

4<sup>th</sup> edition

# Unmet challenges in high risk hematological malignancies: from bedside to clinical practice

Turin, March 26-27, 2026

Starhotels Majestic

*Scientific board:*

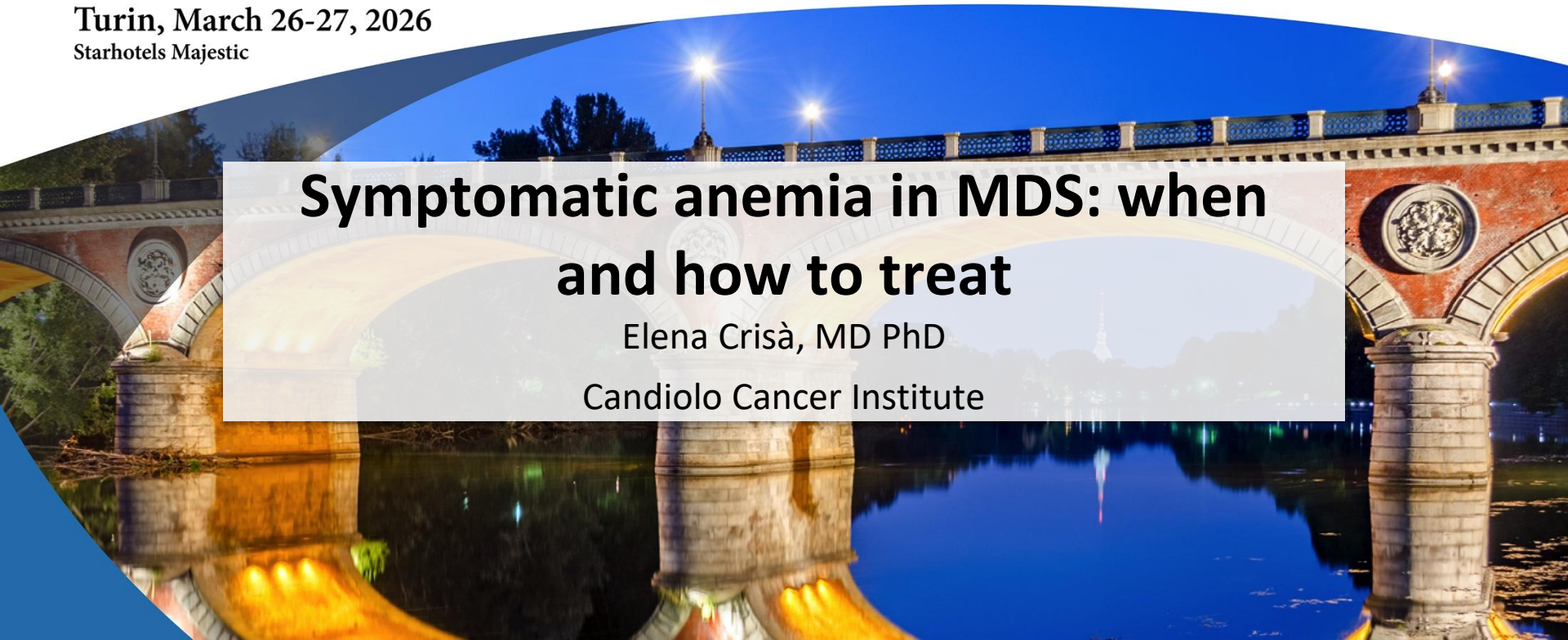
Marco Ladetto (Alessandria)

Umberto Vitolo (Candiolo-TO)

## Symptomatic anemia in MDS: when and how to treat

Elena Crisà, MD PhD

Candiolo Cancer Institute

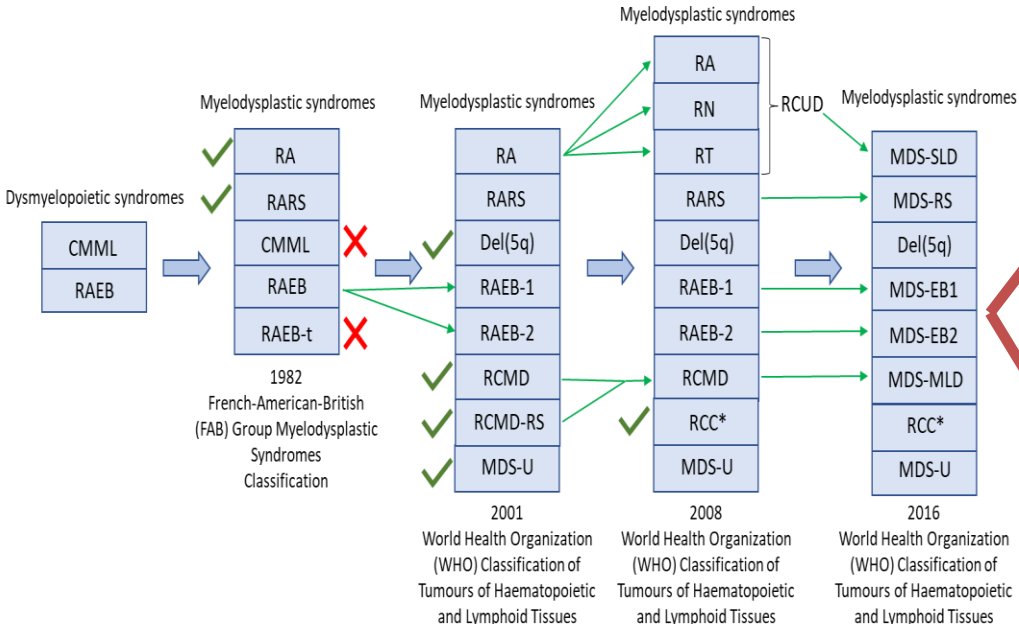


## Disclosures of Elena Crisà

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
GSK						x	
BMS					x		
NOVARTIS							x

# MDS classification has evolved over time

WHO 2022



**Key**

- ✓ = new addition to respective classification
- ✗ = removed from subsequent classification

Leukemia www.nature.com/leu

REVIEW ARTICLE OPEN Check for updates

## The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms

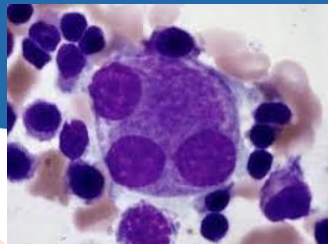
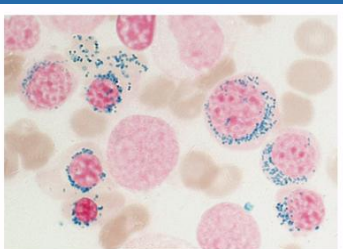
Joseph D. Khoury<sup>1,55</sup>, Eric Solary<sup>2,55</sup>, Oussama Aba<sup>3</sup>, Yasmine Akkari<sup>4</sup>, Rita Alaggio<sup>5</sup>, Jane F. Apperley<sup>6</sup>, Rafael Bejar<sup>7</sup>, Emilio Berti<sup>8</sup>, Lambert Busque<sup>9</sup>, John K. C. Chan<sup>10</sup>, Weina Chen<sup>11</sup>, Xueyan Chen<sup>12</sup>, Wee-Joo Chng<sup>13</sup>, John K. Choi<sup>14</sup>, Isabel Colmenero<sup>15</sup>, Sarah E. Coupland<sup>16</sup>, Nicholas C. P. Cross<sup>17</sup>, Daphne De Jong<sup>18</sup>, M. Tarek Elghetany<sup>19</sup>, Emiko Takahashi<sup>20</sup>, Jean-Francois Emile<sup>21</sup>, Judith Ferry<sup>22</sup>, Linda Fogelstrand<sup>23</sup>, Michaela Fontenay<sup>24</sup>, Ulrich Germing<sup>25</sup>, Sumeet Gujral<sup>26</sup>, Torsten Haferlach<sup>27</sup>, Claire Harrison<sup>28</sup>, Jennelle C. Hodge<sup>29</sup>, Shimin Hu<sup>30</sup>, Joop H. Jansen<sup>30</sup>, Rashmi Kanagal-Shamanna<sup>31</sup>, Hagop M. Kantarjian<sup>31</sup>, Christian P. Kratz<sup>32</sup>, Xiao-Qiu Li<sup>33</sup>, Megan S. Lim<sup>34</sup>, Keith Loebe<sup>35</sup>, Sanam Loghavi<sup>36</sup>, Andrea Marcocci<sup>37</sup>, Soheil Meshkini<sup>38</sup>, Phillip Michaels<sup>39</sup>, Kikkeri N. Naresch<sup>40</sup>, Yasodha Natkunam<sup>41</sup>, Reza Nejaati<sup>42</sup>, German Ott<sup>43</sup>, Eric Padron<sup>44</sup>, Keyur P. Patel<sup>45</sup>, Nikhil Patkar<sup>46</sup>, Jennifer Pircsics<sup>47</sup>, Uwe Platzbecker<sup>48</sup>, Irene Roberts<sup>49</sup>, Anna Schuh<sup>50</sup>, William Sewell<sup>51</sup>, Reiner Siebert<sup>52</sup>, Prashant Tembhare<sup>53</sup>, Jeffrey Tyner<sup>54</sup>, Srdan Verstovsek<sup>55</sup>, Wei Wang<sup>56</sup>, Brent Wood<sup>57</sup>, Wenbin Xiao<sup>58</sup>, Cecilia Yeung<sup>59</sup> and Andreas Hochhaus<sup>60</sup>

ICC 2022

The International Consensus Classification of Myeloid Neoplasms and Acute Leukemias: Integrating Morphological, Clinical, and Genomic Data

Daniel A. Arber, Attilio Orazi, Robert P. Hasserjian, Michael J. Borowitz, Katherine R. Calvo, Hans-Michael Kvasnicka, Sa A. Wang, Adam Bagg, Tiziano Barbui, Susan Branford, Carlos E. Bueso-Ramos, Jorge E. Cortes, Paola Dal Cin, Courtney D. DiNardo, Herve' Dombret, Eric J. Duncavage, Benjamin L. Ebert, Elihu H. Estey, Fabio Facchetti, Kathryn Foucar, Naseema Gangat, Umberto Gianelli, Lucy A. Godley, Nicola Gökbuget, Jason Gotlib, Eva Hellström-Lindberg, Gabriela S. Hobbs, Ronald Hoffman, Elias J. Jabbour, Jean-Jacques Kiladjian, Richard A. Larson, Michelle M. Le Beau, Mignon L-C. Loh, Bob Löwenberg, Elizabeth Macintyre, Luca Malcovati, Charles G. Mullighan, Charlotte Niemeyer, Olatoyosi M. Odenike, Seishi Ogawa, Alberto Orfao, Elli Papaemmanuil, Francesco Passamonti, Kimmo Porkka, Ching-Hon Pui, Jerald P. Radich, Andreas Reiter, Maria Rozman, Martina Rudelius, Michael R. Savona, Charles A. Schiffer, Annette Schmitt-Graeff, Akiko Shimamura, Jorge Sierra, Wendy A. Stock, Richard M. Stone, Martin S. Tallman, Jürgen Thiele, Hwei-Fang Tien, Alexander Tzankov, Alessandro M. Vannucchi, Paresch Vyas, Andrew H. Wei, Olga K. Weinberg, Agnieszka Wierzbowska, Mario Cazzola, Hartmut Döhner and Ayalew Tefferi

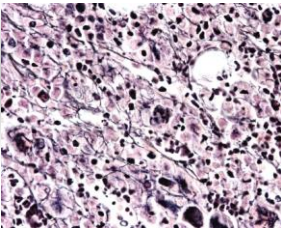
Full blood count and peripheral blood smear



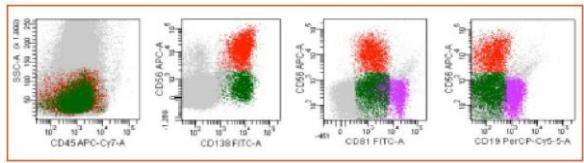
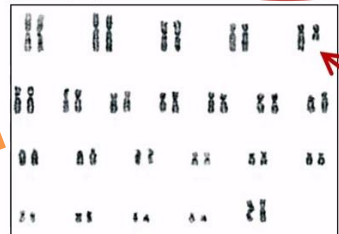
Bone marrow aspirate and biopsy

# Diagnostic tools in MDS

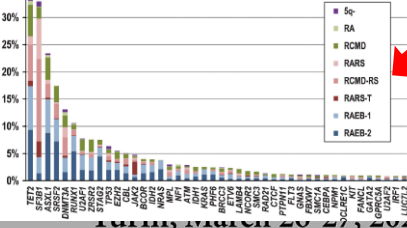
Molecular biology



Del(5q)

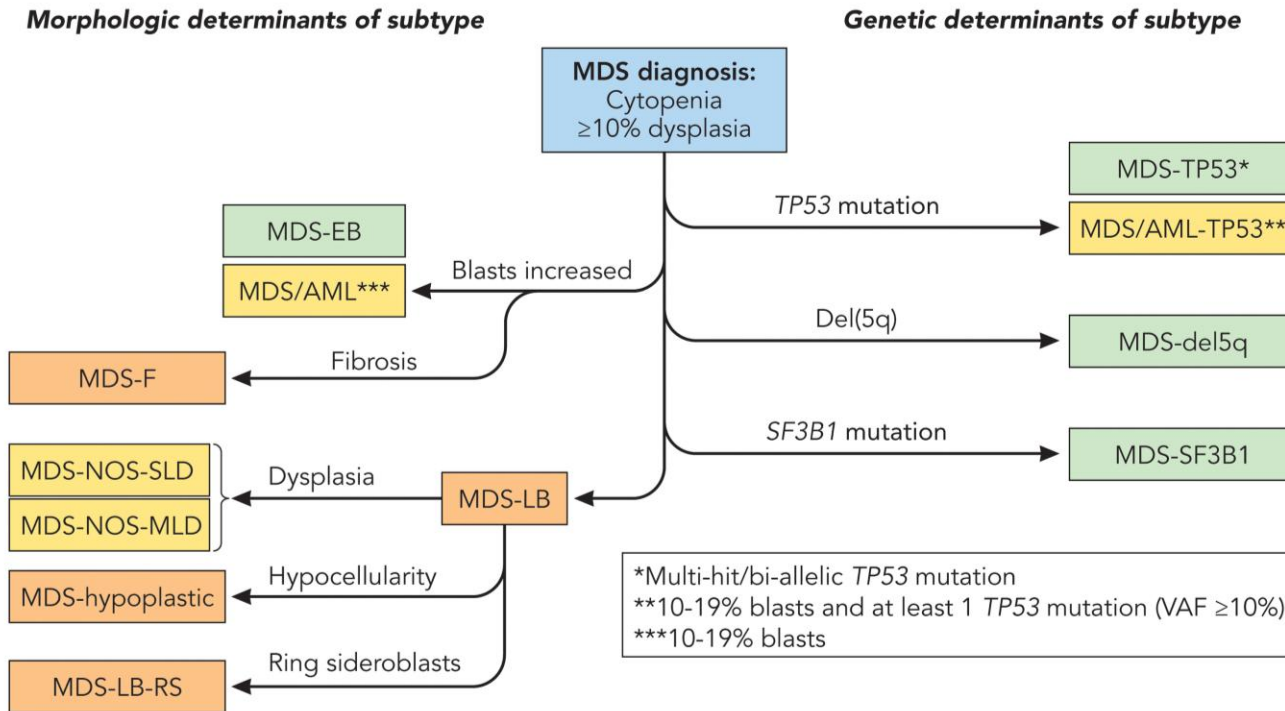


NGS



TP53

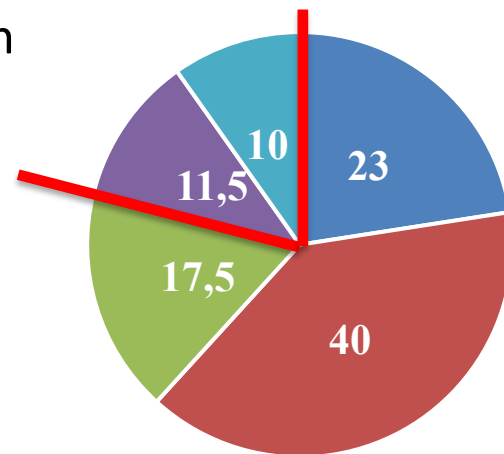
SF3B1



## Anemia in lower risk IPSS-r MDS : a significant clinical burden

% of different risk according to IPSS-revised

- 80% of MDS are in the lower risk category in FISiM registry. In this group:
  - 80% have HB <12 g/dl
  - 48% HB <10 g/dl

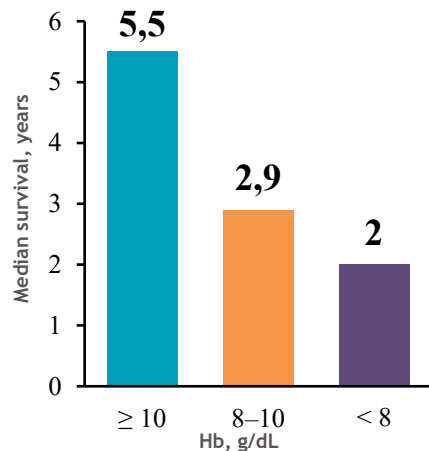


■ Very low ■ Low ■ Intermediate ■ High ■ Very High

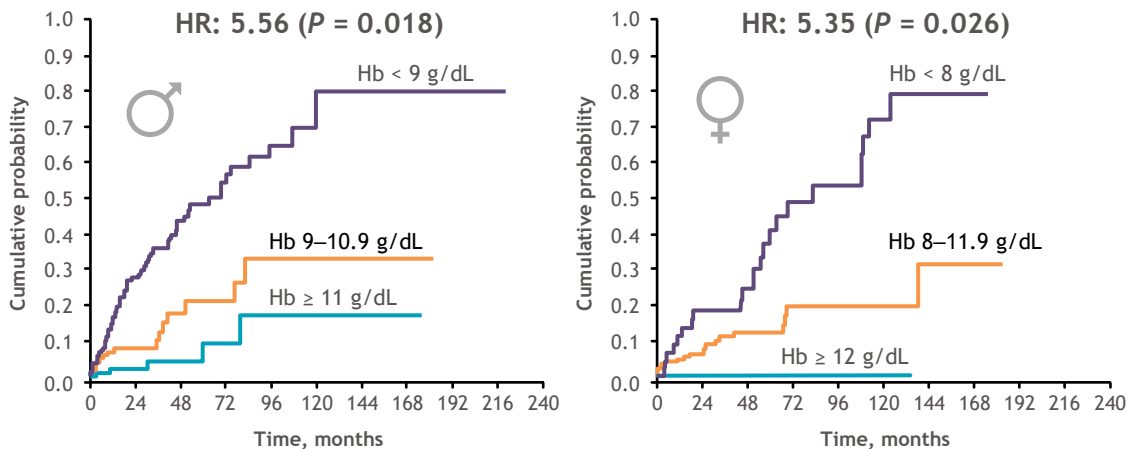
Data on 5503 MDS patients in FISiM registry with available IPSS revised score

# Anemia occurs in up to 90% of patients with MDS resulting in significantly increased risk of mortality

Severity of anemia and OS<sup>3,a</sup>



Probability of non-leukemic death<sup>2,b</sup>



<sup>a</sup>Based on combined international databases of 7012 patients with primary untreated MDS used to create the IPSS-R.<sup>3</sup>

<sup>b</sup>Based on a prospective, observational cohort analysis of 840 patients with MDS at Pavia, Italy and 504 patients with MDS at Düsseldorf, Germany.<sup>2</sup>

Hb, hemoglobin; IPSS-R, International Prognostic Scoring System; MDS, myelodysplastic syndromes; OS, overall survival.

1. Zeidan AM, et al. Blood Rev. 2019;34:1–15; 2. Malcovati L, et al. Haematologica. 2011;96:1433–1440; 3. Greenberg PL, et al. Blood. 2012;120:2454–2465.

# Improving anemia translates into improved survival in lower-risk MDS

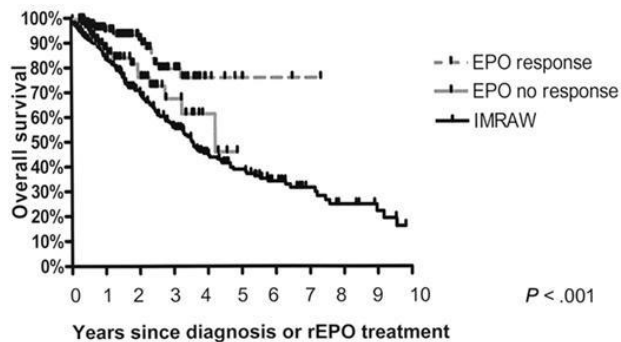
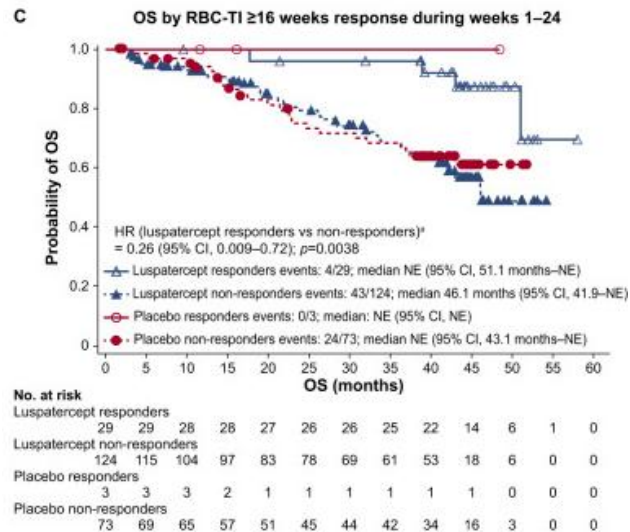
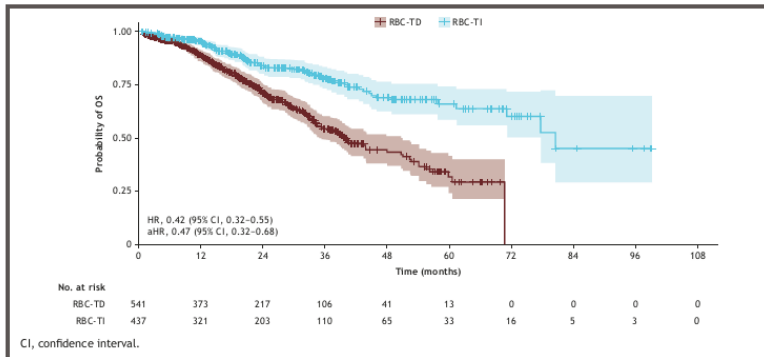
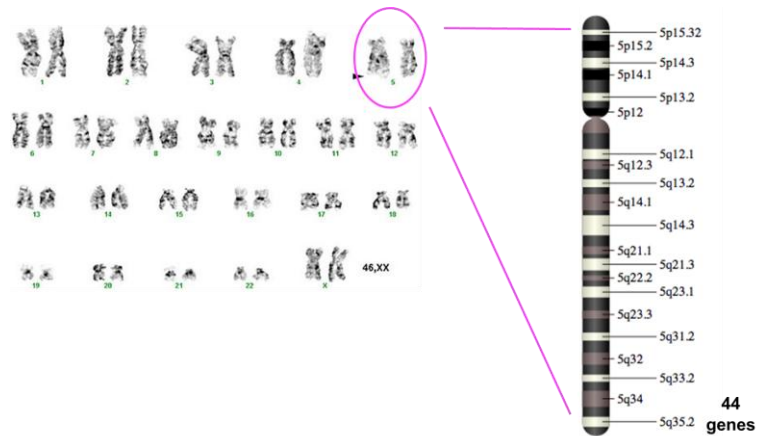
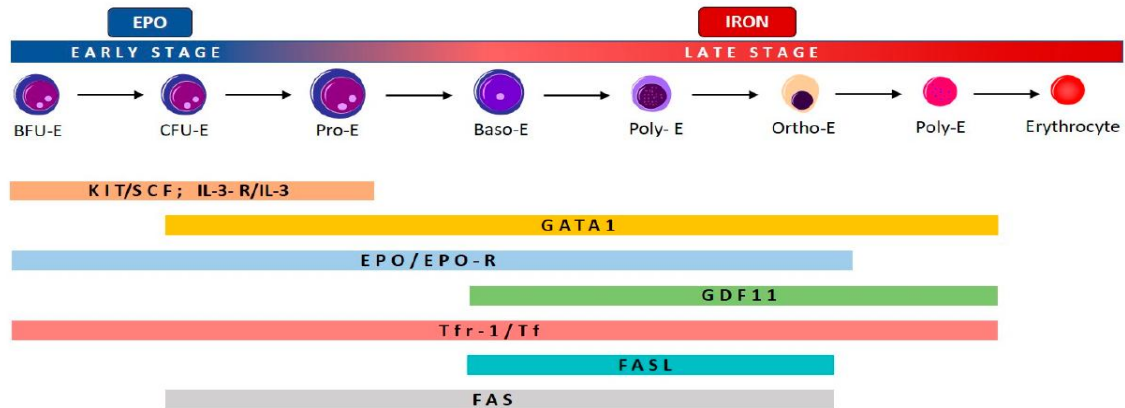
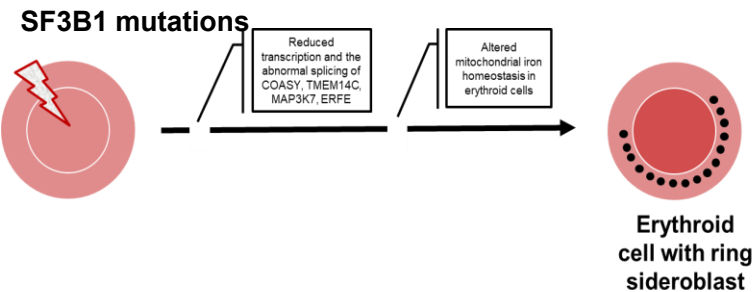


Figure 1. Kaplan-Meier curve for OS



meta-analyses on 6 clinical trials on TD LR-MDS:—3 luspatercept trials (COMMANDS, MEDALIST, and PACE ; 3 lenalidomide trials (5013-MDS-0036 [NCT00065156], 5013-MDS-0047[NCT00179621], and 5013-MDS-0058 [NCT01029262])

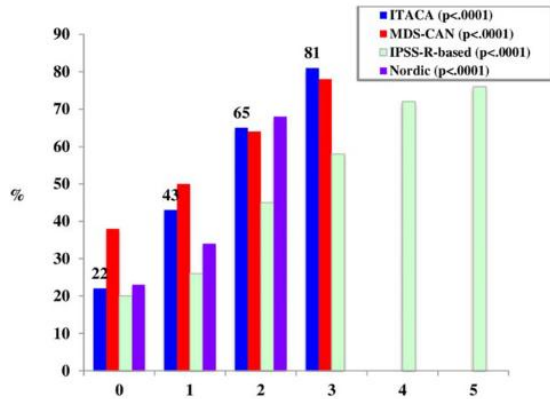
# Anemia in MDS is due to ineffective erythropoiesis



The main pathways involved in anemia in MDS are those regulated by

- Transforming growth factor (TGF)- $\beta$ , which negatively regulates erythrocyte differentiation and maturation
- Erythropoietin (EPO), which acts on the early-stage erythropoiesis.

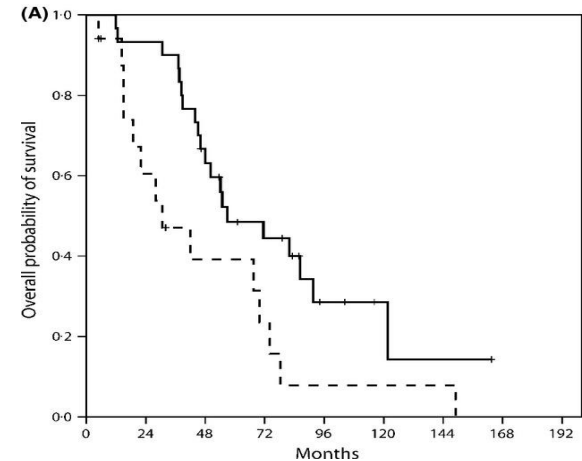
# Recombinant Erythropoietin



Score	ITACA N=681 (p<.0001)		MDS-CAN N=702 (p<.0001)		IPSS-R-based N=524 (p<.0001)		Nordic N=846 (p<.0001)	
	n	% ORR	n	% ORR	n	% ORR	n	% ORR
0	53	22	119	38	5	20	17	23
1	149	43	112	50	7	26	162	34
2	267	65	215	64	36	45	667	68
3	212	81	256	78	91	58		
4					134	72		
5					55	76		

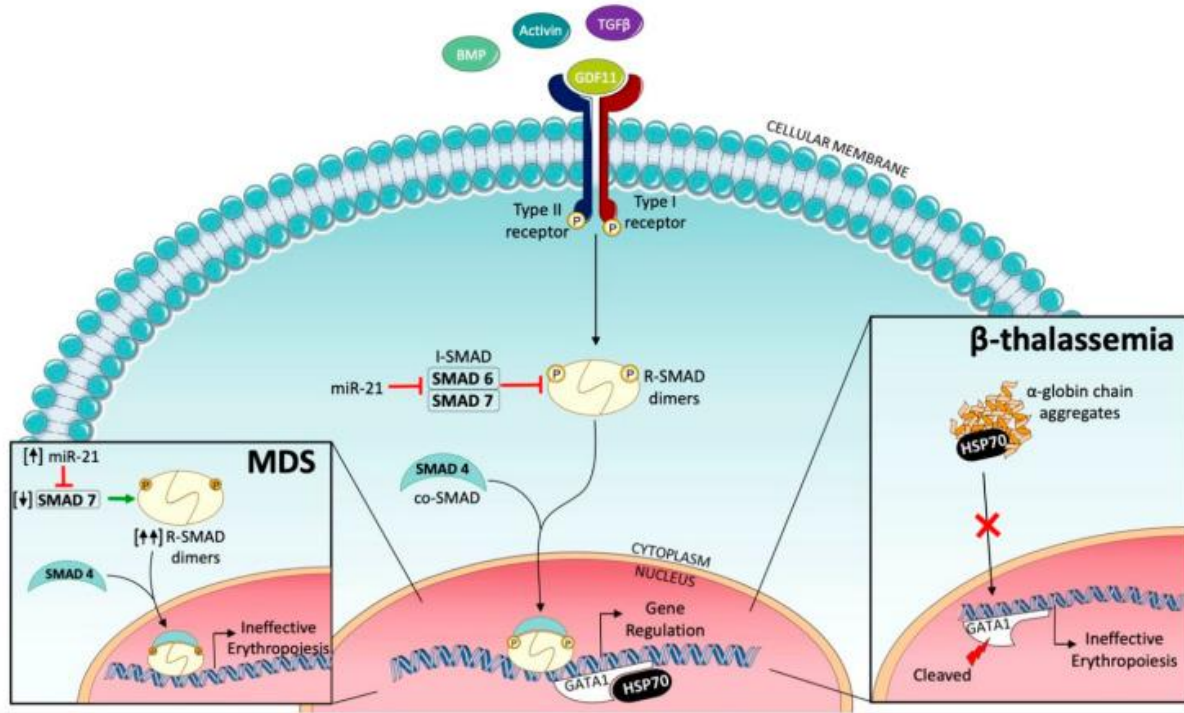
FIGURE 1 Response according to predictive scores.

- **Recombinant Erythropoietin (EPO) & glycosylated forms (darbepoetin) (+/- G-CSF) → current first line treatment of non TD LR MDS**
- Response rates range from 30% to 60% depending on study. Higher if
  - **RBC-TI/low transfusion burden** (ORR 79% vs 54% and 30,6 vs 12.7 mo)
  - Low EPO level (< 200 mIU)
  - IPSS low risk
- Response duration 12-24 months
- Impact of erythroid response on survival and QoL
- no impact on AML progression



OS according to erythroid response:  $P < 0.013$ .

# TGF- $\beta$ superfamily signaling is altered in MDS



- MDS patients display an overactivation of SMAD2/3 signaling due to the altered expression of mir-21 and SMAD7

➔ Luspatercept

# Luspatercept – phase III MEDALIST trial in TD MDS-RS

Patients with MDS<sup>a</sup> (N = 229)

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

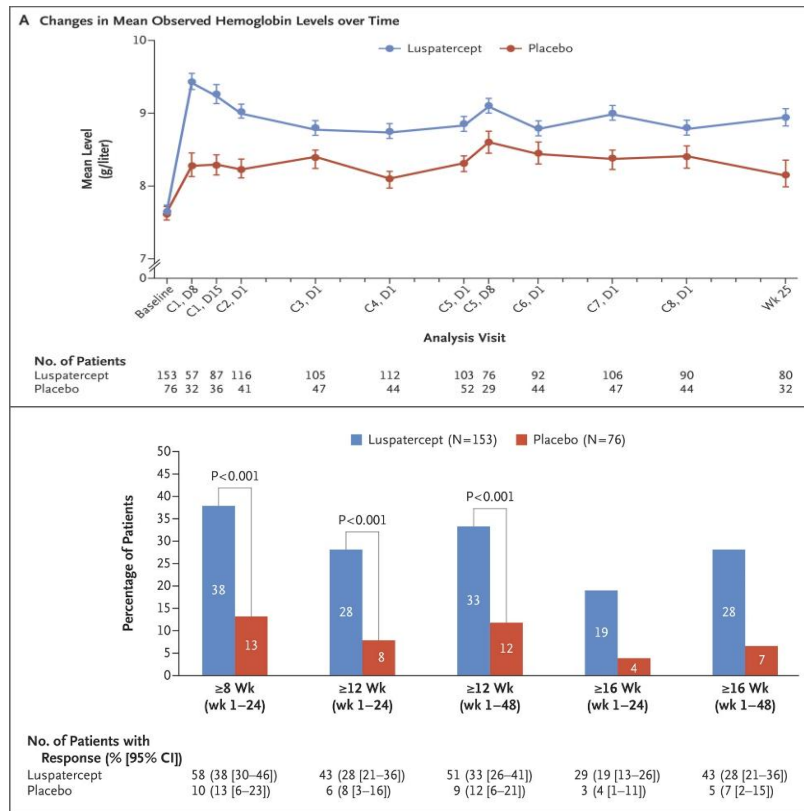
**Luspatercept (n = 153)**  
Starting dose 1.0 mg/kg  
Titration to 1.75 mg/kg allowed  
s.c. every 3 weeks

24 weeks

**Placebo (n = 76)**  
s.c. every 3 weeks

Week 25 Assessment

**Primary endpoint:**  
RBC-TI  $\geq 8$  weeks (Weeks 1-24)



# COMMANDS: phase III trial rEPO vs luspatercept in TD MDS

## Key eligibility criteria

- Aged ≥18 years
- IPSS-R very low-, low-, or intermediate-risk MDS (with or without RS) by WHO 2016, with <5% blasts in BM<sup>a</sup>
- 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

R

1:1

**Luspatercept (n = 178)**  
1.0 mg/kg SC Q3W  
titration up to 1.75 mg/kg

**Epoetin alpha (n = 178)<sup>b</sup>**  
450 IU/kg SC QW  
titration up to 1050 IU/kg

**Response assessment**  
at day 169 and every  
24 weeks thereafter

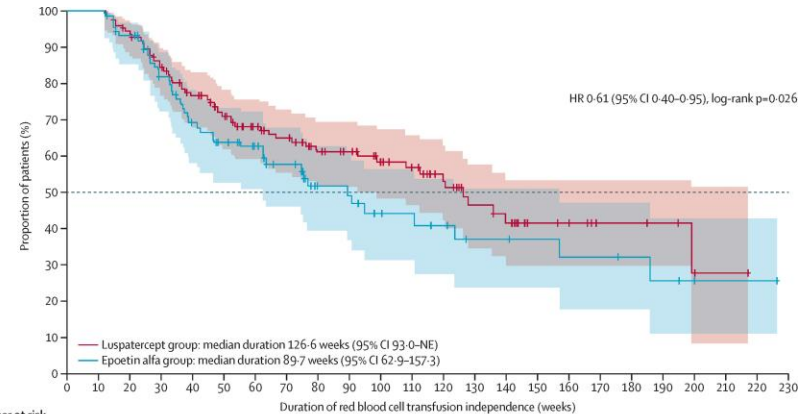
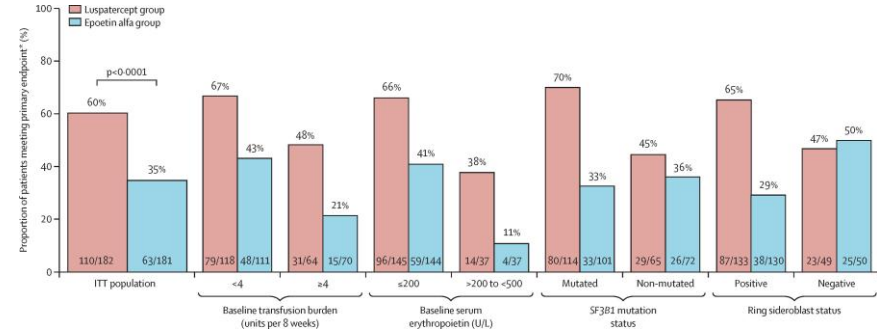
**EOT**  
Due to lack of clinical benefit<sup>c</sup>  
or disease progression per  
IWG criteria

## Primary endpoint (weeks 1-24)

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

## Key secondary endpoints (weeks 1-24)

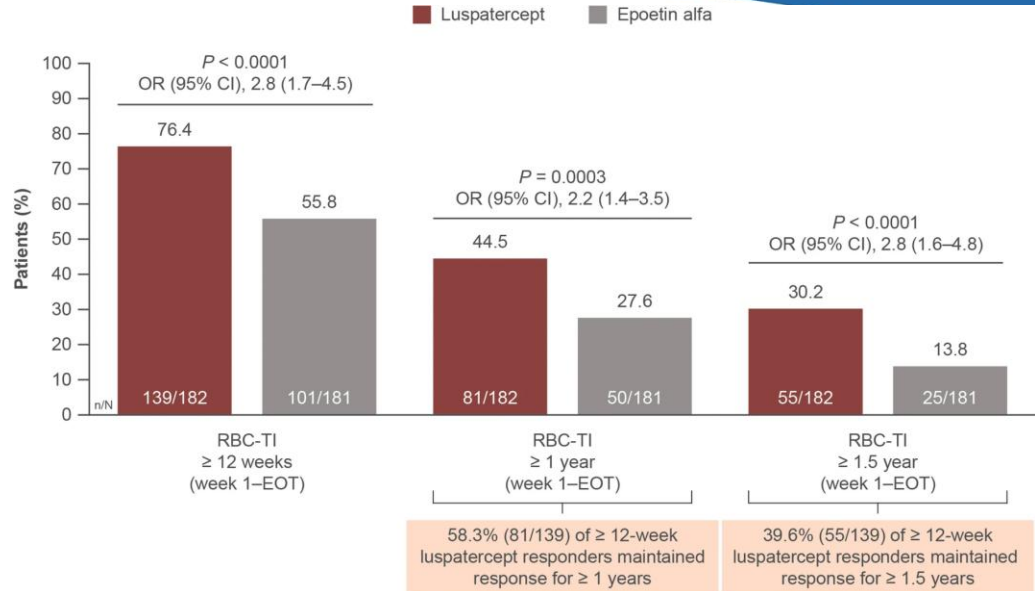
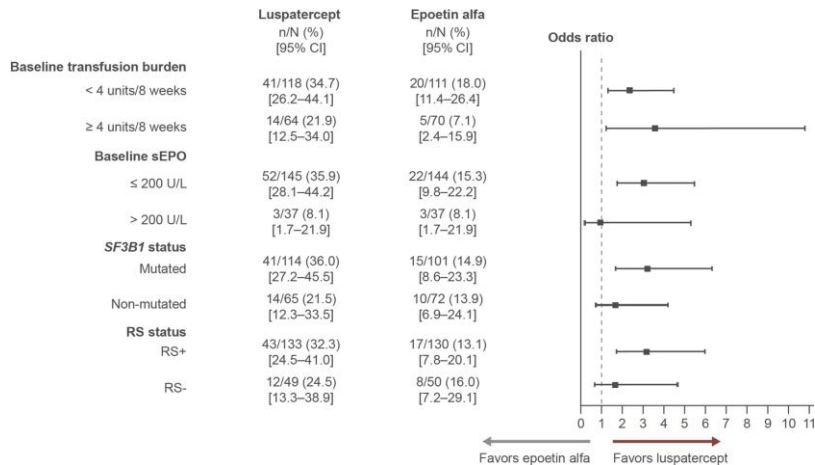
- HI-E response ≥ 8 weeks per IWG 2006 criteria<sup>2</sup>
- RBC-TI: 24 weeks, ≥ 12 weeks
- Preplanned exploratory analysis of RBC-TI: ≥ 24 weeks (weeks 1-48)



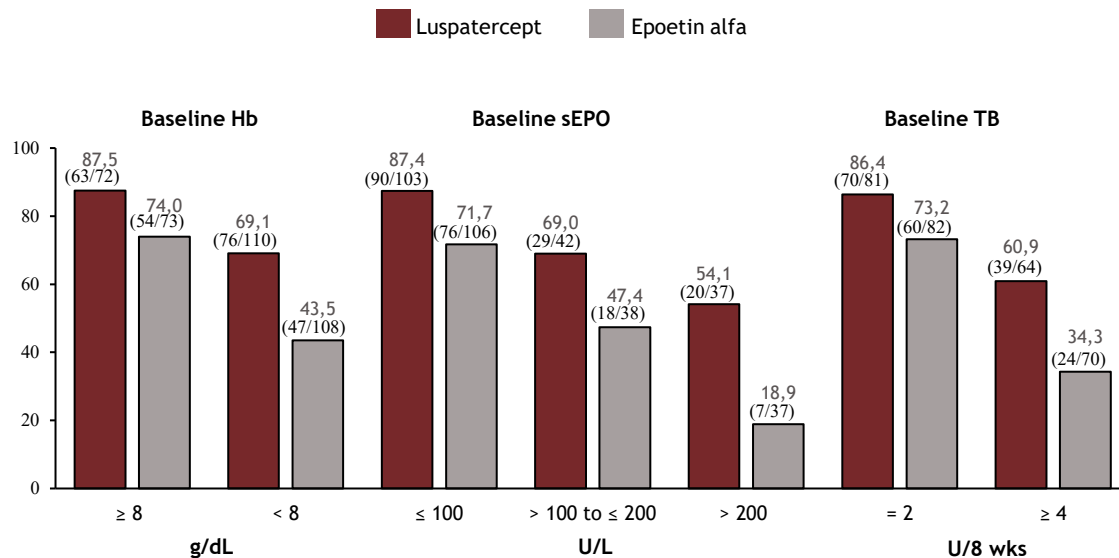
Number at risk (number censored)	124	124	115	100	86	76	65	59	50	46	40	35	28	20	18	10	9	5	4	4	2	1	0	..
Luspatercept group	124	(0)	(2)	(6)	(10)	(14)	(22)	(25)	(31)	(35)	(39)	(43)	(49)	(53)	(54)	(61)	(62)	(66)	(66)	(67)	(68)	(69)	(70)	(-)
Epoetin alpha group	88	(0)	(3)	(8)	(10)	(12)	(18)	(23)	(30)	(31)	(34)	(35)	(36)	(38)	(38)	(40)	(40)	(40)	(41)	(41)	(43)	(44)	(44)	(45)

# COMMANDS: long term results

- Luspatercept continued showing a significant superiority on EPO at later time points
- The rate of response remained superior even in subgroup analysis



# COMMANDS: long term results



patients with less advanced disease characteristics (Hb  $\geq$  8 g/dL; sEPO  $\leq$  100 U/L; TB = 2 U/8 wks) achieved higher response rates and improved durability than those with more advanced disease

MEDALIST<sup>a</sup>Luspatercept (n = 153) vs placebo (n = 76)<sup>1,2</sup>

Fatigue

Any-grade events:<sup>2</sup>  
**30.7% vs 14.5%**Grade 3/4 events:<sup>1</sup>  
**4.6% vs 2.6%***Fatigue occurred more frequently during cycles 1-4 of luspatercept treatment*

HTN

Any-grade events:<sup>2</sup>  
**13.1% vs 9.2%**Grade 3/4 events:<sup>1</sup>  
**3.3% vs 3.9%**

TEE

Any-grade events:<sup>2</sup> **4.6% vs 3.9%***Anti-thrombotic agents were used by 34.0% vs 38.2% of patients, respectively, and 27.5% of patients were on anti-thrombotic agents prior to enrollment<sup>3</sup>*

Discont.

Discontinuations due to TEAEs:<sup>1,2,b</sup> **15.7% vs 7.9%***TEAEs leading to ≥ 2 discontinuations with luspatercept were fatigue (n = 2), sepsis (n = 2) and transformation to AML<sup>3,a</sup>*COMMANDS<sup>4,c</sup>

Luspatercept (n = 182) vs epoetin alfa (n = 179)

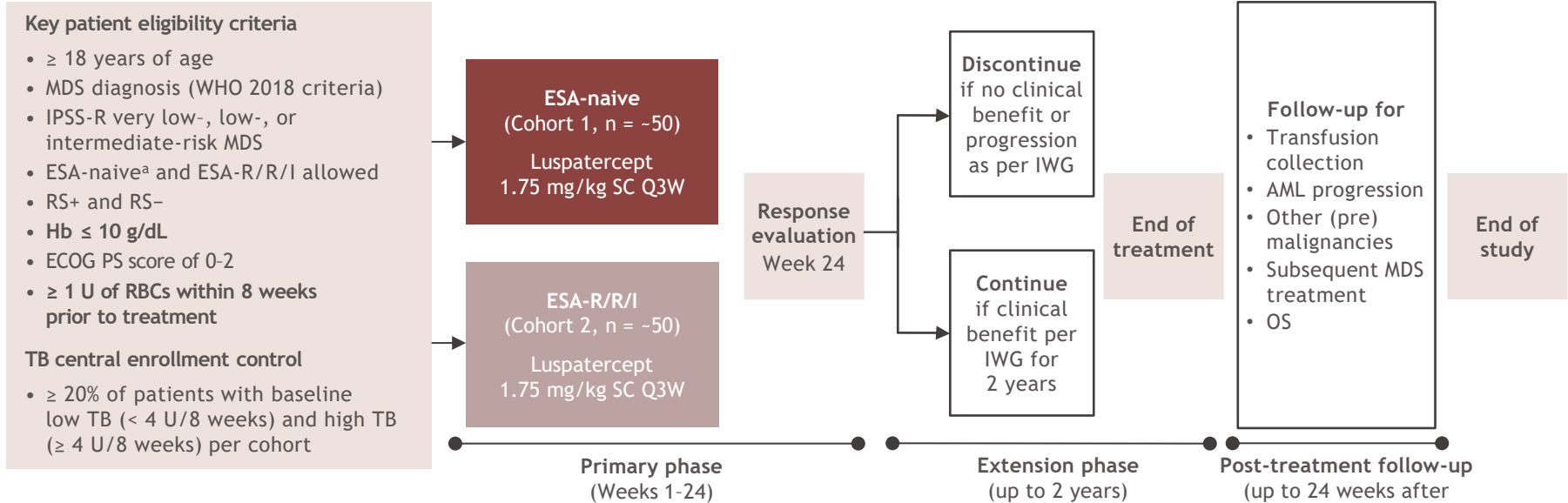
Any-grade events:  
**19% vs 8%**Grade 3/4 events: **1%**  
vs **1%***Fatigue decreased after the first few weeks of treatment*Any-grade events:  
**16% vs 9%**Grade 3/4 events:  
**10% vs 4%***Most hypertension adverse events resolved while on study treatment with medical management and did not lead to drug withdrawal*Any-grade events:  
**7% vs 3%**Grade 3/4 events:  
**4% vs 1%***The incidence of TEEs were similar between the 2 groups when adjusted for exposure*Discontinuations due to TEAEs: **6% vs 3%***Two events were suspected to be related to luspatercept treatment, including non-serious grade 3 dyspnea on exertion and serious grade 4 transformation to AML (n = 1 each)*

• HTN, hypertension.

• 1. Fenaux P, et al. *N Engl J Med* 2020;382:140–151; 2. Santini V, et al. *Blood* 2023;142:915; 4. Della Porta MG, et al. *Lancet Haematol* 2024;11:e646–e658.

# MAXILUS: study design

MAXILUS (NCT06045689) is a phase 3b, open-label, non-randomized, 2-cohort trial



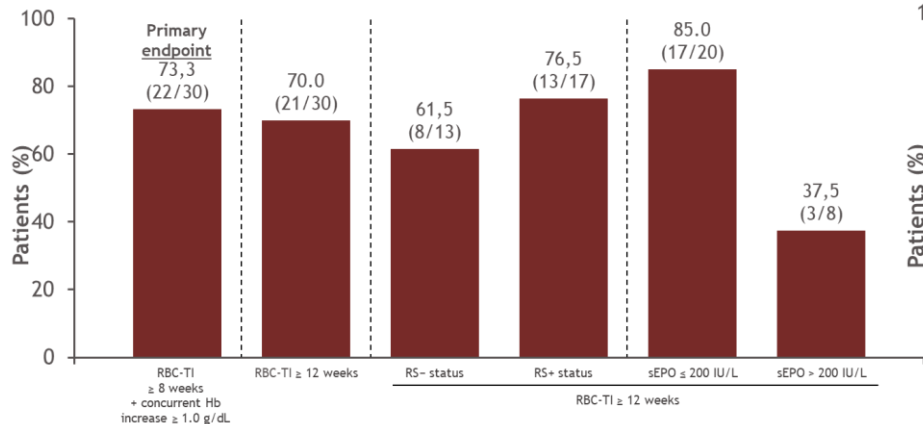
- **Primary endpoint:** RBC-TI for ≥ 8 weeks with a concurrent mean Hb increase of ≥ 1.0 g/dL from Weeks 1 to 24
- **Secondary endpoints:** RBC-TI for ≥ 8 weeks from Weeks 1 to 24, RBC-TI for ≥ 12 weeks from Weeks 1 to 24, disease progression to AML, and safety
- At this preplanned interim analysis (data cutoff date April 14, 2025), ~40% of the ESA-naive cohort and ~80% of the ESA-R/R/I cohort were expected to be eligible for the primary efficacy analysis
- At the primary analysis, ~90% of patients in both cohorts are expected to be eligible for the primary efficacy analysis

AML, acute myeloid leukemia; ECOG PS, Eastern Cooperative Oncology Group performance status; Hb, hemoglobin; IPSS-R, International Prognostic Scoring System-Revised; IWG, International Working Group; MDS, myelodysplastic syndromes; OS, overall survival; Q3W, every 3 weeks; RBC, red blood cell; R/R/I, relapsed/refractory/intolerant; RS, ring sideroblast; SC, subcutaneous; TB, transfusion burden; U, unit; WHO, World Health Organization.

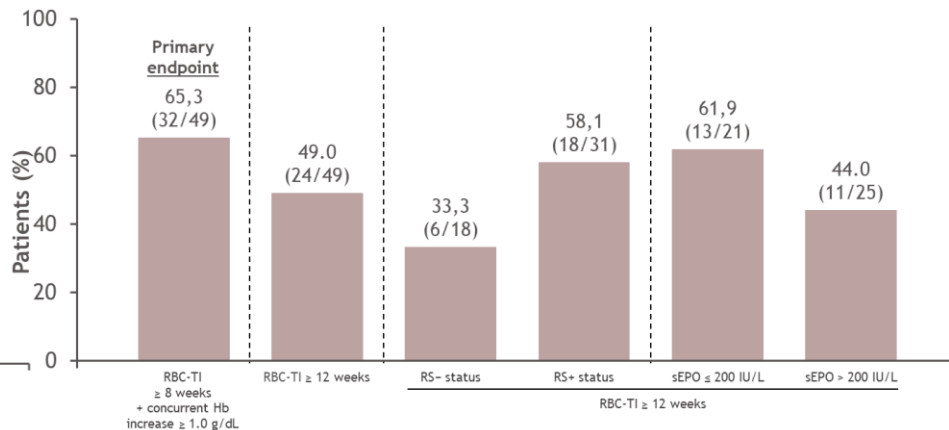
<sup>a</sup>Maximum of 2 doses.

## MAXILUS: RBC-TI (Weeks 1-24)

### ESA-naive cohort



### ESA-R/R/I cohort



Data cutoff date: April 14, 2025. Median (IQR) follow-up was 5.8 (3.3-8.2) months for the ESA-naive cohort.

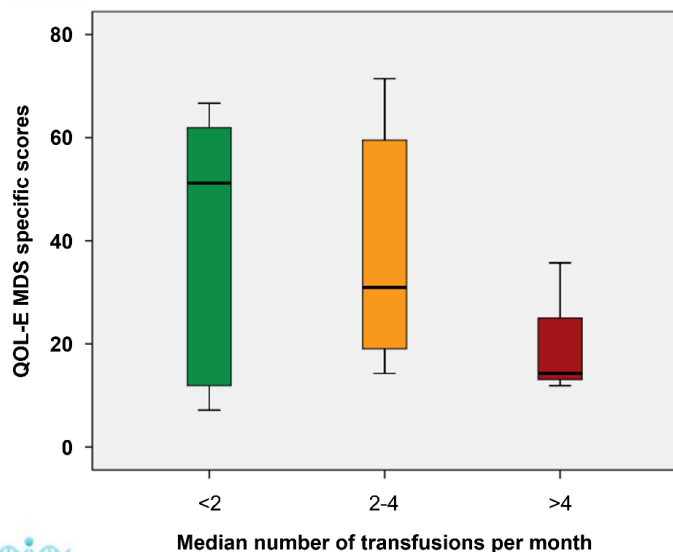
\*Data are from the primary endpoint population which included patients who received their first treatment  $\geq$  24 weeks prior to data cutoff (ESA-naive, n = 30).

# When to stop luspatercept

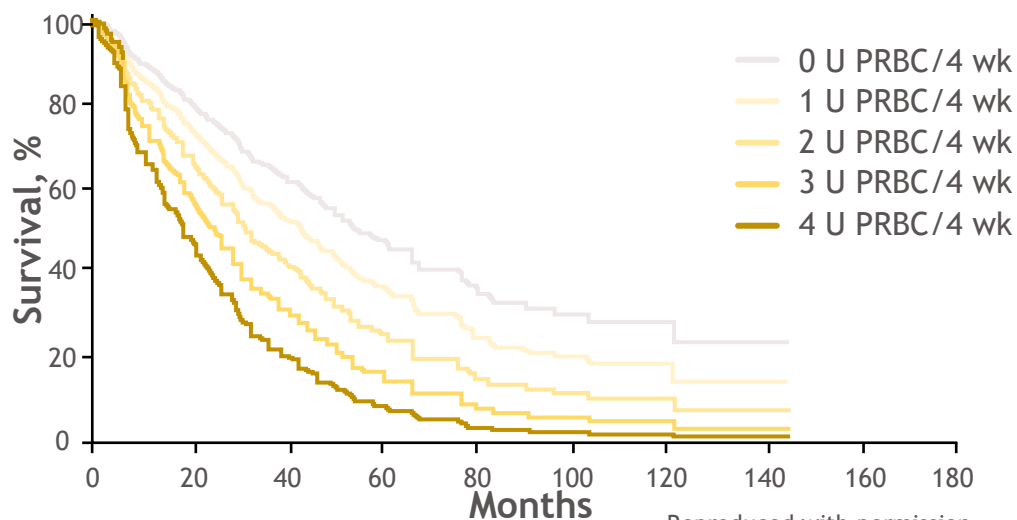
**No response: no decrease in transfusion burden/ no significant increase in Hb levels after 6 weeks at maximum dose 1.75 mg/kg , **no clinical benefit****

**Unacceptable toxicity**

**Response loss**



Crisà E. et al Cancers 2025

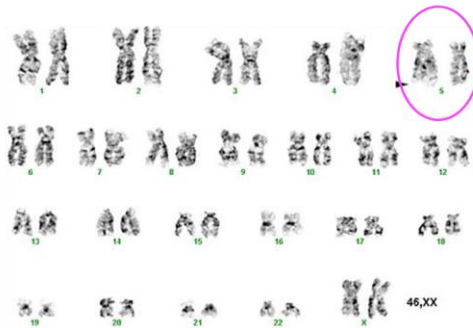


Reproduced with permission from *Haematologica*.<sup>1</sup>

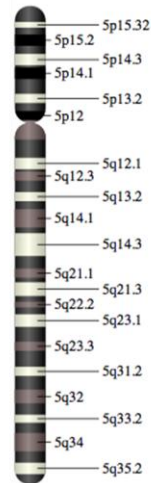
Malcovati L, et al. *Haematologica*. 2006;91:1588–1590

# MDS with del(5q)

		WHO 2022	ICC 2022
Del 5q	MDS with isolated del(5q)	<b>MDS-5q:</b> MDS with low blasts and isolated del 5q or with 1 other cytogenetic abnormality except -7/del(7)	<b>MDS del(5q):</b> MDS with isolated Del 5q or with 1 other cytogenetic abnormality except -7/del(7)

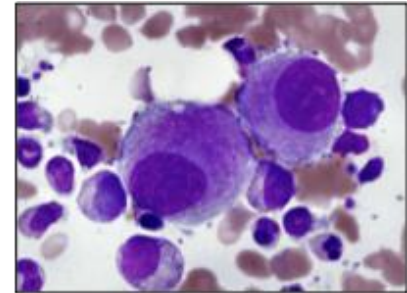


haplodeficiency for several genes located on 5q (particularly CSNK1A1, RPS14, EGR1, miR-145, and miR-146a)  
 →hematological phenotype  
 →selective sensitivity to lenalidomide

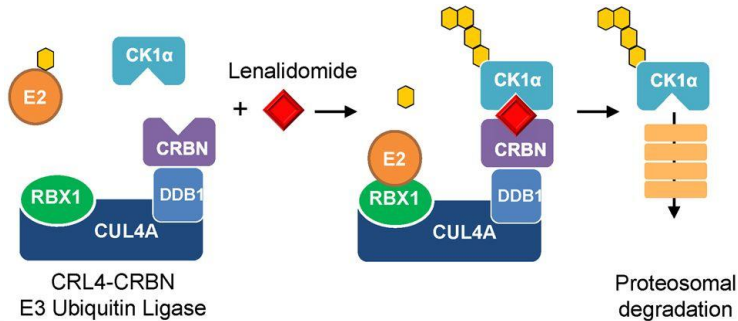


CDR

44 genes



# Lenalidomide in del(5q) MDS



Lenalidomide can lead to red blood cell-transfusion independence (RBC-TI) in 60 - 70% of del(5q) RBC-transfusion dependent MDS patients, and to complete cytogenetic response (CCyR) in 30-40% of the cases.

- Median time to reponse 4-6 weeks

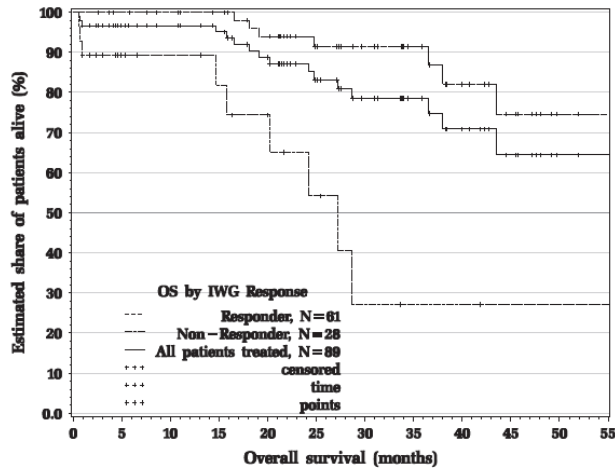
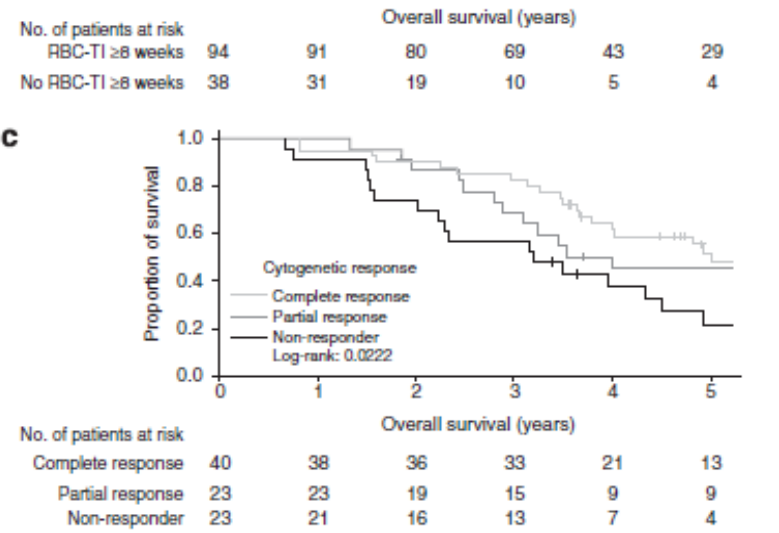


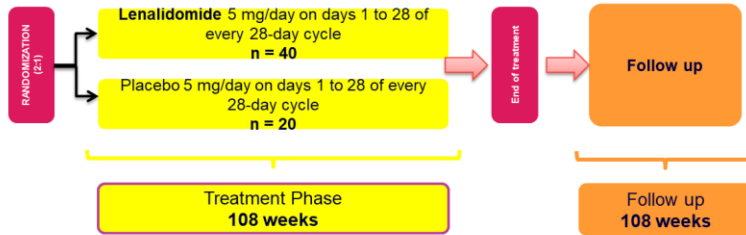
Figure 1. Kaplan-Meier plot showing overall survival of all patients treated and IWG-responders vs IWG-nonresponders.



# Sintra Rev trial : MDS del(5q) non-TD

## Patient Population

- MDS diagnosis (WHO 2008)
- IPSS-Low or Intermediate-1
- No RBC transfusion requirements
- Anemia (Hb<12 g/dL)
- del(5q) MDS solely and/or + other abnormality



## Primary endpoint:

- Time to disease progression

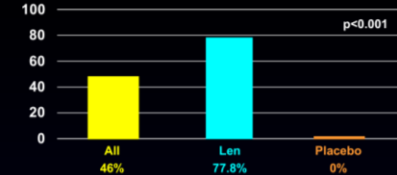
## Key secondary endpoints:

- Erythroid response
- Duration of RBC-TI
- Cytogenetic/marrow response
- Safety
- OS, EFS and time to AML
- Clonal evolution (NGS)

## Low doses of Len reached Erythroid and Cytogenetic responses

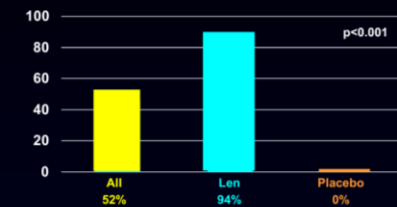
### ✓ Erythroid Response<sup>1</sup>

- ✓ Len (ITT Evaluable) 28/36 (77.8%)
  - ✓ Median Hb at EOT 12.4 g/dL (+2.7 g/dL)
- ✓ Placebo 0 (0%)

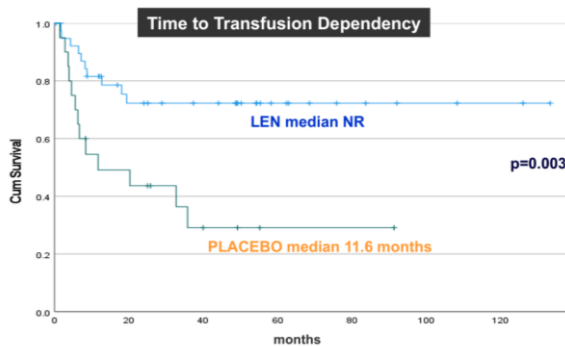


### ✓ Cytogenetic Response<sup>1</sup>

- ✓ Len (ITT Evaluable) 32/34 (94.1%):
  - ✓ 87.5% Complete (28/32)
  - ✓ 12.5% Partial (4/32)
- ✓ Placebo 0 (0%)



<sup>1</sup>IWG MDS 2006 criteria

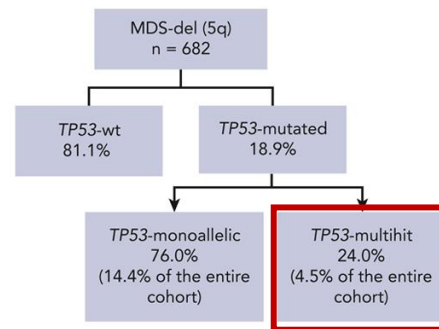


Len decreased in 69.8% the risk of TD: HR 0.302, p 0.005

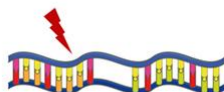
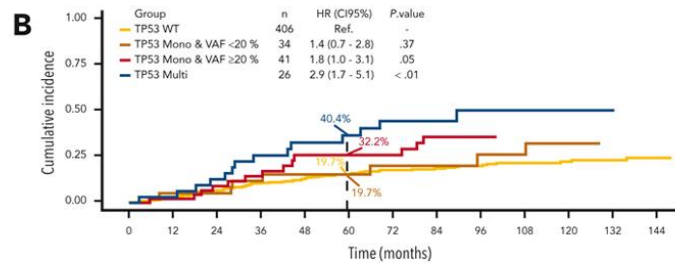
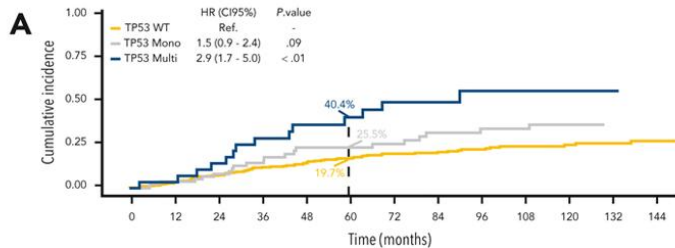
# TP53 and risk of progression to AML in MDS del(5q)

- TP53 mutated at low VAF (<~20%) LEN + close monitoring
- TP53 mutated at high VAF or multi-hit → benefit often modest and transient
  - consider early alternative strategies / transplant (if eligible)
  - monitor clonal evolution
  - calculate IPSS M

## Classification of patients with MDS-del (5q) according to TP53 gene alterations



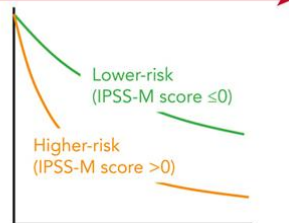
## Risk of AML evolution according to a) TP53 allelic state and b) TP53 VAF cutoff point of 20%



Co-occurring somatic gene mutations

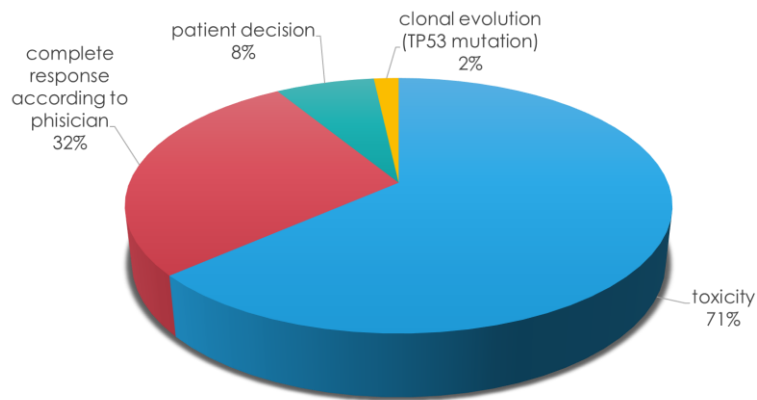
Figure generated using Servier Medical Art

- MDS with truly isolated del(5q)
- MDS-del(5q) with DTA comutation
- MDS-del(5q) with SF3B1 comutation
- MDS-del(5q) with monoallelic TP53 comutation
- MDS-del(5q) with RUNX1 comutation
- MDS-del(5q) with CSNK1A1 comutation



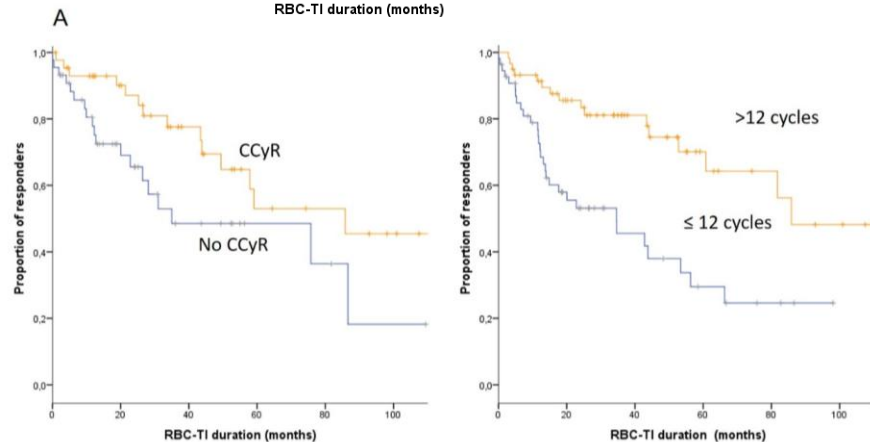
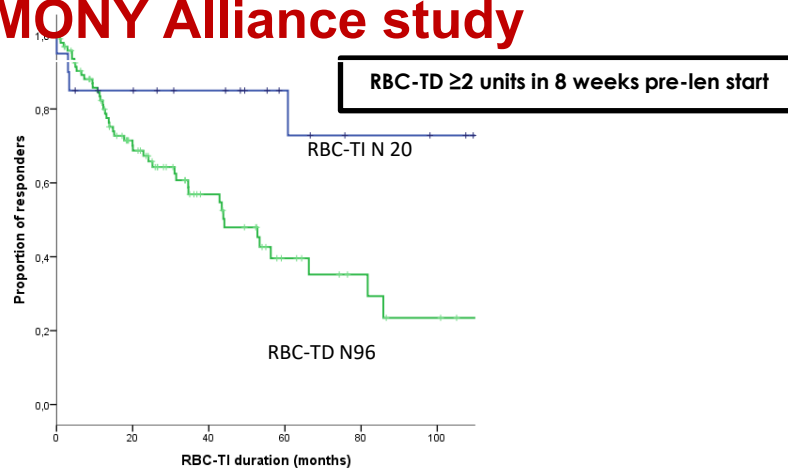
# Retrospective study of lenalidomide discontinuation in patients with MDSdel(5q). A HARMONY Alliance study

## Reason for lenalidomide discontinuation

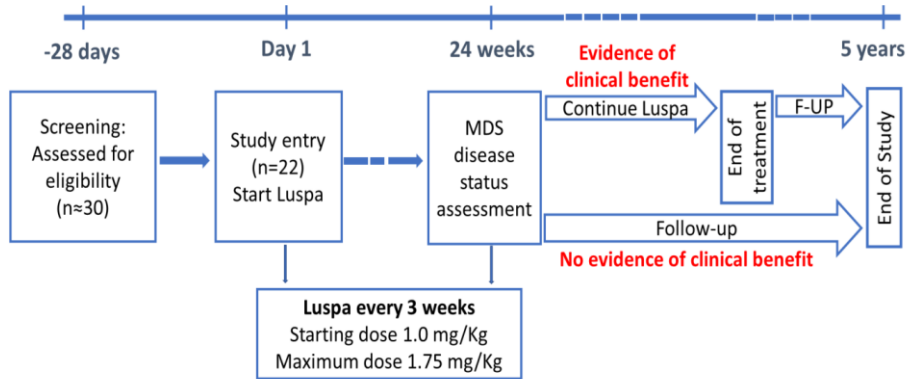


46 patients were re-treated with lenalidomide for response loss and 56% achieved at least a hematological response (3 also a CCyR)

Median FUP from lenalidomide stop:  
40 months (range 2-213)

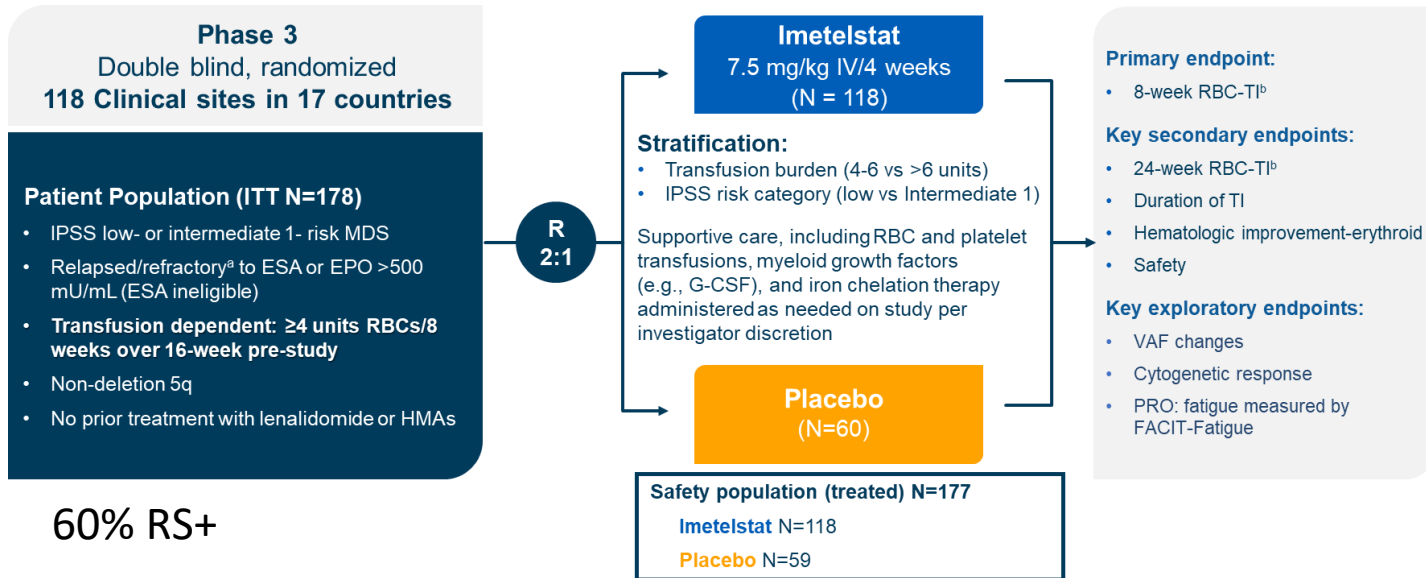
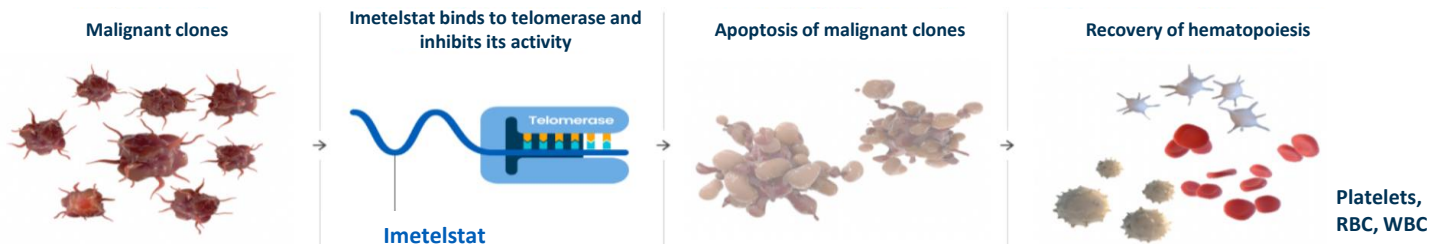


# Luspatercept for the treatment of transfusion-dependent anemia in patients with MDS with del 5q, refractory/resistant/intolerant to prior treatments (QOL-ONE PHOENIX)



- Eight patients (36%) achieved RBC-TI, with concurrent improvements in Hb levels, while maintaining a favorable safety profile
- notable improvement in QoL is reported

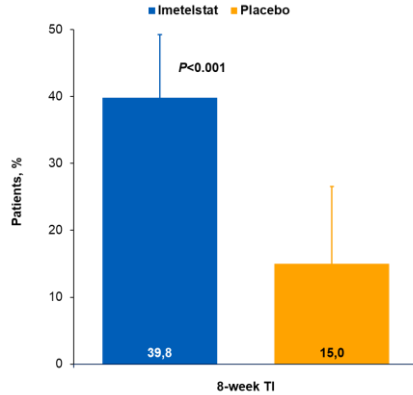
# Imetelstat in Lower Risk MDS: IMerge Phase 3 Trial Design



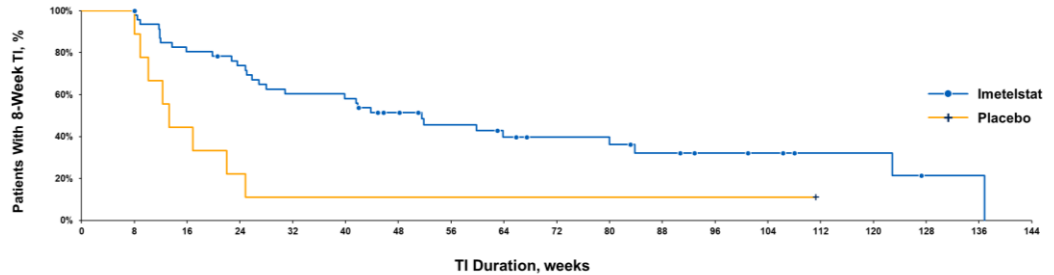
ESA, erythropoiesis-stimulating agent; HMA, hypomethylating agent; LR-MDS, lower risk myelodysplastic syndromes; RBC, red blood cell; TI, transfusion independence; WBC, white blood cell.

1. Asai A, et al. *Cancer Res.* 2003;63(14):3931-3939; 2. Herbert B-S, et al. *Oncogene.* 2005;24(33):5262-5268; 3. Mosoyan G, et al. *Leukemia.* 2017;31(11):2458-2467; 4. Wang X, et al. *Blood Adv.* 2018;2(18):2378-2388; 5. Steensma DP, et al. *J Clin Oncol.* 2021;39(1):48-56;

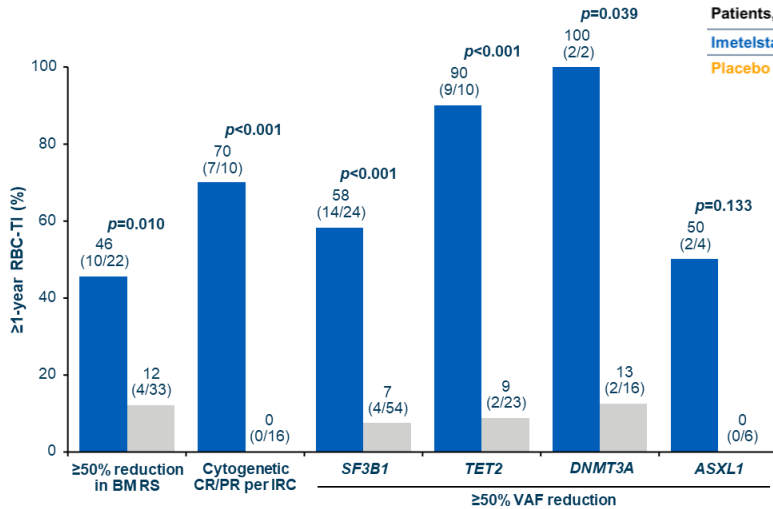
# Higher 8-Week RBC-TI Rate and Longer-Term Duration of RBC-TI with Imetelstat vs Placebo



8-Week TI Responders	Imetelstat (N=47)	Placebo (N=9)	HR (95%CI) <sup>a</sup>	P-Value <sup>b</sup>
Median duration of RBC-TI, weeks (95% CI)	51.6 (26.9–83.9)	13.3 (8.0–24.9)	0.23 (0.09–0.57)	<0.001



Patients, N	TI Duration, weeks																		
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				

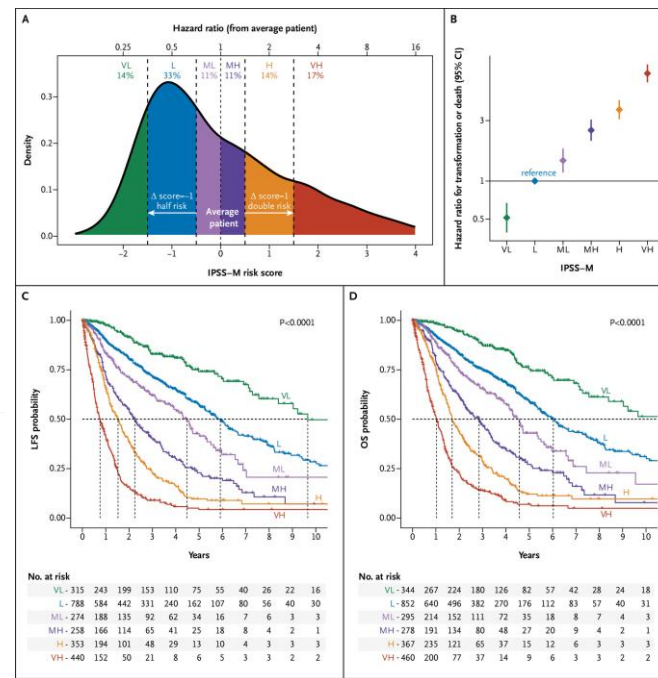
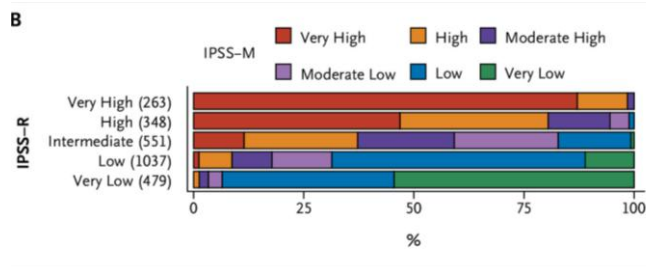


Imetelstat modulates clonal burden, which may suggest disease-modifying potential

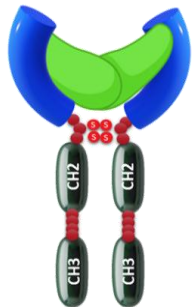
# ALLOGENEIC HSCT IN LOW-INT R-IPSS RISK MDS

## Current recommendation for allogeneic HSCT in lower-risk MDS:

- patients with severe cytopenia (including >2 RBC units per month or life-threatening cytopenias as ANC <0.3 X 10<sup>9</sup>/L or pls <30 X 10<sup>9</sup>/L)
- Patients with progressive disease
- **Patients in whom conventional treatment has failed.**
- Patients with additional unfavorable factors (MB fibrosis or unfavorable IPSS-M).



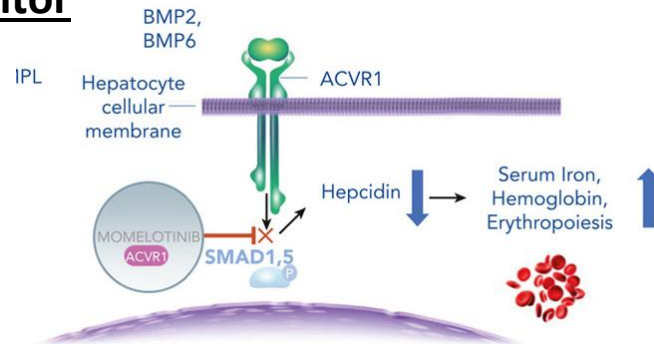
# What next?



## Elritercept (KER-050)

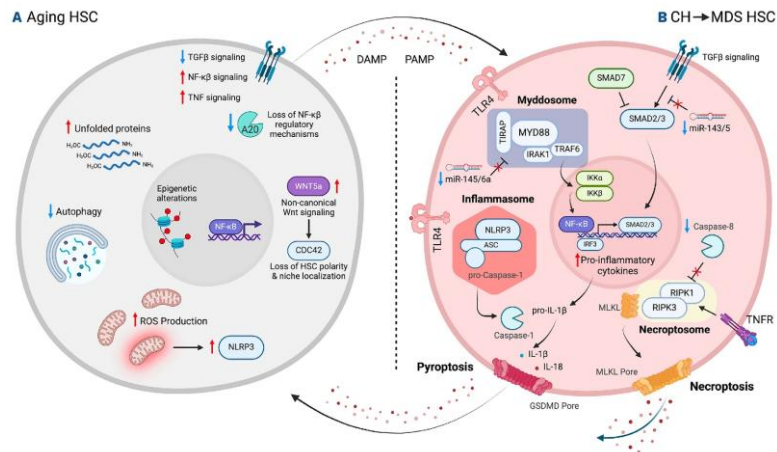
- Designed to inhibit select TGF-beta ligands, including **Activin A**, which has been associated with ineffective hematopoiesis, disease pathogenesis and progression<sup>1,2</sup>

## Momelotinib, a JAK1/JAK2/ACVR1 inhibitor



## Combination strategies:

- Luspatercept +EPO
- Luspatercept +momelotinib



- **Anemia is the prevalent cytopenia in MDS**
- **Anemia and transfusion dependence impact on OS and quality of life**
- **Anemia in MDS is still unmet clinical need as current available treatments (rEPO, luspatercept, lenalidomide, iron chelation) are limited**
- **Treatment of anemia should start early to avoid transfusions /reduce transfusion burden** (ongoing trial with luspatercept in NTD MDS)
- Transplant should be considered in eligible patients, integrating molecular data into treatment decision
- **Possible future perspectives:** therapeutic intervention aimed at restoring hematopoietic homeostasis in the aging population and potentially even preventing MDS ( inhibitors of inflammatory mediators, new targetable immune checkpoints..).

4<sup>th</sup> edition

Unmet challenges in high risk hematological malignancies: from benchside to clinical practice

## Candiolo Cancer Institute: Hematology Team



**Umberto Vitolo**  
MD



**Delia Rota  
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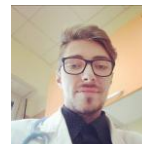
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Schianca**  
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**Marco Fizzotti**  
MD



**Mirko Frascione**  
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MD



**Francesca  
Bonello**  
MD



**Daniela Caravelli**  
MD



# THANK YOU

Turin, March 26-27, 2026  
Starhotels Majestic