FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

CONVEGNO FISiM

Firenze, CSF Montedomini
"Il Fuligno"
24-25 ottobre 2025

Treatment of lower-risk MDS with Lenalidomide and with Elritercept

GESMD

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Disclosures of María Díez Campelo

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
BMS			X			X	
NOVARTIS			X			X	
KEROS			X			X	
ABBIE			X				
GSK						X	
AGIOS			X				
SYROS			X				
CURIS						X	
ASTEX/OTSUKA			X				
CURIS			X			X	
ASCENTAGE FORTREA ASTRAZENECA			X				

- **Lenalidomide (Len) in del(5q)**
  - ✓ Role in transfusion dependent (TD) patients
  - ✓ Early approach in non-TD (NTD)
- **Elritercept**
  - ✓ Mechanism of action
  - ✓ Role in anemic patients
  - ✓ Other data in MDS patients
  - ✓ Next steps in LR-MDS patients

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  - ✓ **Role in transfusion dependent (TD) patients**
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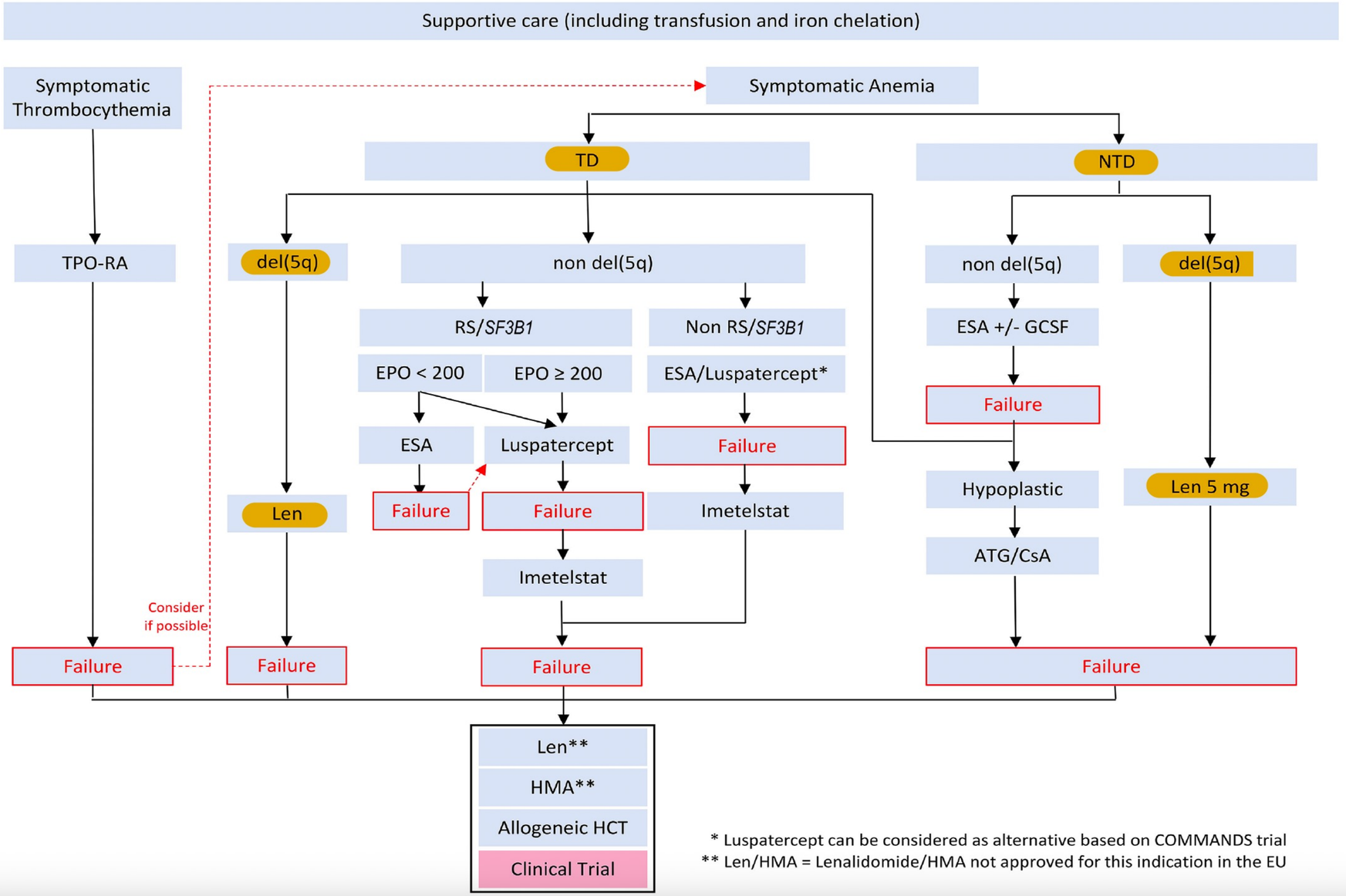
  - ✓ **Next steps in LR-MDS patients**

Treatment options for anemia in LR-MDS

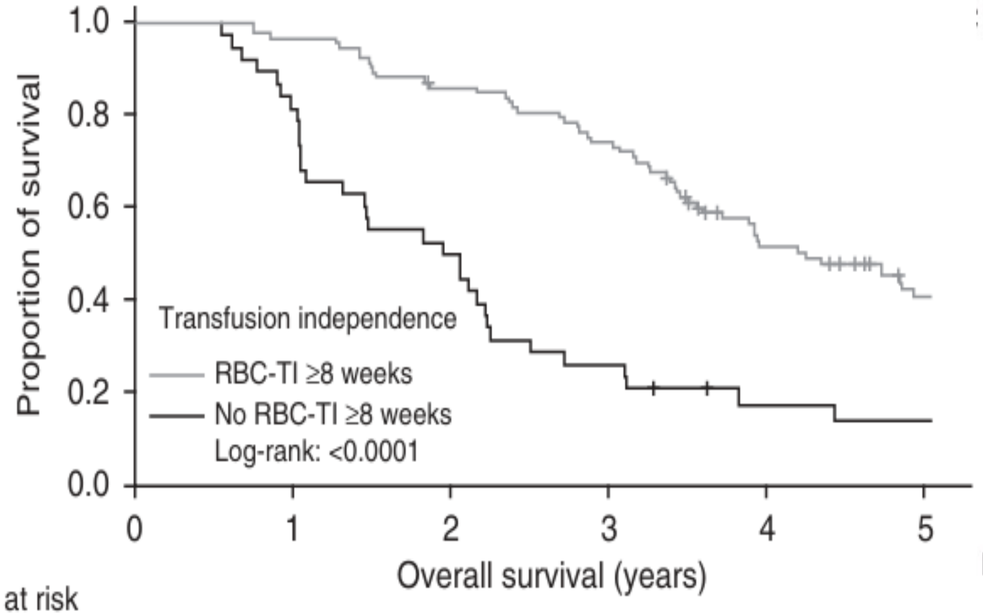
Len is the preferred treatment for symptomatic anemia



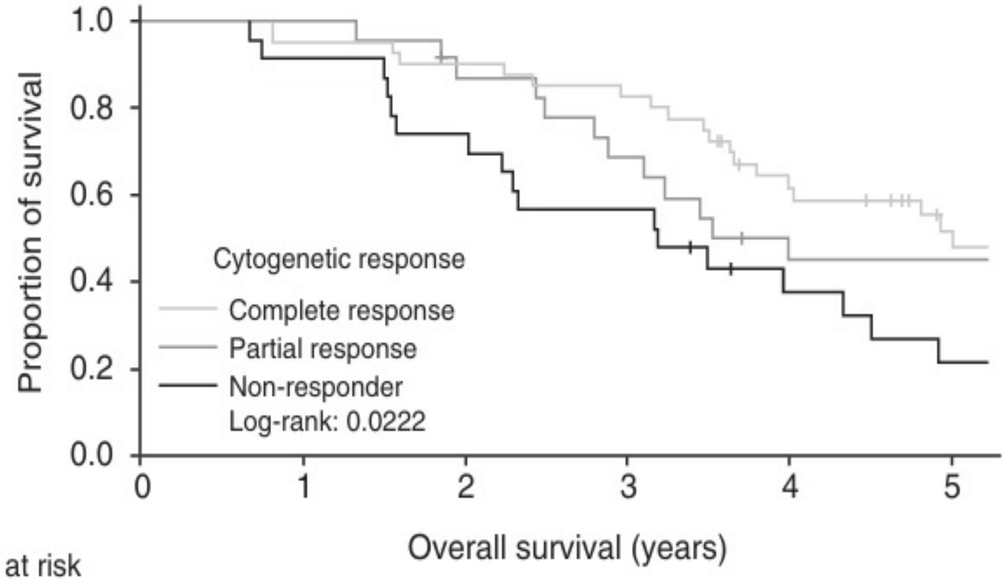
Almuth Maria Anni Merz and Uwe Platzbecker, Haematologica 2025

Len in TD MDS del(5q)

Amazing responses translated into an improved outcomes



No. of patients at risk						
RBC-TI ≥8 weeks	94	91	80	69	43	29
No RBC-TI ≥8 weeks	38	31	19	10	5	4



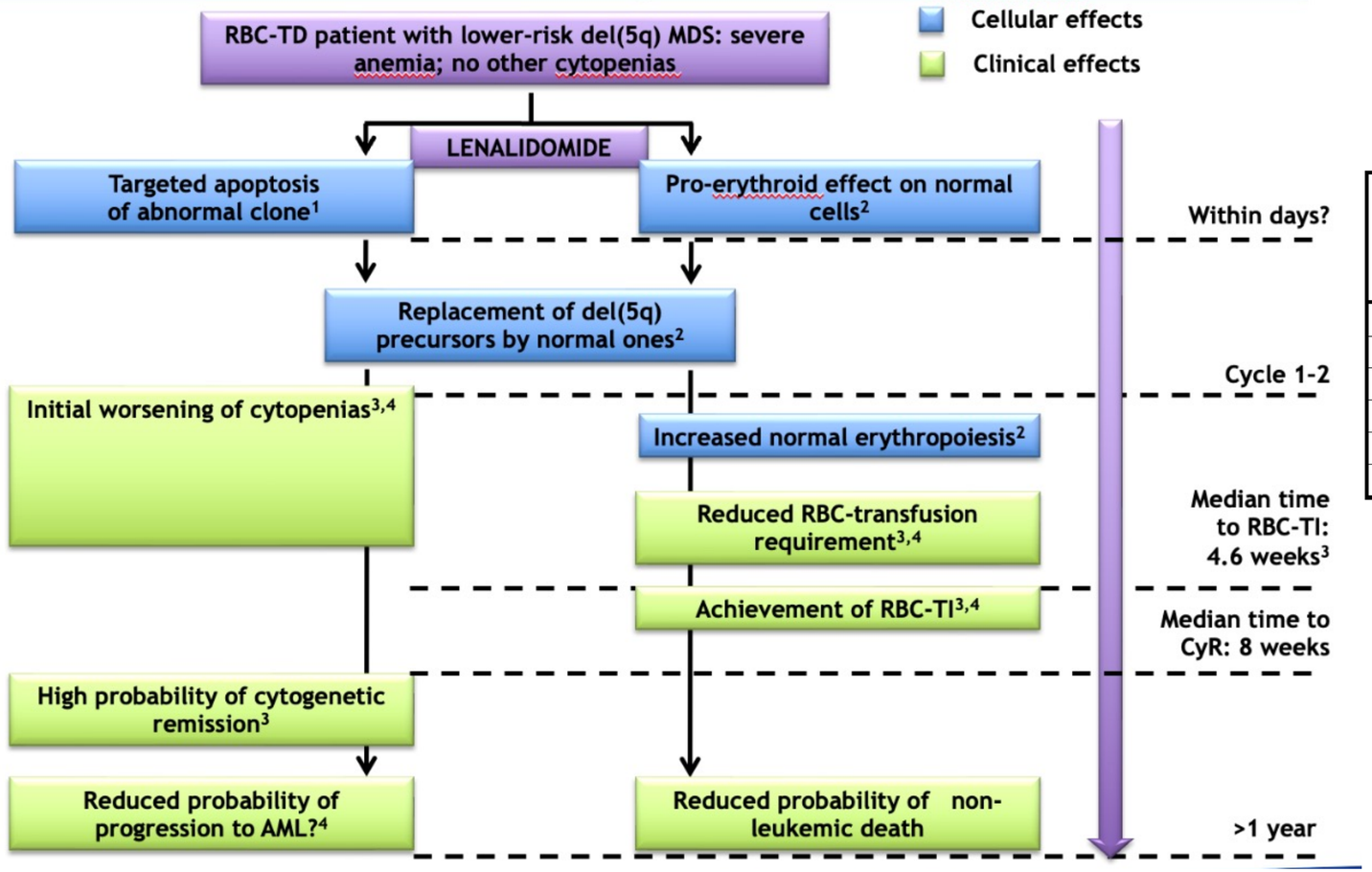
No. of patients at risk						
Complete response	40	38	36	33	21	13
Partial response	23	23	19	15	9	9
Non-responder	23	21	16	13	7	4

- ✓ **Cumulative incidence of AML at 3y 25.1% (lower in responders)**
- ✓ **Median OS 42.4 mo (increased if CyR & TI)**

List, NEJM 2006 *Fenaux, Blood 2011* *List, Leukemia 2014*

Len in TD MDS del(5q)

Adverse events related to targeted del(5q) clone



Most common (>5%) G3/4 adverse events reported

	Overall AEs in MDS-003 Study [17], *n* (%)	Drug-Related AEs in MDS-004 Study [18][a], *n* (%)		
	10 mg[b] (*N* = 148)	LEN 10 mg[c] (*n* = 69)	LEN 5 mg[d] (*n* = 69)	Placebo[d] (*n* = 67)
Neutropenia	81 (55)	52 (75)	51 (74)	10 (15)
Thrombocytopenia	65 (44)	28 (41)	23 (33)	1 (1)
Leukopenia	9 (6)	6 (9)	9 (13)	0 (0)
Anemia	10 (7)	2 (3)	4 (6)	6 (9)
Deep vein thrombosis	4 (3)	4 (6)	1 (1)	1 (1)
Rash	9 (6)	NA	NA	NA

Less frequent adverse events

- Hypothyroidism (6%)
- Secondary neoplasm

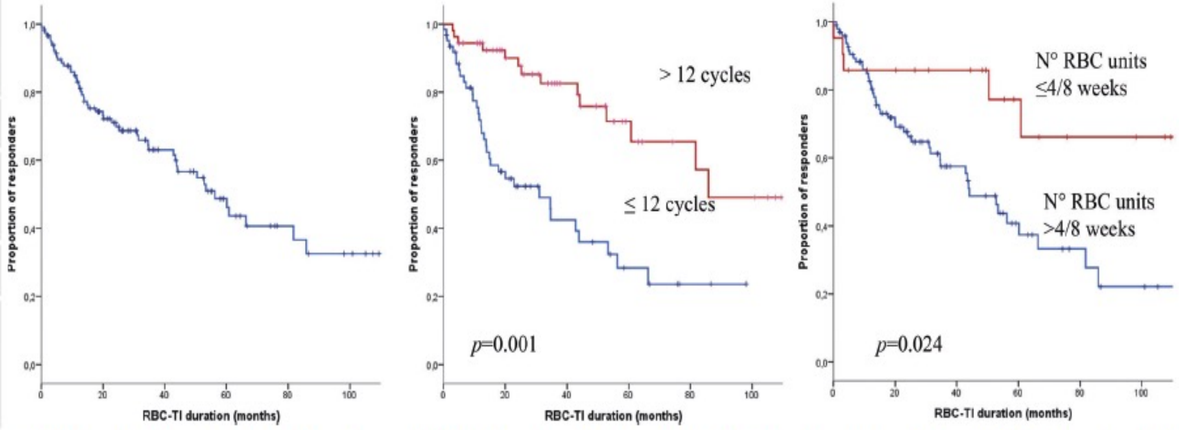
Giagounidis, Ann Hematol 2014 *Komrokji, Ann Oncol, 2015*

Len in TD MDS del(5q)

Discontinuation after therapy is associated with delayed loss of responses, benefit is still present after discontinuation

- ✓ European Retrospective cohort of 118 patients
- ✓ Reasons: intolerance (59%), medical (32%) & patient (8%) decision
- ✓ Lose TI 42.3 % (50/118) + CyR 73.3% (22/30)
- ✓ Median duration of TI after discontinuation 56 mo

Variables	HR	95,0% CI		
		Lower	Upper	*p* value
Age *	1.04	1.00	1.07	0.024
RBC unit/8 weeks >4 at lenalidomide start	3.34	1.18	9.47	0.024
Lenalidomide cycles ≥ 12	0.34	0.18	0.65	0.001
Hemoglobin level at lenalidomide discontinuation*	0.86	0.71	1.03	0.092

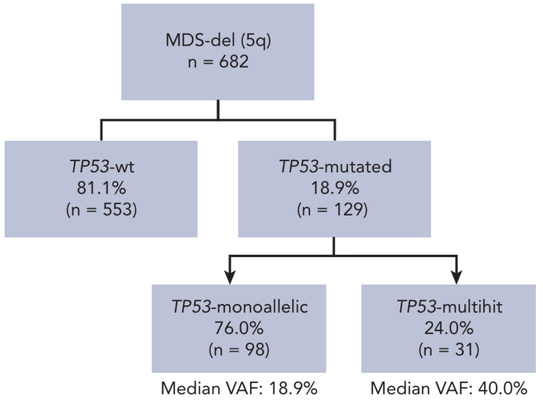


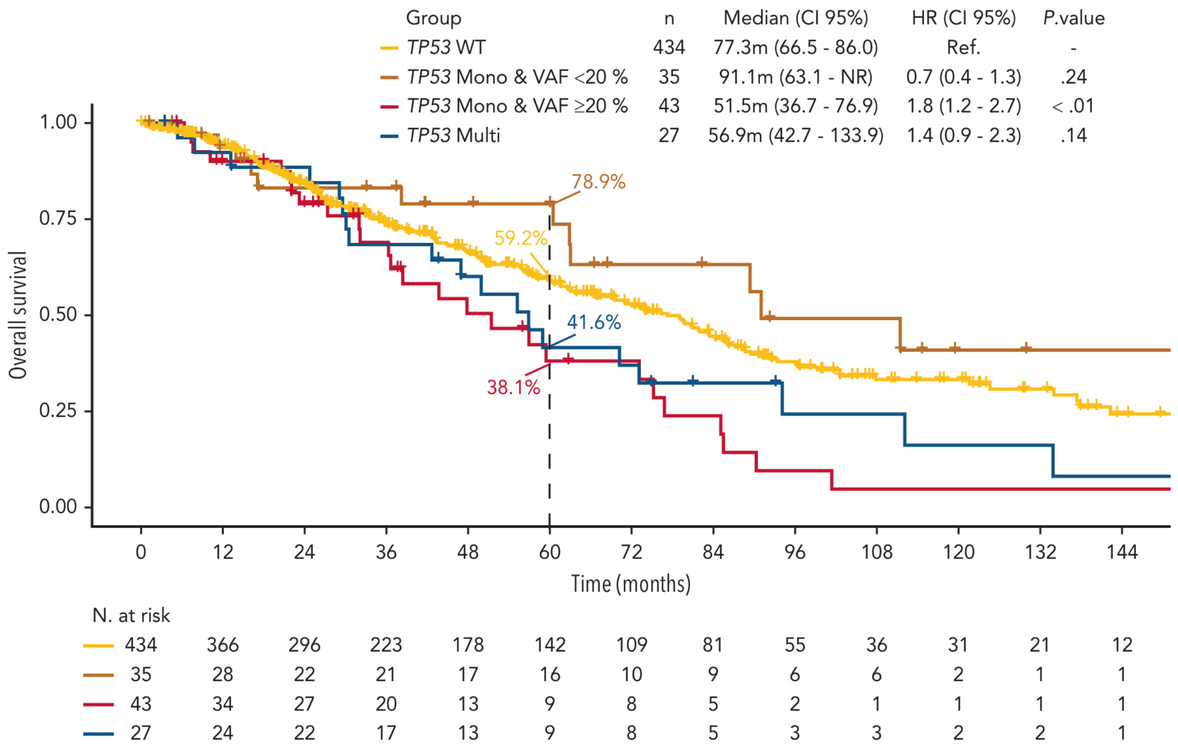
- ✓ Retreatment with Len reached IT in 58% of patients

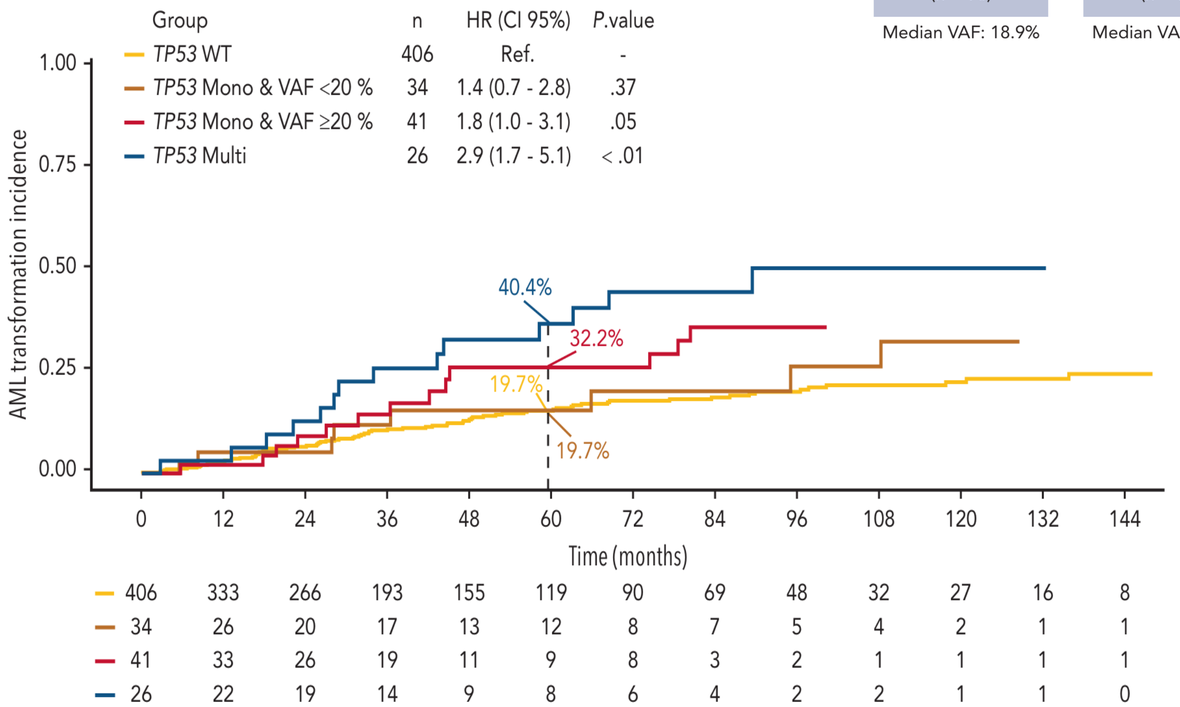
Crisa, Leukemia 2024

Len in TD MDS del(5q)

TP53 mutations reduce Len benefit & increase the risk of AML evolution







Jadersten, JCO 2011

Saft, Haematologica 2014

Mossmer, Leuk 2016

Mallo, BrJHaematol 2013

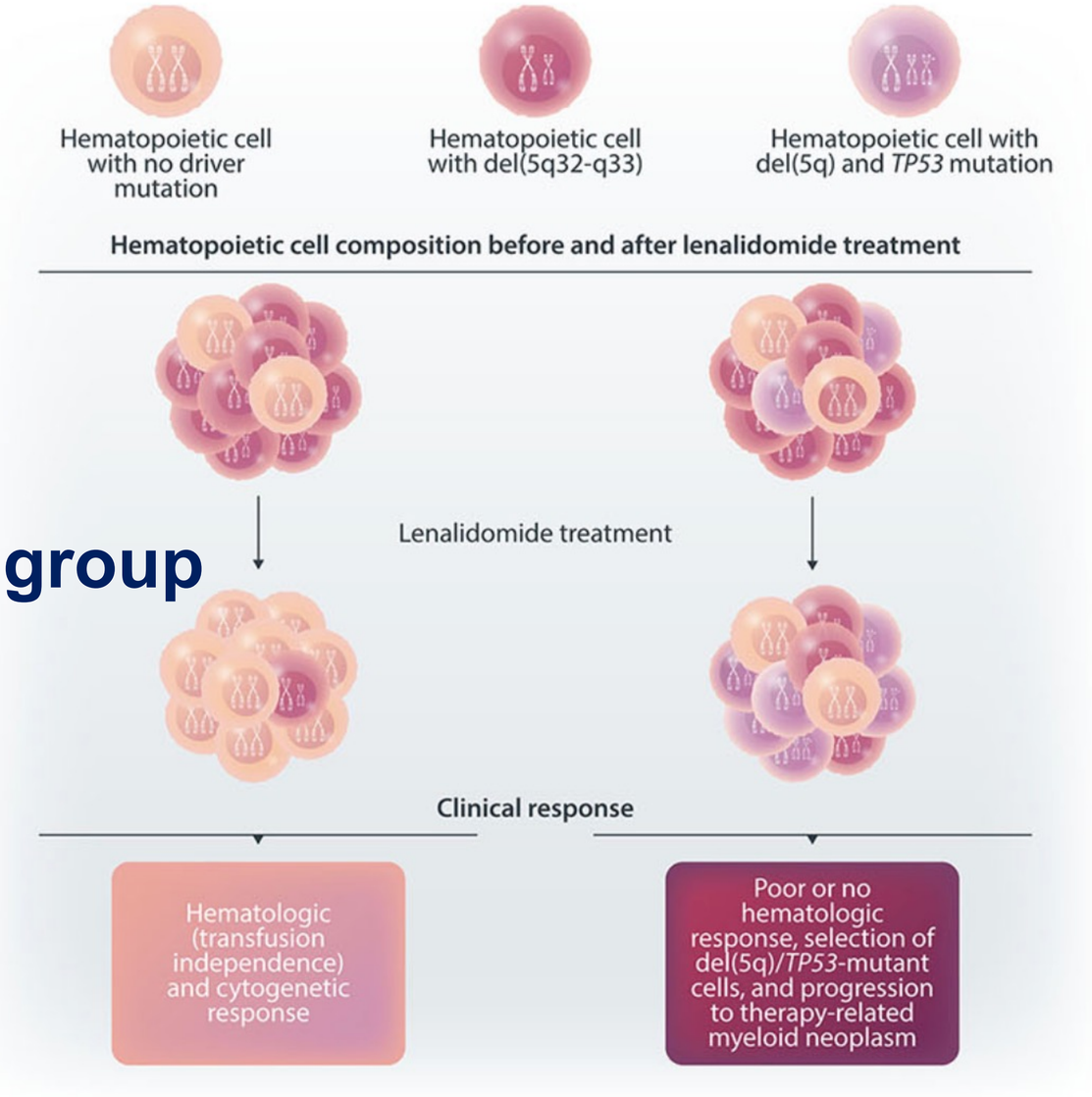
Tefferi, BrJH 2024

Montoro, Blood 2024

Len in TD MDS del(5q)

Len failure need to clear identify reasons and risk

- ✓50% after 2-3y
- ✓Resistance vs clonal evolution
- ✓No clinical trials in this setting
- ✓Luspa (NCT05924100) Italian MDS group
- ✓Azacitidine ORR 56%
- ✓Allo trasplant



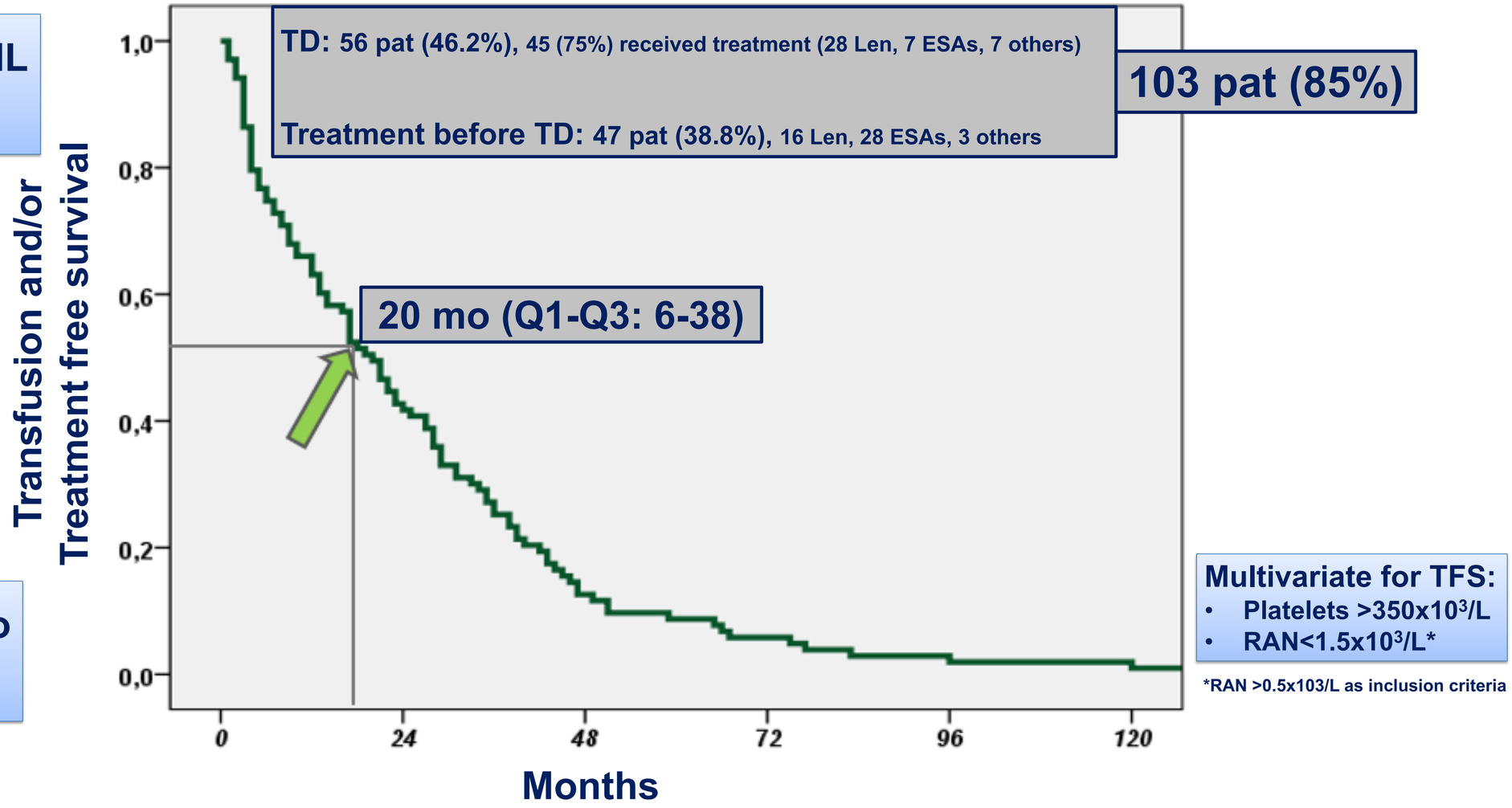
Komrokji, Blood 2011

Garderet, BBMT 2018

Len in Early approach in NTD MDS del(5q)

Spanish and Dusseldorf cohort identified shorter time for TD/need of treatment in NTD patients after diagnosis

- Median Hb 10.2 g/dL
  Q1-Q3 9.5-10.8 g/dL



- AML 23% at 35 mo
- Me OS 80 mo

Multivariate for TFS:
- Platelets >350x10^3/L
- RAN<1.5x10^3/L*

*RAN >0.5x103/L as inclusion criteria

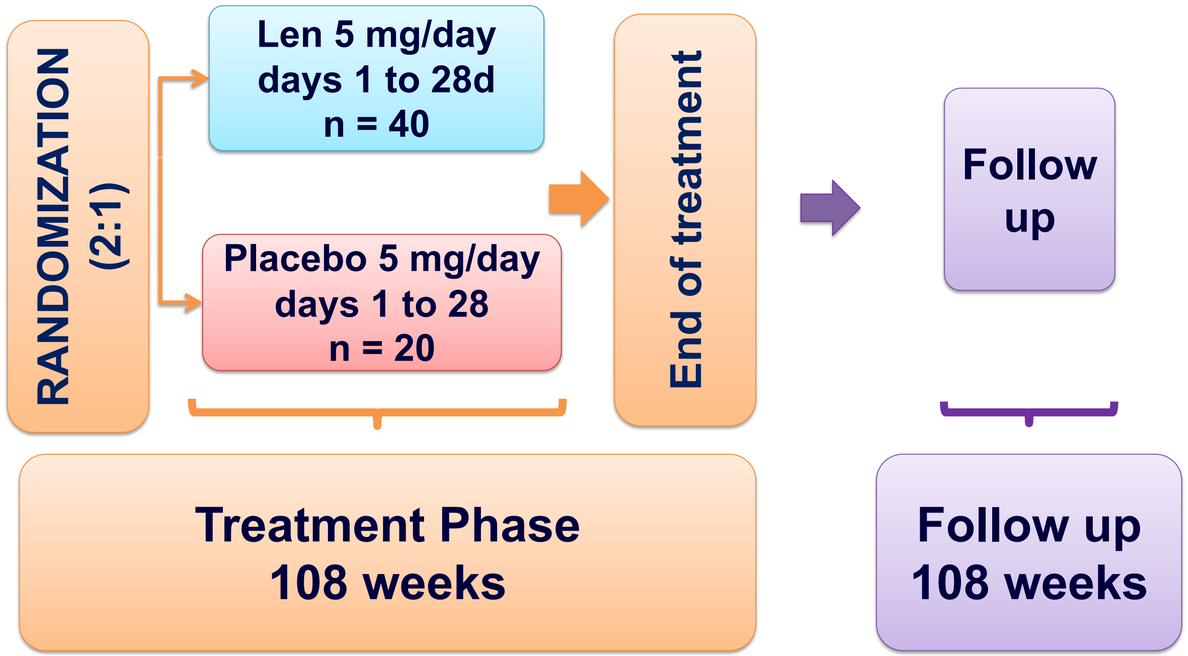
López Cadenas, manuscript in preparation

Len in Early approach in NTD MDS del(5q)

The Sintra-Rev trial is a phase 3, double-blind, randomized, placebo-controlled, multicenter study

Patient Population

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



1st patient: Feb 2010 — 120 months — 62nd patient: Feb 2018

MDS Disease Assessment after 12 weeks and every 6 months thereafter
Discontinue treatment if no clinical benefit and/or disease progression (TD) and/or unacceptable toxicity
No crossover allowed

Díez Campelo & López Cadenas, Lancet Haematology 2024

Len in Early approach in NTD MDS del(5q)

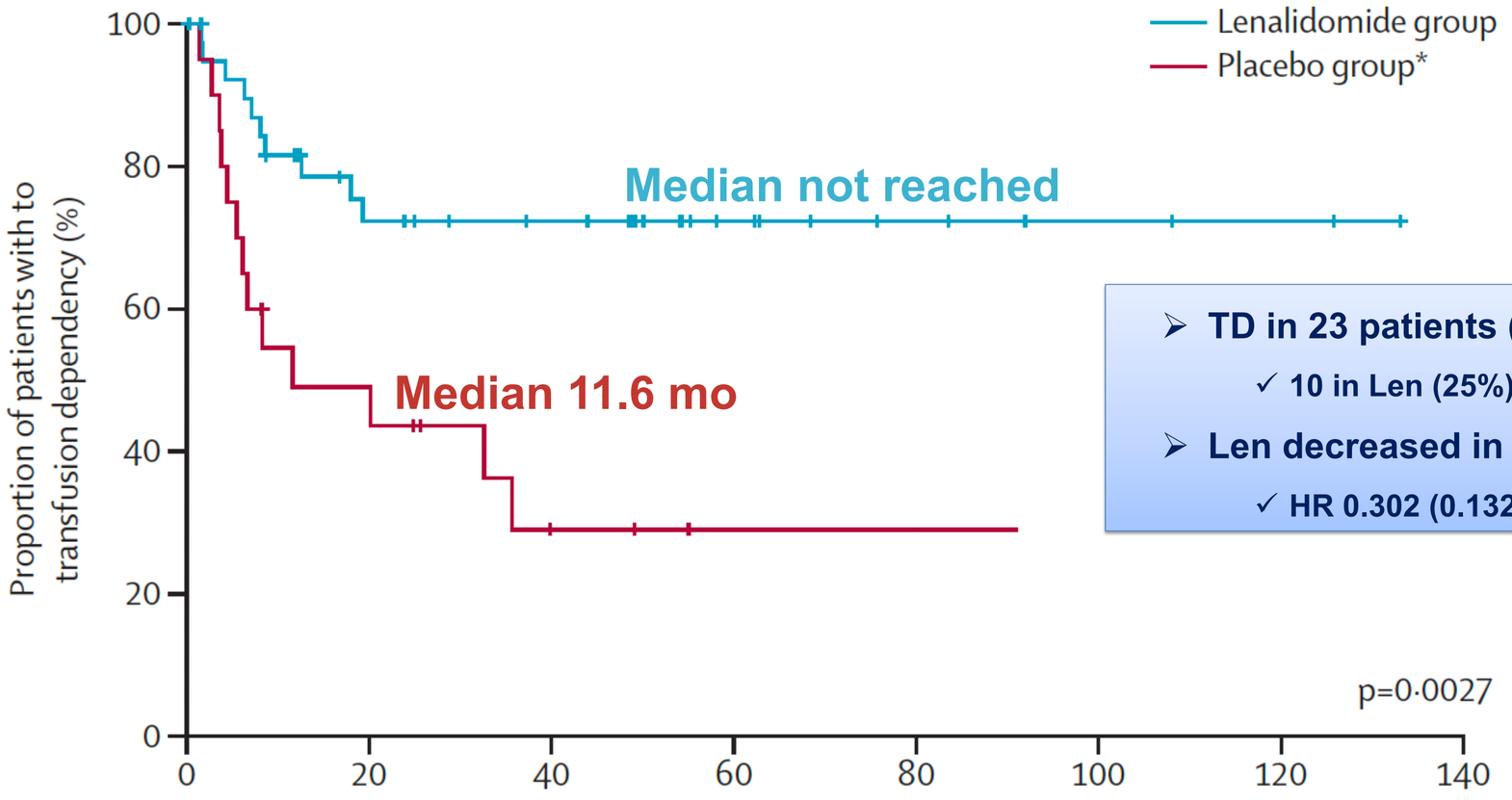
Patients presented symptomatic anemia and no other adverse features

	Total (n=61)	Lenalidomide group (n=40)	Placebo group (n=21)
Age, years	72·2 (65·4–81·9)	72·2 (65·0–82·4)	71·9 (64·7–80·7)
Sex			
Male	11 (18%)	8 (20%)	3 (14%)
Female	50 (82%)	32 (80%)	18 (86%)
ECOG performance status			
0	32 (52%)	21 (53%)	11 (52%)
1	29 (48%)	19 (48%)	10 (48%)
Time from diagnosis,* months	3·6 (1·0–12·1)	2·6 (0·9–11·3)	4·0 (1·7–13·6)
Haemoglobin, g/dL	9·8 (9·1–10·5)	9·8 (9·3–10·7)	9·8 (8·9–10·2)
Neutrophils, $\times 10^9$ cells per L	2·2 (1·5–2·8)	2·1 (1·5–3·2)	2·2 (1·5–2·7)
Platelets $\times 10^9$ cells per L	243 (181–317)	238 (171–312)	272 (200–327)
% of blasts in peripheral blood smears	0 (0–0)	0 (0–0)	0 (0–0)
% of blasts in bone marrow aspirates	1·5 (0·3–3·0)	1·5 (0·6–3·0)	2·0 (0·0–3·0)
IPSS risk category			
Low	43 (70%)	29 (73%)	14 (67%)
Intermediate-1	18 (30%)	11 (28%)	7 (33%)
IPSS-R risk category			
Very low	33 (54%)	25 (63%)	8 (38%)
Low	27 (44%)	15 (38%)	12 (57%)
Intermediate	1 (2%)	0	1 (5%)
IPSS-mol† risk category			
Very low	8/47 (17%)	5/29 (17%)	3/18 (17%)
Low	33/47 (70%)	20/29 (69%)	13/18 (72%)
Moderate low	4/47 (9%)	2/29 (7%)	2/18 (11%)
Moderate high	2/47 (4%)	2/29 (7%)	0

Díez Campelo & López Cadenas, Lancet Haematology 2024

Len in Early approach in NTD MDS del(5q)

Low doses of Len delayed and decreased transfusion dependency



Number at risk (number censored)								
Lenalidomide group	40 (7)	23 (11)	19 (21)	9 (25)	5 (27)	3 (28)	2 (30)	0 (0)
Placebo group	20 (1)	9 (4)	3 (6)	1 (6)	1 (7)	0 (0)	0 (0)	0 (0)

- **TD in 23 patients (38.3%)**
  - ✓ **10 in Len (25%) vs 13 in placebo (65%)**
- **Len decreased in 69.8% the risk of TD**
  - ✓ **HR 0.302 (0.132-0.692), p=0.005**

Díez Campelo & López Cadenas, Lancet Haematology 2024

Len in Early approach in NTD MDS del(5q)

Low doses of Len reached Erythroid and Cytogenetic responses

- **Erythroid response with Len**
  - ✓ w12: 65.6%
  - ✓ Overall: 77.8%
  - ✓ Median Hb increase +2.6 g/dL (EOT visit)
  - ✓ No ER in placebo arm
- **Cytogenetic response with Len**
  - ✓ w12: 79.3%, 58.6% complete + 20.6% partial
  - ✓ Overall: 94.1%, 87.5% complete + 12.5% partial
  - ✓ No CyR in placebo arm

Díez Campelo & López Cadenas, Lancet Haematology 2024

Len in Early approach in NTD MDS del(5q)

Low doses of Len are safe and well tolerated, induced not clinically relevant neutropenia

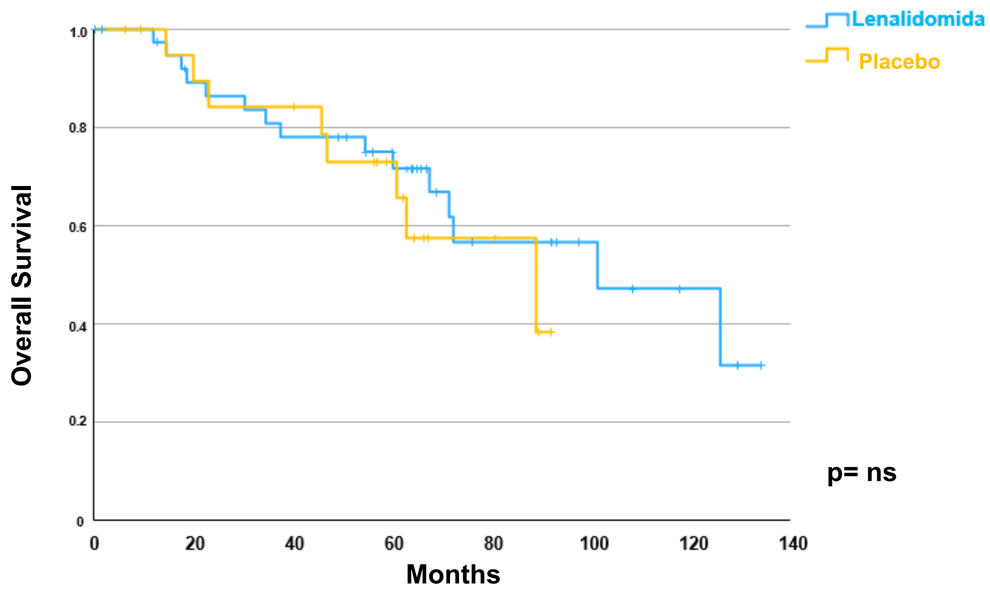
	Grade 1–2*		Grade 3		Grade 4	
	Lenalidomide group (n=38)	Placebo group (n=21)	Lenalidomide group (n=38)	Placebo group (n=21)	Lenalidomide group (n=38)	Placebo group (n=21)
Haematological toxicity						
Neutropenia	6 (16%)	3 (14%)	17 (45%)	1 (5%)	1 (3%)	0
Thrombocytopenia	5 (13%)	0	2 (5%)	0	0	0
Anaemia	3 (8%)	0	1 (3%)	0	0	0
Leukopenia	4 (11%)	0	0	0	0	0
Febrile neutropenia	0	0	1 (3%)	0	0	0
Non-haematological toxicity						
Abdominal pain or discomfort	5 (13%)	1 (5%)	0	0	0	0
Constipation	7 (18%)	0	0	0	0	0
Paraesthesia or dysesthesia	4 (11%)	0	0	0	0	0
Rash or erythema	9 (24%)	3 (14%)	1 (3%)	0	0	0
Pulmonary embolism	0	1 (5%)	1 (3%)	0	0	0
Lung adenocarcinoma†	0	0	1 (3%)	0	0	0
Brain metastases†	0	0	0	0	1 (3%)	0
Asthenia	4 (11%)	2 (10%)	0	0	0	0

Díez Campelo & López Cadenas, Lancet Haematology 2024

Len in Early approach in NTD MDS del(5q)

Low doses of Len did not increase AML evolution

- ✓**Median overall survival 8.4y (no deaths related)**
  - Len 15 pts (37.5%)
  - Placebo 8 pts (38.1%)
- ✓**AML in 11 patients (18%)**
  - Len 6 pts (15%)
    - me 4.3y
    - 2/6 (33.3%) *TP53^{mut}*
    - 2/6 (33.3%) *SF3B1^{mut}*
  - Placebo 5 pts (23.8%)
    - me 4.5y
    - 1/5 (20%) *TP53^{mut}*
    - 2/5 (40%) *SF3B1^{mut}*
- ✓ **PFS 6.8y Len vs 5.3y PBO**
- ✓ **EFS 6.8y Len vs 1.68y PBO**



Patient at risk								
Lenalidomida	40	32	28	22	10	6	3	0
Placebo	21	18	16	10	4	0	0	0

Díez Campelo & López Cadenas, Lancet Haematology 2024

Len in Early approach in NTD MDS del(5q)

Long term FU of patients

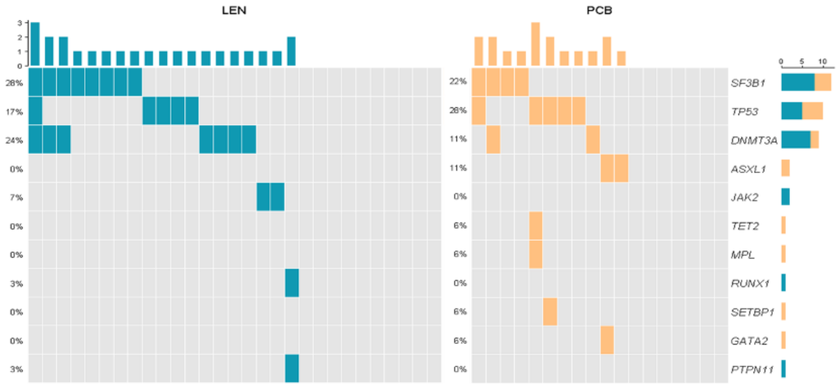
- ✓15 Len patients completed EOE perfect
- ✓received 2y of Len + 2y of FU wo any treatment
- ✓Median FU 30 mo
- ✓No TD in any patient:
  - -80% (12/15) with no treatment
  - -20% received Len (3/12) after 31 mo of EOE
- ✓No SAEs in long term FU

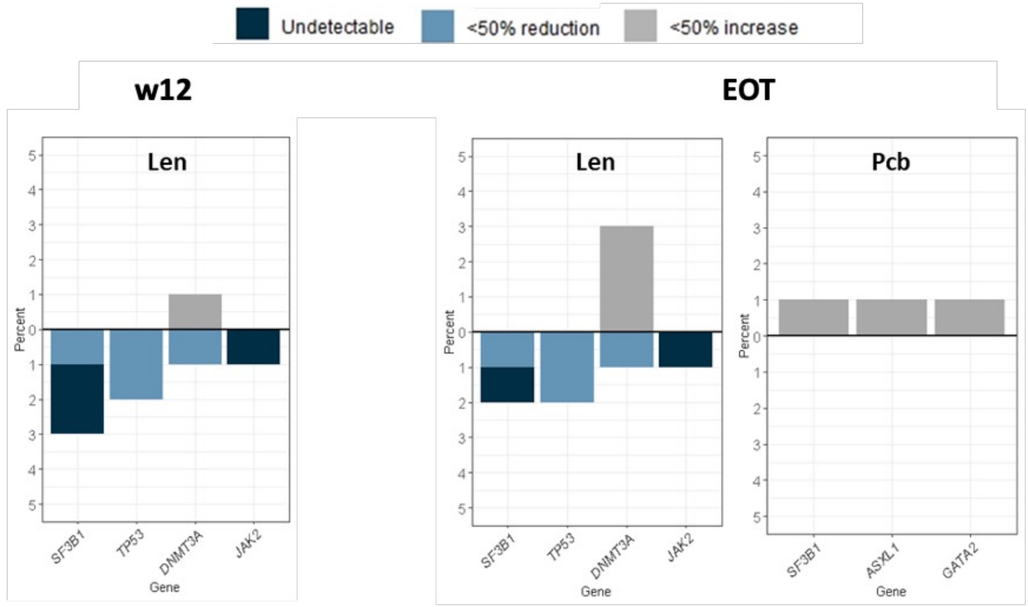
Díez Campelo & López Cadenas, Lancet Haematology 2024

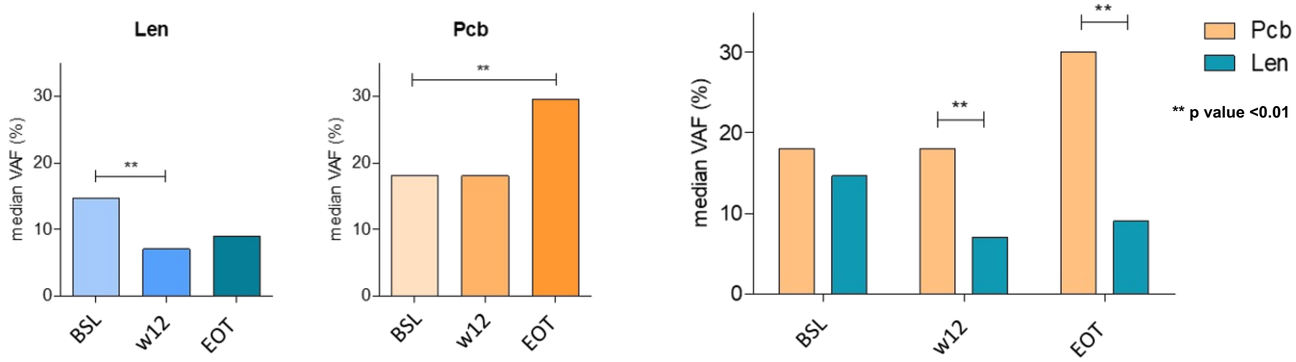
Len in Early approach in NTD MDS del(5q)

Len decreased clonal size while remain stable/increase in PBO

	Total (n=61)	Lenalidomide group (n=40)	Placebo group (n=21)
Next-generation sequencing available data at diagnosis†			
0 mutations	17/47 (36%)	10/29 (35%)	7/18 (39%)
1 mutation	21/47 (45%)	15/29 (52%)	6/18 (33%)
≥2 mutations	9/47 (19%)	4/29 (14%)	5/18 (28%)
TP53 status (at diagnosis)†			
TP53mut (all monoallelic)	10/47 (21%)	5/29 (17%)	5/18 (28%)
Median *TP53* variant allelic frequency (%) and range	22 (5–40)	14 (13–23)	29 (5–40)
TP53wt	37/47 (79%)	24/29 (83%)	13/18 (72%)
SF3B1 status (at diagnosis)†			
SF3B1mut	12/47 (26%)	8/29 (28%)	4/18 (22%)
SF3B1wt	35/47 (75%)	21/29 (73%)	14/18 (78%)







Díez Campelo & López Cadenas, Lancet Haematology 2024

Toribio & Díez Campelo, under review

Len in Early approach in NTD MDS del(5q)

Somatic mutations impact on response and outcomes

RESPONSES	*SF3B1^{MUT}*	*TP53^{MUT}*
Number of patients	12	10
Erythroid response	100%	40%
Cytogenetic response	100%	60%
Duration of response	Shorter	Similar
Transfusion Dependence	37.5% Len & 100% PBO	80% Len & 60%PBO
Time to TD (median)	21.8mo Len & 6.3mo PBO	12.6mo Len & 6.6mo PBO
AML	25% Len & 50% PBO	20% Len & 20% PBO
Time to AML (median)	24mo Len & 16mo PBO	NR/NR

Díez Campelo & López Cadenas, Lancet Haematology 2024

Toribio & Díez Campelo, under review

CURRENT MANAGEMENT OF ANEMIA IN MDS del(5q) PATIENTS IN 2025

2025 personal approach

- **Symptomatic anemia: treat**
- **NTD**
  - **LEN**
    - **Low doses of Len (5 mg/d) x 2y**
    - **NGS mandatory at baseline and during FU**
    - ***TP53*$^{mono\ mut}$: lower responses and risk of AML**
    - ***SF3B1*^{mut}: lower DOR and risk of AML**
  - **ESAs**
    - **if not Len candidates**
    - **low eEPO & isol del(5q)**
    - **shorter DOR**

CURRENT MANAGEMENT OF ANEMIA IN MDS del(5q) PATIENTS IN 2025

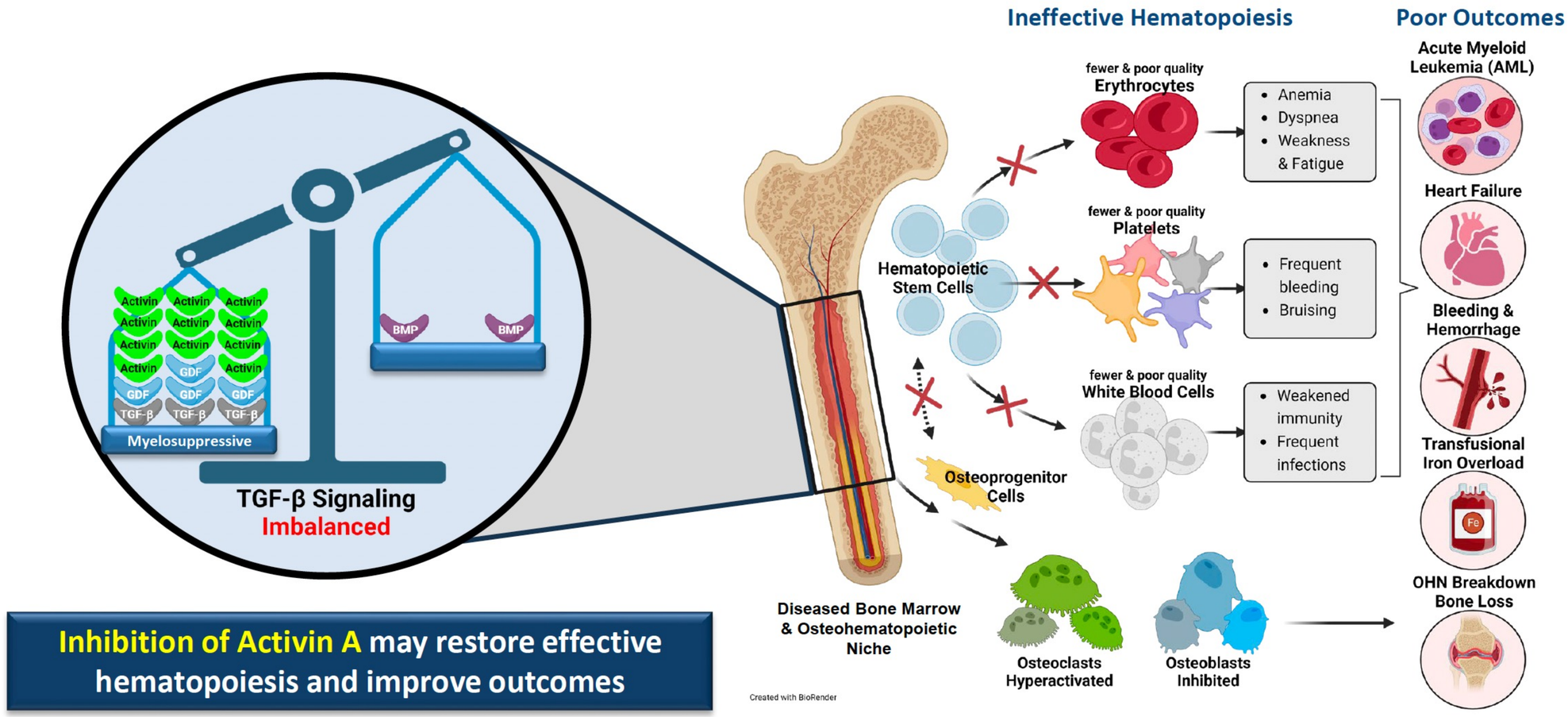
2025 personal approach

- **TD**
  - **Len 10 mg/d x 21 d**
  - ***TP53*^{mut} mandatory: caution in *TP53*^{multihit} patients**
  - ***SF3B1*^{mut} mandatory: shorter DOR and risk of AML**
  - **Discontinuation:** intolerance, in selected patients?
  - **If no response & after failure: confirmed prognosis**

- Lenalidomide (Len) in del(5q)
  - ✓ Role in transfusion dependent (TD) patients
  - ✓ Early approach in non-TD (NTD)
- **Elritercept**
  - ✓ **Mechanism of action**
  - ✓ **Role in anemic patients**
  - ✓ **Other data in MDS patients**
  - ✓ **Next steps in LR-MDS patients**

KER050 for anemia in LR-MDS

Imbalanced TGF-β Signaling in Bone Marrow Results in Ineffective Hematopoiesis and Poor Outcomes in Myelodysplastic Syndromes (MDS)[1,2]



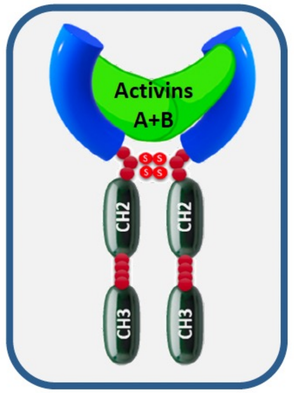
Inhibition of Activin A may restore effective hematopoiesis and improve outcomes

American Society of Hematology

[1]Verma A, et al. *J Clin Inv* 2020
[2]Portale F, et al., *Haematologica*. 2019
BMP = bone morphogenetic protein; GDF = growth differentiation factor; TGF-β = transforming growth factor-β

KER050 for anemia in LR-MDS

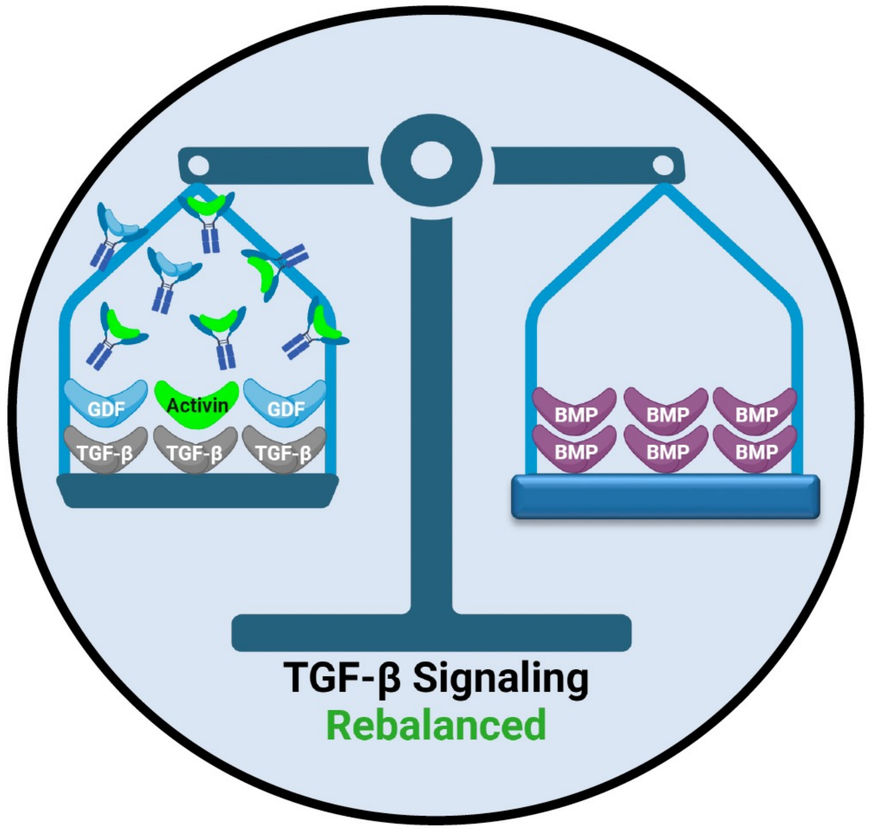
KER-050 (elritercept) is Designed to Target Bone Marrow Disorders of Ineffective Hematopoiesis Including MDS



KER-050 (elritercept)

- Designed to inhibit select TGF-beta ligands, including Activin A, which has been associated with ineffective hematopoiesis, disease pathogenesis and progression[1,2]

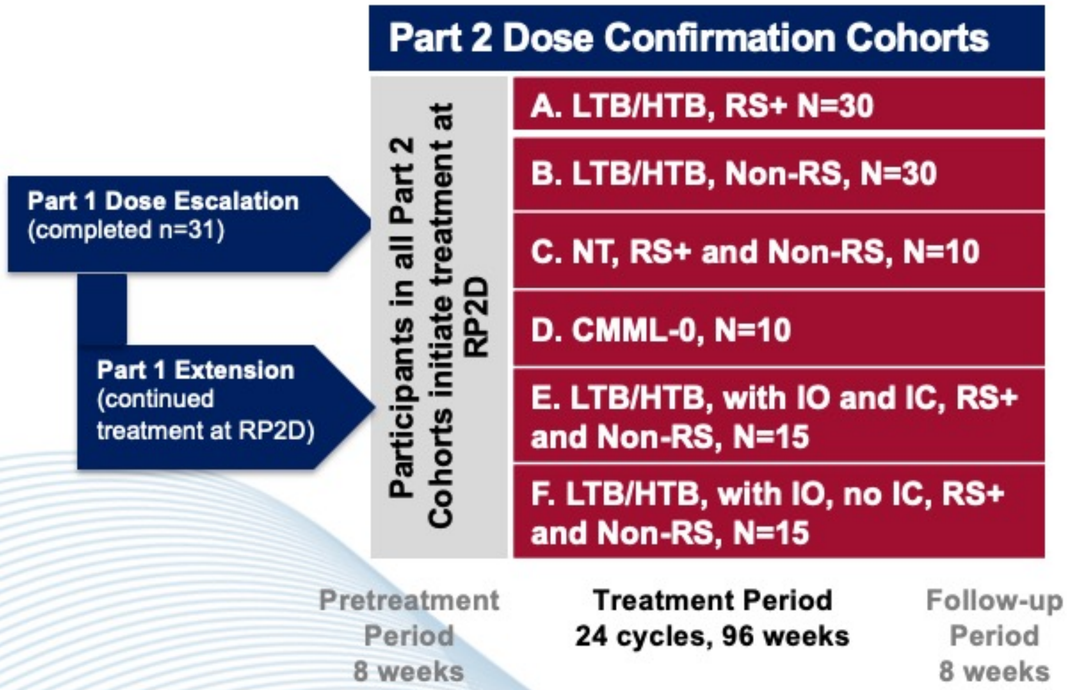
Domain	Effect
Erythropoiesis	ALL stages of differentiation and maturation
Thrombopoiesis	ALL stages of differentiation and maturation
Bone	Increased bone formation
Iron Metabolism	Improved iron utilization



[1]Verma A, et al. *J Clin Inv* 2020
[2]Portale F, et al., *Haematologica*. 2019
BMP = bone morphogenetic protein; GDF = growth differentiation factor; TGF-β = transforming growth factor-β

KER050 for anemia in LR-MDS

3.75-5 mg/Kg Sc every 4w



Key Eligibility Criteria

- MDS per 2016 WHO criteria, RS+ or non-RS, very-low, low-, or intermediate-risk disease (LR-MDS) by IPSS-R with anemia (NT, LTB, HTB)
  - CMML in Cohort D

Primary Objective

- Safety and tolerability

Secondary Endpoints include

- Modified 2006 IWG Hematological Improvement-Erythroid (HI-E)
- Transfusion independence (TI) ≥8 weeks

Status as of Data Cutoff Date

- Part 1 Extension ongoing
- RP2D: 3.75 mg/kg with titration to 5 mg/kg Q4W
- Part 2 Dose Confirmation ongoing and enrolling

Díez Campelo, EHA 2024

KER050 for anemia in LR-MDS

Responders/N (%)	mITT$_{24}$[a]		mITT$_{24}$ + EPO < 500 U/L[b]	
	All (N=81)	HTB (N=46)	All (N=66)	HTB (N=35)
Overall Response[c]	**45/81 (55.6)**	**23/46 (50.0)**	**40/66 (60.6)**	**20/35 (57.1)**
Modified IWG 2006 HI-E[d]	**40/81 (49.4)**	**22/46 (47.8)**	**35/66 (53)**	**19/35 (54.3)**
RS+	33/57 (57.9)	19/33 (57.6)	29/51 (56.9)	16/29 (55.2)
non-RS	7/24 (29.2)	3/13 (23.1)	6/15 (40)	3/6 (50)
TI ≥8 weeks[e]	**26/63 (41.3)**	**16/46 (34.8)**	**25/50 (50.0)**	**15/35 (42.9)**
RS+	**22/45 (48.9)**	**13/33 (39.4)**	**21/40 (52.5)**	**12/29 (41.4)**
non-RS	**4/18 (22.2)**	**3/13 (23.1)**	**4/10 (40)**	**3/6 (50)**

HI-E and TI response rates in mITT$_{24}$ participants with HTB were similar to those observed in the overall mITT$_{24}$ population, supporting the potential for elritercept (KER-050) to treat a broad array of patients with LR-MDS including those with greater bone marrow dysfunction

Díez Campelo, EHA 2024

KER050 for anemia in LR-MDS

- Most frequent TEAEs (in ≥ 15% of participants regardless of causality were:
  - Diarrhea (24; 27.6%)
  - Fatigue (22; 25.3%)
  - Dyspnea (18; 20.7%)
  - Dizziness (17; 19.5%)
  - COVID-19 & Nausea (16; 18.4% each)
  - Anemia (15; 17.2%)
- Majority of the TEAEs were mild (Gr 1) to moderate (Gr 2)
- 4 treatment-related TESAEs of Injection site reaction (Gr 2), Dyspnea (Gr 3), Syncope (Gr 3) and Gastric neoplasm (Gr 3) occurred in 1 participant each
  - Gastric neoplasm, Dyspnea and Syncope were assessed as not related to study treatment by the Sponsor due to underlying co-morbidities
- Fatal TEAEs (Cardiac failure, MI and Sudden death) occurred in 3 (3.4%) participants; all were assessed as not related by both the PI and the Sponsor
- No participants progressed to AML

Category	RP2D (N=87) n (%)
Any TEAE	85 (97.7)
Any treatment-related TEAE	37 (42.5)
Any TESAE	38 (43.7)
Any treatment-related TESAE	4 (4.6)
Any TEAE leading to death	3 (3.4)
Any TEAE leading to KER-050 discontinuation	13 (14.9)

***Treatment-related TEAEs leading to KER-050 discontinuation: ISR, Platelet count increased, and Dyspnoea**
Unrelated TEAEs leading to KER-050 discontinuation: Nodular melanoma, NSCLC, MI, Dementia Alzheimer's type, Dyspnoea, Cardiac failure, and COPD and Cardiac failure congestive (both in 1 participant)

Treatment-related = considered to be related to the study treatment by the treating investigator.
Number and percent of participants with events were summarized.

Díez Campelo, EHA 2024

KER050 for anemia in LR-MDS

Updated results in 2025, confirmed benefit in HTB and non-RS

Hematological responses observed in broad array of participants

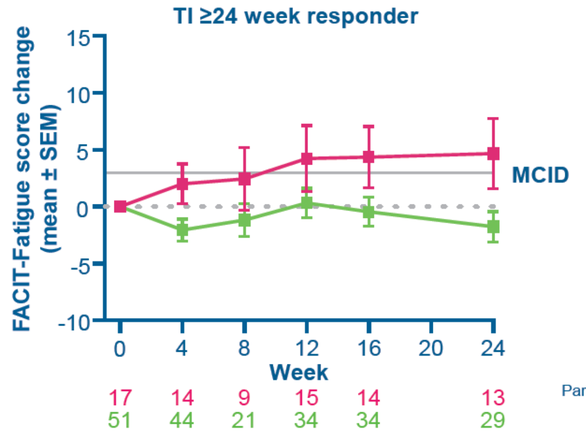
Responders/N (%)	$mITT_{24}$[a]		$mITT_{24}$ + EPO n <500 U/L[b]	
	All (N=87)	HTB (N=51)	All (N=71)	HTB (N=39)
Overall response[c]	48/87 (55.2)	25/51 (49.0)	43/71 (60.6)	22/39 (56.4)
Modified IWG 2006 HI-E[d]	42/87 (48.3)	24/51 (47.1)	37/71 (52.1)	21/39 (53.8)
RS+	33/59 (55.9)	19/35 (54.3)	29/52 (55.8)	16/30 (53.3)
Non-RS	9/28 (32.1)	5/16 (31.3)	8/19 (42.1)	5/9 (55.6)
TI ≥8 weeks	27/69 (39.1)	16/51 (31.4)	26/55 (47.3)	15/39 (38.5)
RS+	22/47 (46.8)	13/35 (37.1)	21/41 (51.2)	12/30 (40.0)
Non-RS	5/22 (22.7)	3/16 (18.8)	5/14 (35.7)	3/9 (33.3)

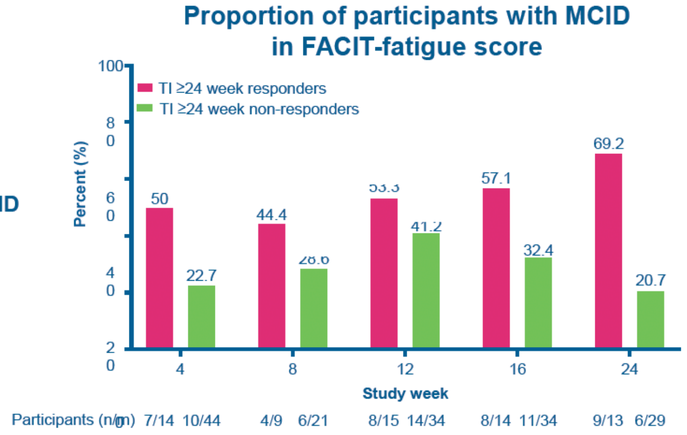
Giagounidis, EHA 2025

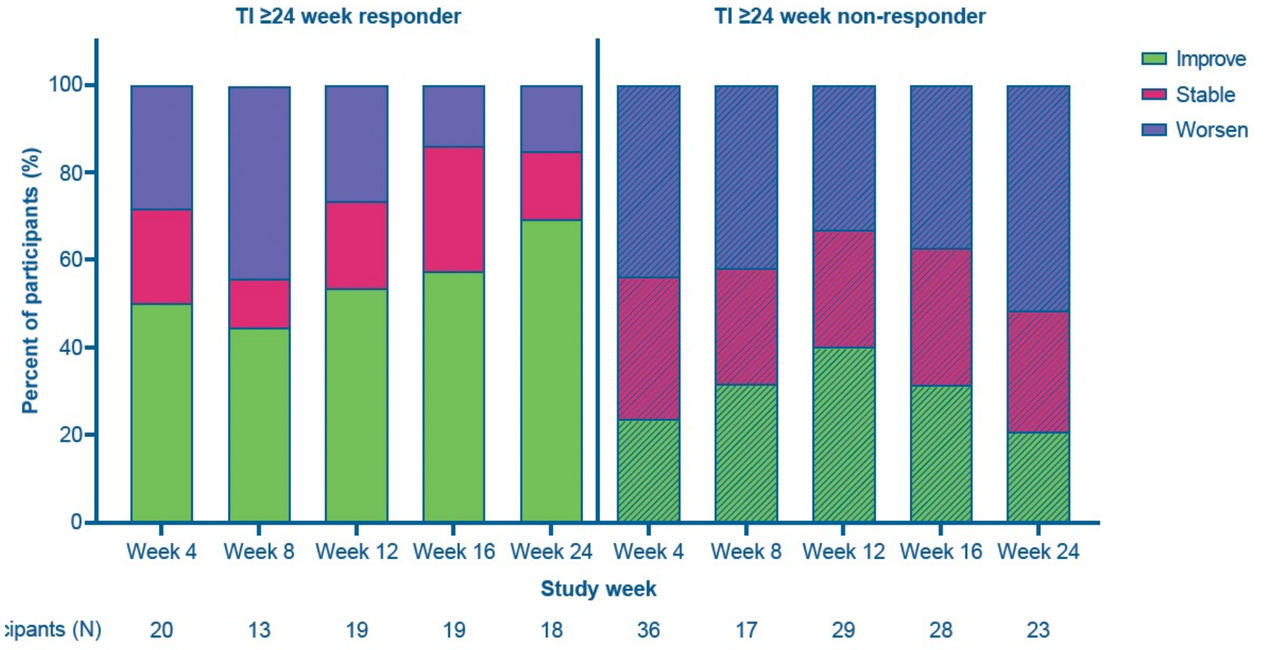
KER050 for anemia in LR-MDS

Updated results in 2025, QoL improved among responders

Sustained and clinically meaningful improvements in FACIT-Fatigue scores observed with elritercept treatment







TI response duration	Change from baseline in FACIT-Fatigue score at Week 24, mean (SEM)		Mean difference, responder vs non-responder
	Responder	Non-responder	
TI ≥24 weeks	4.7 (3.1), n=13	-1.8 (1.3), n=29	6.5

ta for mITT$_{24}$ participants with baseline FACIT-Fatigue scores (n=1 missing) for TI ≥24 weeks responder, assessed from Weeks

Giagounidis, EHA 2025

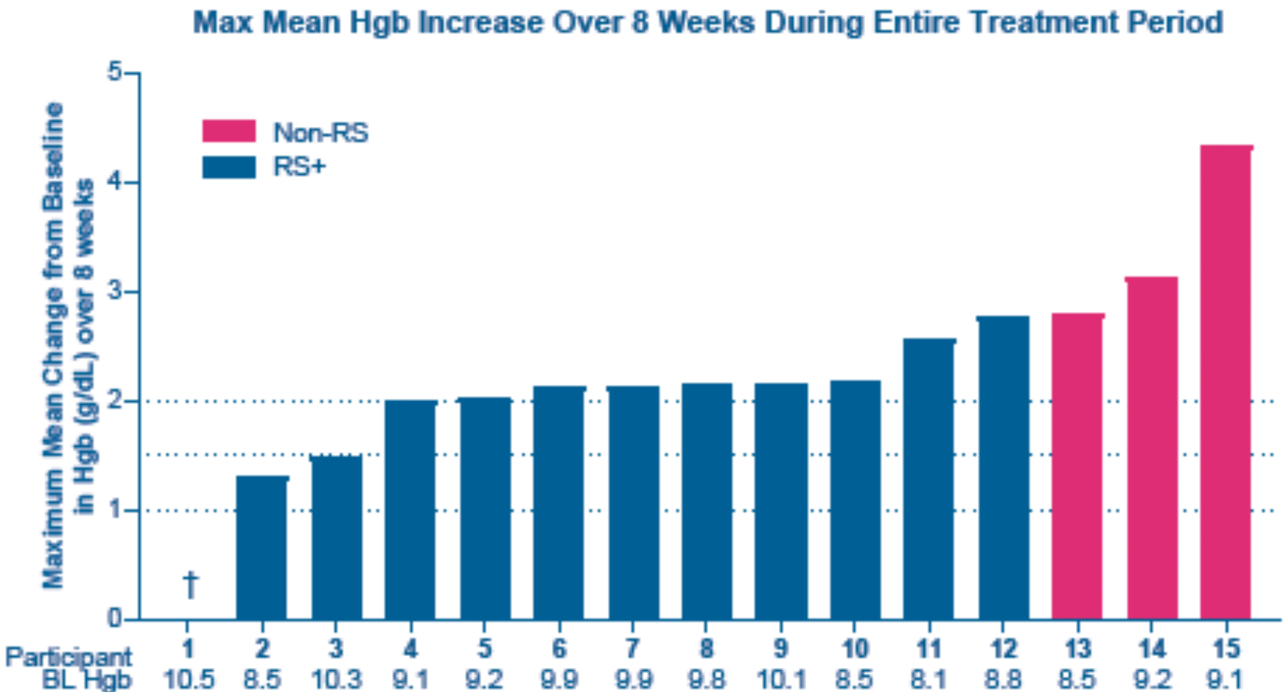
KER050 for anemia in LR-MDS

Updated results in 2025, in NTD anemia, confirmed benefit

Robust hematological responses observed in most NT participants, regardless of RS status

- Maximum mean change increases in Hgb over any 8-week period during elritercept treatment:
  - 14 (93.3%) had an increase of ≥1.0 g/dL
  - 13 (86.7%) had an increase of ≥1.5 g/dL
  - 12 (80%) had an increase of ≥2.0 g/dL

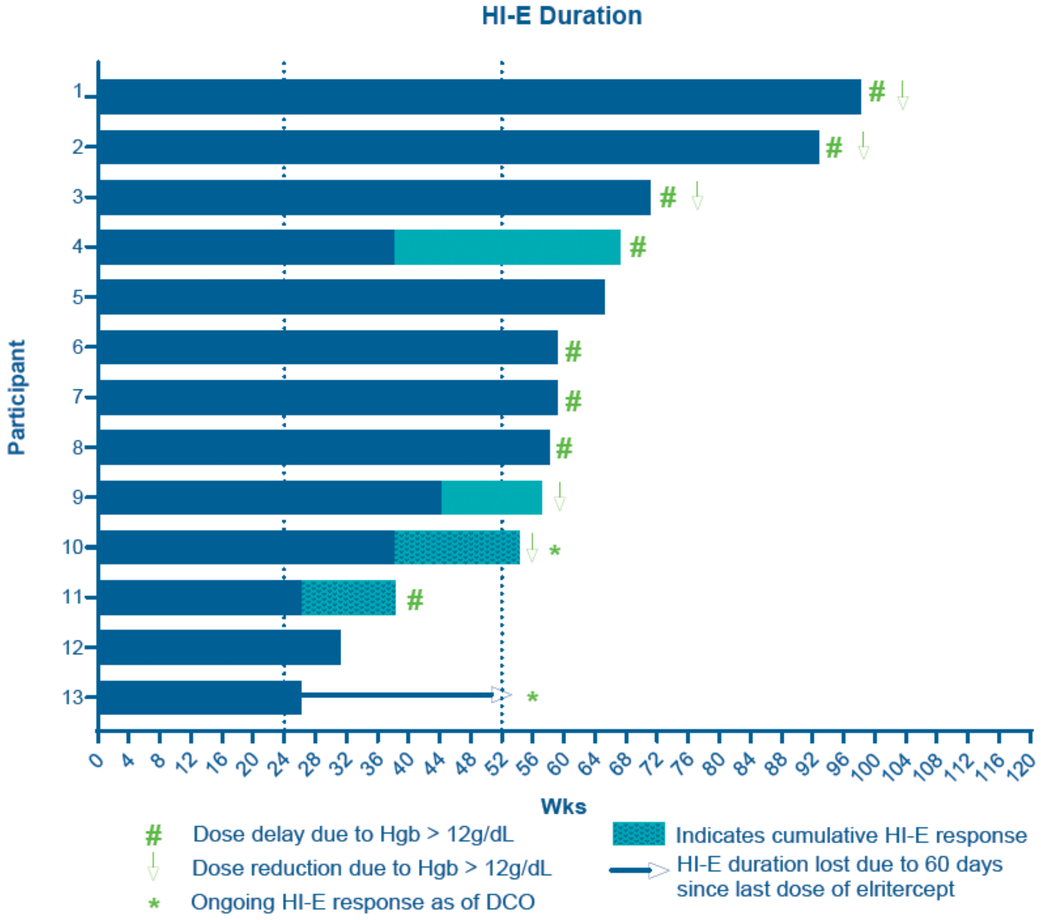
Population	NT (n=15) responders/n (%)
HI-E*	**13/15 (86.7%)**
RS+	10/11 (90.9%)
Non-RS	3/4 (75.0%)

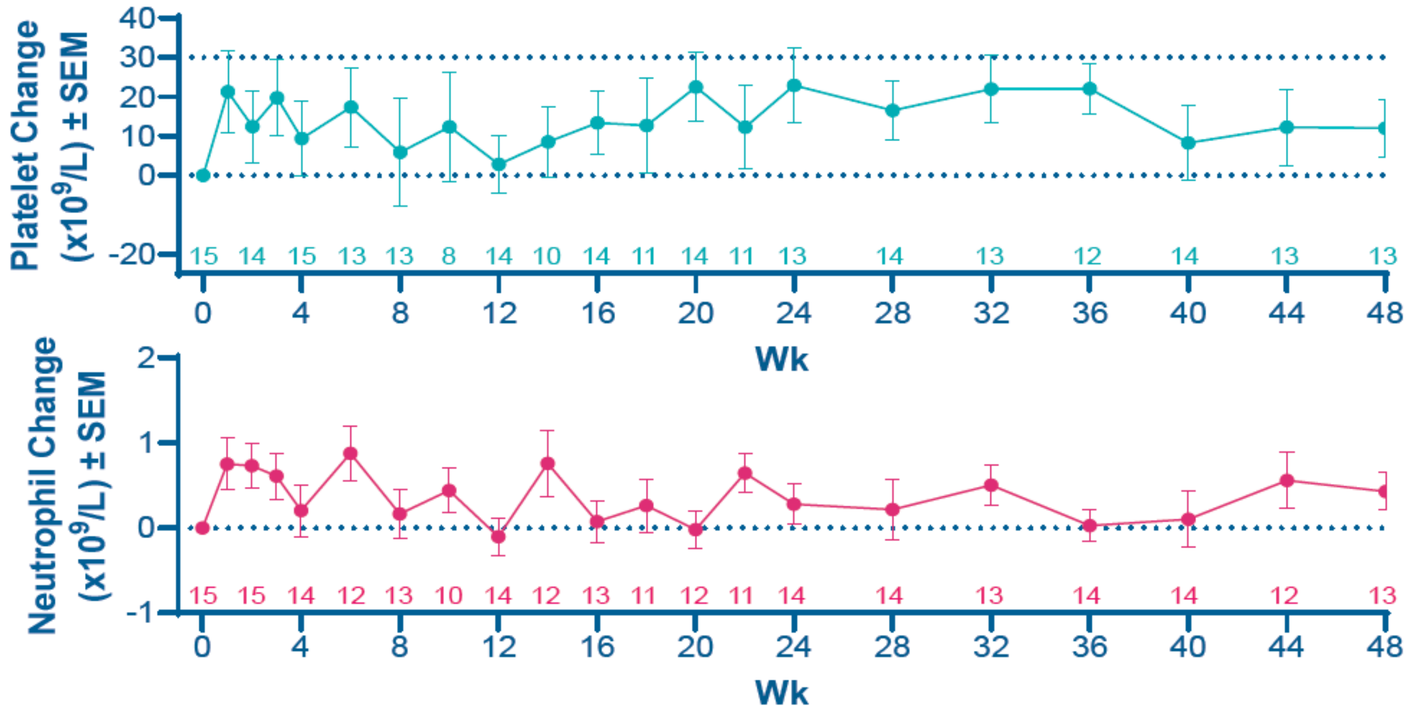


Valcárcel, EHA 2025

KER050 for anemia in LR-MDS

NTD anemia patients: prolonged responses, improved BM function



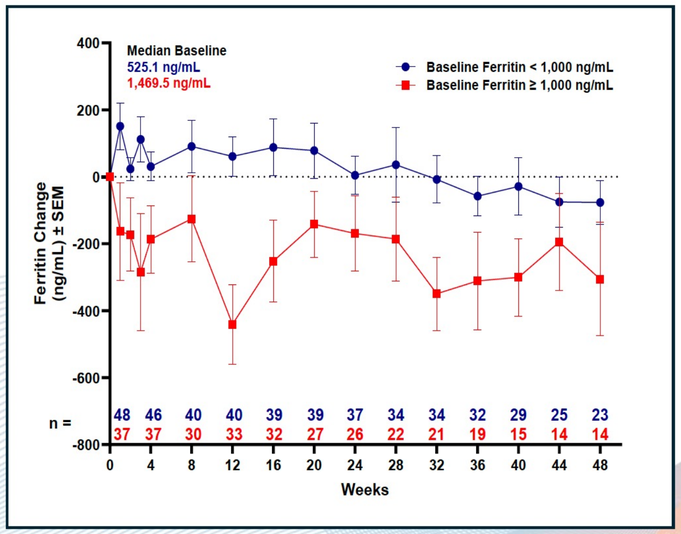


Valcárcel, EHA 2025

Reduced ferritin and increased bone specific alkaline phosphatase in participants with LR-MDS treated with KER-050 support potential to rebalance the osteohematopoietic niche

Rapid and Sustained Decreases in Serum Ferritin Observed with Elritercept Treatment

- Treatment guidelines recognize serum ferritin ≥1,000 ng/ml as an indicator of IO in at-risk patients
- Serum ferritin ≥ 1,000 ng/ml may be an independent predictor of mortality risk in patients with LR-MDS[1]



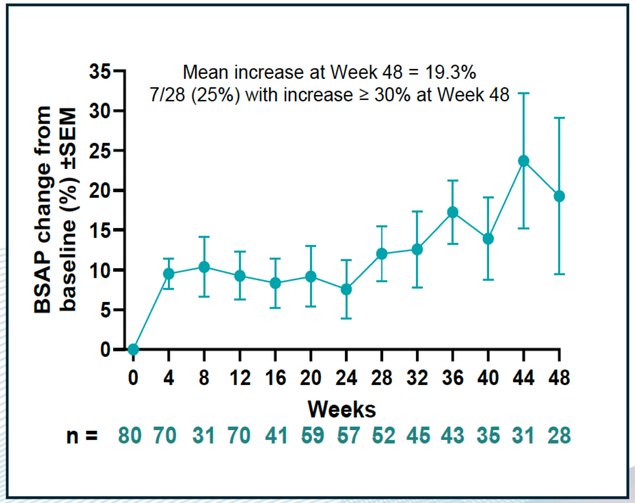
Among study participants with baseline ferritin ≥1,000 ng/ml and at least 1 post-baseline ferritin measurement (N=37):

- 19 (51%) showed decreases to <1000 ng/ml while on treatment
- 29 (78%) showed a ≥20% reduction in ferritin while on treatment
- 2 participants, including one who was NT, discontinued iron chelator therapy

Elritercept has potential to ameliorate iron overload in participants with MDS, regardless of baseline transfusion burden

Observed Increases in BSAP Support Potential of Elritercept to Restore OHN Function and Provide Benefits Beyond Erythropoiesis

- BSAP is a marker of activity of osteoblasts (bone forming cells in the OHN)
- Dysregulated TGF-β signaling in the OHN suppresses osteoblast activity and disrupts osteoblast interactions with hematopoietic precursors that support functional hematopoiesis[1,2,3]



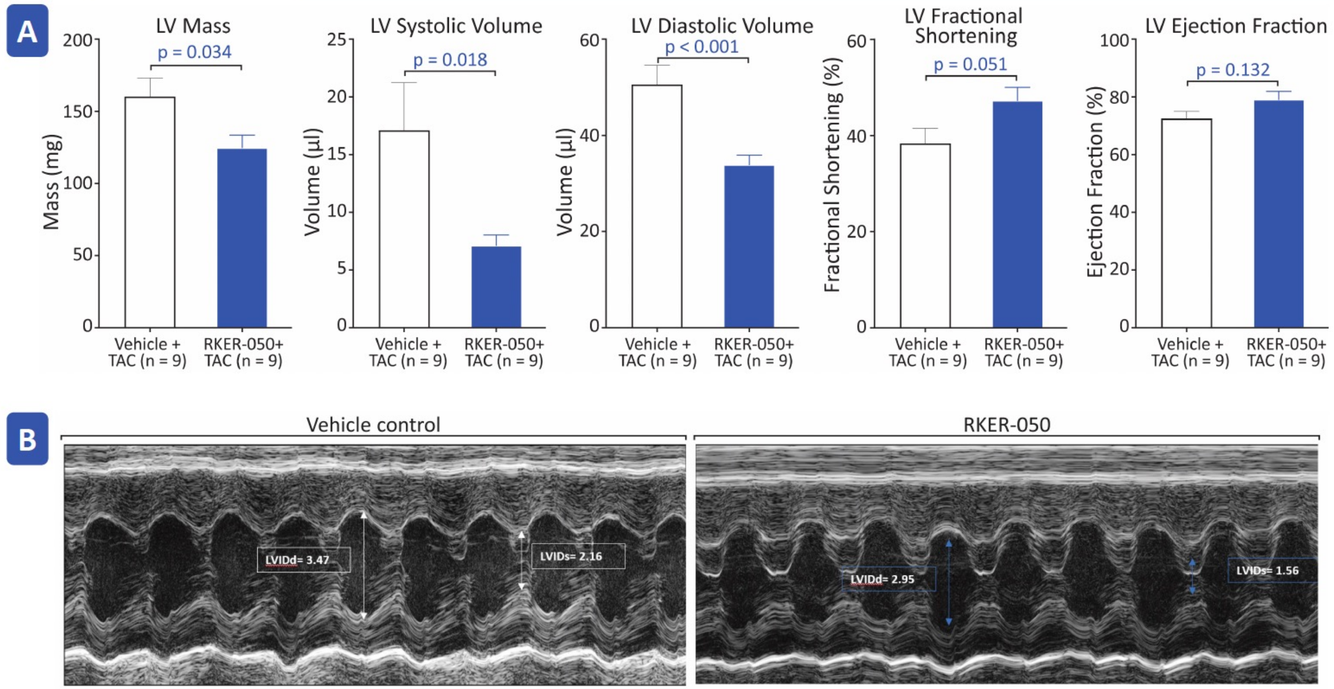
- Elritercept-mediated inhibition of TGF-β ligands anticipated to increase osteoblast activity
  - Dose-dependent increases in BSAP were observed following single doses of elritercept in healthy post-menopausal women[4]
- Sustained increases in BSAP were observed with elritercept in this generally elderly population with LR-MDS:
  - Increases were observed regardless of hematologic response, baseline transfusion burden, or RS status

Observed increases in BSAP support potential for elritercept to restore the OHN

Valcárcel, EHA 2024

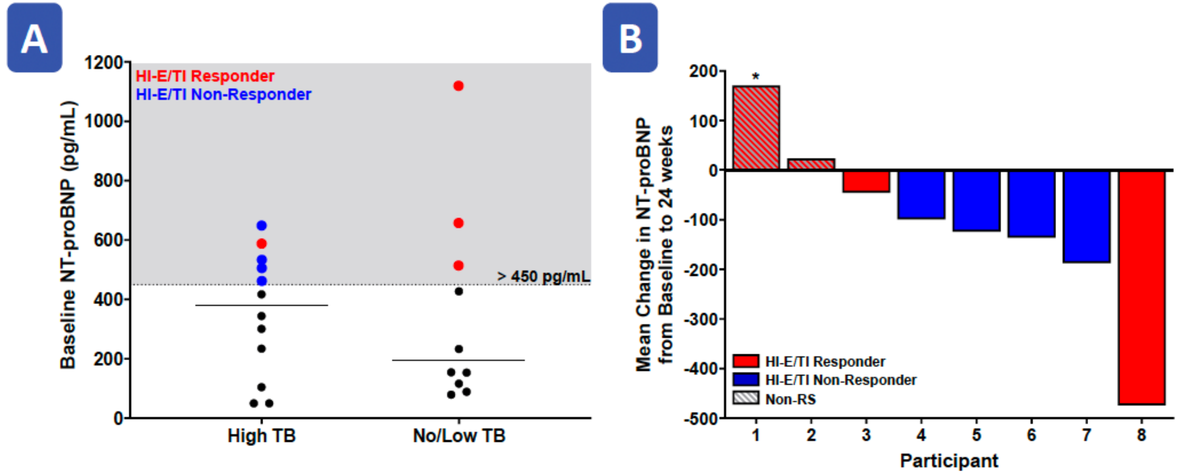
Activin A inhibition by KER-050 is associated with evidence of cardiovascular benefit: Translation of preclinical observations to humans with MDS

Improved cardiac function and morphology in mice with anemia



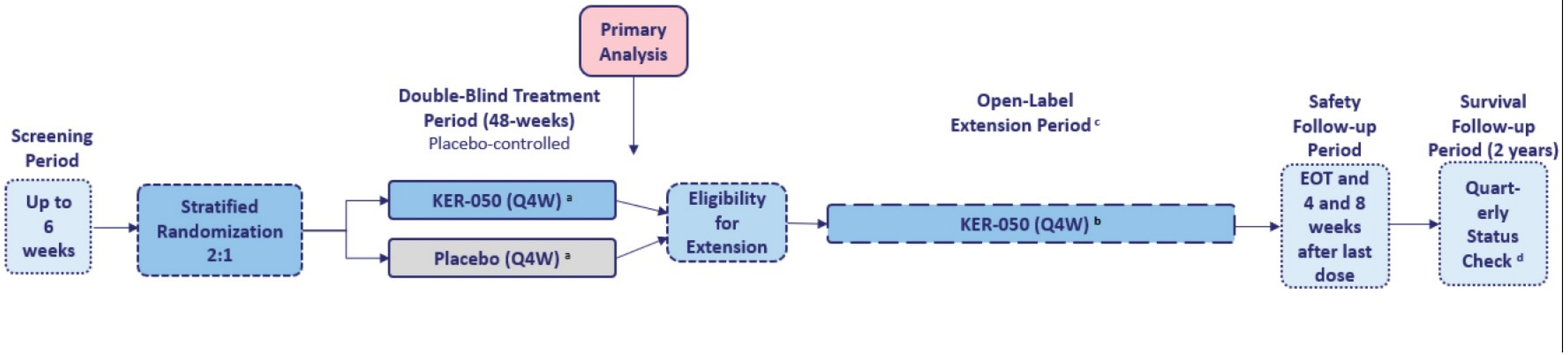
Tan, EHA 2024

Reduced NT-proBNP serum levels regardless of hematological response



NEXT STEPS: registration trials

2nd line Renew trial, LUSPA naïve patients



1st line trial, COMMANDS like trial

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

Randomized 1:1

Elritercept
3.75 mg/Kg sc Q4w
Titration up to 5 mg/Kg

Epo alpha
450IU/Kg sc 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[b] 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

ELRITERCEPT
in anemic LR-MDS PATIENTS

- **Novel TGF-B inhibitor**
  - **Responses in HTB and non-RS patients**
  - **Favourable safety profile and administration (Q4w)**
  - **Improved QoL among responders**
  - **Trilineage responses**
  - **Iron overload improvement**
  - **Cardiac function?**
  - **Under review in 2nd line (Luspa naïve) and 1st line (vs ESAs)**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