Recent progress in the treatment of lower risk MDS

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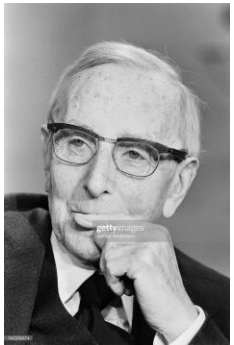
GFM



Recent treatments of lower risk MDS

- Lower risk MDS: where is the limit ?
- Treatment of anemia of lower risk MDS
- Treatment of thrombocytopenia of lower risk MDS
- Chelation therapy ?
- Treatment of MDS with autoimmune/autoinflammatory disorders

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IPSS -R

Table 3. IPSS-R Prognostic Score Values

Prognostic variable	0	0.5	1	1.5	2	3	4
Cytogenetics	Very Good		Good		Intermed-iate	Poor	Very Poor
BM Blast %	≤2		>2-<5%		5-10%	>10%	
Hemoglobin	≥10		8-<10	<8			
Platelets	≥100	50-<100	<50				
ANC	≥0.8	<0.8					

Table 4. IPSS-R Prognostic Risk Categories/Scores

RISK GROUP	RISK SCORE
Very Low	≤1.5
Low	>1.5-3
Intermediate	>3-4.5
High	>4.5-6
Very High	>6

Treatment Objectives

- Higher risk MDS
  - IPSS intermediate-2 or high

  or R-IPSS very high, high and intermediate (> 3.5)
  - Delay disease progression
  - Prolong survival
- Lower risk MDS
  - IPSS low or intermediate-1

  or R-IPSS very low, low , int <4
  - Improve blood cytopenias *(mainly anemia)*
  - Improve quality of life

Somatic mutations in MDS: 85-90% of the patients

- splicing factors SF3B1, SRSF2
- Methylation: DNMT3a, TET2, IDH1/2
- Chromatin modification: ASXL1,EZH 2
- TP53, RAS,RUNX 1
- Rare:
  - NPM1, FLT3
  - JAK2, CALR, MPL

IPSS-M

Category	Variable	Multivariable model: hazard ratio[#] (95% CI)	Weight w	Scaling x^{mean}
confounder	$^{y_{10}}$ **Age**, in years	1.23 (1.05 - 1.43)	N/A	N/A
	Sex:Male	1.22 (1.06 - 1.41)	N/A	N/A
	Type:Secondary/Therapy-related	1.36 (1.10 - 1.68)	N/A	N/A
clinical	% **Bone Marrow Blasts**, in %	1.42 (1.30 - 1.55)	0.352	0.922
	$^{y_{100}}$ min(**Platelets**,250), in x10^9/L	0.80 (0.72 - 0.89)	-0.222	1.41
	Hemoglobin, in g/dL	0.84 (0.81 - 0.88)	-0.171	9.87
cytogenetics	**IPSS-R category vector**[&]	1.33 (1.21 - 1.47)	0.287	1.390
gene main effects 17 variables, 16 genes	***TP53***^{multi}	3.27 (2.38 - 4.48)	1.18	0.0710
	MLL^{PTD}	2.22 (1.49 - 3.32)	0.798	0.0247
	FLT3$^{ITD+TKD}$	2.22 (1.11 - 4.45)	0.798	0.0108
	SF3B1^{Sq}	1.66 (1.03 - 2.66)	0.504	0.0166
	NPM1	1.54 (0.78 - 3.02)	0.430	0.0112
	RUNX1	1.53 (1.23 - 1.89)	0.423	0.126
	NRAS	1.52 (1.05 - 2.20)	0.417	0.0362
	ETV6	1.48 (0.98 - 2.23)	0.391	0.0216
	IDH2	1.46 (1.05 - 2.02)	0.379	0.0429
	CBL	1.34 (0.99 - 1.82)	0.295	0.0473
	EZH2	1.31 (0.98 - 1.75)	0.270	0.0588
	U2AF1	1.28 (1.01 - 1.61)	0.247	0.0866
	SRSF2	1.27 (1.03 - 1.56)	0.239	0.158
	DNMT3A	1.25 (1.02 - 1.53)	0.221	0.161
	ASXL1	1.24 (1.02 - 1.51)	0.213	0.252
	KRAS	1.22 (0.84 - 1.77)	0.202	0.0271
	SF3B1$^{\alpha}$	0.92 (0.74 - 1.16)	-0.0794	0.186
gene residuals[$] 1 variable, 15 genes	min(**Nres**,2) Possible values are 0,1 or 2	1.26 (1.12 - 1.42)	0.231	0.388

0.5 1 2 3 5

Hematological parameters as continuous variables

IPSS-R cytogenetic categories,

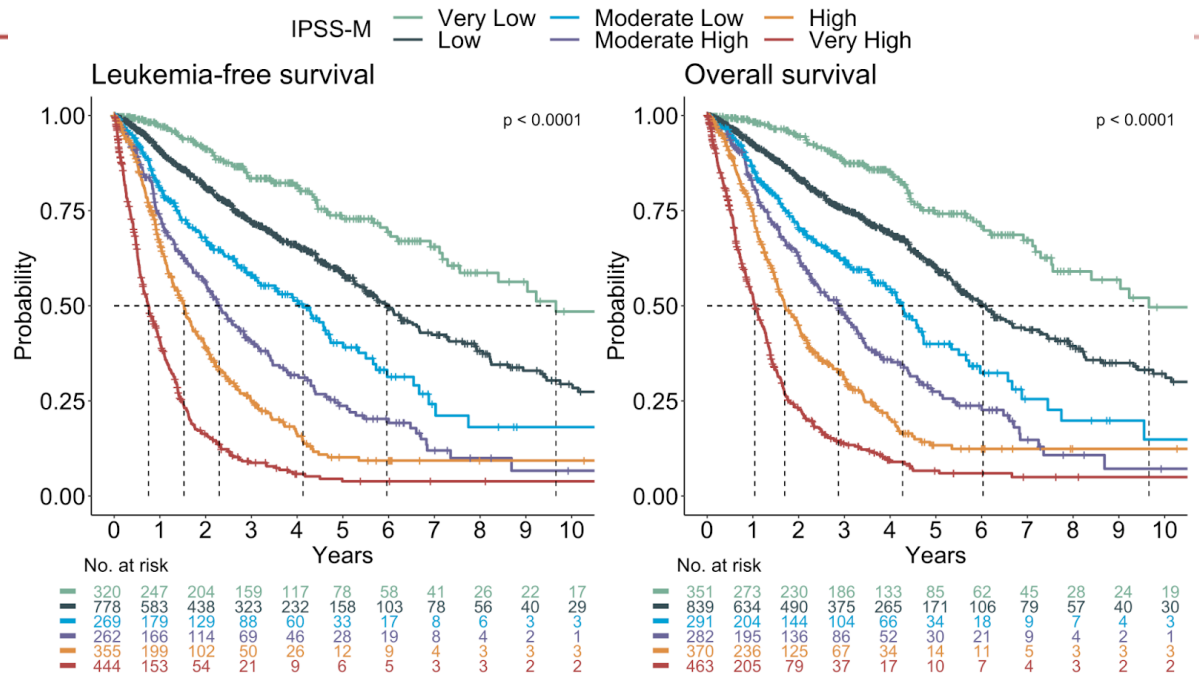
17 Variables from 16 genes

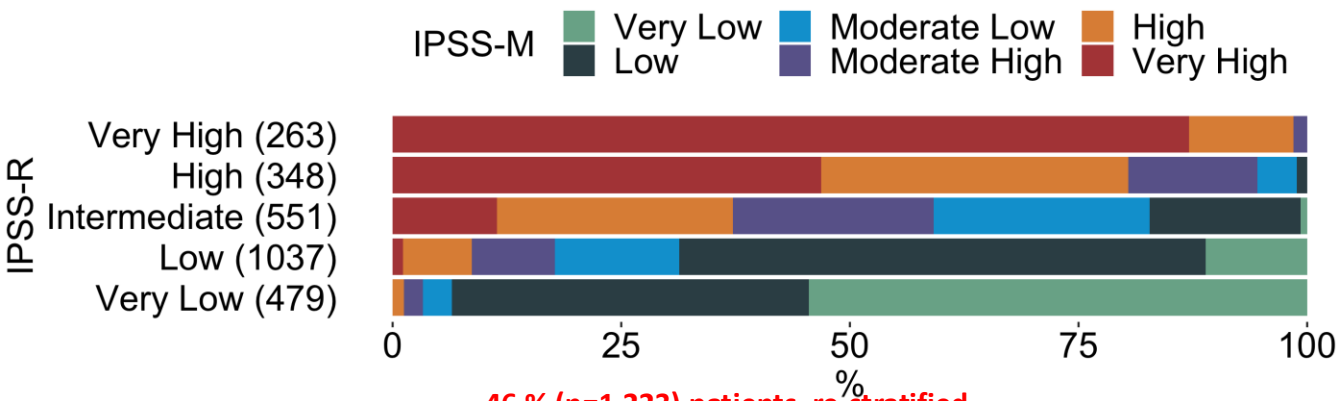
1 Variable from 15 residual genes ^
Number of mutated genes (0, 1 ou 2)

gènes résiduels : ***BCOR, BCORL1, CEBPA, ETNK1, GATA2, GNB1, IDH1, NF1, PHF6, PPM1D, PRPF8, PTPN11, SETBP1, STAG2, WT1***

Elsa Bernard et al. ASH 2021

IPSS-M risk categories **Very low | low | low moderate | high moderate | high | very high**





46 % (n=1 223) patients re-stratified

7% (n=196) patients re-stratified by more than one strata

Mutations with largest clinical significance in MDS

- SF3B1
  - Alone of with «favorable » mutations (TET2…)
  - With unfavorable mutations (RUNX1….)
- TP53
  - Biallelic: *complex karyotype* with del 17p, del 5q
  - Monoallelic *(non complex karyotype*)
    - Isolated del 5q
    - others

- IDH1
- IDH2
- (FLT3, NPM1)

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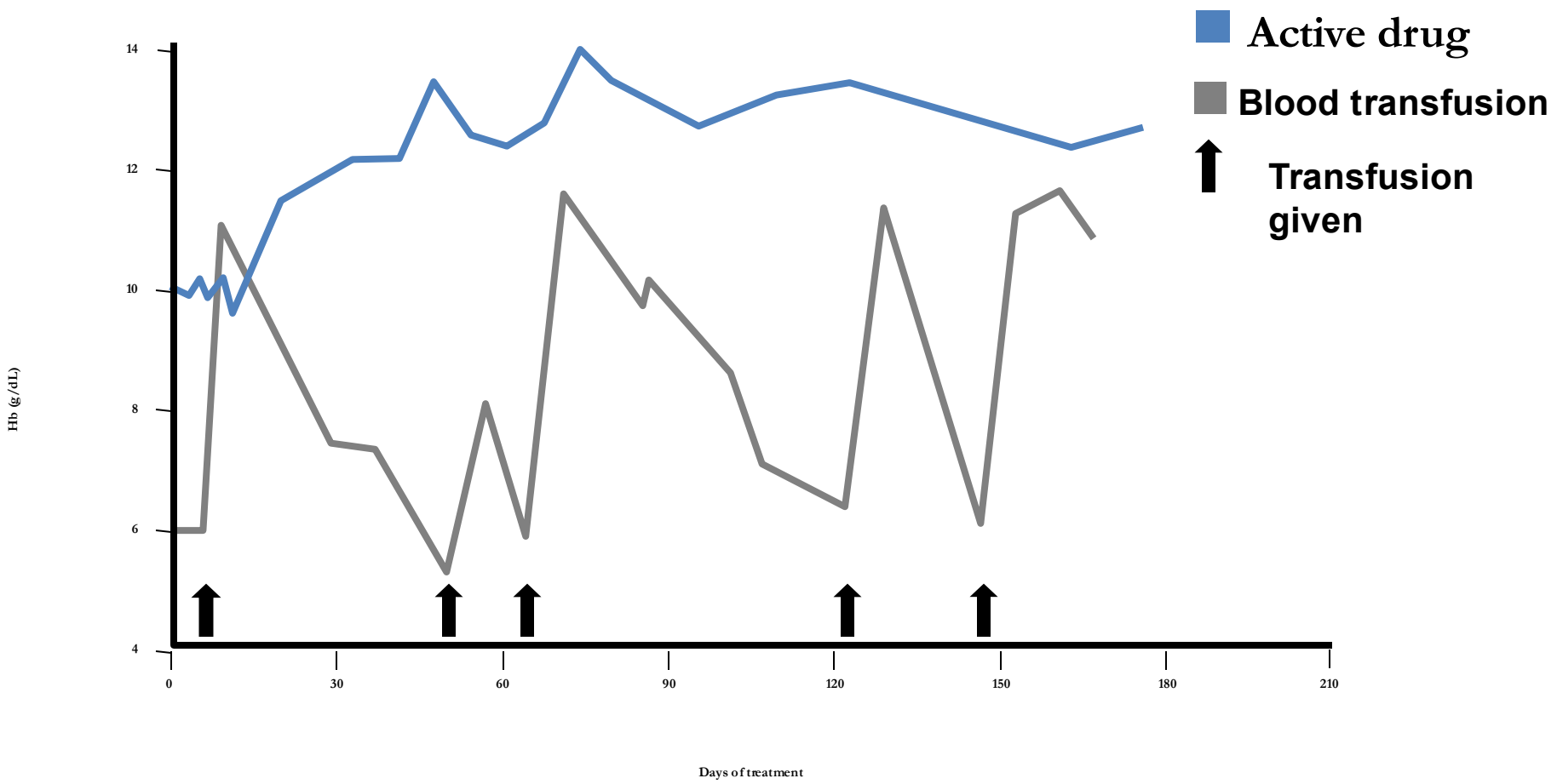
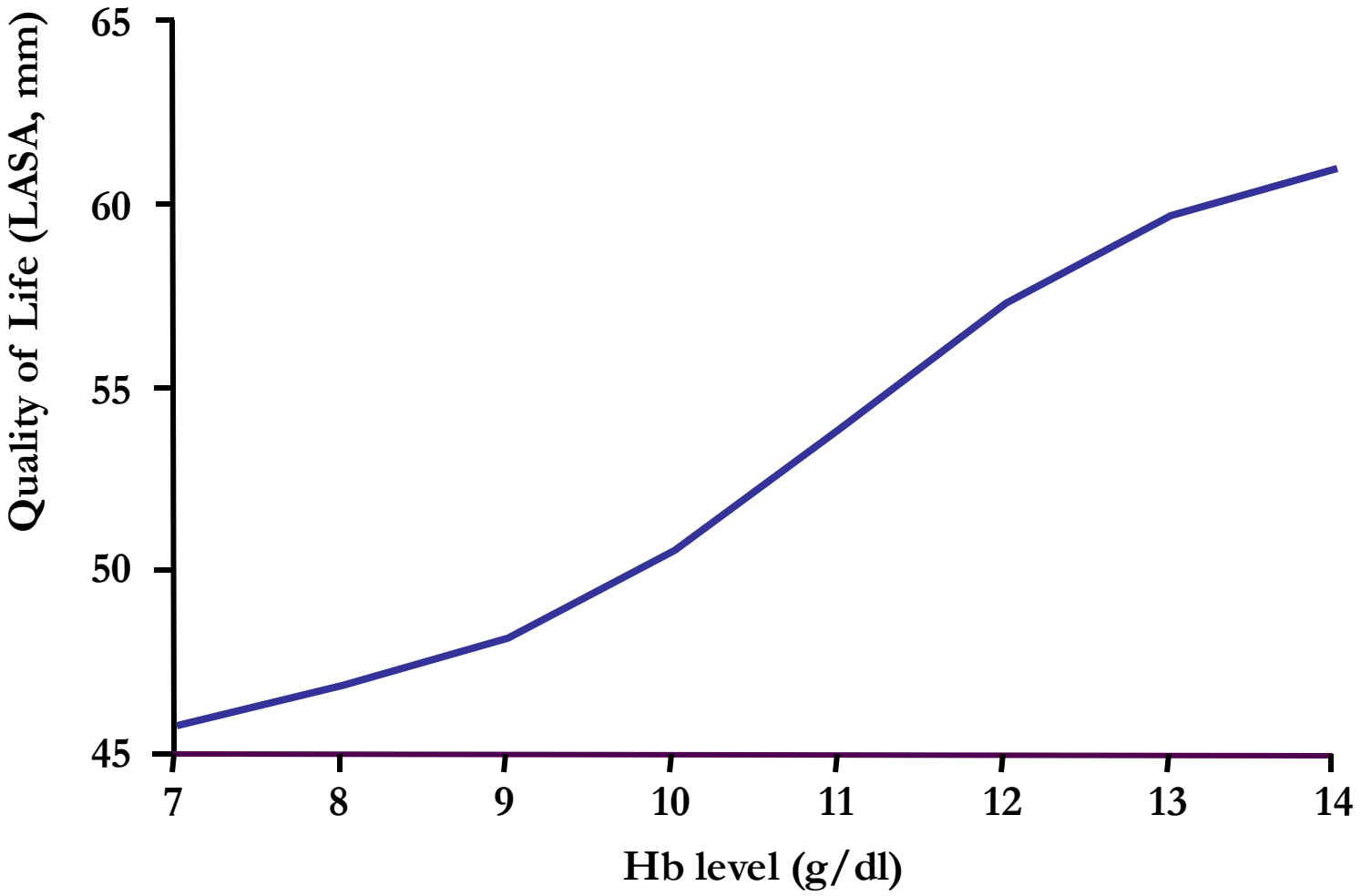

Active drug
Blood transfusion
Transfusion given
Hb (g/dL)
14
12
10
8
6
4
0
30
60
90
120
150
180
210
Days of treatment

Quality of Life is correlated to Hb levels



LASA: Linear Analog Scale Assessment

Crawford et al. *Cancer* 2002; 95: 888–95

Treatments of lower risk MDS: How to prevent anemia recurrence?

- First line treatment
  - ESAs (EPO and darbepoetin) (non del 5q)
    - 50% responses
    - Median duration 20 to 24 months
  - Lenalidomide (del 5q)
    - 65% transfusion independence
    - 50% complete cytogenetic response
    - Median duration 2.2 years

Treatments of lower risk MDS: How to prevent anemia recurrence?

- Second line treatments
  - Immunosuppressive drugs
    - 40% response rate
    - Selected population
  - Lenalidomide (non del 5q)
    - 25-30% transfusion independence
    - Median duration 35-40 weeks
  - Hypomethylating agents
    - 20-30% response

Early start of LEN in MDS with del 5q ?

SINTRA –REV trial (M Diez Campelo, ASH 2020 and ASH 2022)

- Patients with Hb <12g, no RBC TD
- randomized between LEN (5mg/d) or placebo

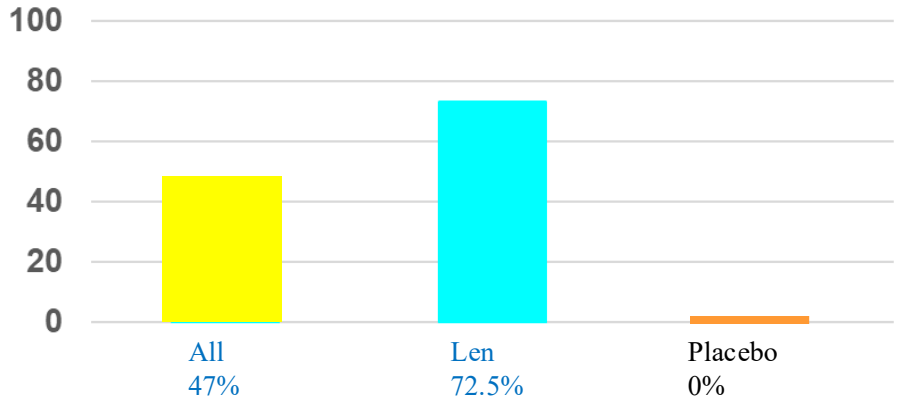
GESMD

Groupe Francophone des Myélodysplasies

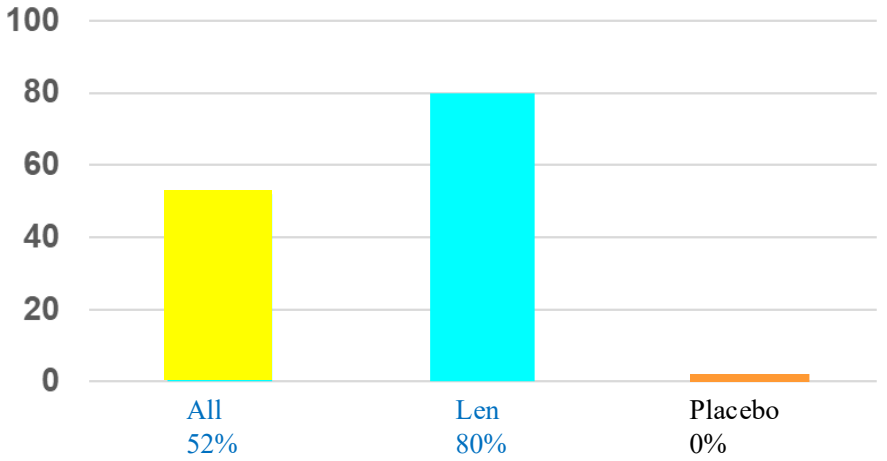
Sintra-Rev Clinical Trial

Low doses of Len improved Erythroid and Cytogenetic responses

✓ **Erythroid Response**



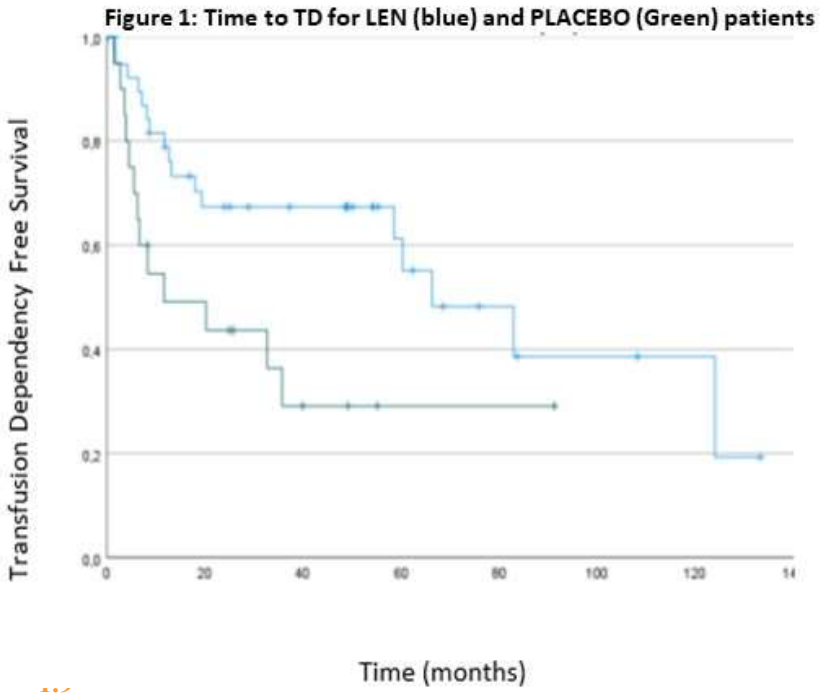
✓ Cytogenetic Response



Sintra-Rev Clinical Trial

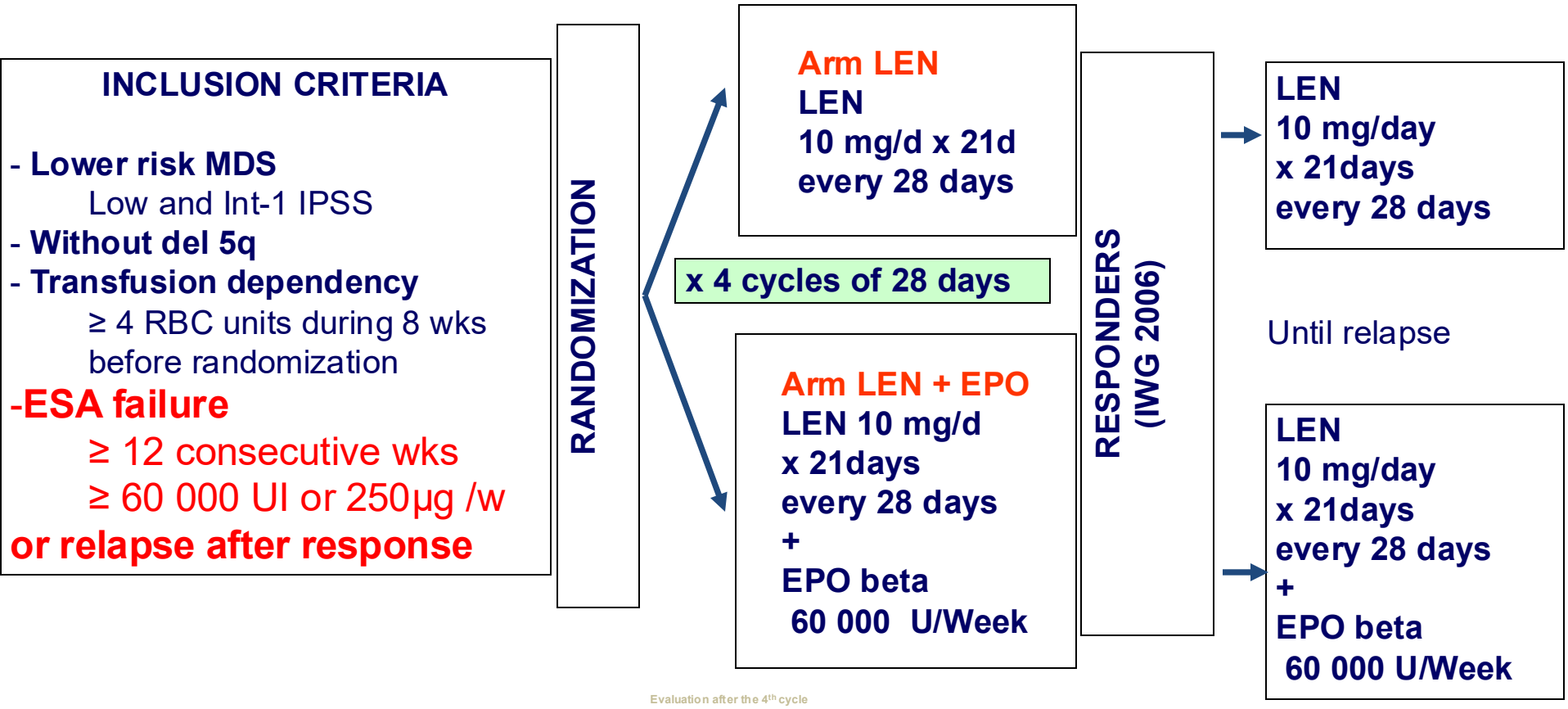
Low doses of Len delayed and decreased transfusion dependency

Median time to Transfusion Dependency (median 66.3 vs 11.6 months)



LEN+ EPO in lower risk MDS without del 5q

Groupe Francophone des Myélodysplasies



A Toma and F Dreyfus, Leukemia 2015

Groupe Francophone des Myélodysplasies

Erythroid response and RBC-TI

(patients who received >= 4 cycles n= 99)

	LEN + EPO N = 50	LEN N = 49	
Erythroid response (IWG 2006)	**52%**	**30.6%**	**RR = 1.7** **p= 0.03**

Presented by : Andréa Toma, MD PhD - APHP - France

New drugs for anemia of non del 5q lower risk MDS

- Metapivat/etavopivat
- Spliceosome inhibitors
- Imetelstat (telomerase inhibitor)
- Daratumumab (CD 38 inhibitor)
- Fc enginered antibody BI 836858 (MDSC inhibition)
- Inhibition of the NLRP3 inflammasome (including of S 100A9)
- TLR inhibition
- HIF hydroxylase inhibitors (Roxadustat)
- Asunercept (blockade of the CD 95 ligand system)
- IDH1 and IDH2 inhibitors
- Luspatercept (ligand trap to inhibit negative regulators of late-stage erythropoiesis, including GDF11 and activin B)

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RESEARCH ARTICLE

Roxadustat for the treatment of anemia in patients with lower-risk myelodysplastic syndrome: Open-label, dose-selection, lead-in stage of a phase 3 study

David H. Henry[1] | John Glaspy[2] | Rosemary Harrup[3] | Moshe Mittelman[4] | Amy Zhou[5] | Hetty E. Carraway[6] | Charles Bradley[7] | Gopal Saha[7] | Katharina Modelska[7] | Pamela Bartels[7] | Robert Leong[7] | Kin-Hung P. Yu[7]

- HIF hydroxylase inhibitor
- Lower risk MDS with sEPO<400 and low RBC transfusion requirement
- N=24, TI in 9 (37.5%)
- No major side effects

original reports

Imetelstat Achieves Meaningful and Durable Transfusion Independence in High Transfusion–Burden Patients With Lower-Risk Myelodysplastic Syndromes in a Phase II Study

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- N=38
- 63% of patients IPSS Low and 37% Int-1
- Median RBC transfusion requirement 8 units/8weeks

Parameters	n = 38
8-week TI, n (%)	16 (42%)
Duration of TI[a], weeks, median (range)	85.9 (8.0 – 140.9)
24-week TI, n (%)	11 (29)
HI-E per IWG 2006, n (%)	26 (68)

2023 ASCO® ANNUAL MEETING

IMerge

IMerge: Results From a Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Imetelstat in Patients With Heavily Transfusion Dependent Non-Del(5q) Lower-Risk Myelodysplastic Syndromes Relapsed/Refractory to Erythropoiesis Stimulating Agents

Amer Zeidan, MBBS MHS,[1] Uwe Platzbecker, MD,[2] Valeria Santini, MD,[3] Pierre Fenaux, MD, PhD,[4] Mikkael A. Sekeres, MD,[5] Michael Robert Savona, MD,[6] Yazan F. Madanat, MD,[7] Maria Diez-Campelo, MD, PhD,[8] David Valcarcel-Ferreiras, MD, PhD,[9] Thomas Ilmer, MD,[10] Anna Jonasova, PhD,[11] Petra Belohlavkova, PhD,[12] Laurie Sherman, BSN,[13] Tymara Berry, MD,[13] Souria Dougherty, MBA,[13] Sheetal Shah, BS,[13] Libo Sun, PhD,[13] Ying Wan, MD, PhD,[13] Fei Huang, PhD,[13] and Rami Komrokji, MD[14]

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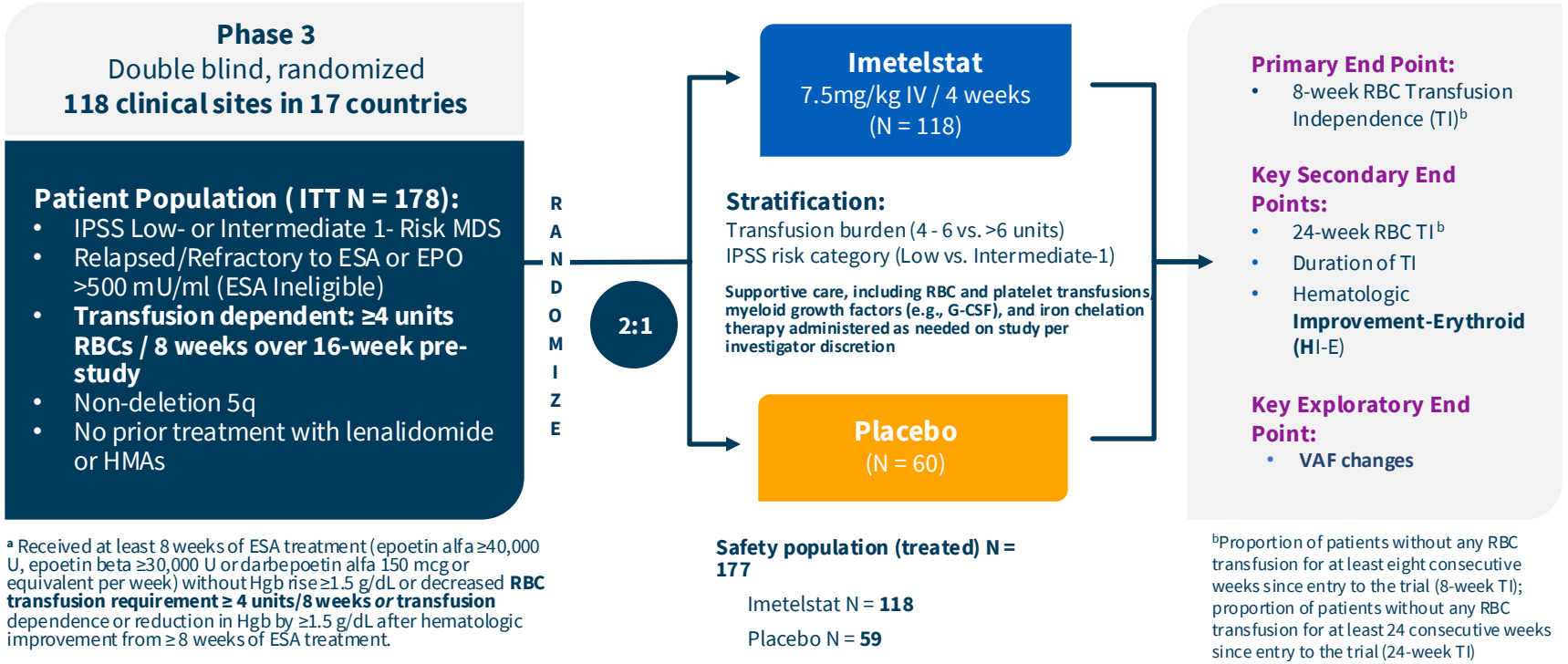


[a] Received at least 8 weeks of ESA treatment (epoetin alfa ≥40,000 U, epoetin beta ≥30,000 U or darbepoetin alfa 150 mcg or equivalent per week) without Hgb rise ≥1.5 g/dL or decreased **RBC transfusion requirement ≥ 4 units/8 weeks *or* transfusion** dependence or reduction in Hgb by ≥1.5 g/dL after hematologic improvement from ≥ 8 weeks of ESA treatment.

Safety population (treated) N = 177

Imetelstat N = **118**

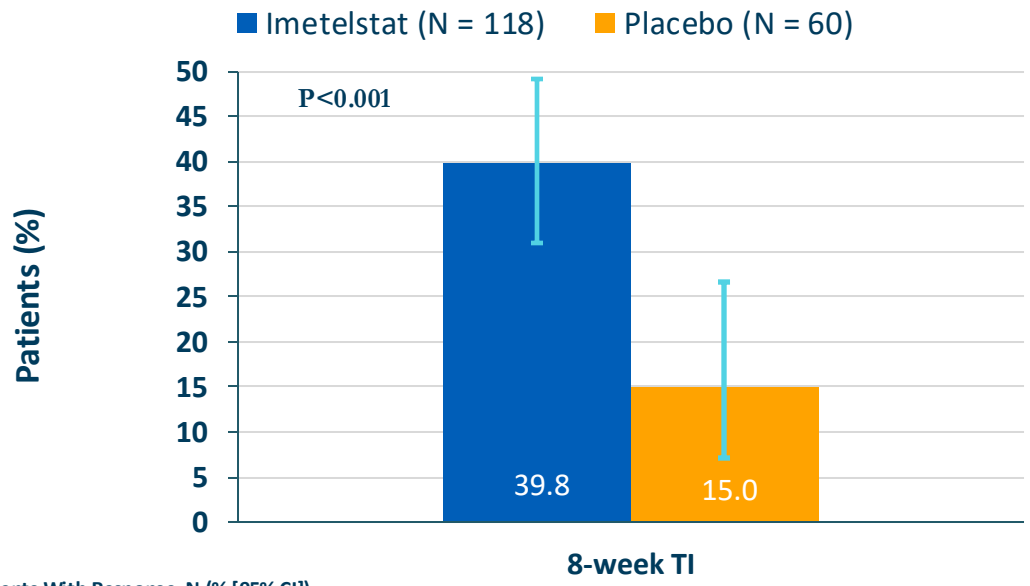
Placebo N = **59**

[b] Proportion of patients without any RBC transfusion for at least eight consecutive weeks since entry to the trial (8-week TI); proportion of patients without any RBC transfusion for at least 24 consecutive weeks since entry to the trial (24-week TI)

Baseline Patient and Disease

Characteristic	Imetelstat (N = 118)	Placebo (N = 60)
Median age, y (range)	72 (44-87)	73 (39-85)
Male, n (%)	71 (60)	40 (66)
Median time since diagnosis, y (range)	3.5 (0.1-26.7)	2.8 (0.2-25.7)
WHO classification, n (%) RS+ RS-	 73 (62) 44 (37)	 37 (62) 23 (38)
IPSS risk category n (%) Low Intermediate-1	 80 (68) 38 (32)	 39 (65) 21 (35)
Median pretreatment hemoglobin,[a] g/dL (range)	7.92 (5.3-10.1)	7.80 (6.1-9.2)
Median prior RBC transfusion burden, RBC units / 8 weeks (range)	6 (4-33)	6 (4-13)
Prior RBC transfusion burden, n (%) ≥4 to ≤6 units / 8 weeks >6 units / 8 weeks	 62 (53) 56 (48)	 33 (55) 27 (45)
Median sEPO, mU/mL (range)	174.9 (6.0-4460.0)	277.0 (16.9-5514.0)
sEPO level, n (%) ≤500 mU/mL >500 mU/mL	 87 (74) 26 (22)	 36 (60) 22 (37)
Prior erythropoiesis stimulating agents use, n (%)	108 (92)	52 (87)
Prior luspatercept use,[b] n (%)	7 (6)	4 (7)

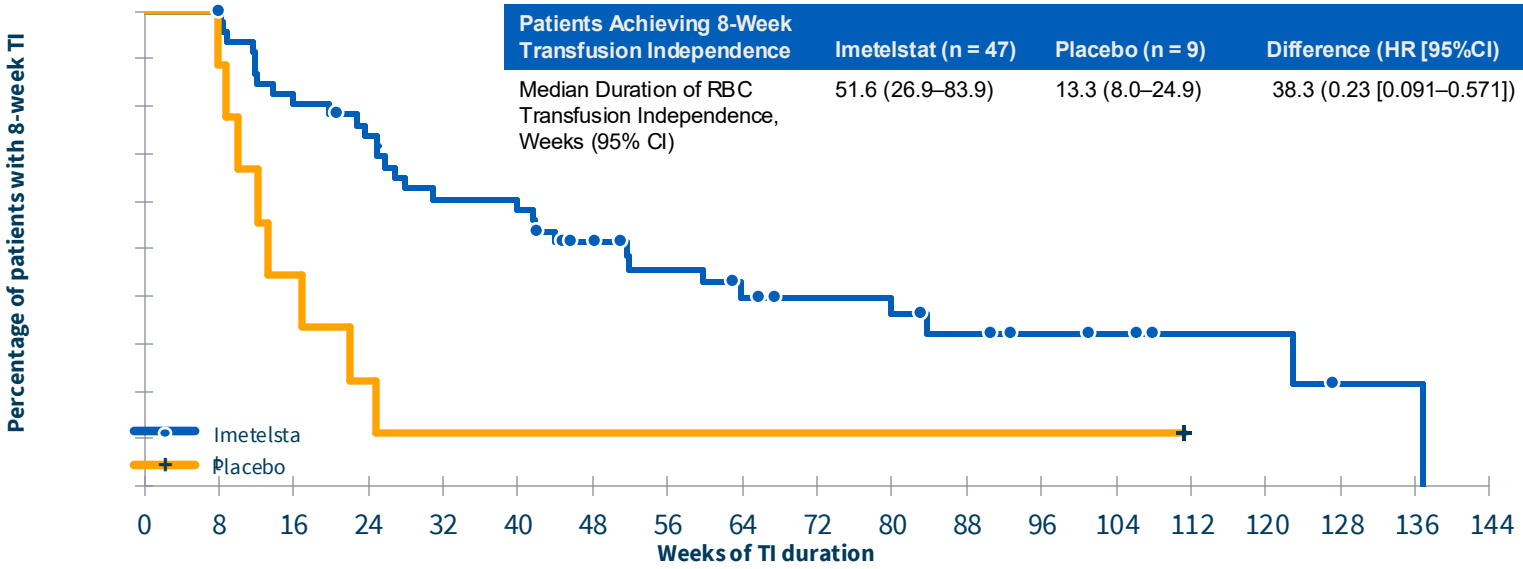
Primary End Point: 8-Week RBC TI Rate Significantly Higher With Imetelstat vs Placebo Overall



Patients With Response, N (% [95% CI])	
Imetelstat	47 (39.8 [30.93 – 49.25])
Placebo	9 (15.0 [7.10 – 26.57])

Imetelstat 8-Week RBC-TI Responders Have Significantly Longer Duration of Transfusion Independence vs Placebo

Patients Achieving 8-Week Transfusion Independence	Imetelstat (n = 47)	Placebo (n = 9)	Difference (HR [95%CI)	P-value
Median Duration of RBC Transfusion Independence, Weeks (95% CI)	51.6 (26.9–83.9)	13.3 (8.0–24.9)	38.3 (0.23 [0.091–0.571])	<0.001



Number of patients

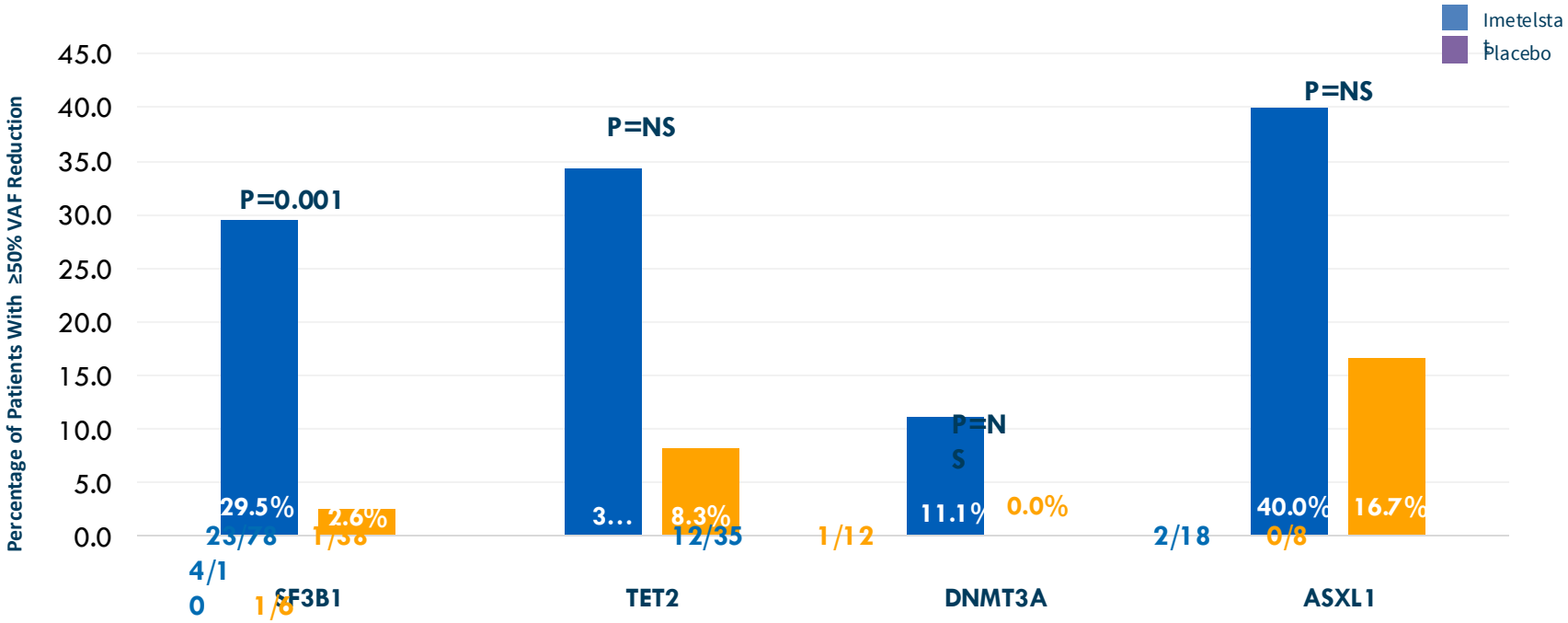
Imetelstat	47	47	37	33	27	26	20	16	13	11	11	8	6	5	3	3	1	1	0
Placebo	9	9	4	2	1	1	1	1	1	1	1	1	1	1	0				

Consistent with Prior Clinical Experience, the Most Common SAEs Were Cytopenias in Cycles 1 – 3

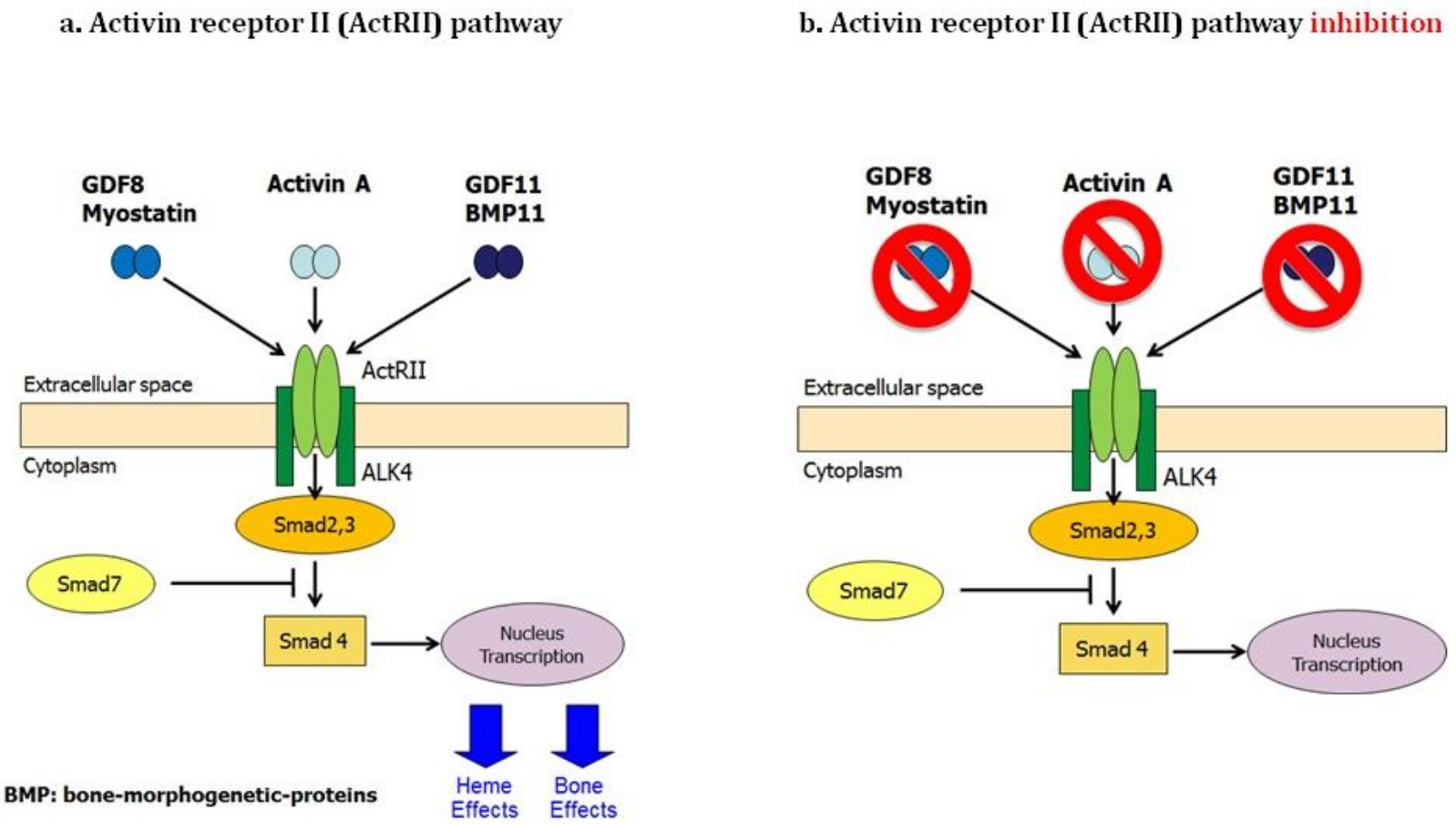
- No new safety signals were observed
- Non-hematologic AEs were generally low grade
- The most frequent AEs with imetelstat were thrombocytopenia and neutropenia
  - A majority of patients with Grade 3-4 thrombocytopenia and neutropenia experienced them during Cycles 1-3
- No cases of Hy's Law or drug-induced liver injury observed
  - The incidence of grade 3 liver function test abnormalities were similar in both treatment groups

AE, n (%)	Imetelstat (N = 118)		Placebo (N = 59)	
	Any Grade	Grade 3 – 4	Any Grade	Grade 3 – 4
Hematologic				
Thrombocytopenia	89 (75)	73 (62)	6 (10)	5 (8)
Neutropenia	87 (74)	80 (68)	4 (7)	2 (3)
Anemia	24 (20)	23 (19)	6 (10)	4 (7)
Leukopenia	12 (10)	9 (8)	1 (2)	0
Other				
Asthenia	22 (19)	0	8 (14)	0
Edema peripheral	13 (11)	0	8 (14)	0
Pyrexia	9 (8)	2 (2)	7 (12)	0
COVID-19	22 (19)[c]	2 (2)[d]	8 (14)[c]	3 (5)[d]
Diarrhea	14 (12)	1 (1)	7 (12)	1 (2)
Constipation	9 (8)	0	7 (12)	0
Headache	15 (13)	1 (1)	3 (5)	0
Hyperbilirubinemia	11 (9)	1 (1)	6 (10)	1 (2)
Investigation: ALT increased[a]	14 (12)	3 (3)	4 (7)	2 (3)

More Patients With Imetelstat vs Placebo Had ≥50% VAF Decrease in *SF3B1*, *TET2*, *DNMT3A*, *ASXL1* Mutations



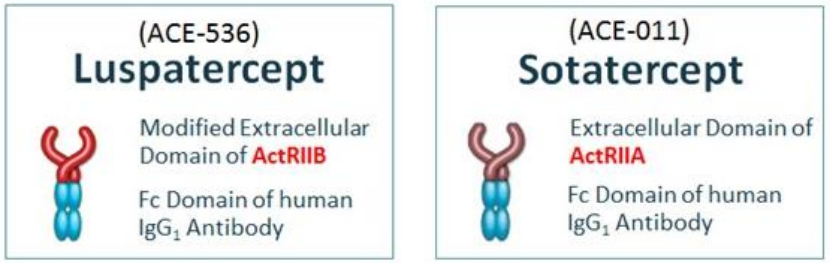
TGF beta inhibition



Luspatercept

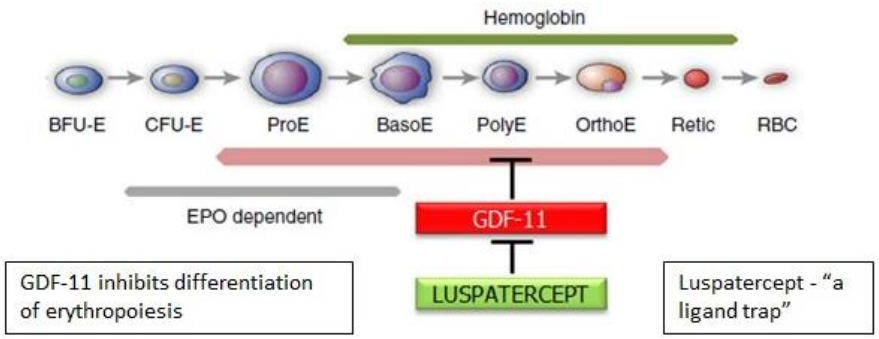
Figure 2:

a. Structure of Luspatercept and Sotatercept



Activin A Binding	**No**	**Yes**
Bone Increase	**No**	**Yes**
RBC Increase	**Yes**	**Yes**

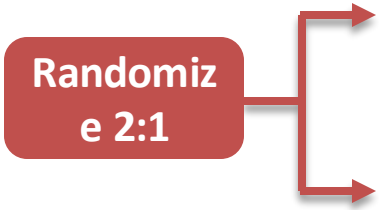
b. Mechanism of action of Luspatercept



MEDALIST Trial
Study Design – A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study

Patient Population

- MDS-RS (WHO): ≥ 15% RS or ≥ 5% with *SF3B1* mutation
- < 5% blasts in bone marrow
- No del(5q) MDS
- IPSS-R Very Low-, Low-, or Intermediate-risk
- Prior ESA response
  - Refractory, intolerant
  - ESA naive: EPO > 200 U/L
- Average RBC transfusion burden ≥ 2 units/8 weeks
- No prior treatment with disease-modifying agents (e.g. iMIDs, HMAs)



Luspatercept 1.0 mg/kg (s.c.) every 21 days
n = 153

Dose titrated up to a maximum of 1.75 mg/kg

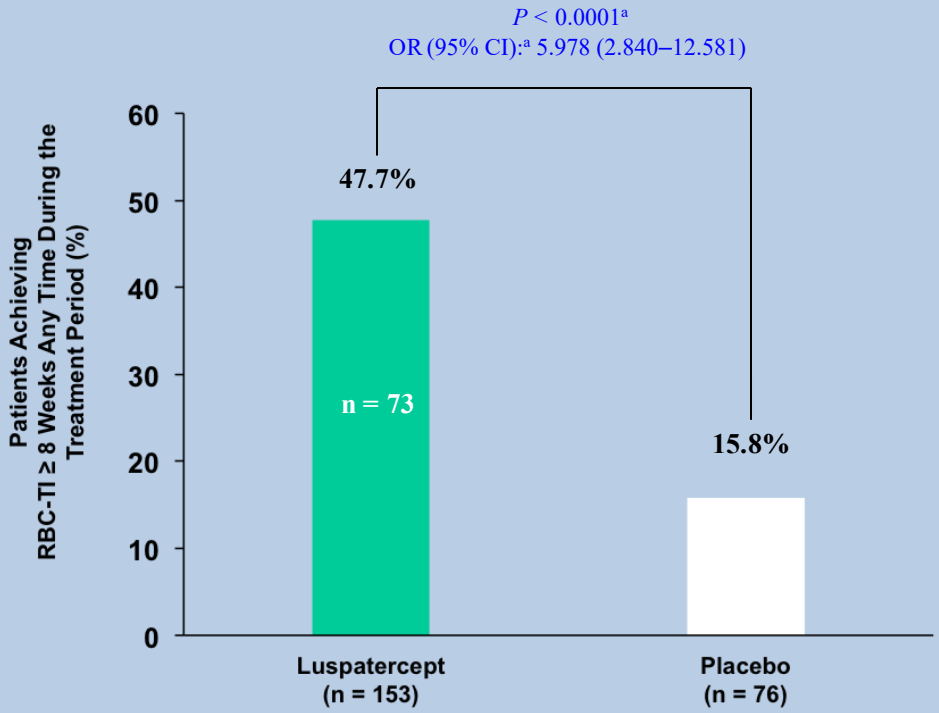
Placebo (s.c.) every 21 days
n = 76

Disease & Response Assessment week 24 & every 6 months Treatment discontinued for lack of clinical benefit or disease progression per IWG criteria; no crossover allowed

Subjects followed ≥ 3 years post final dose for AML progression, subsequent MDS treatment and overall survival

Data cutoff: May 8, 2018 Includes last subject randomized + 48 weeks.
EPO, erythropoietin; HMA, hypomethylating agent; iMID, immunomodulatory drug; IWG, International Working Group; s.c., subcutaneously; *SF3B1*, splicing factor 3b subunit 1;
WHO, World Health Organization.

MEDALIST Trial
A Randomized, Phase 3 Study of Luspatercept in MDS RS
RBC-TI ≥ 8 weeks Achieved any time during treatment period



- **Primary endpoint previously reported: 37.9%** luspatercept versus **13.2%** placebo patients achieved RBC-TI ≥ 8 weeks during Weeks 1–24 ($P < 0.0001$)[1]

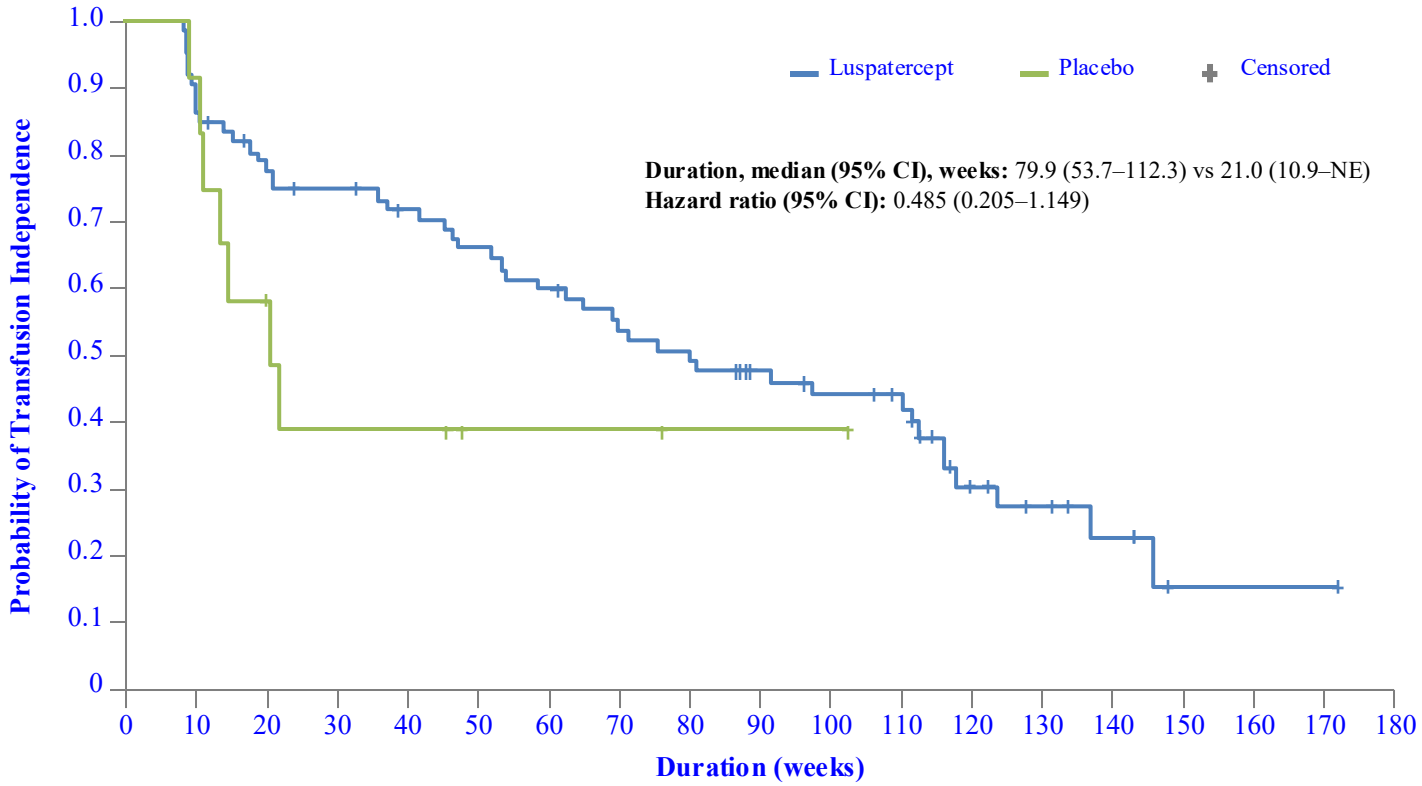
[a]

1. MEDALIST authors. Blood. 2018;132:abstract 1.

RBC-TI ≥ 8 weeks by baseline transfusion burden

RBC-TI ≥ 8 Weeks Over the Entire Treatment Period	Luspatercept (n = 153)	Placebo (n = 76)	Luspatercept Minus Placebo	
			OR (95%CI)[a]	*P* Value[a]
Average baseline RBC transfusion requirement, n/N (%)				
≥ 6 U/8 weeks	14/66 (21.2)	2/33 (6.1)	4.17 (0.89–19.60)	0.0547
≥ 4 to < 6 U/8 weeks	20/41 (48.8)	2/23 (8.7)	10.00 (2.07–48.28)	0.0013
< 4 U/8 weeks	39/46 (84.8)	8/20 (40.0)	8.36 (2.51–27.83)	0.0002

Cumulative Duration of RBc-ti ≥ 8 weeks[a] IN ALL RESPONDERS



Number of patients[b]

Luspatercept	73	63	55	52	48	44	40	35	32	27	24	22	11	8	5	1	1	1
Placebo	12	11	7	4	4	2	2	2	1	1	1							

[a] Cumulative duration of RBC-TI ≥ 8 weeks is defined as the sum of all durations of RBC-TI for patients achieving RBC-TI ≥ 8 weeks during the entire treatment phase.
[b] In the intent-to-treat population; patients who maintained response were censored from the analysis.

NE, not estimable.

SAFETY

Disease progression

Summary of Disease Progression, n (%)	Luspatercept (n = 153)	Placebo (n = 76)
Progression to HR-MDS or AML	8 (5.2)	4 (5.3)
HR-MDS	5 (3.3)	2 (2.6)
AML	3 (2.0)	2 (2.6)

AML, acute myeloid leukemia; HR-MDS, higher-risk myelodysplastic syndromes.

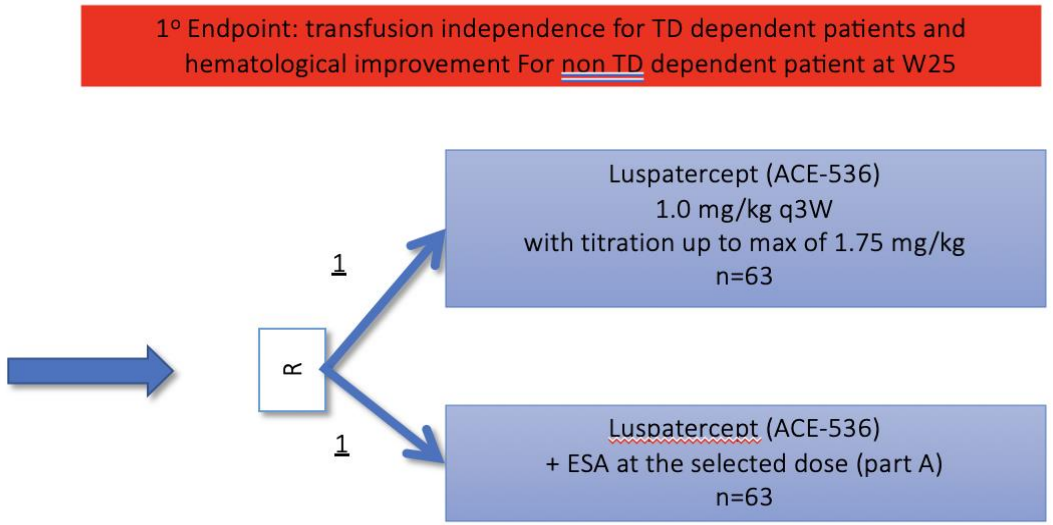
Perspectives with Luspatercept

- Combinations with
  - EPO
  - Lenalidomide
- Use en MDS without ring cells
  - Commands trial (Luspa vs EPO)
  - Combola trial

Groupe Francophone des Myélodysplasies

Luspa+/- EPO: Combola Trial (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



Groupe Francophone des Myélodysplasies

Luspatercept versus epoetin alfa for treatment of anemia in ESA-naive lower-risk myelodysplastic syndromes patients requiring RBC transfusions: data from the phase 3 COMMANDS study

Matteo Giovanni Della Porta,[1,2] Uwe Platzbecker,[3] Valeria Santini,[4] Amer M. Zeidan,[5] Pierre Fenaux,[6] Rami S. Komrokji,[7] Jake Shortt,[8] David Valcarcel,[9] Anna Jonasova,[10] Sophie Dimicoli-Salazar,[11] Ing Soo Tiong,[12] Chien-Chin Lin,[13] Jiahui Li,[14] Jennie Zhang,[14] Ana Carolina Giuseppi,[14] Sandra Kreitz,[15] Veronika Pozharskaya,[14] Karen L. Keeperman,[14] Shelonitda Rose,[14] Jeevan K. Shetty,[15*] Sheida Hayati,[14] Sadanand Vodala,[14] Andrius Degulys,[16,17] Stefania Paolini,[18] Thomas Cluzeau,[19] Guillermo Garcia-Manero[20]

[1]Cancer Center IRCCS Humanitas Research Hospital, Milan, Italy; [2]Department of Biomedical Sciences, Humanitas University, Milan, Italy; [3]Medical Clinic and Policlinic 1, Hematology and Cellular Therapy, University Hospital Leipzig, Leipzig, Germany; [4]MDS Unit, Hematology, University of Florence, AOUC, Florence, Italy; [5]Department of Internal Medicine, Yale School of Medicine and Yale Cancer Center, Yale University, New Haven, CT; [6]Service d'Hématologie Séniors, Hôpital Saint-Louis, Université Paris 7, Paris, France; [7]Moffitt Cancer Center, Tampa, FL; [8]Monash University and Monash Health, Melbourne, VIC, Australia; [9]Hospital Universitari Vall d'Hebron, Barcelona, Spain; [10]Medical Department Hematology, Charles University General University Hospital, Prague, Czech Republic; [11]Hôpital Haut-Lévêque, Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France; [12]Malignant Haematology & Stem Cell Transplantation, The Alfred, Melbourne, Victoria, Australia; [13]Department of Laboratory Medicine, National Taiwan University Hospital, Taipei, Taiwan; [14]Bristol Myers Squibb, Princeton, NJ; [15]Celgene International Sàrl, a Bristol-Myers Squibb Company, Boudry, Switzerland; [16]Hematology, Oncology and Transfusion Medicine Center, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania; [17]Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, Vilnius, Lithuania.; [18]IRCCS University Hospital of Bologna, "Seràgnoli" Institute of Hematology, Bologna, Italy, Italy; [19]Département d'Hématologie Clinique, Université Cote d'Azur, CHU Nice, Nice, France; [20]Department of Leukemia, University of Texas MD Anderson Cancer Center, Houston, TX.
*At the time of the study

Presentation number S102

The COMMANDS study

The COMMANDS study (NCT03682536) is a phase 3, global, open-label, randomized trial comparing the efficacy and safety of luspatercept versus epoetin alfa for the treatment of anemia due to IPSS-R LR-MDS in ESA-naive patients who require RBC transfusions

Key eligibility criteria

- ≥ 18 years of age
- IPSS-R very low-, low, or intermediate-risk MDS (with or without RS) by WHO 2016, with < 5% blasts in bone marrow[a]
- Required RBC transfusions (2–6 pRBC units/8 weeks for a minimum of 8 weeks immediately prior to randomization)
- Endogenous sEPO < 500 U/L
- ESA-naive

Patients stratified by:

- Baseline sEPO level
- Baseline RBC transfusion burden
- RS status

Randomize 1:1

Luspatercept (N = 178)
1.0 mg/kg s.c. Q3W
titration up to 1.75 mg/kg

Epoetin alfa (N = 178)[b]
450 IU/kg s.c. QW
titration up to 1050 IU/kg

Response assessment at day 169 and every 24 weeks thereafter

End treatment
Due to lack of clinical benefit[c] or disease progression per IWG criteria

Post-treatment safety follow-up

- Monitoring for other malignancies, HR-MDS or AML progression, subsequent therapies, survival
- For 5 years from first dose or 3 years from last dose, whichever is later

[a]MDS with del(5q) were excluded. [b]2 patients randomized to the epoetin alfa arm withdrew consent prior to receiving their first dose; [c]Clinical benefit defined as transfusion reduction of ≥ 2 pRBC units/8 weeks versus baseline; AML, acute myeloid leukemia; ESA, erythropoiesis-stimulating agent; IPSS-R, Revised International Prognostic Scoring System; IWG, International Working Group; LR-MDS, lower-risk MDS; MDS, myelodysplastic syndromes; pRBC, packed RBC; QW, once weekly; Q3W, every 3 weeks; RBC, red blood cell; RS, ring sideroblasts; s.c., subcutaneously; sEPO, serum erythropoietin; WHO, World Health Organization.

Della Porta MG, et al. EHA 2023 [Abstract #S102]

Study endpoints

Composite primary endpoint (weeks 1-24)

- RBC-TI for ≥ 12 weeks **WITH CONCURRENT** mean hemoglobin increase ≥ 1.5 g/dL

Secondary endpoints (weeks 1-24)

- HI-E response ≥ 8 weeks per IWG criteria
- RBC-TI for 24 weeks
- RBC-TI for ≥ 12 weeks

Secondary and exploratory endpoints

- Duration of RBC-TI for ≥ 12 weeks (week 1–EOT)
- Impact of baseline mutations on response
- Subgroup analyses

- The data cutoff date for this planned interim analysis was August 31, 2022
  - This prespecified interim analysis was planned for when ~300 patients had either completed 24 weeks of treatment or discontinued prior to completing 24 weeks of treatment (at 85% of information for the primary endpoint)

Safety

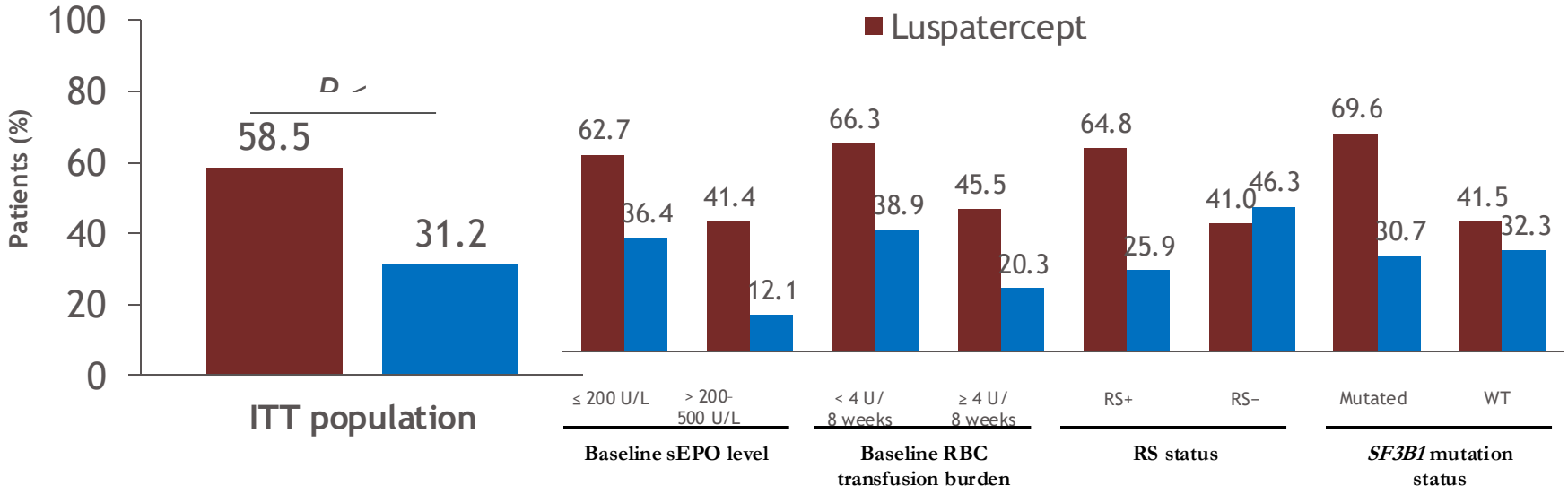
- Treatment discontinuation
- TEAE
- HR-MDS/AML progression
- Death

HI-E, hematological improvement-erythroid; RBC-TI, RBC transfusion independence; TEAE, treatment-emergent adverse event.

Della Porta MG, et al. EHA 2023 [Abstract #S102]

Primary endpoint: luspatercept superior to epoetin alfa

- Of 301 pts included in the efficacy analysis, 86 (58.5%) patients receiving luspatercept and 48 (31.2%) epoetin alfa achieved the primary endpoint
  - Achievement of the primary endpoint favored luspatercept or was similar to epoetin alfa for all subgroups analyzed

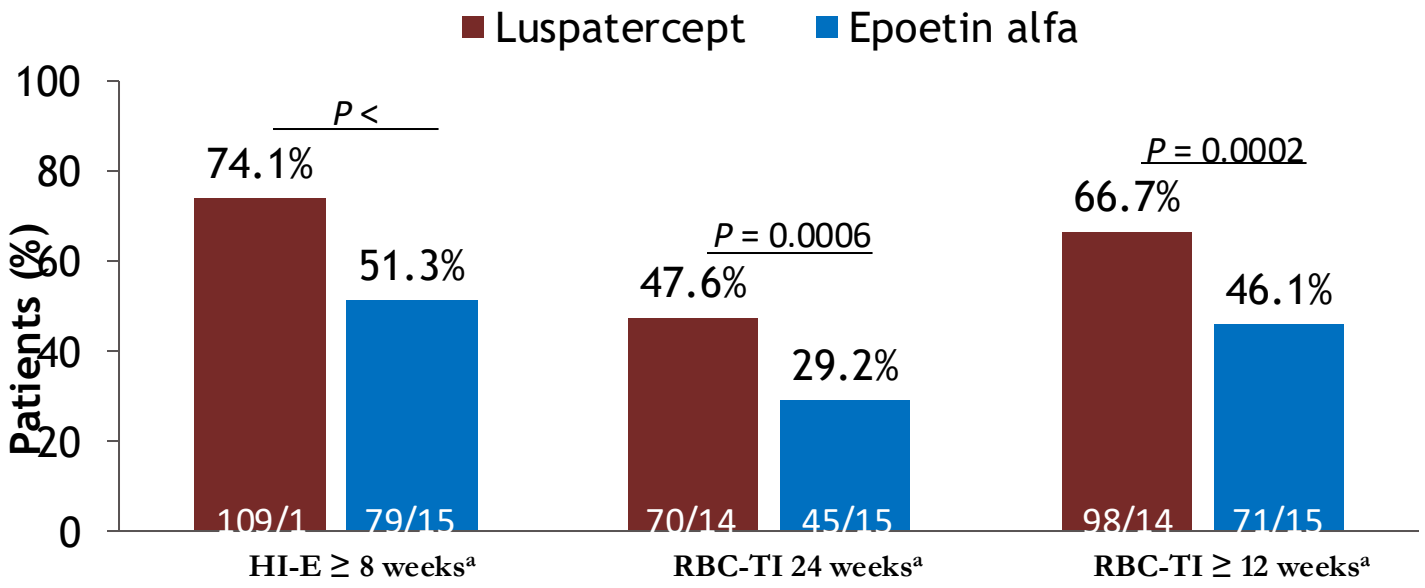


This prespecified interim analysis included 301 patients who had either completed 24 weeks of treatment or discontinued priorto completing 24 weeks of treatment.

Della Porta MG, et al. EHA 2023 [Abstract #S102]

Secondary endpoints: luspatercept superior to epoetin alfa

	Luspatercept (N = 147)	Epoetin alfa (N = 154)
Time to first RBC transfusion (week 1-EOT)	n = 93 168.0 (64.0–323.0)	n = 116 42.0 (22.0–55.0)

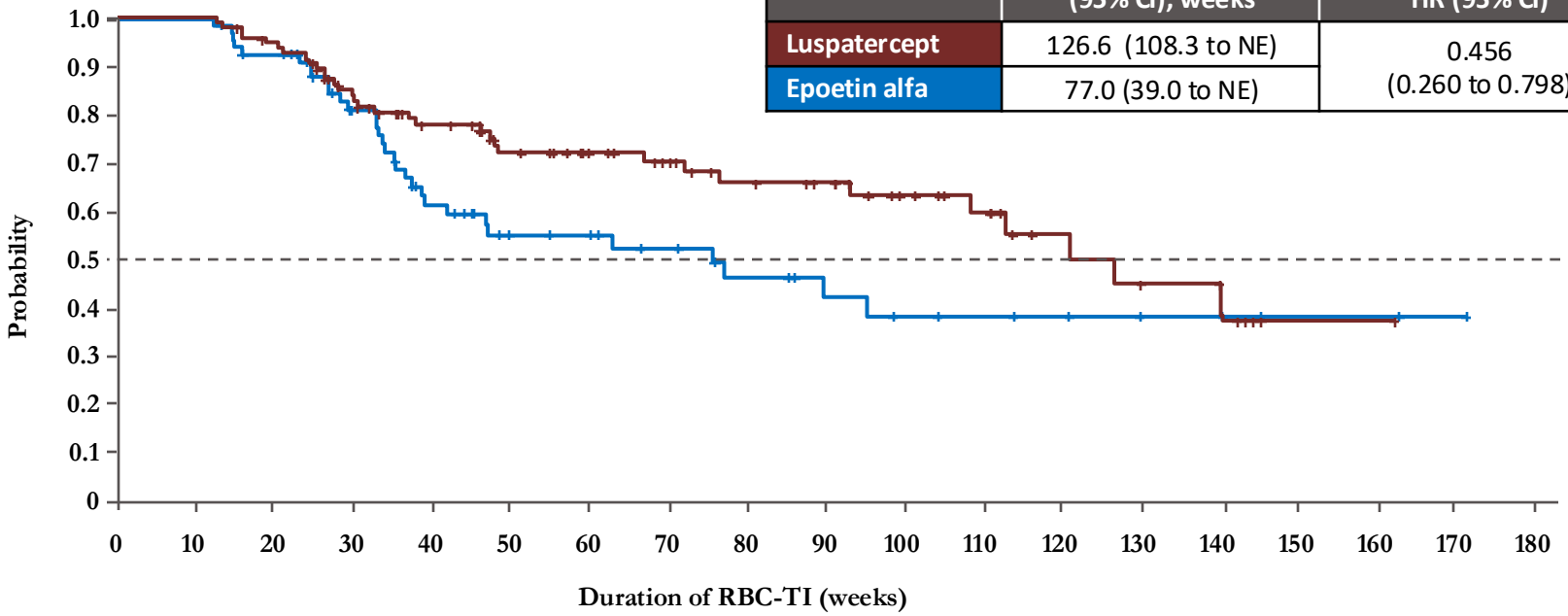


[a]During weeks 1-24.

Della Porta MG, et al. EHA 2023 [Abstract #S102]

Duration of RBC-TI ≥ 12 weeks[a]

	Median duration (95% CI), weeks	HR (95% CI)
Luspatercept	126.6 (108.3 to NE)	0.456 (0.260 to 0.798)
Epoetin alfa	77.0 (39.0 to NE)	



No. at risk																			
Luspatercept	98	98	91	74	61	49	42	37	31	28	21	17	11	8	6	1	1	0	
Epoetin alfa	71	71	63	47	33	24	23	19	15	11	9	8	7	5	5	2	2	1	0

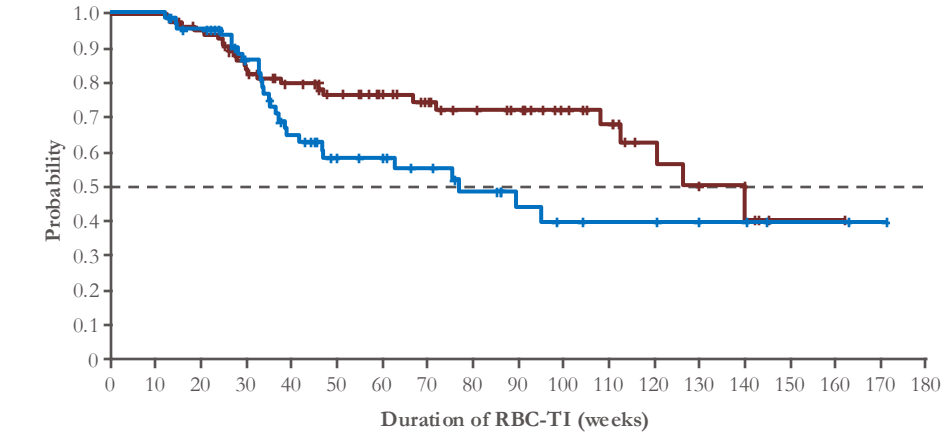
EOT, end of treatment; NE, not estimable; RBC-TI, red blood cell transfusion independence.
[a]In ITT responders during weeks 1–EOT.

Della Porta MG, et al. EHA 2023 [Abstract #S102]

Duration of RBC-TI ≥ 12 weeks[a]: sEPO subgroups

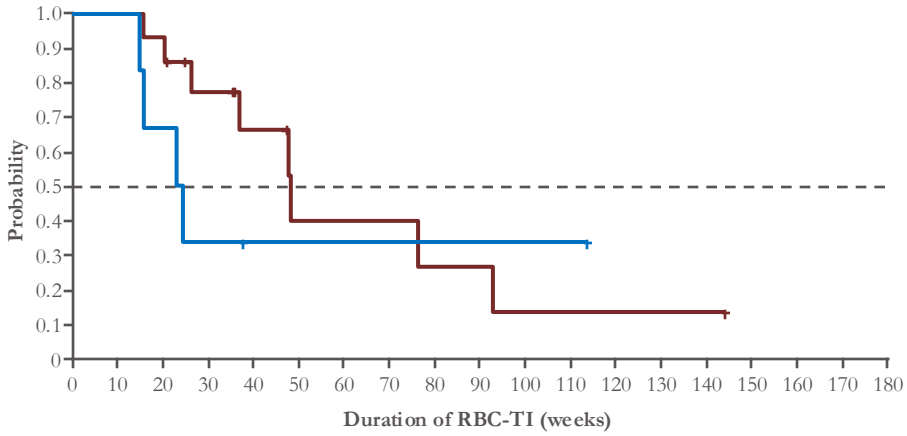
Median duration (95% CI), weeks	Luspatercept	Epoetin alfa	HR (95% CI)
sEPO ≤ 200 U/L	140.1 (112.7 to NE)	77.0 (41.9 to NE)	**0.601 (0.348 to 1.038)**
sEPO >200-500 U/L	48.3 (26.3 to 93.0)	23.9 (14.9 to NE)	**0.624 (0.186 to 2.092)**

sEPO ≤ 200 U/L



No. at risk																		
Luspatercept	84	84	78	65	55	46	39	34	29	26	20	16	10	7	5	1	1	0
Epoetin alfa	65	65	59	45	32	23	22	18	14	10	8	7	7	5	5	2	2	1	0

sEPO > 200-500 U/L



No. at risk																		
Luspatercept	14	14	13	9	6	3	3	3	2	2	1	1	1	1	1	0		
Epoetin alfa	6	6	4	2	1	1	1	1	1	1	1	1	0					

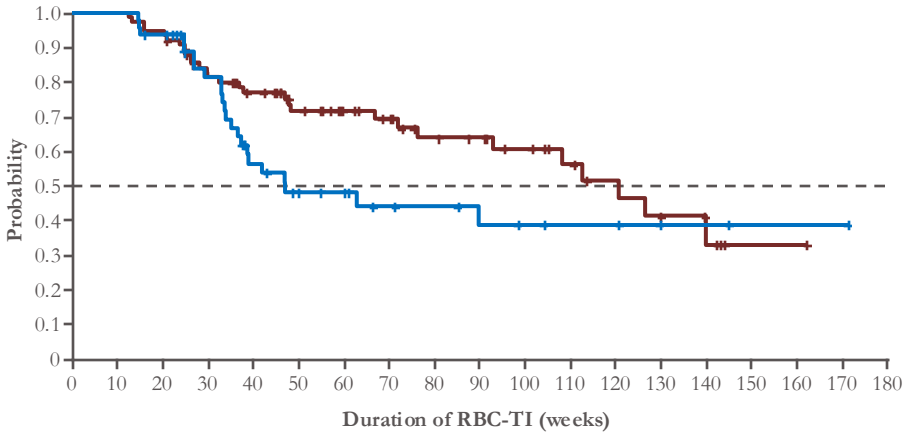
EOT, end of treatment; NE, not estimable; RBC-TI, red blood cell transfusion independence.
[a]In ITT responders during weeks 1–EOT.

Della Porta MG, et al. EHA 2023 [Abstract #S102]

Duration of RBC-TI ≥ 12 weeks[a]: RS subgroups

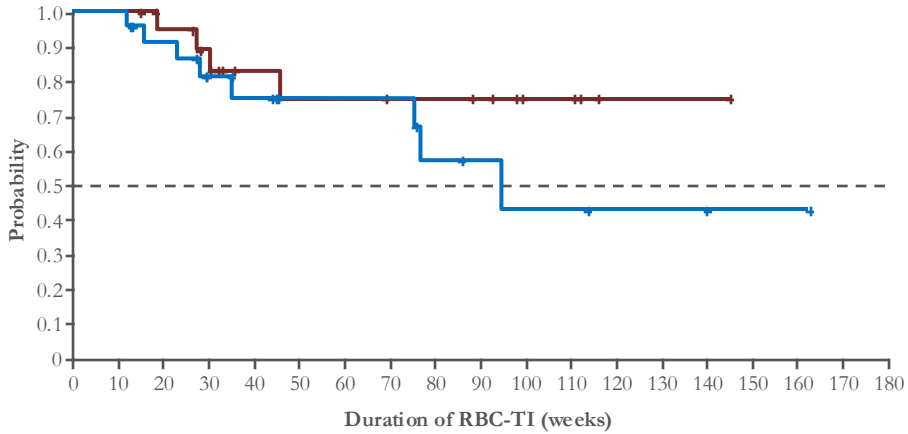
Median duration (95% CI), weeks	Luspatercept	Epoetin alfa	HR (95% CI)
RS+	120.9 (76.4 to NE)	47.0 (36.6 to NE)	**0.626 (0.361 to 1.085)**
RS–	NE (46.0 to NE)	95.1 (35.3 to NE)	**0.492 (0.148 to 1.638)**

RS+



No. at risk																		
Luspatercept	77	77	73	59	51	40	33	29	23	21	17	13	10	7	5	1	1	0
Epoetin alfa	48	48	44	33	21	15	14	10	9	7	6	5	5	3	3	1	1	1	0

RS–



No. at risk																	
Luspatercept	21	21	18	15	10	9	9	8	8	7	4	4	1	1	1	0	
Epoetin alfa	23	23	19	14	12	9	9	9	6	4	3	3	2	2	2	1	1	0

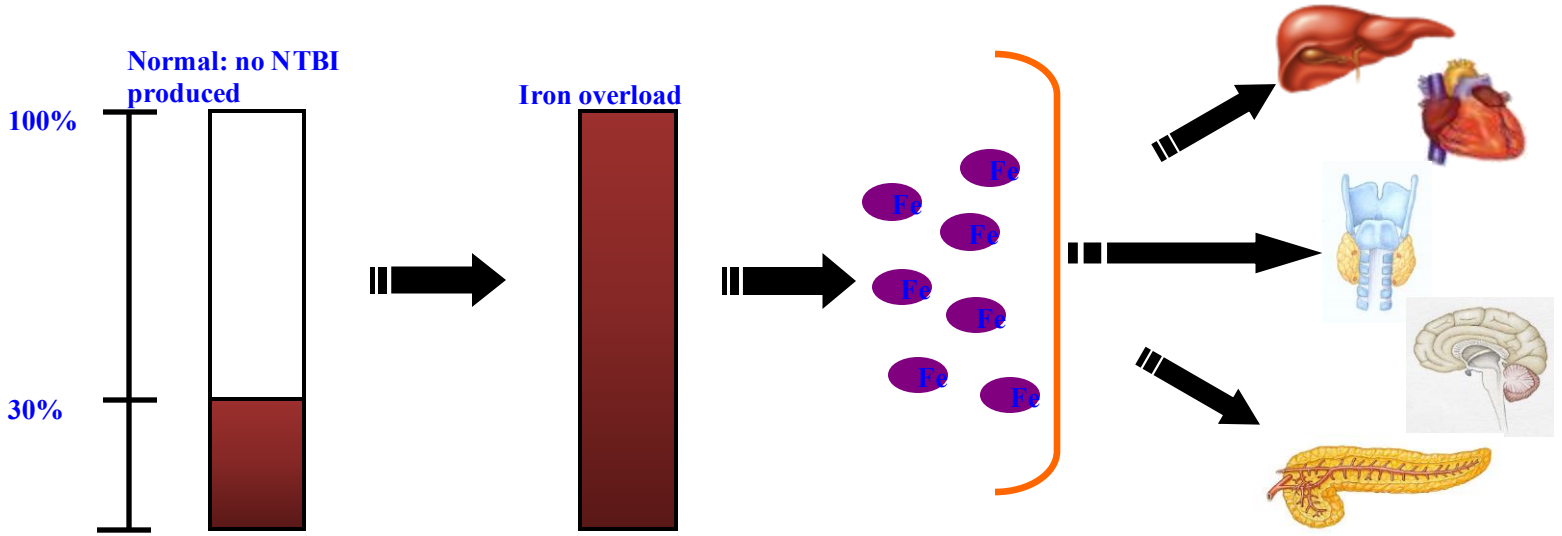
EOT, end of treatment; NE, not estimable; RBC-TI, red blood cell transfusion independence.
[a]In ITT responders during weeks 1–EOT.

Della Porta MG, et al. EHA 2023 [Abstract #S102]

Recent treatments of lower risk MDS

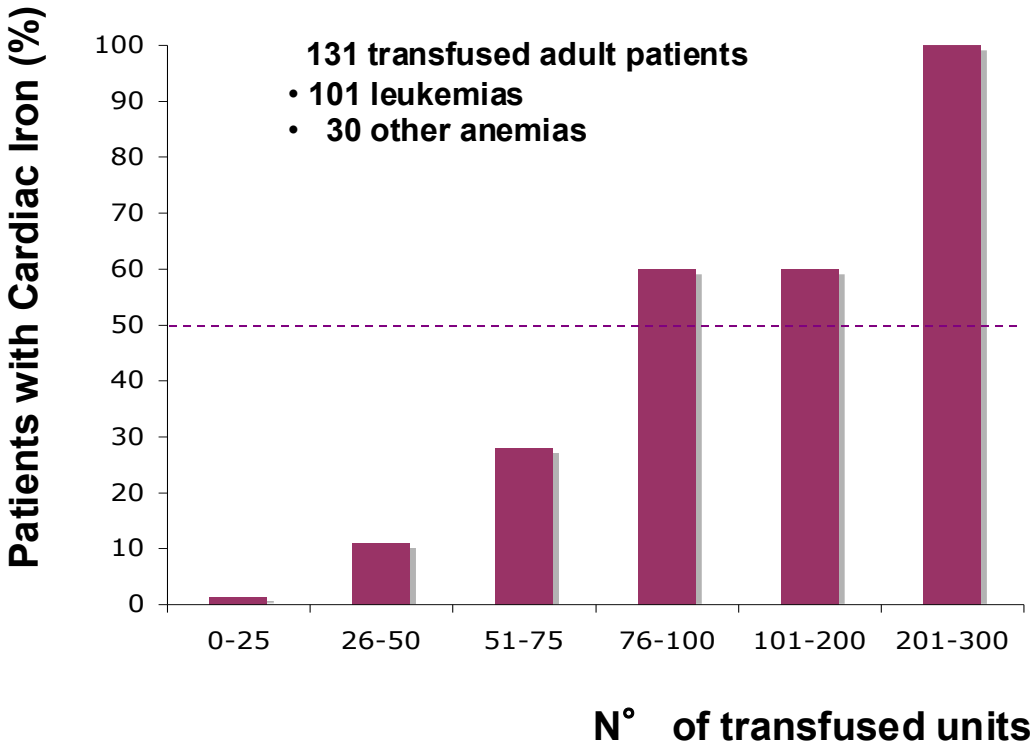
- Lower risk MDS: where is the limit ?
- Treatment of anemia of lower risk MDS
- Treatment of thrombocytopenia of lower risk MDS
- Chelation therapy ?
- Treatment of MDS with autoimmune/autoinflammatory disorders

Accumulation of non transferrin bound iron (NTBI or LPI) in organs



NTBI = non-transferrin bound iron.

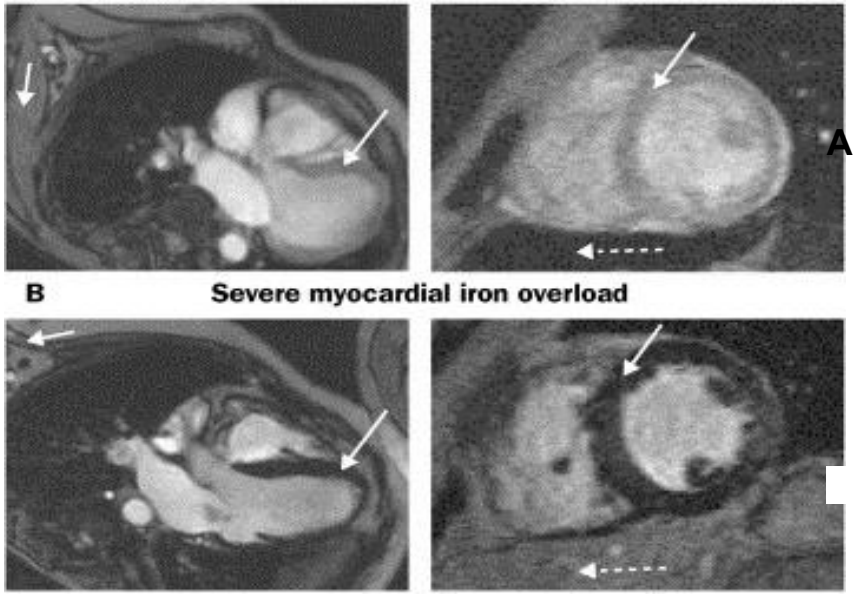
Correlation between n° of transfusions and heart iron overload



Buja LM, Roberts WC. Am J Med. (1971) 51:209-21.

MRI can evaluate iron overload (T2*)

Normal myocardial iron

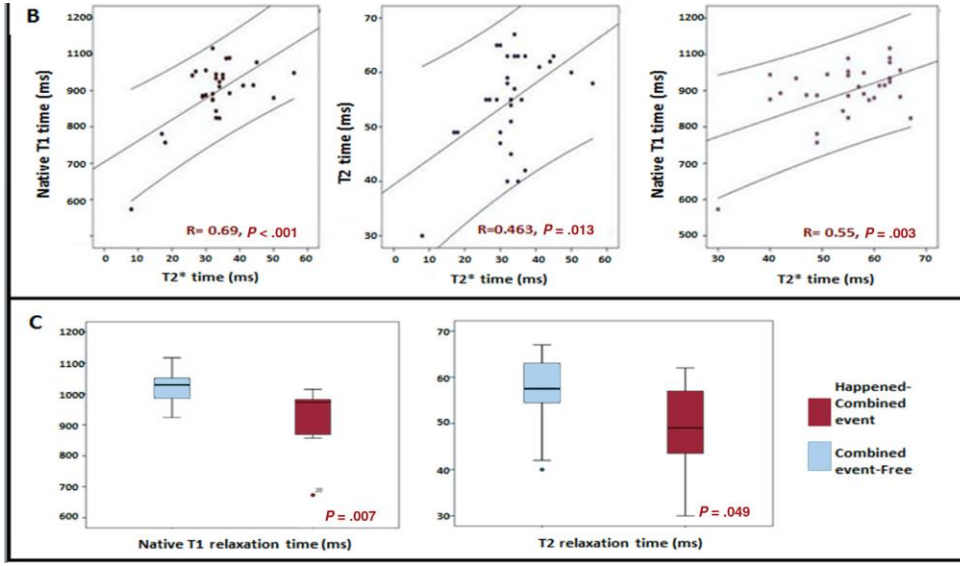


http://oernst.f5lvg.free.fr/liver/iron.html

Groupe Francophone des Myélodysplasies

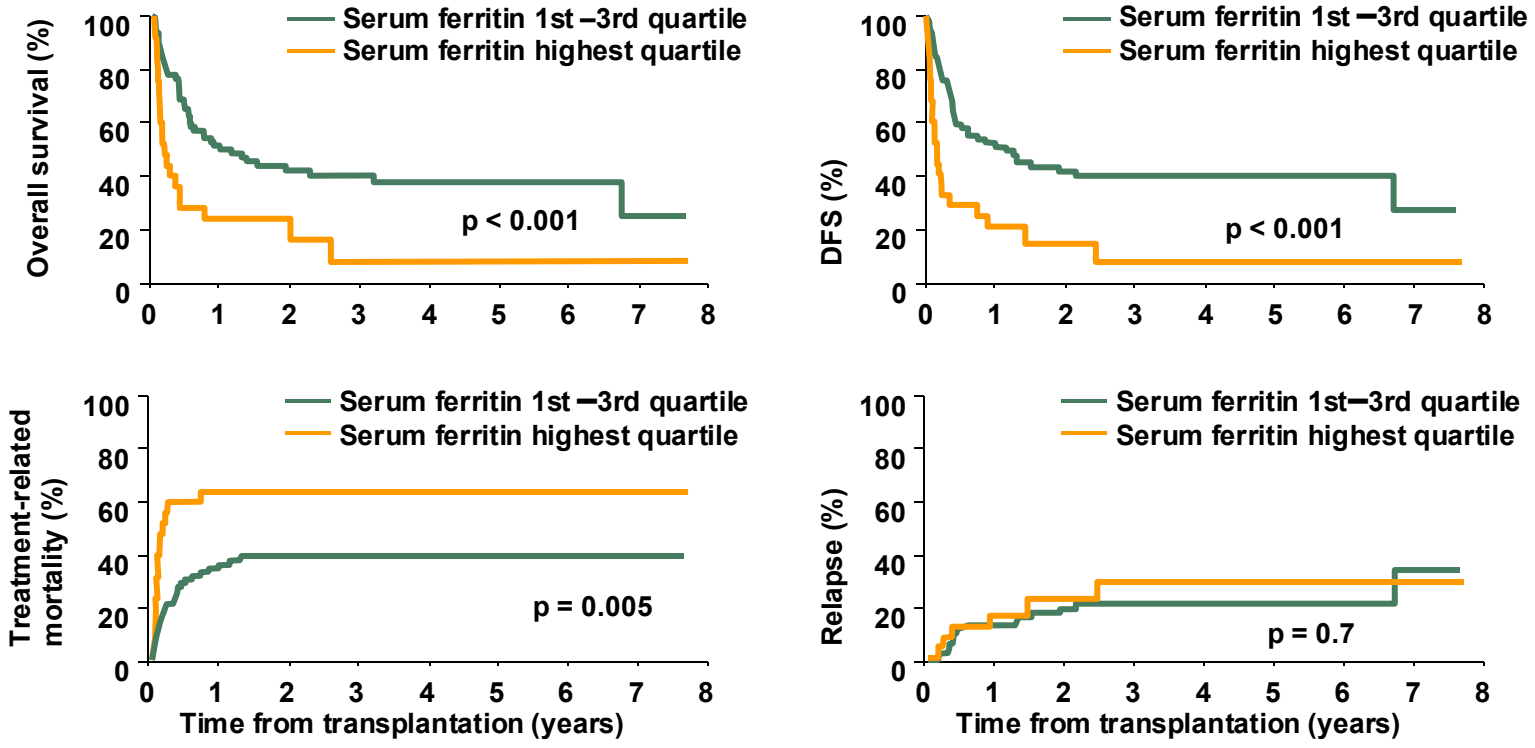
Usefulness of myocardial T_1 and T_2 mapping with magnetic resonance in transfusion-dependent patients with low-risk myelodysplastic syndrome

Marta Alonso-Fernández-Gatta,[a,b,◇,*] Ana Martín-García,[a,b,◇] María Díez-Campelo,[c] Agustín C. Martín-García,[a,b] Félix López-Cadenas,[c] and Pedro L. Sánchez[a,b]



GESMD

Allo SCT results according to serum ferritin level



DFS = disease-free survival.

Armand P, et al. Blood. 2007;109:4586-8.

Safety and Efficacy, Including EFS, of Deferasirox Versus Placebo in Iron-Overloaded Patients with Low- and Int-1-Risk MDS: Outcomes from the Randomized, Double-Blind Telesto Study

Angelucci,Ann Int Med, 2020

- 225 pts : Deferasirox (n=149) or Placebo (n=76)
- EFS: composite primary endpoint (cardiac, liver failure transformation to AML,death)
- Median EFS :1440 day for Deferasirox vs 1091 days for Placebo : 36.4% risk reduction (P=0.015)

Figure 1. Kaplan-Meier curve of event-free survival

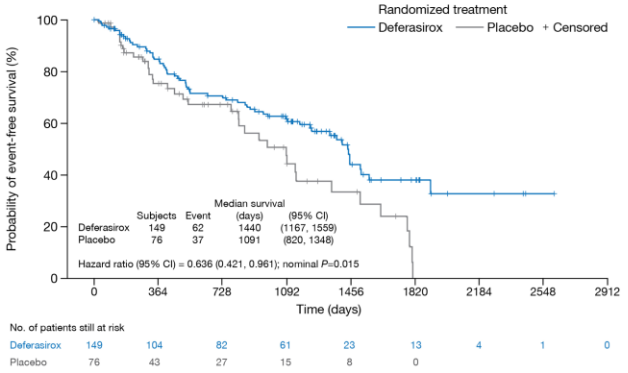
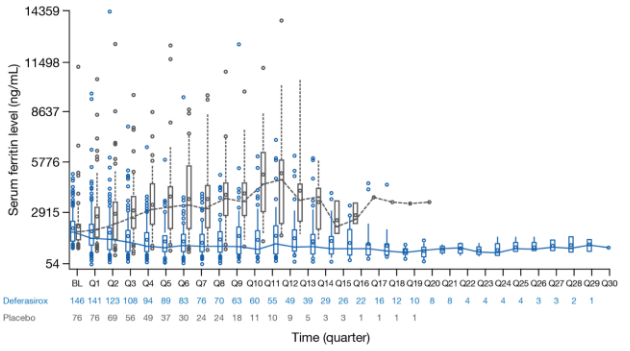
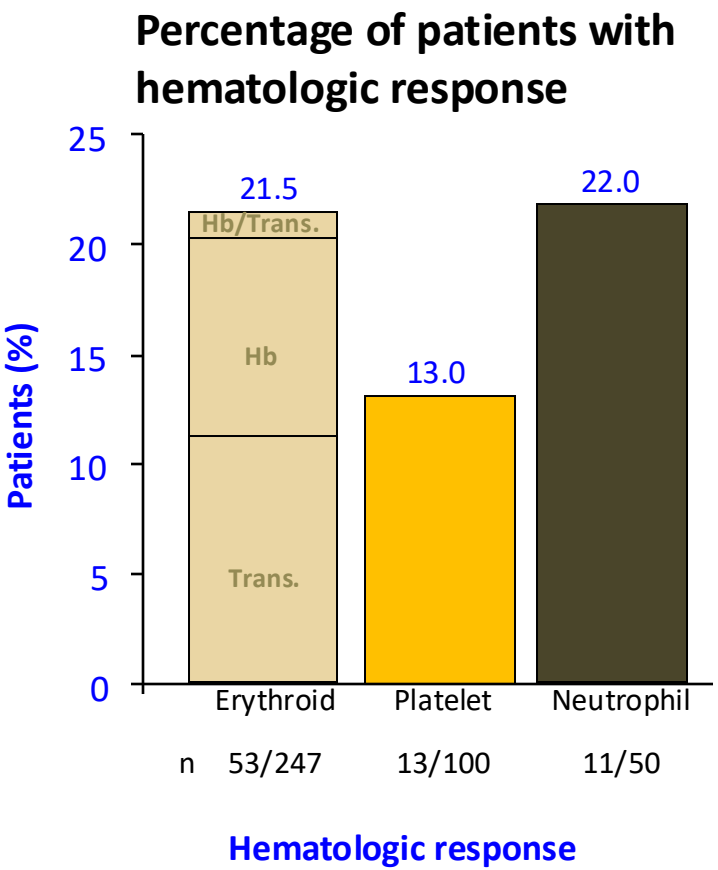


Figure 2. Serum ferritin levels over time by treatment group



Whiskers mark 10th and 90th percentiles, boxes show lower and upper quartiles, horizontal line shows the median and o represents the mean; values outside 10th–90th percentile are plotted as o
NE, not evaluable

Improvement of cytopenias



Gattermann N, et al. *Haematologica*. 2012;97:1364-71.

bjh research paper

Deferasirox reduces oxidative DNA damage in bone marrow cells from myelodysplastic patients and improves their differentiation capacity

Tamara Jiménez-Solas,[1,2] Félix

Summary

The Pharmacogenomics Journal (2020) 20:664–671
https://doi.org/10.1038/s41397-020-0154-5

ARTICLE

Genome-wide transcriptomics leads to the identification of deregulated genes after deferasirox therapy in low-risk MDS patients

Jesús María Hernández Sánchez[1] · Eva Lumbreras[1] · María Díez-Campelo[2] · Teresa González[1,2] · Diego Alonso López[3] · María Abáigar[1] · Mónica del Rey[1] · Ana África Martín[2] · Raquel de Paz[4] · Sara Erquiaga[5] · Beatriz Arrizabalaga[5] · Jesús María Hernández-Rivas[1,2] · Ana Eugenia Rodríguez Vicente[1]

Recent treatments of lower risk MDS

- Lower risk MDS: where is the limit ?
- Treatment of anemia of lower risk MDS
- Treatment of thrombocytopenia of lower risk MDS
- Chelation therapy ?
- Treatment of MDS with autoimmune/autoinflammatory disorders

VOLUME 28 · NUMBER 3 · JANUARY 20 2010

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Safety and Efficacy of Romiplostim in Patients With Lower-Risk Myelodysplastic Syndrome and Thrombocytopenia

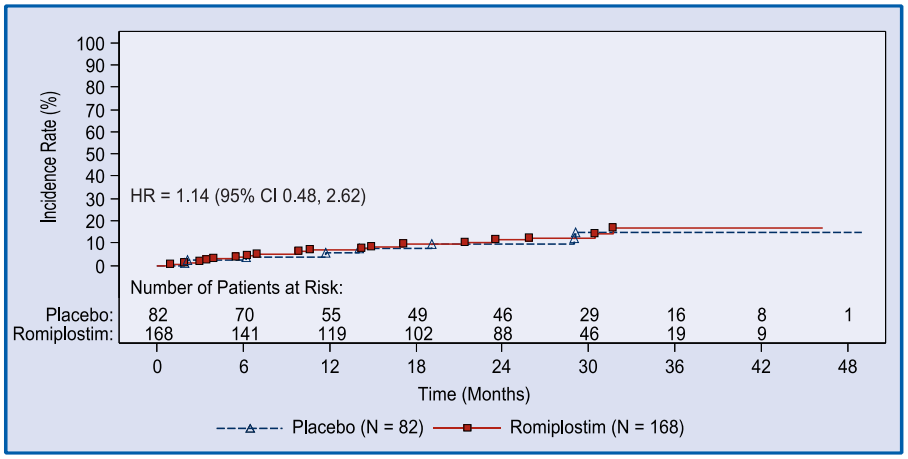
Hagop Kantarjian, Pierre Fenaux, Mikkael A. Sekeres, Pamela S. Becker, Adam Boruchov, David Bowen, Eva Hellstrom-Lindberg, Richard A. Larson, Roger M. Lyons, Petra Muus, Jamile Shammo, Robert Siegel, Kuolung Hu, Janet Franklin, and Dietmar P. Berger

- N=44, lower risk MDS
- platelets <50G/l
- 300 to 1500 ug/week
- Evaluation at week 4
- 50% response
- Transient increase in marrow blasts in 15% of the patients

Treatment with Romiplostim, a Thrombopoietin-Receptor Agonist, in Thrombocytopenic Patients with Low or Intermediate-1 Risk Myelodysplastic Syndrome: Updated Follow-up Results for Acute Myeloid Leukemia and Survival from a Randomized, Double-Blind, Placebo-Controlled Study

Hagop Kantarjian,[1] Ghulam Mufti,[2] Pierre Fenaux,[3] Mikkael Sekeres,[4] Jeffrey Szer,[5] Uwe Platzbecker,[6] Andrea Kuendgen,[7] Gianluca Gaidano,[8] Wieslaw Wiktor-Jedrzejczak,[9] Anne Meibohm,[10] Angela Lopez,[11] Aristoteles Giagounidis[12]

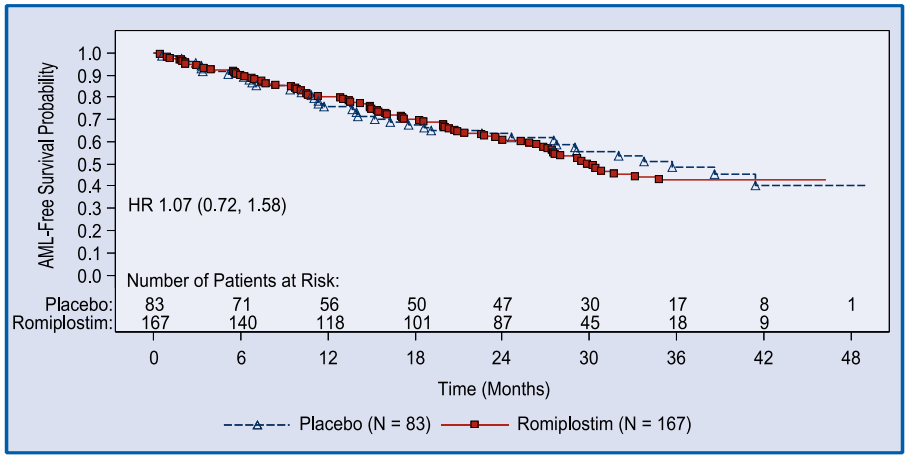
Figure 2. Incidence of AML, on Treatment and During Long-term Follow-up to March 2013



Includes all randomized patients who received at least 1 dose of the investigational product. Cumulative incidence rates are estimated using the Kaplan-Meier methods.
Total observational time is the time from randomization to the last available long-term contact or end-of-study for patients who did not enter long-term follow-up.
HR, hazard ratio; CI, confidence interval.

HR, hazard ratio; CI, confidence interval.

Figure 4. AML-Free Survival, on Treatment and During Long-term Follow-up to March 2013



Includes all randomized patients who received at least 1 dose of the investigational product.
Total observational time is the time from randomization to the last available long-term contact or end-of-study for patients who did not enter long-term follow-up.
HR, hazard ratio; CI, confidence interval.

Eltrombopag for Low-Risk Myelodysplastic Syndromes With Thrombocytopenia: Interim Results of a Phase-II, Randomized, Placebo-Controlled Clinical Trial (EQOL-MDS)

Esther Natalie Oliva, MD[1]; Marta Riva, MD[2]; Pasquale Niscola, MD[3]; Valeria Santini, MD[4]; Massimo Breccia, MD[5]; Valentina Giai, MD[6]; Antonella Poloni, MD[7]; Andrea Patriarca, MD[8]; Elena Crisà, MD[8]; Isabella Capodanno, MD[9]; Prassede Salutari, MD[10]; Gianluigi Reda, MD[11]; Nicola Cascavilla, MD[12]; Dario Ferrero, MD[13]; Attilio Guarini, MD[14]; Giovanni Tripepi, PhD[15]; Giuseppe Iannì, BSc[16]; Emilio Russo, PhD[17]; Andrea Castelli, MD[18]; Bruno Fattizzo, MD[11,19]; Germana Beltrami, MD[20]; Monica Bocchia, MD[21]; Alfredo Molteni, MD[22]; Pierre Fenaux, MD[23]; Ulrich Germing, MD[24]; Alessandra Ricco, MD[25]; Giuseppe A. Palumbo, MD, PhD[26]; Stefana Impera, MD[27]; Nicola Di Renzo, MD[28]; Flavia Rivellini, MD[29]; Francesco Buccisano, MD[30]; Aspasia Stamatoullas-Bastard, MD[31]; Anna Marina Liberati, MD[32]; Anna Candoni, MD[33]; Ilaria Maria Delfino, BSc[1]; Maria Teresa Arcadi, BSc[34]; Patrizia Cufari, BSc[1]; Lorenzo Rizzo, MD[35]; Irene Bova, BSc[36]; Maria Grazia D'Errigo, BSc[36]; Gina Zini, MD[37,38]; and Roberto Latagliata, MD[39]

DOI https://doi.org/10.1200/JCO.22.02699

- N=169 (112 vs 57)
- Eltrombopag 50 to 300mg/d
- 42% vs 11 % response
- 63% still responders at 60 months
- Significant bleeding improvement
- 17% vs 17% MDS/AML progression

bjh research paper

Eltrombopag for myelodysplastic syndromes or chronic myelomonocytic leukaemia with no excess blasts and thrombocytopenia: a French multicentre retrospective real-life study

Comont et al, Brit J Haematol, 2021

Thibault Comont,[1] Mathieu Meunier,[2] Summary

- ELT in 50 MDS and 11 with CMML, with no excess of marrow blasts and platelet <50 G:L
- Platelet response in 47 (77%) patients.
- median duration of response 8 (0–69) months.
- None of the eight still responders who discontinued ELT had relapsed, at a median of 16 (6–23) months after ELT discontinuation.
- Although 36% of the patients were anti-coagulated or anti-aggregated only 10% of patients had Grade ≥3 bleeding events.
- Thrombotic events in six (10%) patients, who all but one had a medical history of arterial or venous thrombosis.
- Progression to AML in four (7%) patients.

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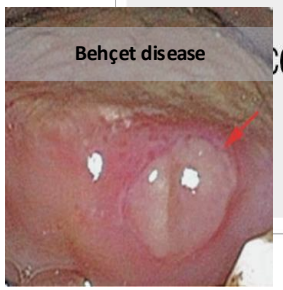
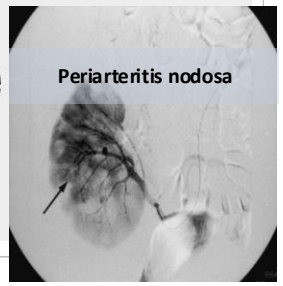
Recent treatments of lower risk MDS

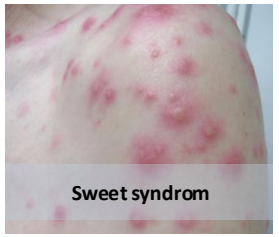
- Lower risk MDS: where is the limit ?
- Treatment of anemia of lower risk MDS
- Treatment of thrombocytopenia of lower risk MDS
- Chelation therapy ?
- Treatment of MDS with autoimmune/autoinflammatory disorders

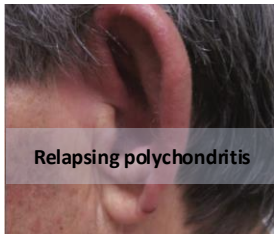
Association MDS/CMML - SIAD

- ~ 15-20% of MDS/CMML are associated with Systemic Inflammatory and Autoimmune Diseases (SIAD)
- SIAD often atypical
- SIAD association generally has no impact on prognosis in MDS/CMML patients

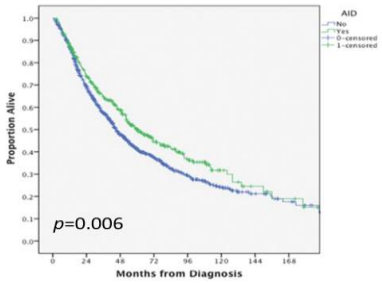




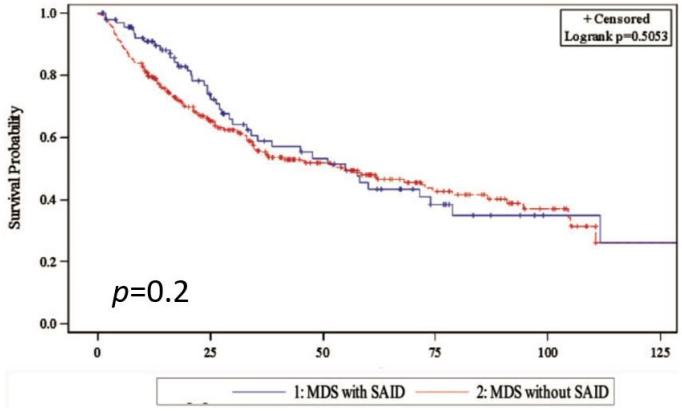




Komrokji *et al.* Am J Hematol. 2016
- n = 1408
- 391/1408 (28%) avec SIAD, 171/391 hypothyroidism



Mekinian *et al.* Rheumatology. 2016
- n = 788 MDS/CMML
- 123/788 (16%) with SIAD



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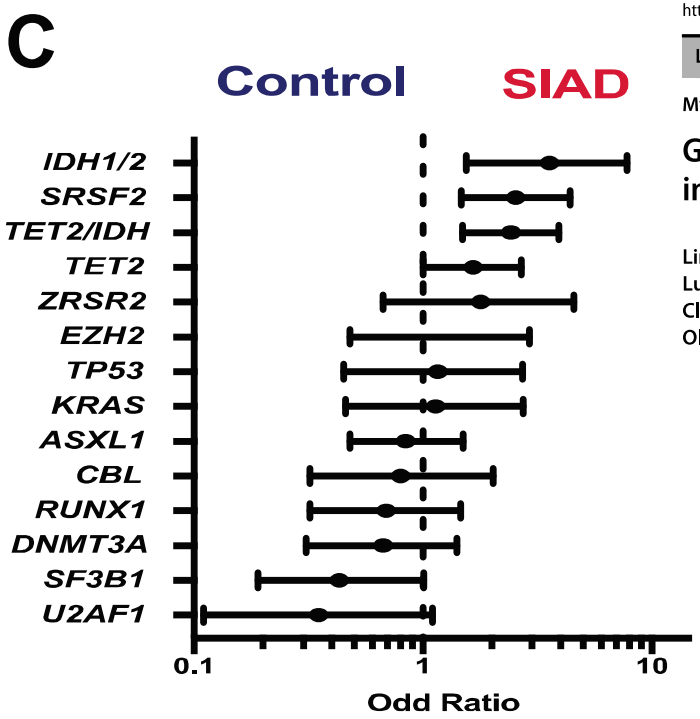
ORIGINAL ARTICLE
Korean J Intern Med 2020;35:457-464
https://doi.org/10.3904/kjim.2018.247

KJIM

Mutation of ten-eleven translocation-2 is associated with increased risk of autoimmune disease in patients with myelodysplastic syndrome

Yoon-Jeong Oh[1,*], Dong-Yeop Shin[2,3,*], Sang Mee Hwang[4], Sung-Min Kim[5], Kyongok Im[5], Hee Sue Park[6], Jung-Ah Kim[6], Yeong Wook Song[7], Ana Márquez[8], Javier Martín[8], Dong-Soon Lee[5,6], and Jin Kyun Park[7]



Leukemia (2021) 35:2720–2724
https://doi.org/10.1038/s41375-021-01152-1

LETTER

Myelodysplastic syndrome

Genomic landscape of MDS/CMML associated with systemic inflammatory and autoimmune disease

Lin-Pierre Zhao[1,2,3] · Maxime Boy[2,3] · Célia Azoulay[2] · Emmanuelle Clappier[4] · Marie Sébert[1,5] · Ludivine Amable[2] · Jihene Klibi[2] · Kamel Benlagha[2] · Marion Espéli[2,3] · Karl Balabanian[2,3] · Claude Preudhomme[6,7] · Alice Marceau-Renaut[6,7] · Lina Benajiba[5,8] · Raphaël Itzykson[1,9] · Arsène Mekinian[10] · Olivier Fain[10] · Antoine Toubert[2,3,11] · Pierre Fenaux[1,5] · Nicolas Dulphy[2,3,11] · Lionel Adès[1,5]

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Contents lists available at ScienceDirect

Leukemia Research

journal homepage: www.elsevier.com/locate/leukres

Efficacy of Azacitidine in autoimmune and inflammatory disorders associated with myelodysplastic syndromes and chronic myelomonocytic leukemia

Jean-Baptiste Fraison[a,*,1], Arsène Mekinian[b,1], Eric Grignano[c], Jean-Emmanuel Kahn[d], Jean-Benoit Arlet[e], Olivier Decaux[f], Guillaume Denis[g], Anne-Laure Buchdahl[h], Mohamed Omouri[i], Gwenola Maigne[j], Achille Aouba[j], Nathalie Leon[k], Sabine Berthier[l], Eric Liozon[m], Sophie Park[n], Claude Gardin[o], Olivier Lortholary[p], Julien Rossignol[c], Pierre Fenaux[q], Olivier Fain[b,1], Thorsten Braun[o,1]

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- 22 patients treated with AZA for autoimmune disorders (AID) associated with MDS/CMML
- Response of AID to Azacitidine in 19 patients (86%)
- Reduction or discontinuation of steroids and/or immunosuppressive therapy possible in 16 cases (73%).

LETTER

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MYELODYSPLASTIC NEOPLASM

A Phase II prospective trial of azacitidine in steroid-dependent or refractory systemic autoimmune/inflammatory disorders and VEXAS syndrome associated with MDS and CMML

Arsene Mekinian[1,27]✉, Lin Pierre Zhao[2,27], Sylvie Chevret[3], Kristell Desseaux[3], Laurent Pascal[4], Thibaut Comont[5], Alexandre Maria[6], Pierre Peterlin[7], Louis Terriou[8], Maud D'Aveni Piney[9], Marie-Pierre Gourin[10], Norbert Vey[11], Odile Beyne Rauzy[5], Vincent Grobost[12], Holy Bezanahary[13], Sophie Dimicoli-Salazar[14], Anne Banos[15], Stefan Wickenhauser[16], Benoit De Renzis[17], Eric Durot[18], Shanti Natarajan-Amé[19], Laurent Voillat[10], Fatiha Chermat[2], Karine Lemaire[2], Vincent Jachiet[1], Chantal Himberlin[18], Sylvain Thépot[20], Jose Miguel Torregrosa Diaz[21], Laurent Frenzel[22], Emmanuel Gyan[23], Guillaume Denis[24], Pierre Hirsch[25], Olivier Kosmider[26], Lionel Ades[2], Olivier Fain[1] and Pierre Fenaux[2]

- N=30
- 66% response on SAID
- 59% hematological response

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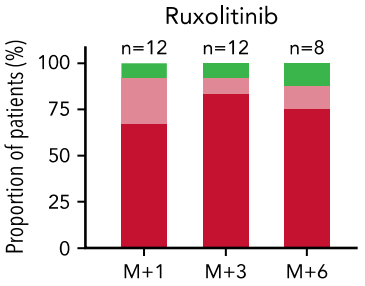
UBA 1 mutation (VEXAS) and MDS

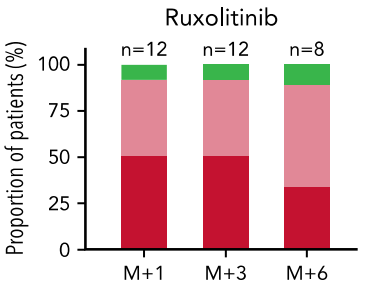
- VEXAS: Autoinflammatory disease , X linked,cutaneous lesions, vacuoles in granulocytes,
- MDS in 40% of the cases

TO THE EDITOR:

Ruxolitinib is more effective than other JAK inhibitors to treat VEXAS syndrome: a retrospective multicenter study

Maël Heiblig,[1] Marcela A. Ferrada,[2,*] Matthew T. Koster,[3,*] Thomas Barba,[4,*] Mathieu Gerfaud-Valentin,[5] Arsène Mékinian,[6] Henrique Coelho,[7] Gaelle Fossard,[1] Fiorenza Barraco,[1] Lionel Galicier,[8] Boris Bienvenu,[8] Pierre Hirsch,[9] Guillaume Vial,[10] Anne Blandine Boutin,[11] Joris Galland,[12] Guillaume Le Guenno,[13] Adrien Bigot,[14] Kenneth J. Warrington,[3] Tanaz A. Kermani,[15] Peter C. Grayson,[2] Bhavisha A. Patel,[16] David B. Beck,[17,18] Yvan Jamilloux,[5,†] Pierre Fenaux,[19,†] and Pierre Sujobert[20]





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LETTER

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MYELODYSPLASTIC NEOPLASM

A Phase II prospective trial of azacitidine in steroid-dependent or refractory systemic autoimmune/inflammatory disorders and VEXAS syndrome associated with MDS and CMML

Arsene Mekinian[1,27]✉, Lin Pierre Zhao[2,27], Sylvie Chevret[3], Kristell Desseaux[3], Laurent Pascal[4], Thibaut Comont[5], Alexandre Maria[6], Pierre Peterlin[7], Louis Terriou[8], Maud D'Aveni Piney[9], Marie-Pierre Gourin[10], Norbert Vey[11], Odile Beyne Rauzy[5], Vincent Grobost[12], Holy Bezanahary[13], Sophie Dimicoli-Salazar[14], Anne Banos[15], Stefan Wickenhauser[16], Benoit De Renzis[17], Eric Durot[18], Shanti Natarajan-Amé[19], Laurent Voillat[10], Fatiha Chermat[2], Karine Lemaire[2], Vincent Jachiet[1], Chantal Himberlin[18], Sylvain Thépot[20], Jose Miguel Torregrosa Diaz[21], Laurent Frenzel[22], Emmanuel Gyan[23], Guillaume Denis[24], Pierre Hirsch[25], Olivier Kosmider[26], Lionel Ades[2], Olivier Fain[1] and Pierre Fenaux[2]

- N=30
- 13 (52% VEXAS patients)
- 75% response on VEXAS symptoms
- 59% hematological response

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Recent treatments of lower risk MDS

- Lower risk MDS: where is the limit ?
- Treatment of anemia of lower risk MDS
- Treatment of thrombocytopenia of lower risk MDS
- Chelation therapy ?
- Treatment of MDS with autoimmune/autoinflammatory disorders
- Should some lower risk MDS be transplanted ?

Bone Marrow Transplantation (2017) **52,** 209–215

www.nature.com/bmt

ORIGINAL ARTICLE

Allogeneic haematopoietic stem cell transplant in patients with lower risk myelodysplastic syndrome: a retrospective analysis on behalf of the Chronic Malignancy Working Party of the EBMT

M Robin[1], R Porcher[2,3], W Zinke-Cerwenka[4], A van Biezen[5], L Volin[6], G Mufti[7], C Craddock[8], J Finke[9], C Richard[10], J Passweg[11], A Peniket[12], J Maertens[13], G Sucak[14], T Gedde-Dahl[15], A Vitek[16], A Nagler[17], D Blaise[18], D Beelen[19], N Maillard[20], R Schwerdtfeger[21], T de Witte[22] and N Kroger[23]

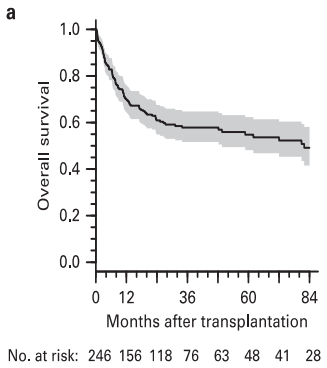

Figure 1. OS, PFS and cumulative incidence of NRM. OS, PFS and cumulative incidence of NRM are shown in (**a**, **b** and **c**), respectively. Grey shaded areas represent the 95% pointwise confidence interval.

TRM post allo SCT Recent GFM experience

- *CPX 351 trial* (median age 62) (Peterlin Lancet Hematol, 2023)
  - N=29
  - TRM: 5/29 (17%)
- *allo risk trial* (median age 62) (Robin, ASH 2021)
  - N= 58
  - TRM: 11/ 58 (19%)

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Allo risk trial (Robin, ASH 2021)

63 patients with donor

15 patients without donor

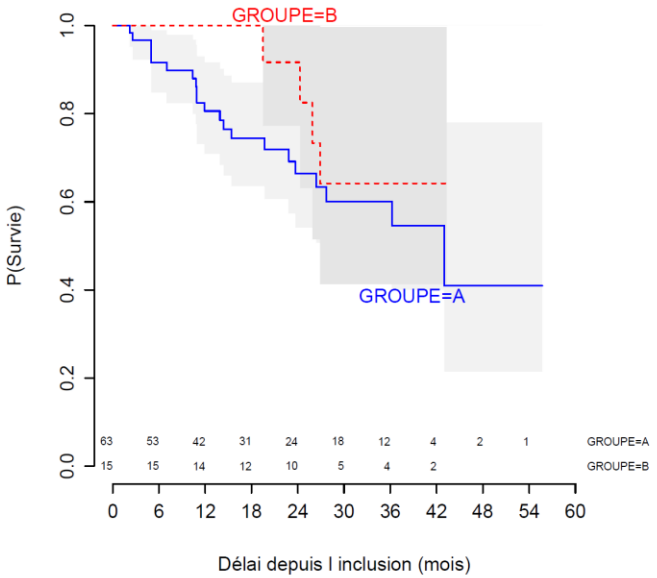
✓ 3 yr OS 60 vs 64%

58 (92%) patients trasplanted

✓ 4 dises related deaths

✓ 11 (19%) TRM

✓ 6 death relapse /progression



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Should lower risk MDS be transplanted ?

- NO
  - RARS with normal karyotype and isolated SF3B1 mutation
- YES
  - IPSS/ IPSS-R progression
  - TP53 mutation with VAF > 20%, or if VAF increases
  - Lower risk MDS with del 5q failing LEN

Allo in lower risk MDS ?

- Other patients: take into account
  - age, comorbidities
  - donor
  - Response to treatment
  - Importance of cytopenias
  - *Mutations ?*
  - Progression
  - Patient choice

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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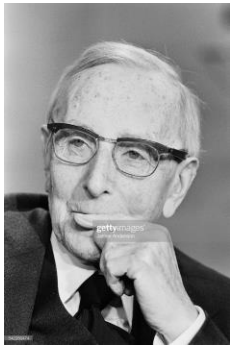

Groupe Francophone des Myélodysplasies

- 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


EMSCO
MYELODYSPLASTIC
SYNDROMES


gfm
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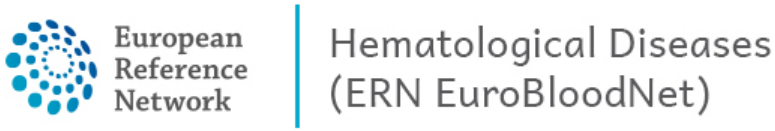
FISM
FONDAZIONE
ITALIANA
SINDROMI
MIELODISPLASTICHE


D·MDS
Deutsche MDS-Studiengruppe


GESMD


European
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10th Translational Research Conference Myelodysplastic Syndromes, Overlap MDS/MPN Disorders and Clonal Hematopoiesis

Malahide (Dublin), Ireland
October 16-18, 2026
#ESHMDS2026

Chairs: **Pierre Fenaux, Katharina Götze, Mikkael Sekeres**

DEADLINE FOR ABSTRACTS: JULY 6th, 2026

To register and for further information: www.esh.org - info@esh.org