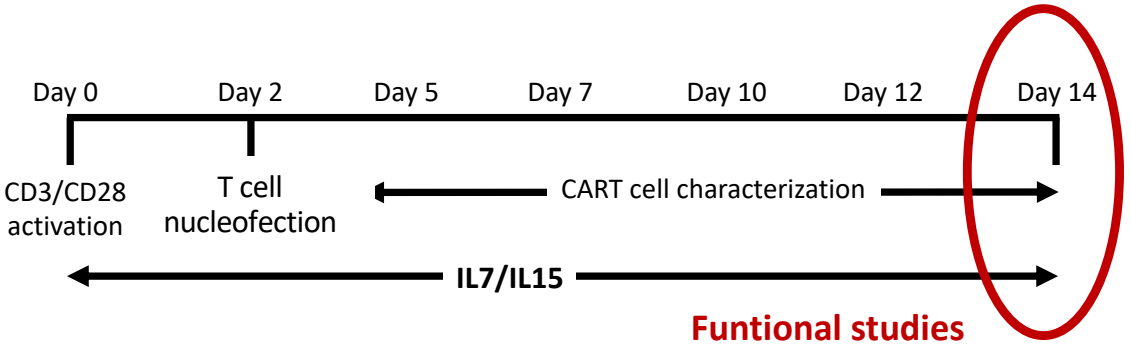
Calviño C (2023). Front. Immunol. 14:1270843.

Functionality of TCRKO/HLA-IKO CAR-T cells

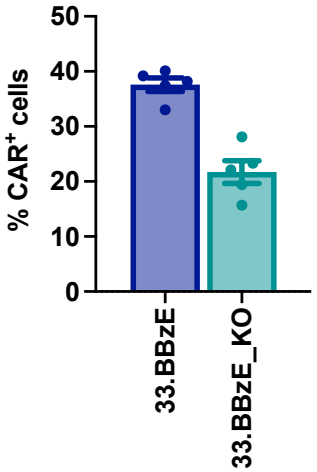
Allogeneic CD33 CAR-T

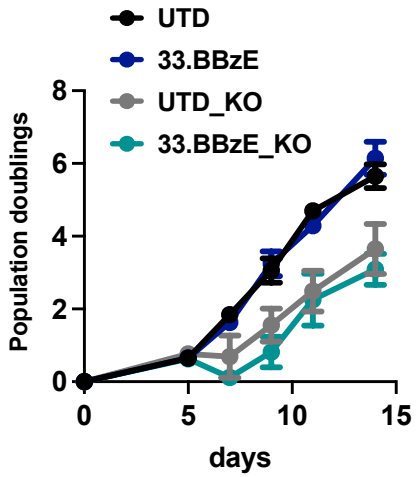
CD4/CD8 isolation

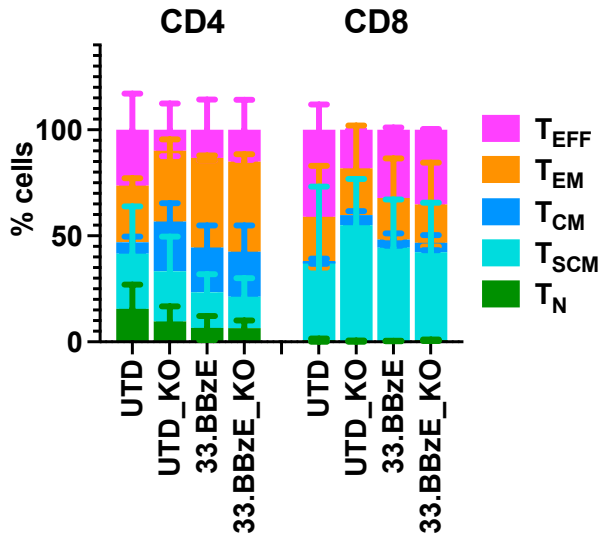
Healthy donors
AML patients

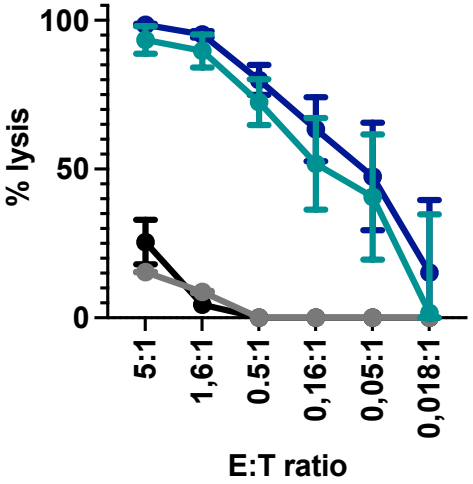


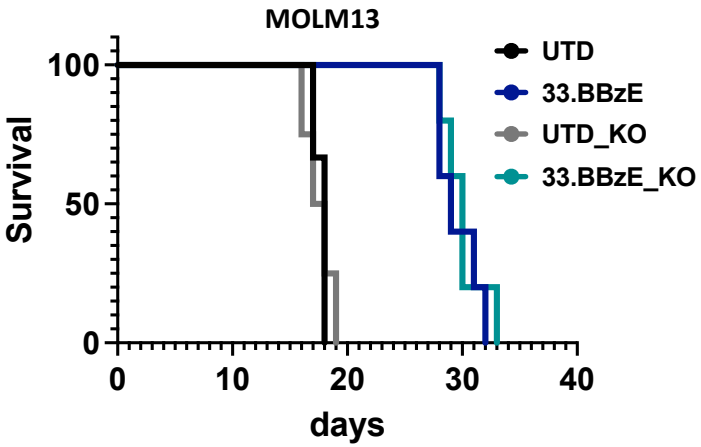
Funtional studies
- ***In vitro***
- ***In vivo***







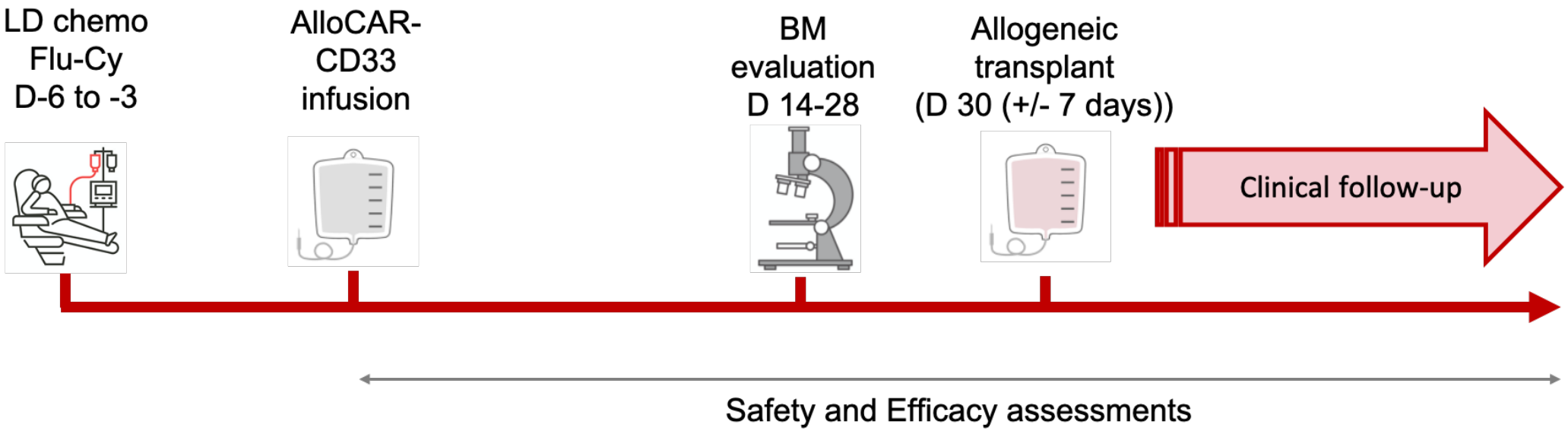




Courtesy of Dr Alfonso

Calviño C (2023). Front. Immunol. 14:1270843.

Design

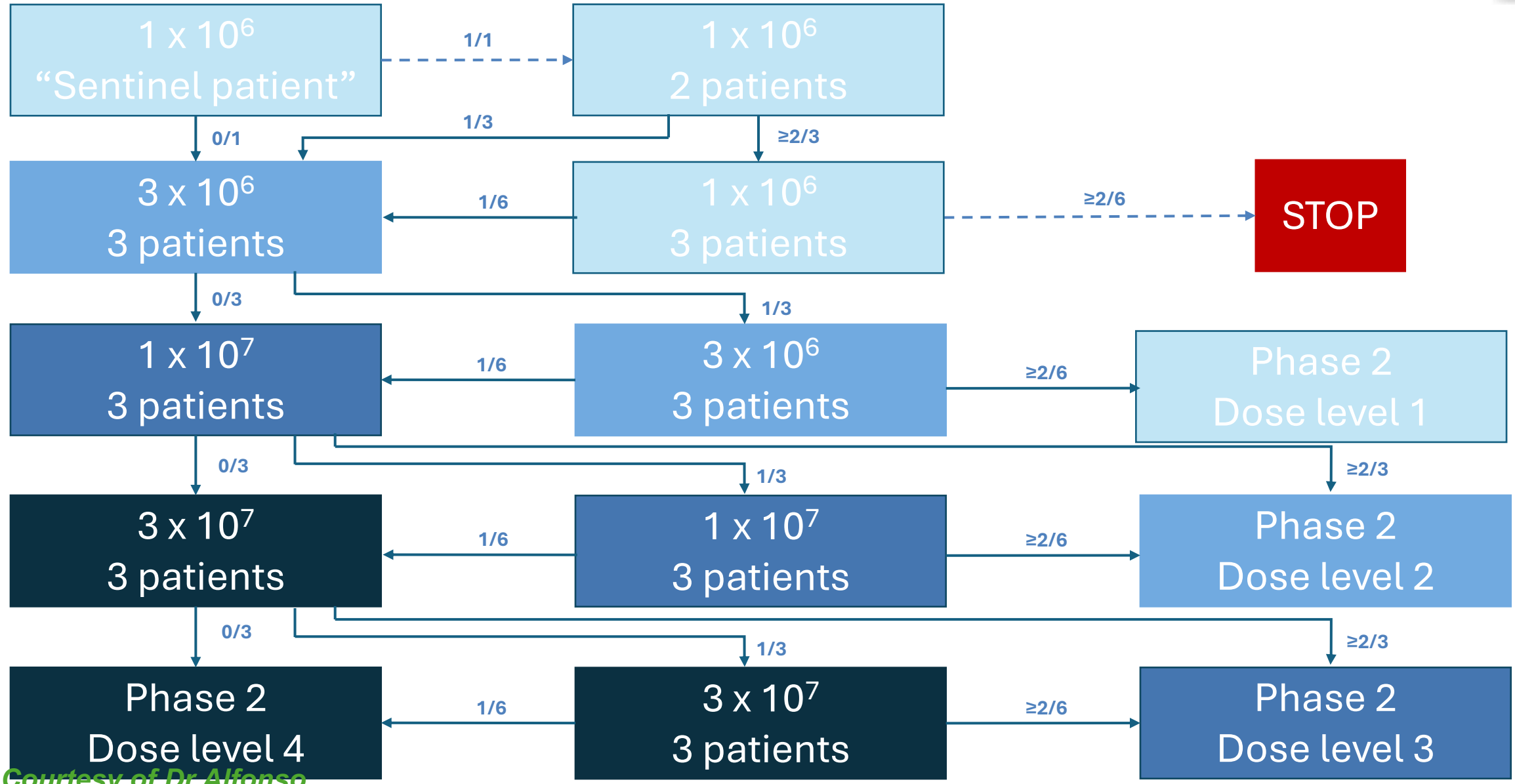


LD: Cyclophosphamide 300 mg/m^2 + fludarabine 30 mg/m2 on days −5, −4 and −3

Courtesy of Dr Alfonso

Allogeneic CD33 CAR-T

Dose scalation



Courtesy of Dr Alfonso

Inclusion Criteria

1. Diagnosis of AML or high risk MDS (IPSS-R intermediate, high or very high).
2. Relapsed or refractory disease defined as:
   - AML: 1. Relapse after ≥2 prior lines of therapy or 1 prior line with prior alloSCT; 2. Persistence of leukemic cells (≥ 5% in marrow) or documented extramedullary disease after at least two cycles of intensive induction; (i.e. 3+7 and FLAGIDA or similar),
   - MDS: 1. Relapse after ≥1 prior lines of therapy including alloSCT; 2. Persistent blast (≥10% in bone marrow) in spite of prior salvage treatment before alloSCT
3. Have exhausted all available treatments, such as targeted therapies.
4. Eligible for allogeneic transplant and with an identified donor.

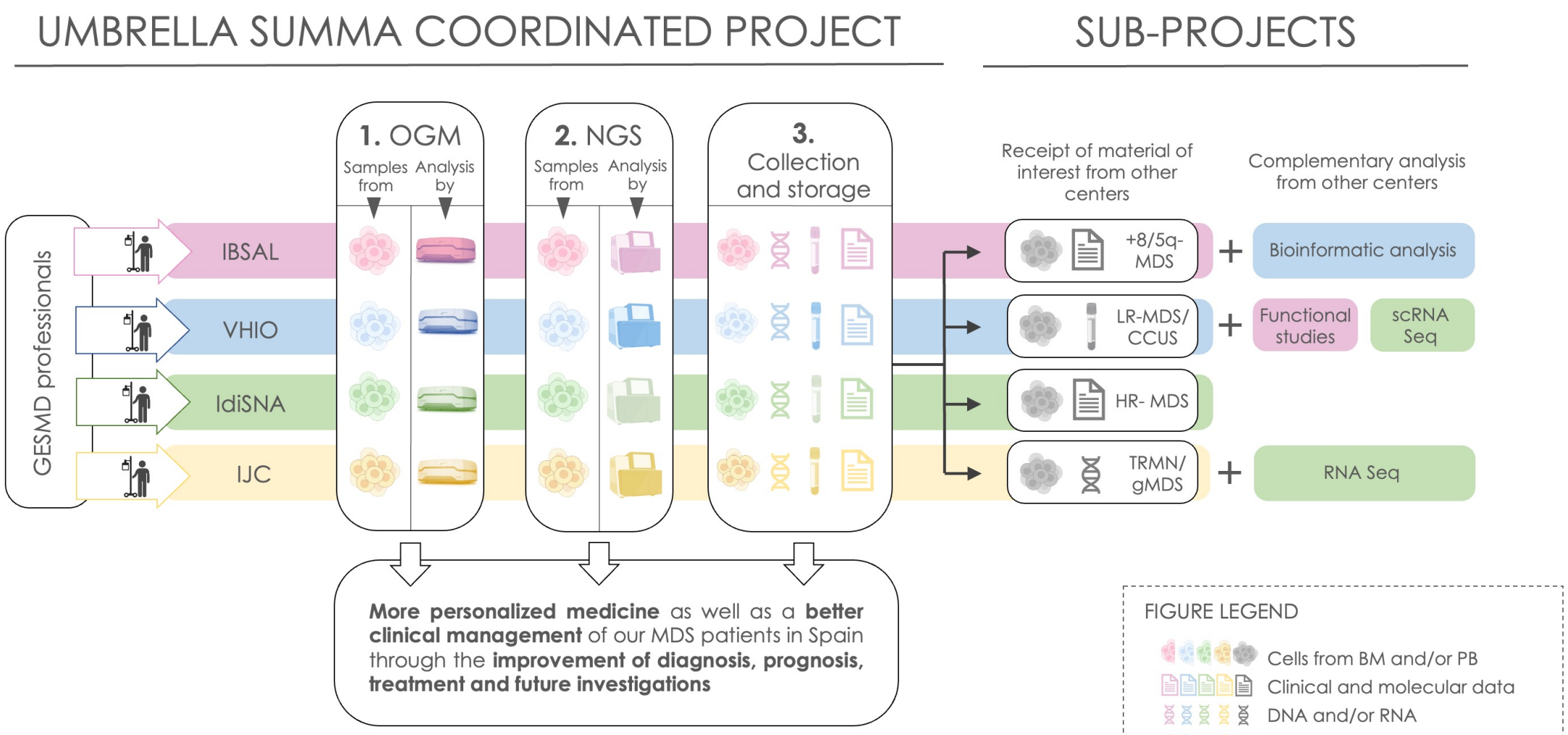
Courtesy of Dr Alfonso

UMBRELLA SUMMA LEGACY

Unified platforM for a Better integRal Evaluation of myeLodyspLastic syndromes in spAin-Strategy for Unraveling personalized genoMic Medicine in public heAlth system incorporating patient reported outcomes

PI: María Díez Campelo
CoIP: David Valcárcel

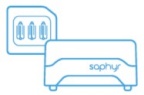
UMBRELLA SUMMA



UMBRELLA SUMMA Legacy

OBJETIVES

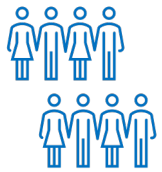
1. To develop a coordinated strategy that integrates the clinical, genetic, and molecular data of patients diagnosed with MDS at the national level within the National Health System. This strategy will include the incorporation of data to the RESMD **(1.1)**, the creation of a biobank of MDS-specific samples **(1.2)**, and the integration of Patient-Reported Outcome Measures (PROMs) and Patient-Reported Experience Measures (PREMs) **(1.3)**.



2. To validate new diagnostic tools in patients with MDS through:

- OPTICAL GENOME MAPPING (OGM) **(2.1):** Application in patients with no detectable cytogenetic alterations and/or without mitosis.
- DIGITIZATION OF BONE MARROW IMAGES **(2.2)**: Data capture and processing for diagnostically challenging cases, such as low-risk MDS without excess blasts, MDS with bone marrow fibrosis, and cases with uncertain blast counts.

UMBRELLA SUMMA Legacy



3. Evaluate the value of genomic, transcriptomic, and/or proteomic analysis as a predictive strategy in patients with MDS under special conditions, through:

- PATIENTS WITH MDS AND *TP53* MUTATIONS (3.1)
- PATIENTS WITH THERAPY-RELATED MYELOID NEOPLASMS (3.2)
- IDENTIFICATION AND CHARACTERIZATION OF PATIENTS WITH GERMLINE PREDISPOSITION (3.3)

4. Develop interoperable artificial intelligence (AI) tools that efficiently integrate clinical, molecular, and morphological information from patients with MDS, to create advanced algorithms that optimize diagnosis, prognosis, and personalized treatment. This objective includes the implementation and validation of preexisting AI models, such as AIPSS-MDS, as well as the development of new models that are fed by integrated and standardized data, ensuring their clinical applicability and compliance with international standards for interoperability and data security.

5. Promote training, dissemination, and knowledge sharing through the organization of working groups aimed at healthcare professionals and patients, using all of the above tools, including digitized virtual images, to improve diagnostic understanding and the management of the most relevant medical conditions.

GESMD

FISIM CLINICAL TRIALS

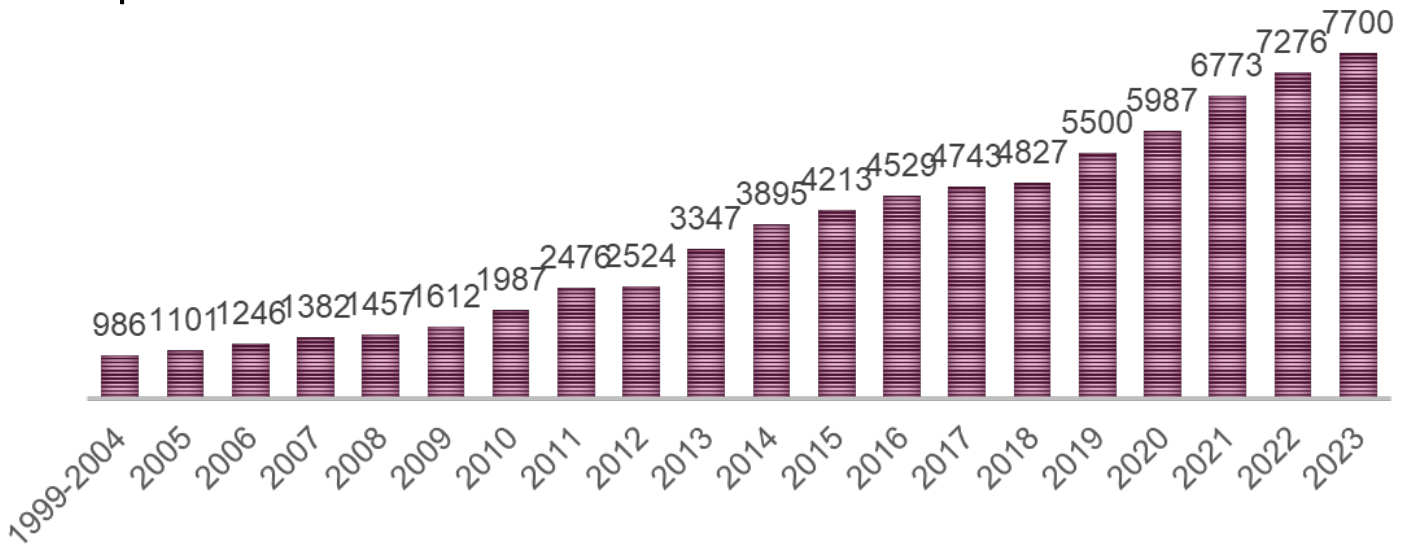
Valeria Santini

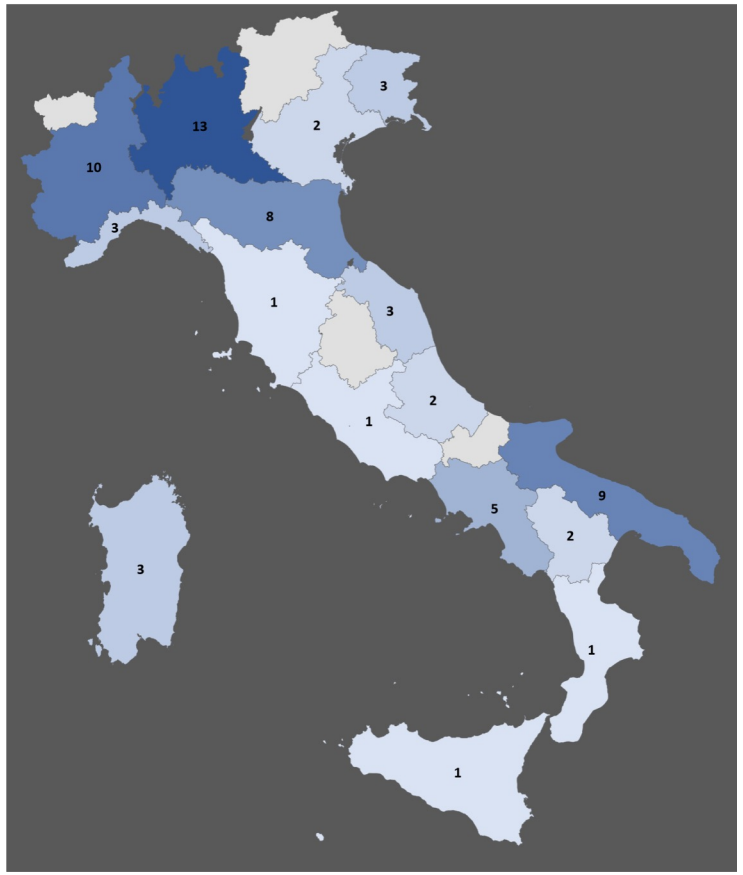
FONDAZIONE
ITALIANA
SINDROMI
MIELODISPLASTICHE

FISiM-MDS: Registry

Adult patients affected with myelodysplastic syndromes and myelodysplastic/myeloproliferative neoplasms enrolled in the Italian network of pathology registry

- **Study design**: pathology registry. 7700 patients with MDS and MDS/MPN from 67 Italian centers within 24 Years
- **Objectives**:
  - Census of all cases of MDS diagnosed by FISiM centers
  - Record the most important clinical-laboratory information, the treatment and follow up of the patients-> real-world picture
  -Carry out biological, clinical and observational studies to improve the prognosis of MDS patients.





FISIM Clinical trials

Recently completed studies

- Iron-mediated tissue damage in acquired ineffective erythropoiesis
- Hypocellular myelodysplastic syndromes (h-MDS)
- Real-world study on luspatercept in MDS-RS
- Lenalidomide discontinuation in MDS del(5q)- Harmony

Ongoing trials

Observational trials

- Lower risk MDS with predominant thrombocytopenia
- FISIM-MDS NGS

Phase II trials

- Low risk MDS: REMARK
- High risk CMML: PATROL

Work in progress

FISIM
FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

Pilo et al. Leu Res 2022 ; Calabretto G et al. Leukemia 2022; Lanino L et al. Am J *Hematol*. 2023;

FISIM ongoing trials

FONDAZIONE
ITALIANA
SINDROMI
MIELODISPLASTICHE

Lower risk MDS with predominant thrombocytopenia

Impact of the thrombocytopenia severity on the clinical evolution in patients with “lower risk” (very low-low-intermediate IPSS-R) myelodysplastic syndrome: retrospective study from disease registry

(Anna Calvisi, Enrico Balleari)

Study design: Multicenter, retrospective observational study. Patients with MDS from 67 Italian centers

Patients population:

- MDS at IPSS –r very low, low or intermediate
- thrombocytopenia <100000/mmc at diagnosis
- Available data on molecular characterization , treatment and outcome

Endpoints

- Progression free survival
- Overall survival
- Time to AML
- Response to treatments

According to platelets level at diagnosis:

- 100-50000/µl
- 50-30000/µl
- <30000/µl

FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

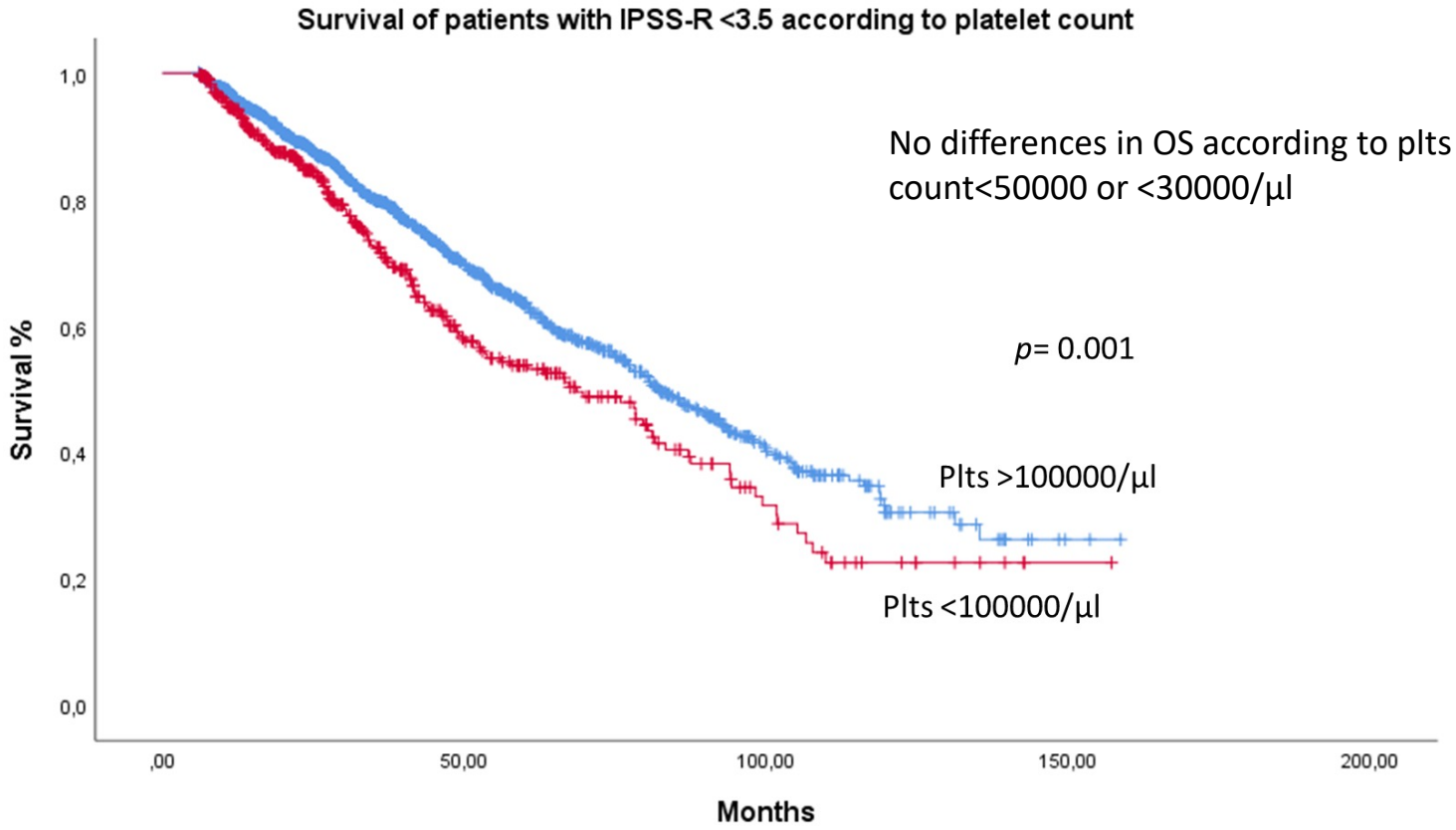
Lower risk MDS with predominant thrombocytopenia

1905 pts with IPSS-R <3.5 and follow up >=6 months

⇩

479 patients with plts<100000/µl

PLTS/µl	N°
50000-100000	350
30000-50000	76
<30000	53



Ongoing data cleaning for PFS, molecular characterization , coexisting immunological disorders and therapy

FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

FISiM-NGS-MDS

(Prof. Matteo Della Porta)

- **Study design**: No-profit, prospective observational study. 882 patients with MDS from 28 Italian participating centers within 5 Years

- **Objectives**:

  Primary:

  define the clinical utility of mutational screening in the diagnostic work-up and classification of MDS defined according to WHO criteria and to IPSS-R risk categories, developing precision medicine program in MDS patients based on real-world data

  Secondary:

  - assess the implementation of diagnostic and therapeutic guidelines in a real world context
  - evaluate the impact of specific interventions
  - identify predictors of response to specific treatments

FISiM-NGS-MDS

Inclusion criteria:

- Age ≥ 18 years
- Diagnosis of myelodysplastic syndrome or myelodysplastic/myeloproliferative neoplasms (chronic myelomonocytic leukemia, CMML) according to 2016 WHO classification criteria
- Ability to give informed consent according to ICH/EU GCP, and national/local regulations.

Exclusion criteria:

- Lack of written informed consent
- Lack of biological samples (blood, bone marrow aspirate)

FISiM
FONDAZIONE
ITALIANA
SINDROMI
MIELODISPLASTICHE

D·MDS
Deutsche MDS-Studiengruppe

Update:
D-MDS Studygroup and EMSCO

16.10.2025

Active interventional Studies (according to AMG/CTR)

LR/HR	Acronym	Title	IMP	Countries	Sample size	Status
LR	REMARK	*A phase II, open-label, multicenter study of orally administered RVU120 for the treatment of anemia in patients with lower-risk myelodysplastic neoplasms (MDS)*	**RVU120**		N=41 (single-arm	Recruitment completed
LR	LUSPLUS	*A phase IIIb, open-label, single arm study to evaluate the efficacy and safety of luspatercept in patients with lower-risk MDS and ring-sideroblastic phenotype (MDS-RS)*	**Luspatercept**		N=55 (single-arm)	Recruitment completed
LR	LENNON	*A phase II, open-label, single arm study to evaluate the efficacy of luspatercept in erythropoiesis-stimulating agent naive lower-risk MDS patients with or without ring sideroblasts who do not require RBC transfusions*	**Luspatercept**		N=30 (single-arm)	Recruiting **N=18/30**
HR	PALOMA	*Primary comparison of liposomal anthracycline based treatment versus conventional care strategies before allogeneic stem cell transplantation in patients with higher risk MDS and oligoblastic AML*	**CPX-351** (Vyxeos®) (random. vs. CCR)		N=150 (two-arm)	Recruitment completed
HR	IMPRESS	*A phase II study evaluating the efficacy and safety of imetelstat in patients with HR myelodysplastic syndromes or AML failing HMA-based therapy*	**Imetelstat**		N=46 (single-arm)	Recruitment completed
HR	PATROL	*A Phase II study of Azacitidine (AZA) combined with Venetoclax (VEN) and Tagraxofusp (TAG) in patients with higher higher-risk chronic myelomonocytic leukemia (CMML)*	**Tagraxofusp** (in comb. with AZA and VEN)		N=24 (single-arm)	Some sites are initiated, pending study drug availability
HR	AZALOX	*A Phase Ib/II multicenter open-label study evaluating the safety and efficacy of escalating doses of PXS-5505 in combination with 5-Azacitidine for pan LOX/LOXL inhibition in patients diagnosed with Myelodysplastic Neoplasms (MDS) or Chronic Myelomonocytic Leukemia (CMML)*	**PXS 5505** (in comb. with AZA**)**		N=42 (single-arm)	**N=1/42**

Active interventional Studies (according to AMG/CTR)

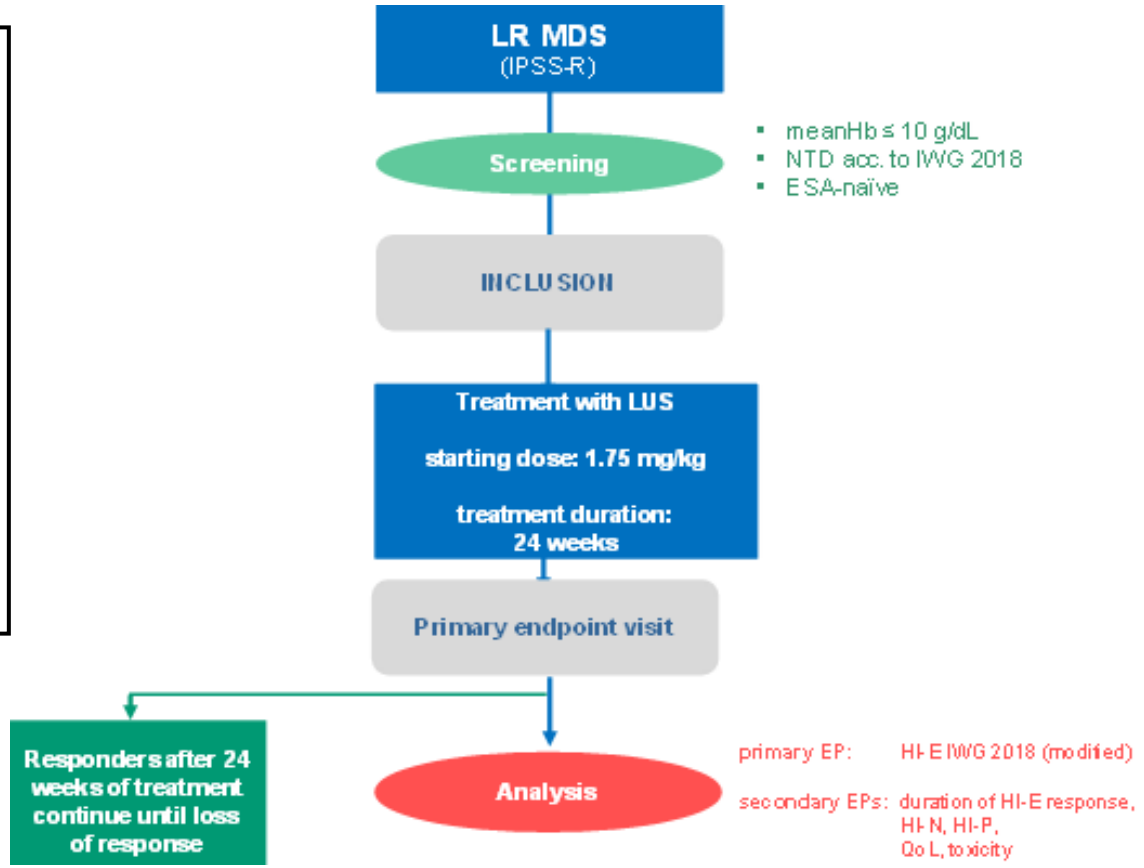
LR/HR	Acronym	Title	IMP	Countries	Sample size	Status
LR	LENNON	*A phase II, open-label, single arm study to evaluate the efficacy of luspatercept in erythropoiesis-stimulating agent naive lower-risk MDS patients with or without ring sideroblasts who do not require RBC transfusions*	Luspatercept		N=30 (single-arm)	Recruiting **N=18/30**

Essential inclusion criteria

- Diagnosis of MDS according to WHO classification
- Very low, low, or intermediate-risk disease with up to 3.5 points according to the Revised International Prognostic Scoring System (IPSS-R)
- Non-transfusion-dependent (NTD) according to IWG 2018
- Symptomatic anemia: mean baseline Hb < 10 g/dL

Essential exclusion criteria

- Secondary MDS
- Known clinically significant anemia due to iron, vitamin B12, or folate deficiency
- autoimmune disorders, hereditary hemolytic anemia, or gastrointestinal bleeding
- Prior allogeneic or autologous stem cell transplantation
- ECOG > 2
- Previous ESA treatment



Active interventional Studies (according to AMG/CTR)

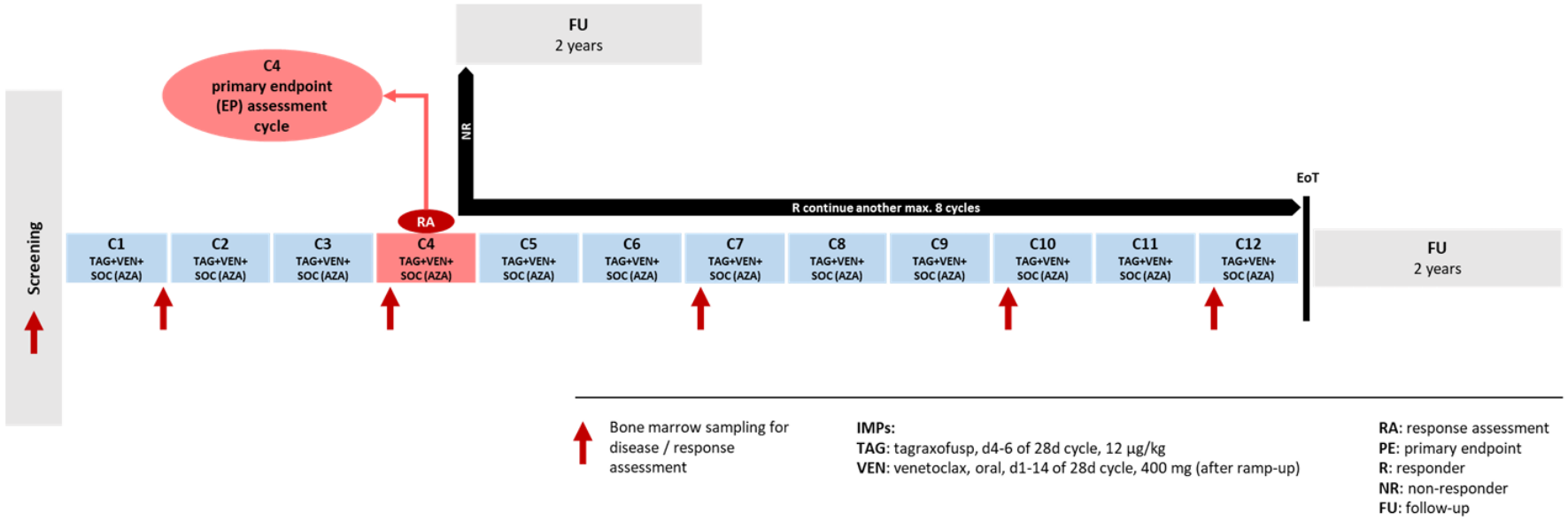
LR/HR	Acronym	Title	IMP	Countries	Sample size	Status
CMML	PATROL	*A Phase II study of Azacitidine (AZA) combined with Venetoclax (VEN) and Tagraxofusp (TAG) in patients with higher higher-risk chronic myelomonocytic leukemia (CMML)*	**Tagraxofusp** (in comb. with AZA and VEN)		N=24 (single-arm)	Some sites are initiated, pending study drug availability

Essential inclusion criteria

- CMML diagnosis according to WHO 2022 criteria
- CPSS risk: intermediate-2 or high-risk (HR) CMML
- AZA treatment according to standard therapy
- ECOG: 0–2

Essential exclusion criteria

- CMML with t(5;12) or PDGFRB rearrangement, treatable with imatinib
- Blasts in bone marrow or peripheral blood ≥ 20%
- Patients with known CNS involvement



Active interventional Studies (according to AMG/CTR)

supported by Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

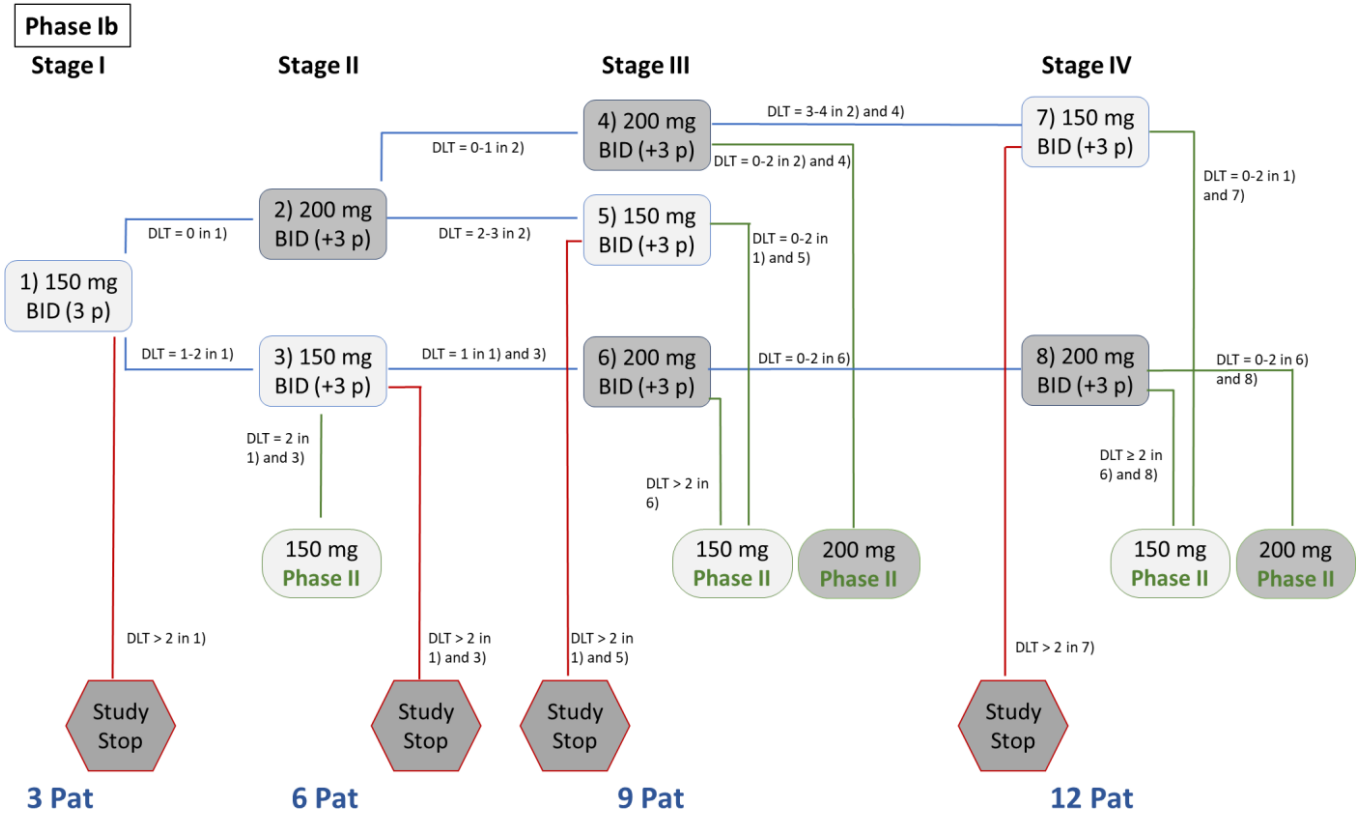
LR/HR	Acronym	Title	IMP	Countries	Sample size	Status
HR-MDS, CMML	AZALOX	*A Phase Ib/II multicenter open-label study evaluating the safety and efficacy of escalating doses of PXS-5505 in combination with 5-Azacitidine for pan LOX/LOXL inhibition in patients diagnosed with Myelodysplastic Neoplasms (MDS) or Chronic Myelomonocytic Leukemia (CMML)*	**PXS 5505** (in comb. with AZA)		N=42 (single-arm)	Recruiting **N=1/42**

Essential inclusion criteria

- For MDS: IPSS-R: high or very high with Hb < 8 g/dl
- For CMML: CPSS classification: intermediate-2 or high
- ECOG ≤ 2
- Transfusion dependency within the last 16 weeks

Essential exclusion criteria

- Previous combination treatment with AZA and VEN
- Allogeneic HSCT or solid organ transplantation
- Use of cytotoxic chemotherapeutic agents, corticosteroids (prednisone ≤ 10 mg/day or corticosteroid equivalent permitted), or immunomodulatory agents (e.g., thalidomide, lenalidomide) within 28 days prior to study entry



Active non-interventional Studies

LR/HR	Acronym	Title	IMP	Countries	Sample size	Status
LR	PRO-RED	*Longitudinal, App-based Assessment of Varying Red Blood Cell Transfusion Strategies and their Association with Patient-Reported and Clinical Outcomes in Lower-Risk MDS Patients*	**n.a.**		N=60 (single-arm)	Recruiting **N=47/60**
LR/HR	MDS-Registry	*Prospective and retrospective data collection on diagnosis, treatment and course of disease of myelodysplastic syndromes in adults*	**n.a.**		Appr. N=1200 newly documented patients + appr. N=8400 already documented patients	Recruiting **N>7000/9600**
	VEXAS-Registry	*Multicenter national VEXAS registry with accompanying biomaterial collection*	**n.a.**		N=45 per year	Recruiting **N>50**

supported by Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

Active non-interventional Studies

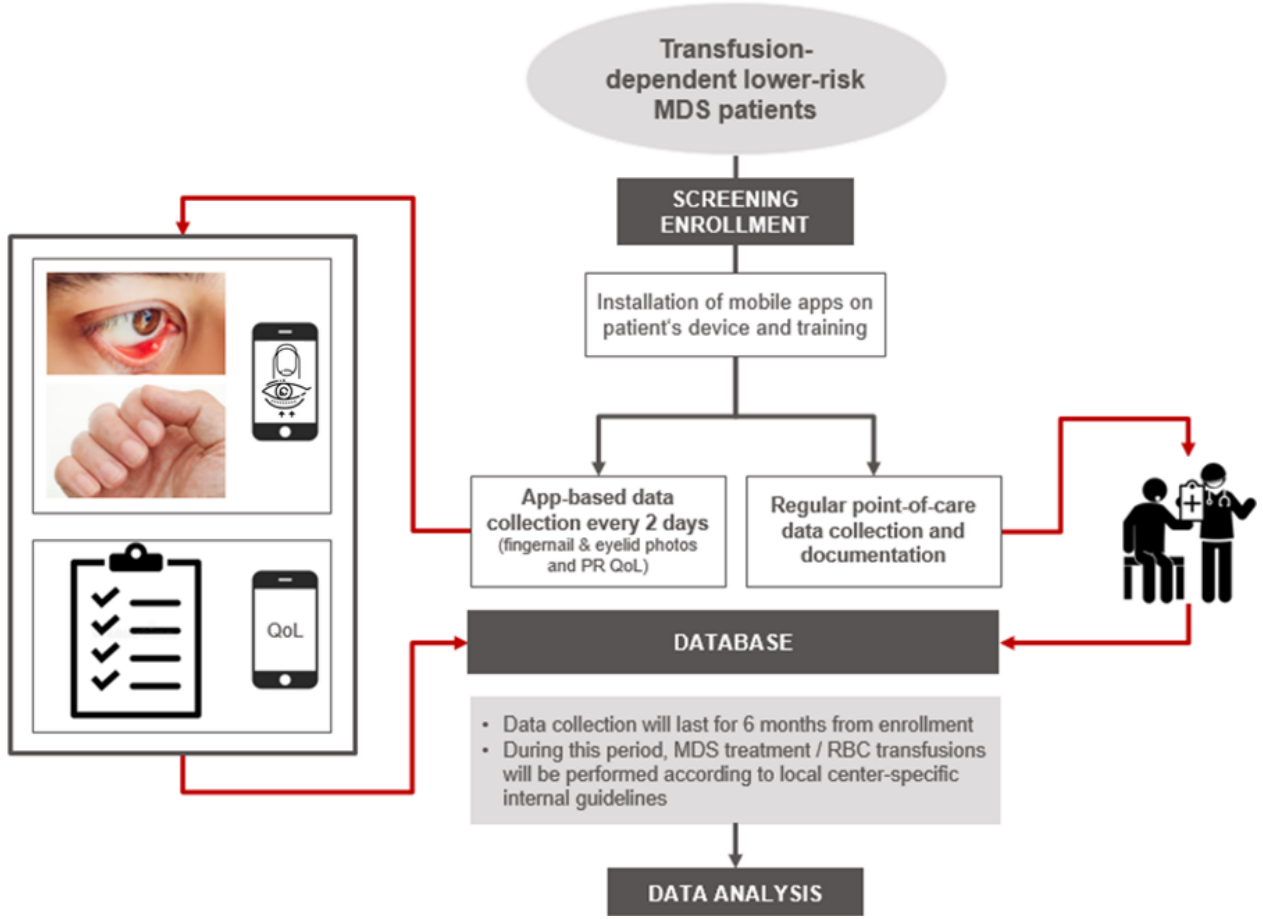
LR/HR	Acronym	Title	IMP	Countries	Sample size	Status
LR	PRO-RED	*Longitudinal, App-based Assessment of Varying Red Blood Cell Transfusion Strategies and their Association with Patient-Reported and Clinical Outcomes in Lower-Risk MDS Patients*	n.a.		N=60 (single-arm)	Recruiting **N=47/60**

Essential inclusion criteria

- Confirmed diagnosis of lower-risk MDS (IPSS-R very low, low, intermediate up to 3.5 points) or MDS/MPN overlap including MDS/MPN-RS-T, MDS/MPNu, aCML or non-proliferative CMML according to WHO criteria as determined by microscopic analyses of the bone marrow and peripheral complete blood count (CBC)
- Symptomatic transfusion dependent anemia defined as having received ≥3 units of RBCs within the last 16 weeks prior to screening

Essential exclusion criteria

- Patients who are unable to use the PRO-RED app or questionnaires provided for the study



Active non-interventional Studies

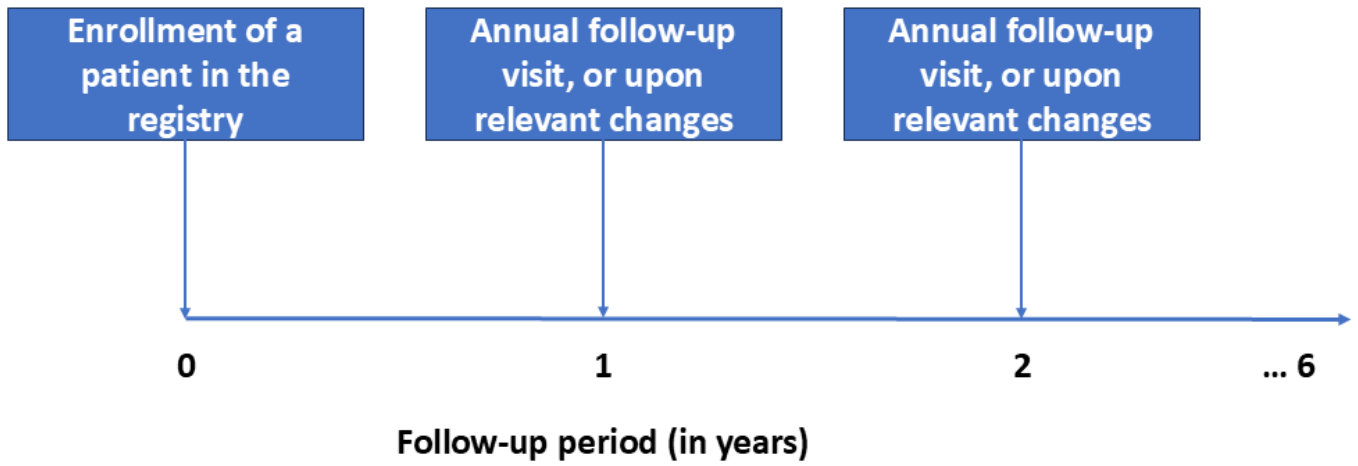
LR/HR	Acronym	Title	IMP	Countries	Sample size	Status
LR/HR	MDS-Registry	*Prospective and retrospective data collection on diagnosis, treatment and course of disease of myelodysplastic syndromes in adults*	**n.a.**		Appr. N=1200 newly documented patients + appr. N=8400 already documented patients	Recruiting **N>7000/9600**

Essential inclusion criteria

- MDS, MDS-MPD-Disease including AML with signs of dysplasia (AML-MRC) according to WHO-classification, t-MDS, t-AML with blasts <30%, MDS-associated diseases: ICUS, CHIP & CHOP
- Availability of follow-up

Essential exclusion criteria

- Other myeloid neoplasms



→ https://www.mds-register.de/

Active non-interventional Studies

VEXAS REGISTER

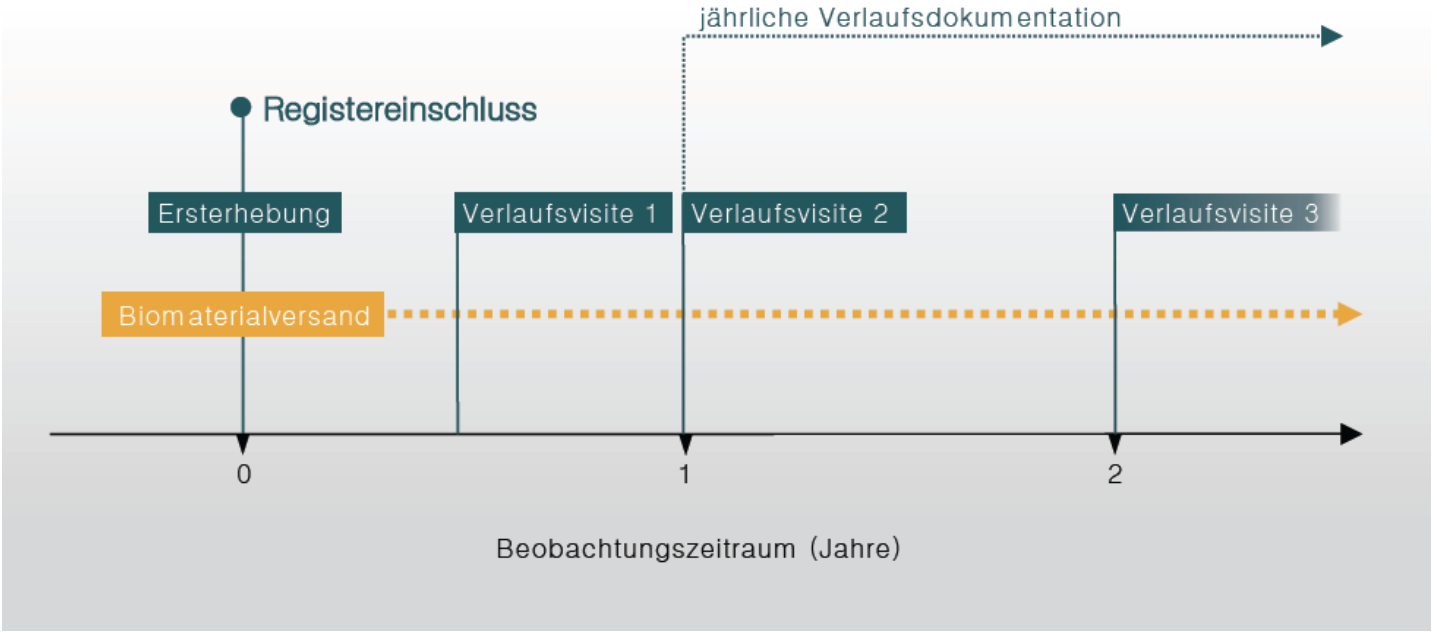
LR/HR	Acronym	Title	IMP	Countries	Sample size	Status
	VEXAS-Registry	*Multicenter national VEXAS registry with accompanying biomaterial collection*	**n.a.**		N=45 per year	Recruiting **N>50**

Essential inclusion criteria

- Confirmed diagnosis of VEXAS syndrome (molecular genetic evidence of a UBA1 mutation)

Essential exclusion criteria

- Patients with comorbidities and a non-curative intended therapy



→ https://vexas.net/

Finished Studies

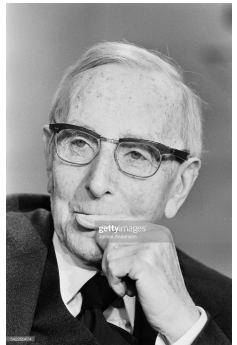
LR/HR	Acronym	Title	IMP	Countries	Sample size	Status
HR	SAMBA	*Single agent JNJ-56022473 in MDS and AML patients failing hypomethylating agent based therapy*	**Talacotuzumab**		N=43	*Leukemia*
LR	EUROPE	*Prospective validation of a predictive model of response to Romiplostim in patients with IPSS low or intermediate-1 risk myelodysplastic syndrome (MDS) and thrombocytopenia*	**Romiplostim**		N=75	*Leukemia*
CMML	DACOTA	*A randomized phase III study of Decitabine (DAC) with or without hydroxyurea (HY) versus HY in patients with advanced proliferative chronic myelomonocytic leukemia (CMML)*	**Decitabine**		N=168	*JCO*
HR	BERGAMO	*A phase II study evaluating the efficacy and safety of Bemcentinib in patients with myelodysplastic syndromes failing standard of care therapy*	**Bemcentinib**		N=43	*Leukemia*
LR	SINTRA-REV	*Multicenter, randomized, double-bling, phase III study of REVLIMID (Lenalidomide) versus placebo in patients witn low risk myelodysplastic syndrome (low and internediate-1 IPSS) with alteration in 5q- and anemia without the need of transfusion*	**Lenalidomid**		N=61	*Lancet Haematol*
LR & HR	IDEAL	*A single-arm phase II multicenter study of IDH2 (AG-221) inhibitor in patients with IDH2 mutated myelodysplastic syndrome*	**Enasidenib**		N=68 (3 cohorts)	Not published yet
LR	LUCAS	*A Phase II, Open-Label, Multicenter Study of Orally Administered CA-4948 for the Treatment of Anemia in Patients With Very Low, Low or Intermediate Risk Myelodysplastic Syndromes (MDS)*	**Emavusertib (CA-4948)**		N=38/84 (2 cohorts)	*ASH 2024 & EHA 2025*
LR	CANFIRE	*A Phase II, Single-Arm, Open-Label Study to Assess the Efficacy and Safety of Canakinumab for the Treatment of Anemia in Patients With IPSS-R Very Low, Low, or Intermediate Risk Myelodysplastic Syndromes or MDS/MPN*	**Canakinumab**		N=11/41	
LR	IMerge	*A Study to Evaluate Imetelstat (GRN163L) in Transfusion-Dependent Subjects With IPSS Low or Intermediate-1 Risk Myelodysplastic Syndrome (MDS) That is Relapsed/Refractory to Erythropoiesis-Stimulating Agent (ESA) Treatment*	**Imetelstat**	among others	N=178	*Lancet*

GFM clinical trials September 2025

Groupe Francophone des Myélodysplasies

Université Paris Cité

UNIVERSITÉ PARIS 13



GFM clinical trials

- Higher risk MDS
  - First line
  - Second line or beyond
  - Allo SCT
  - CMML
  - MDS with TP 53 mutation

- Lower risk MDS
  - First line
  - Second line or beyond
  - Associated with autoimmune or auto inflammatory diseases

Groupe Francophone des Myélodysplasies

GFM clinical trials

- Higher risk MDS
  - First line
  - Second line or beyond
  - Allo SCT
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- Lower risk MDS
  - First line
  - Second line or beyond
  - Associated with autoimmune or auto inflammatory diseases

Groupe Francophone des Myélodysplasies

Onureg-Ven : A phase 1b-2 study
(Colombe Saillard)

Groupe Francophone des Myélodysplasies

Target population	Previously untreated higher-risk myelodysplastic syndromes ineligible for allogenic transplantation
Study design	Multicenter, l phase 1b-2 study
Objectives of the Trial	**Primary objective** in the phase 1b is to establish maximum tolerated dose (MTD) and determine recommended phase 2 dose-schedule (RP2DS) by evaluating safety and tolerability of Onureg (CC-486) and VENETOCLAX combination, in previously untreated patients with HR-MDS not eligible for transplant. When MTD/RP2D will be determined, phase 2 dose expansion part of the study will open for enrollment. **Primary objective in phase 2** is to assess preliminary efficacy (CR rate) of the R2PD of Onureg-VEN combination.

	Oral AZA	Venetoclax
Level -1	200 mg QD d1-d7	400 mg QD d1-d14
Level 1	200 mg QD d1-d14	400 mg QD d1-d14
Level 2	300 mg QD d1-d14	400 mg QD d1-d14

GFM clinical trials

- Higher risk MDS
  - First line
  - Second line or beyond
  - Allo SCT
  - CMML
  - MDS with TP 53 mutation

- Lower risk MDS
  - First line
  - Second line or beyond
  - Associated with autoimmune or auto inflammatory diseases

Groupe Francophone des Myélodysplasies

Impress (cooperation with the German MDS group) (L
Adès for the GFM)

- Imetelstat in higher risk MDS and AML having failed AZA (+/-Venetoclax)

GFM clinical trials

- Higher risk MDS
  - First line
  - Second line or beyond
  - Allo SCT
  - CMML
  - MDS with TP 53 mutation

- Lower risk MDS
  - First line
  - Second line or beyond
  - Associated with autoimmune or auto inflammatory diseases

Groupe Francophone des Myélodysplasies

Ongoing

1) VENTOGRAFT: Venetoclax + AZA + DLI in MDS relapsing post allo SCT (T Cluzeau,M Robin)

2)Upfront allo SCT in patients with marrow blasts <15% (M Robin)

3) MRD ALLO MDS (M Robin)

Groupe Francophone des Myélodysplasies

GFM clinical trials

- Higher risk MDS
  - First line
  - Second line or beyond
  - Allo SCT
  - CMML
  - MDS with TP 53 mutation

- Lower risk MDS
  - First line
  - Second line or beyond
  - Associated with autoimmune or auto inflammatory diseases

Groupe Francophone des Myélodysplasies

Advanced CMML(R Itzykson)

- AZA + VEN (AVENHIR trial)

GFM clinical trials

- Higher risk MDS
  - First line
  - Second line or beyond
  - Allo SCT
  - CMML
  - MDS with TP 53 mutation

- Lower risk MDS
  - First line
  - Second line or beyond
  - Associated with autoimmune or auto inflammatory diseases

Groupe Francophone des Myélodysplasies

Higher risk MDS with TP53 mutation (T Cluzeau)

- AZA+ ATO
- AZA+ Niclosamide

GFM clinical trials

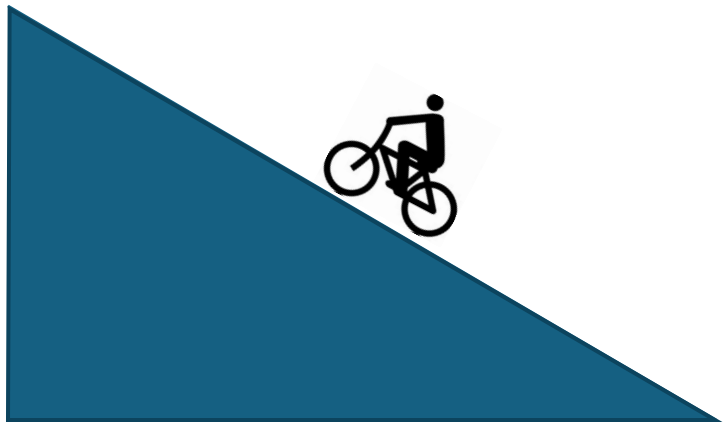
- Higher risk MDS
  - First line
  - Second line or beyond
  - Allo SCT
  - CMML
  - MDS with TP 53 mutation

- Lower risk MDS
  - First line
  - Second line or beyond
  - Associated with autoimmune or auto inflammatory diseases

Groupe Francophone des Myélodysplasies

Groupe Francophone des Myélodysplasies

Randomized trial evaluating early versus late introduction of Epoetin Alfa (EPREX®) in patients with low-risk myelodysplastic syndromes



GFM-EPO-PRETAR

Sophie PARK
CHU de Grenoble Alpes

Numéro EudraCT: 2016-000327-10

Numéro ClinicalTrials.gov: NCT02992860

GFM clinical trials

- Higher risk MDS
  - First line
  - Second line or beyond
  - Allo SCT
  - CMML
  - MDS with TP 53 mutation

- Lower risk MDS
  - First line
  - Second line or beyond
  - Associated with autoimmune or auto inflammatory diseases

Groupe Francophone des Myélodysplasies

Combola Trial (non sideroblastic lower risk MDS) (L Adès)

- Patients with lower risk MDS according to IPSS classification (LOW, INT-1) without RS
- failed to achieved a response or who subsequently relapse after ESA (at least 60000 U EPO-a over at least 12weeks or equivalent), without disease progression (Or ineligible to ESA defined by EPO > 500 UI/l)
- Hemogobin < 9 gr/dl or Transfusion dependant(at least 3 RBCs
- No del(5q) MDS

1º Endpoint: transfusion independence for TD dependent patients and hematological improvement For non TD dependent patient at W25

R

1

Luspatercept (ACE-536)
1.0 mg/kg q3W
with titration up to max of 1.75 mg/kg
n=63

1

Luspatercept (ACE-536)
+ ESA at the selected dose (part A)
n=63

Groupe Francophone des Myélodysplasies

Groupe Francophone des Myélodysplasies

LODEFI

Phase II therapeutic trial evaluating low-dose deferasirox (DFX) in patients with resistant low-risk myelodysplastic syndrome (MDS) or post-erythropoiesis-stimulating agent (ESA) relapse"

Pr Sophie PARK

Promoteur :
CHU de Grenoble
Délégation à la Recherche Clinique et à l'Innovation
Pavillon Dauphiné
CS 10217
38043 Grenoble Cedex 09

Protocole en vigueur : version 8.0 du 20220304
Lettre d'information et de consentement : version 3.1 du 23/11/2018

Version 6.0 du 18062021

Registry of MDS-RS treated by Luspatercept+ EPO (M D'Aveni, T Comont)

- MDS-RS patients included in the GFM registry
- Treated with Luspatercept according to approved schedule
- ***EPO added in case of failure***

Groupe Francophone des Myélodysplasies

Etude Luspamark (S Park)

- evaluation of biomarkers associated with fatigue with Luspatercept treatment

Etude ATOMYELO (T Cluzeau)

- Phase I/II
- SMD de faible risque avec anémie dépendante des transfusions
- Possible sans limite de nombre de traitements antérieurs !
- ATO oral fabriqué par l'IGR
- En se basant sur l'essai GFM (Vey et coll, JCO)

GFM clinical trials

- Higher risk MDS
  - First line
  - Second line or beyond
  - Allo SCT
  - CMML
  - MDS with TP 53 mutation

- Lower risk MDS
  - First line
  - Second line or beyond
  - Associated with autoimmune or auto inflammatory diseases

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Next steps in VEXAS with MDS (cooperation with MINHEMON/VEXAS group)

- New JAK inhibitors : Momelotinib (M Heiblig)
- ASTX 030 (T Comont)

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Perspectives on clinical trials in MDS in Europe

- Recently completed cooperative EMSCO studies
- Current studies
- How can we envisage the future ?

COMMENTARY

blood advances

TO THE EDITOR:

An agenda to advance research in myelodysplastic syndromes: a TOP 10 priority list from the first international workshop in MDS

Maximilian Stahl,[1] Omar Abdel-Wahab,[2] Andrew H. Wei,[3] Michael R. Savona,[4] Mina L. Xu,[5] Zhuoer Xie,[6] Justin Taylor,[8] Daniel Starczynowski,[9] Guillermo F. Sanz,[10-12] David A. Sallman,[6] Valeria Santini,[13] Gail J. Roboz,[14] Mrinal M. Patnaik,[7] Eric Padron,[6] Olatoyosi Odenike,[15] Aziz Nazha,[16] Stephen D. Nimer,[8] Ravindra Majeti,[17] Richard F. Little,[18] Steven Gore,[18] Alan F. List,[19] Vijay Kutchroo,[20] Rami S. Komrokji,[6] Tae Kon Kim,[4] Nina Kim,[18] Christopher S. Hourigan,[21] Robert P. Hasserjian,[22] Stephanie Halene,[23] Elizabeth A. Griffiths,[24] Peter L. Greenberg,[17] Maria Figueroa,[8] Pierre Fenaux,[25] Fabio Efficace,[26] Amy E. DeZern,[27] Matteo G. Della Porta,[28] Naval G. Daver,[29] Jane E. Churpek,[30] Hetty E. Carraway,[31] Andrew M. Brunner,[32] Uma Borate,[33] John M. Bennett,[34] Rafael Bejar,[35] Jacqueline Boultwood,[36] Sanam Loghavi,[37] Jan Philipp Bewersdorf,[2] Uwe Platzbecker,[38] David P. Steensma,[39] Mikkael A. Sekeres,[8] Rena J. Buckstein,[40] and Amer M. Zeidan[23]

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Review

Classification, risk stratification and response assessment in myelodysplastic syndromes/neoplasms (MDS): A state-of-the-art report on behalf of the International Consortium for MDS (icMDS)

Maximilian Stahl [a], Jan Philipp Bewersdorf [b], Zhuoer Xie [c], Matteo Giovanni Della Porta [d], Rami Komrokji [c], Mina L. Xu [e], Omar Abdel-Wahab [b], Justin Taylor [f], David P. Steensma [g], Daniel T. Starczynowski [h], Mikkael A. Sekeres [f], Guillermo Sanz [i,j,k], David A. Sallman [c], Gail J. Roboz [l], Uwe Platzbecker [m], Mrinal M. Patnaik [n], Eric Padron [c], Olatoyosi Odenike [o], Stephen D. Nimer [f], Aziz Nazha [p], Ravi Majeti [q], Sanam Loghavi [r], Richard F. Little [s], Alan F. List [t], Tae Kon Kim [u], Christopher S. Hourigan [v], Robert P. Hasserjian [w], Stephanie Halene [x], Elizabeth A. Griffiths [y], Steven D. Gore [s], Peter Greenberg [z], Maria E. Figueroa [f], Pierre Fenaux [aa], Fabio Efficace [ab], Amy E. DeZern [ac], Naval G. Daver [ad], Jane E. Churpek [ae], Hetty E. Carraway [af], Rena Buckstein [ag], Andrew M. Brunner [ah], Jacqueline Boultwood [ai], Uma Borate [aj], Rafael Bejar [ak], John M. Bennett [al], Andrew H. Wei [am], Valeria Santini [an], Michael R. Savona [u], Amer M. Zeidan [x,*]

Table 1. Top 10 list of MDS collaborative priority research goals

Priority research goals
1. To establish a new standard of care for frontline higher-risk MDS
2. To develop better treatment options for DNA methyltransferase inhibitor (DNMTi)-refractory MDS
3. To develop effective strategies for *TP53*-mutated MDS
4. To advance novel treatment strategies to impact the underlying pathophysiology of lower-risk MDS
5. To conduct clinical trials in a collaborative international effort with emphasis on equal access and on PROs
6. To formulate unified diagnostic criteria and classification subgroups for MDS
7. To establish and systematically validate clinically meaningful response criteria for MDS therapy
8. To establish tools to predict, and ultimately reduce, risk of progression of CH to MDS and other hematological malignancies in clinical practice
9. To establish linked clinical databases and biobanks allowing sharing of data
10. To improve the development and dissemination of reliable preclinical models of MDS

A few additional suggestions for international clinical trials in higher risk MDS

- We have now better response criteria (IWG 2018 ad 2023)
- Large patient numbers and surrogate endpoints needed
- Avoid some exclusion criteria
- Parallel trials on different continents
  - APR 246 in MDS with TP 53 mutation (T Cluzeau, D Salmann)
  - ABNL MARRO (M Savona)
- Prespecified subgroup analysis (based particularly on genetics)
- Avoid the systematic « intention to treat dogma »(especially for relapsing patients)
- For TP53 mutation, close cooperation with solid tumor specialists

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but what we need most is effective drugs !

Department of hematology and immunology
of Hospitals St Louis, R Debré, Avicenne
APHP and University of Paris

Hôpital St Louis

- 7 services of adult hematology (H Dombret, N Boissel, G Socié, B Arnulf, E Oksenhendler, P Fenaux, C Thiéblemont)
- ICU (E Azoulay)
- pneumology (A Tazi)

Hôpital Robert Debré

- pediatric hématology service (A Baruchel)
- Sickle cell disease unit(M Benkerrou)

Hôpital Avicenne

- Adult hematology service (C Gardin)

Université de Paris

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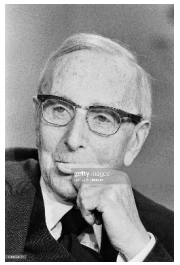

Groupe Francophone des Myélodysplasies

- Activates clinical trials in MDS (35 centers in France and Belgium + Switzerland)
- Website: www. gfmgroup.org
- Online registry of French MDS cases
- Close cooperation with:
  - a patient support group
  - the International MDS Foundation
  - the European Leukemia Net

Groupe Francophone des Myélodysplasies