

VI Reunión

GESMD



**NUEVAS ALTERNATIVAS DE
TRATAMIENTO DE LA ANEMIA EN
SMD DE BAJO RIESGO**

© Getty Images

Joaquin Sanchez Garcia
Servicio de Hematología
Hospital Reina Sofia.
MIBIC-Universidad Cordoba

Impacto en QoL

Daño orgánico

Table 3. Predictive factors of QOL-E scores

QOL index ^a	Factor	Univariate analysis		Multivariate analysis [†]	
		Effect (95% CI) ^a	p value	Effect (95% CI) ^a	p value
QOL-E, Physical	Age (1 year)	-0.73 (-1.00, -0.46)	<0.0001	-0.48 (-0.74, -0.22)	0.0003
	Charlson's index (2-5 vs 0-1) ^b	-16.3 (-23.0, -9.5)	<0.0001	-14.2 (-20.4, -8.0)	<0.0001
	Hb (1 g/dL) ^l	+2.48 (+1.50, +3.45)	<0.0001	+1.69 (+0.71, +2.67)	0.0008
	Transfusions (yes vs no) [†]	-9.1 (-13.6, -4.7)	0.0002	-7.2 (-11.7, -2.6)	0.0029
	Time from baseline (1 month)	-0.22 (-0.45, +0.01)	0.061	-0.29 (-0.52, -0.06)	0.014
QOL-E, Functional	Age (1 year)	-0.34 (-0.66, -0.01)	0.042	-0.01 (-0.33, +0.30)	0.93
	Charlson's index (2-5 vs 0-1) ^b	-14.8 (-22.6, -7.1)	0.0002	-15.5 (-22.9, -8.1)	<0.0001
	Hb (1 g/dL) ^l	+3.79 (+2.49, +5.09)	<0.0001	+2.99 (+1.61, +4.36)	<0.0001
	Transfusions (yes vs no) [†]	-13.0 (-19.3, -6.6)	0.0002	-8.3 (-15.1, -1.6)	0.017
	Time from baseline (1 month)	-0.10 (-0.47, +0.27)	0.60	-0.21 (-0.59, +0.16)	0.26

Ann Hematol (2015) 94:779–787

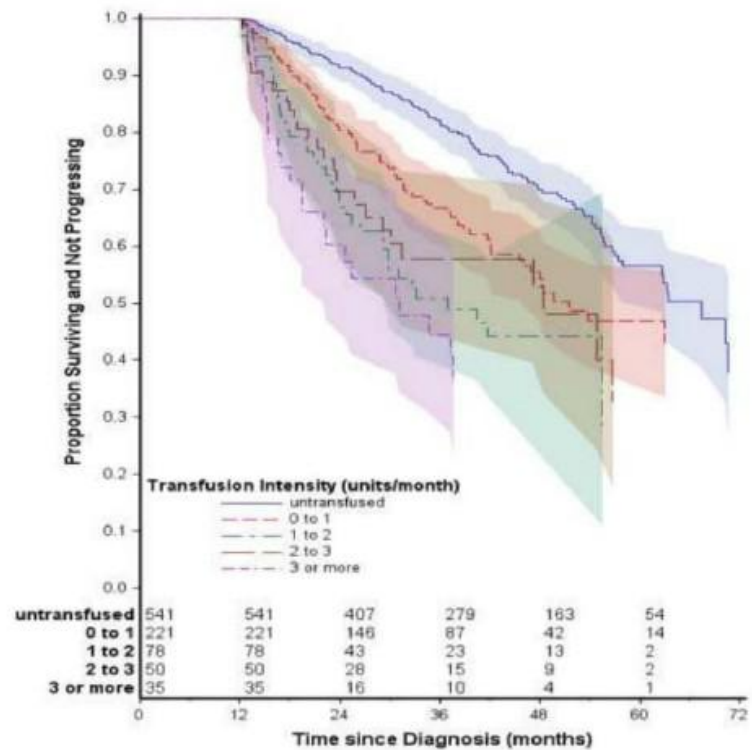
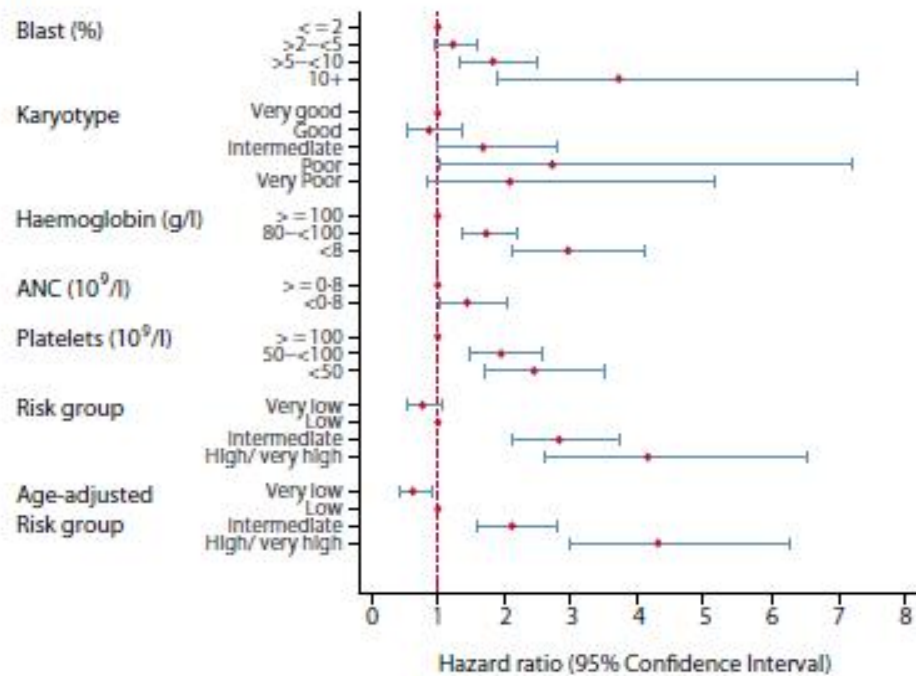
Table 5 Baseline and evolution of organ complications (N=263)

Complication	Total, n (%)	Mean±SD number of PRBC transfusions at start of complication	Mean±SD SF levels at start of complication, µg/L
Cardiac	53 (20.2 %) ^a	53.6±61.2 ^b	1945.4±1527.6 ^c
Hepatic	30 (11.4 %) ^d	58.7±73.7 ^e	2387.2±1722.2 ^f
Endocrine	26 (9.9 %) ^g	60.7±59.2 ^f	1839.2±1593.7 ^e
Arthropathies	10 (3.8 %) ^f	48.1±42.4 ^b	4718.2±6094.7 ⁱ

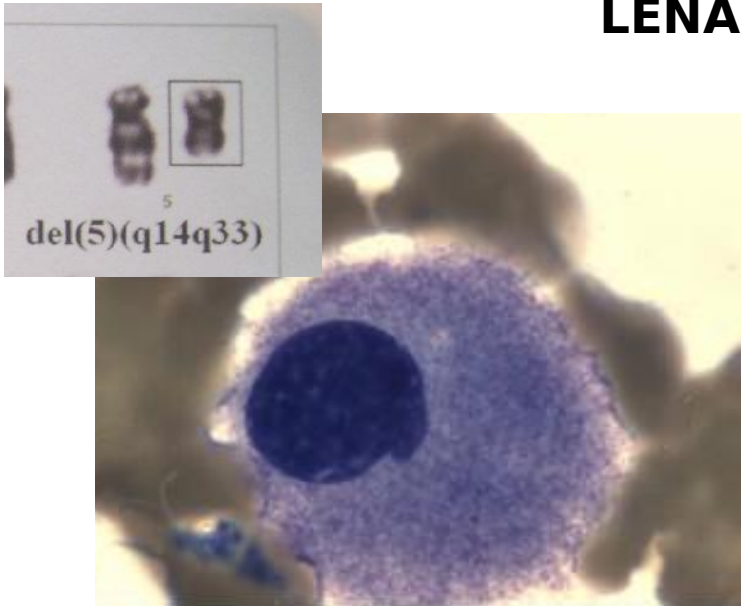
CI confidence interval, PRBC packed red blood cells, SD standard deviation, SF serum ferritin

PROGNOSTIC IMPACT OF TRANSFUSION INTENSITY ON SURVIVAL THE UEMDS REGISTRY N=1000

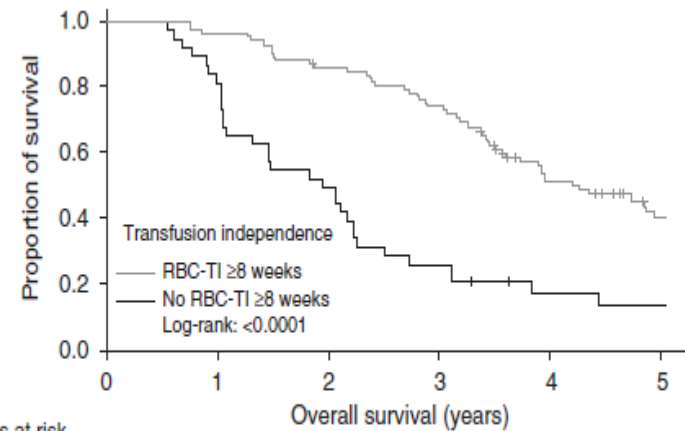
(B)



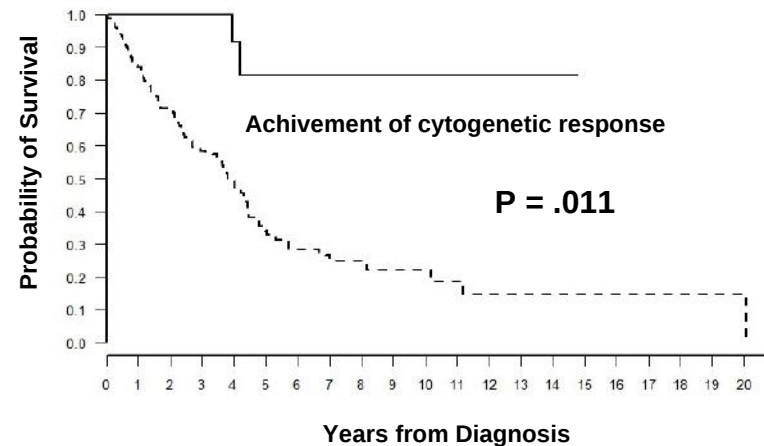
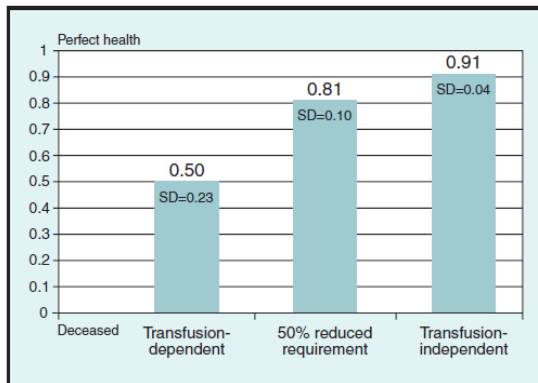
IMPORTANCIA DE CONSEGUIR INDEPENDENCIA TRANSFUSIONAL LENALIDOMIDA EN SMD DEL50



b



No. of patients at risk	0	1	2	3	4	5
RBC-TI ≥8 weeks	94	91	80	69	43	29
No RBC-TI ≥8 weeks	38	31	19	10	5	4



VI Reunión

GESMD

Referencia	N	Dosis mg	Respuesta% MH(IT) Duracion	Respuesta cCGT	Ajuste Dosis
Raza A, Blood 2008 MDS002 Low-Int1 sin del5q	214 FASE II	10	43(26) 41 wks	8.5% (4/47)	54.7%
Sibon D, BJH 2012 Low-Int1 sin del5a	31 RETR	5-10 ± EPO	48(37)	NE	32%
Yang Y, Exp Ther Med 2013 del5a Low-Int1 sin	30 RETR	10	NE/0	0	NE
Santini V, ASH meeting 2015 del5q Low-Int1 sin	160 FASE III	10	26.9% 32 wks		31.9%

A PHASE 3 STUDY OF LENALIDOMIDE VERSUS PLACEBO IN RBC TRANSFUSION DEPENDENT PATIENTS WITH LR MDS WITHOUT DEL5Q UNRESPONSIVE OR REFRACTORY TO ESAS

Table. Key efficacy data.

Response	LEN (n = 160)	PBO (n = 79)
RBC-TI \geq 56 days, n (%)	43 (26.9)*	2 (2.5)
Duration of RBC-TI \geq 56 days, median (95% CI), weeks ^a	32.9 (20.7–71.1)	NE (NE–NE)
RBC-TI \geq 168 days, n (%)	28 (17.5)	0

^aResponding pts only.* $P < 0.001$.

ORIGINAL ARTICLE

Lenalidomide with or without erythropoietin in transfusion-dependent erythropoiesis-stimulating agent-refractory lower-risk MDS without 5q deletion

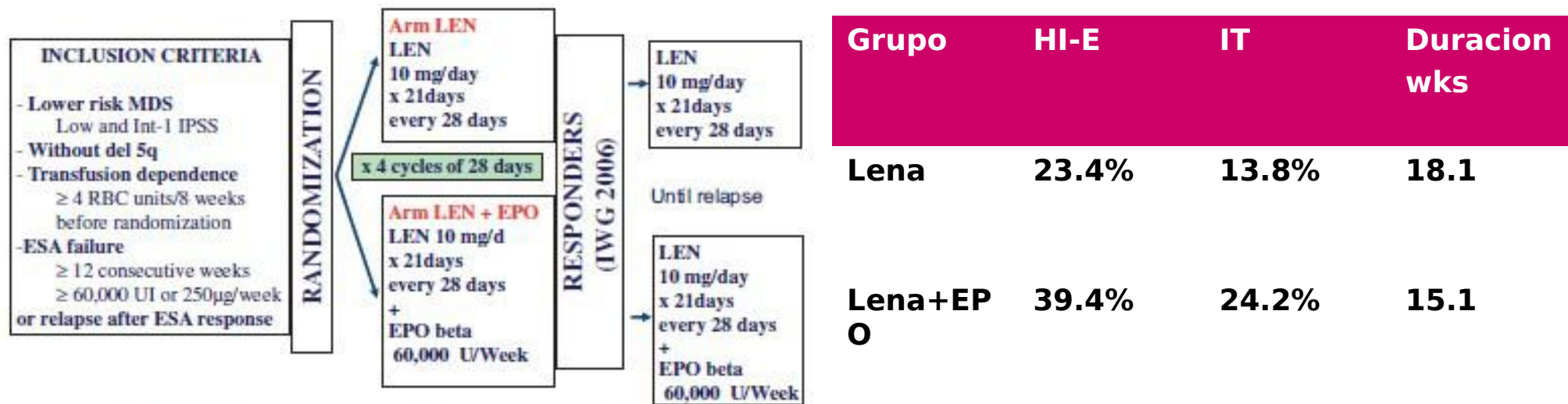


Figure 1. GFM-LENEPO 2008 study treatment plan (registered at clinicaltrials.gov (NCT01718379), EudraCT number 2008-008262-12).

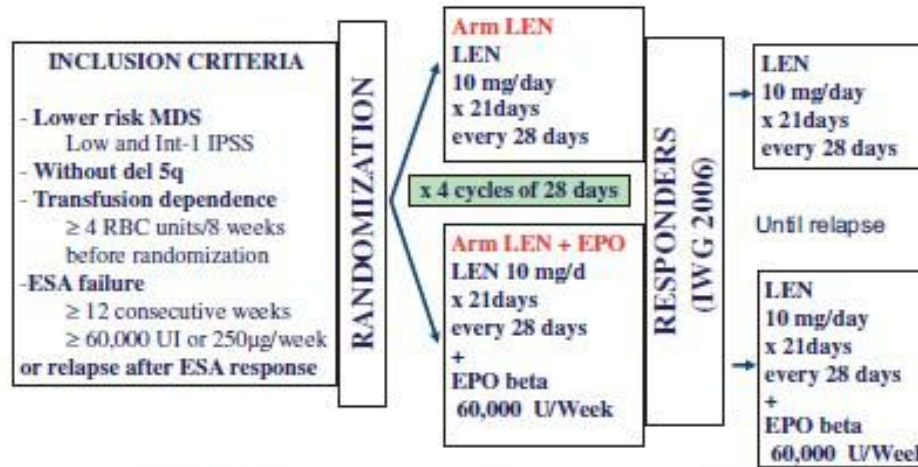


Figure 1. GFM-LENEPO 2008 study treatment plan (registered at clinicaltrials.gov (NCT01718379), EudraCT number 2008-008262-12).

G- POLIMORFISMO CEREBLON PREDICTOR INDEPENDIENTE DE RESPUESTA

Mutaciones en SF3B1 (75%), TET2 (45%), DNMT3A (20%) ASXL1 (19%)

VI Reunión

GESMD

**EFICACIA Y SEGURIDAD DEL USO DE
LENALIDOMIDA EN PACIENTES AFECTOS DE
SINDROME MIELODISPLASICO SIN DELECCION
5Q.
Estudio Lena No-5q RESMD**

Autores: J Sánchez-García, M Díaz-Campelo, F Ramos, R Andreu, S Osorio, J Casaño, J Serrano y G Sanz.

VI Reunión

GESMD

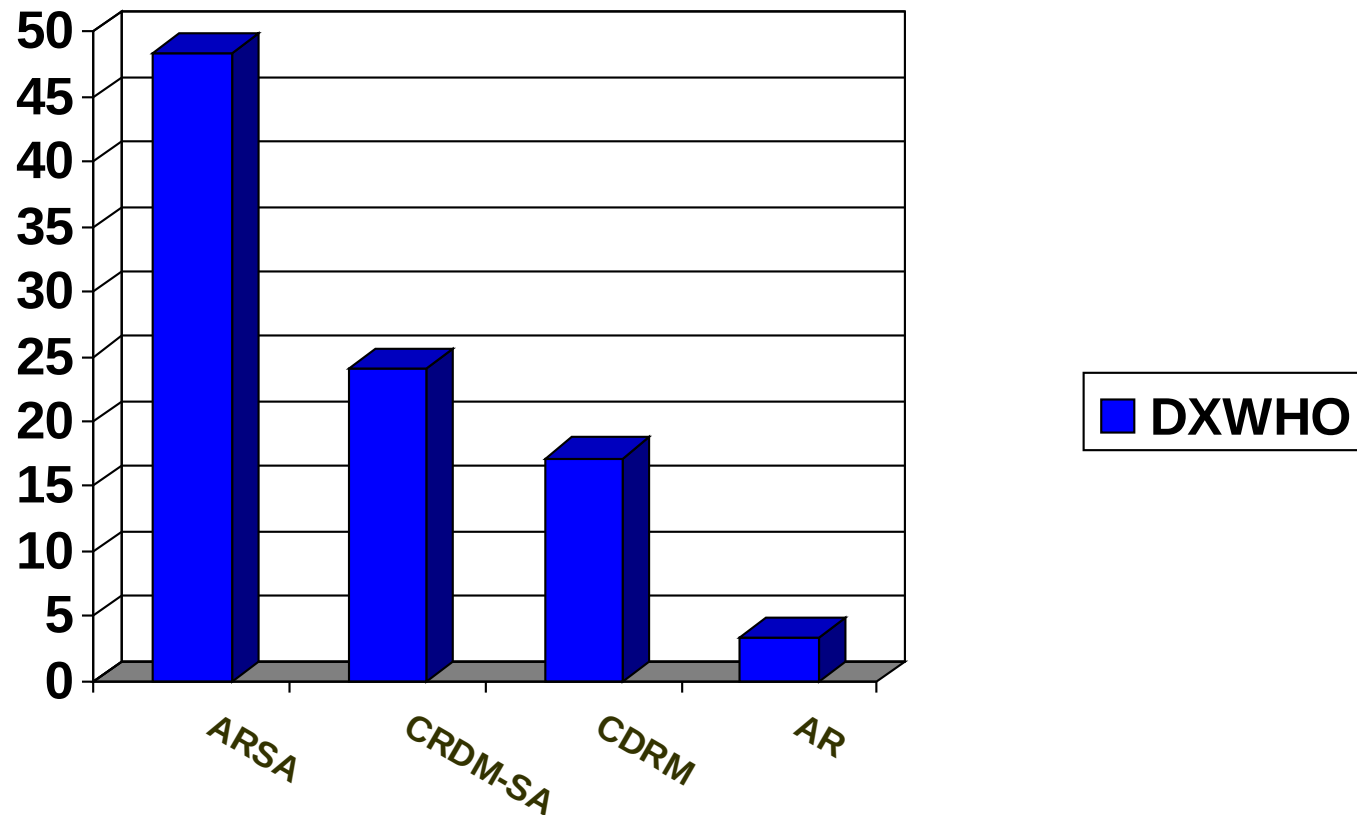
116 Pacientes incluidos en el RESMD con lenalidomida como tratamiento sin del5q de 45 centros (31 con 1-2 casos)

Se han recibido un total de 35 CRDs procedentes de 5 hospitales (30% de los posibles casos)

Se incluyen para análisis 29 pacientes con datos completos y del5 excluido

CARACTERÍSTICAS CLÍNICAS DE LA SERIE

Mediana Edad: 68.7 (40-86a).....Sexo: ...72.4% varones y 27.6% mujeres



RESULTADOS N=29

Cariotipo	N (%)
Normal	22 (76)
-Y	3 (10)
Traslocaciones	
t(2;3), t(6;11)	2(7)
+8	1(3)
del11q23	1(3)
IPSS-bajo (62.1%) e Int-1 (37.9%)	

Características pre-Lena	N (%)
Dependencia transfusional	29 (100)
CH 8 wks previas	5 (2-16)
Mediana (rango)	
Tratamientos previos:	
AEEs	24 (83)
G-CSF	14 (48)
AZA	6 (21)
ATG	0
Tiempo Dx-Lena meses	36(4-122)
Mediana (rango)	

**Características
Tratamiento con Lena**

N (%)

Dosis 10mg/24h

22(75)

Mediana de ciclos (rango)

3 (1-24)

**Independencia
transfusional**

5 (17-25)

Efectos Secundarios

Toxicidad Hematologica

5 (17)

Toxicidad Hepatica

1 (3.5)

Toxicidad cutánea

1(3.5)

Tratamientos posteriores

AZA

14 (48)

QT

3 (10)

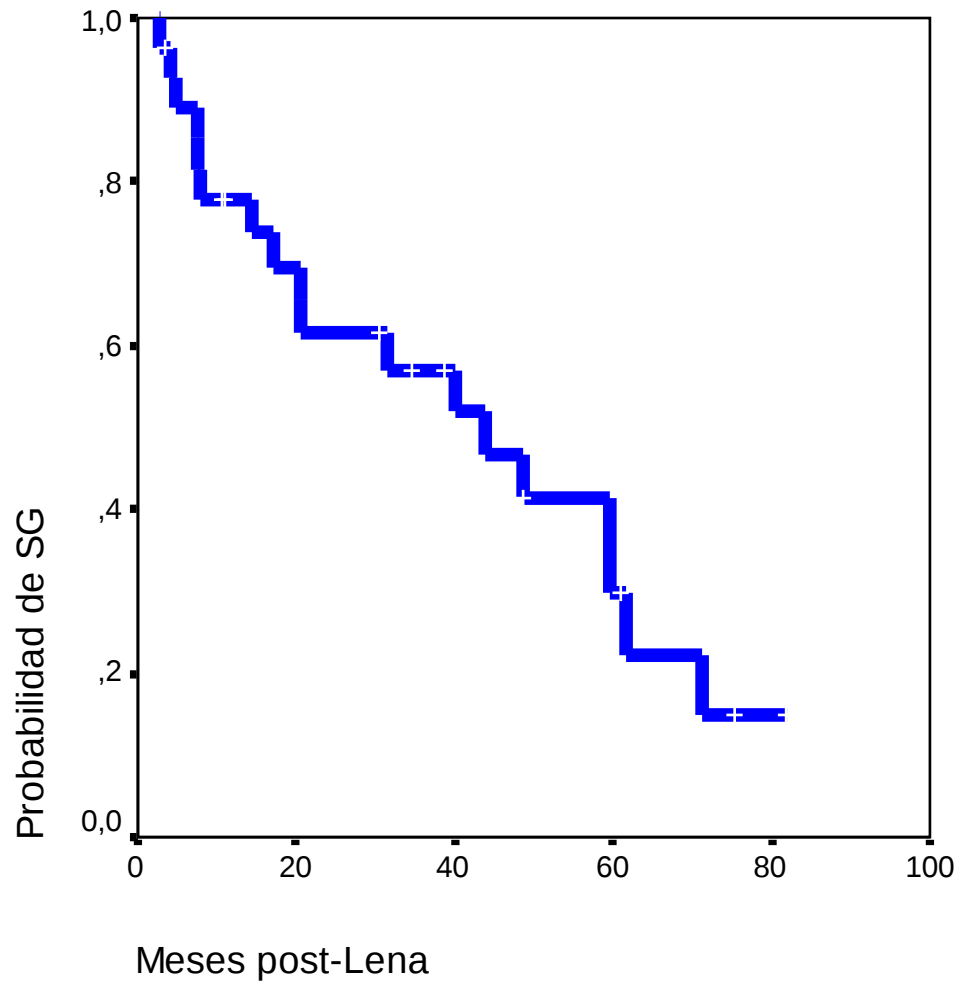
VI Reunión

GESMD

Edad	DxWHO	Cario	IPSS	TTo previos	N de ciclos	Duración respuesta Semanas
64	ARS	46 XX	Bajo	AEEs+GCSF	3	12
73	CRDM-SA	46 X,-Y JAK2 neg	Bajo	AEEs+GCSF	10	32
50	ARS	46 XY	Bajo	AEEs+GCSF	24	76
76	CRDM	46 XY	Bajo	AEEs	9	20
86	ARS	46 XX	Bajo	AEEs+GCSF	19	76+

Mediana duración de respuesta: 32 semanas (12-76)

2-tLAM



Mediana de Supervivencia post-Lena: 43 meses (95%IC 21-66)

Un 25% de pacientes con SMD de bajo riesgo sin del5q pueden alcanzar IT con lenalidomida con mediana de duración de respuesta 32s

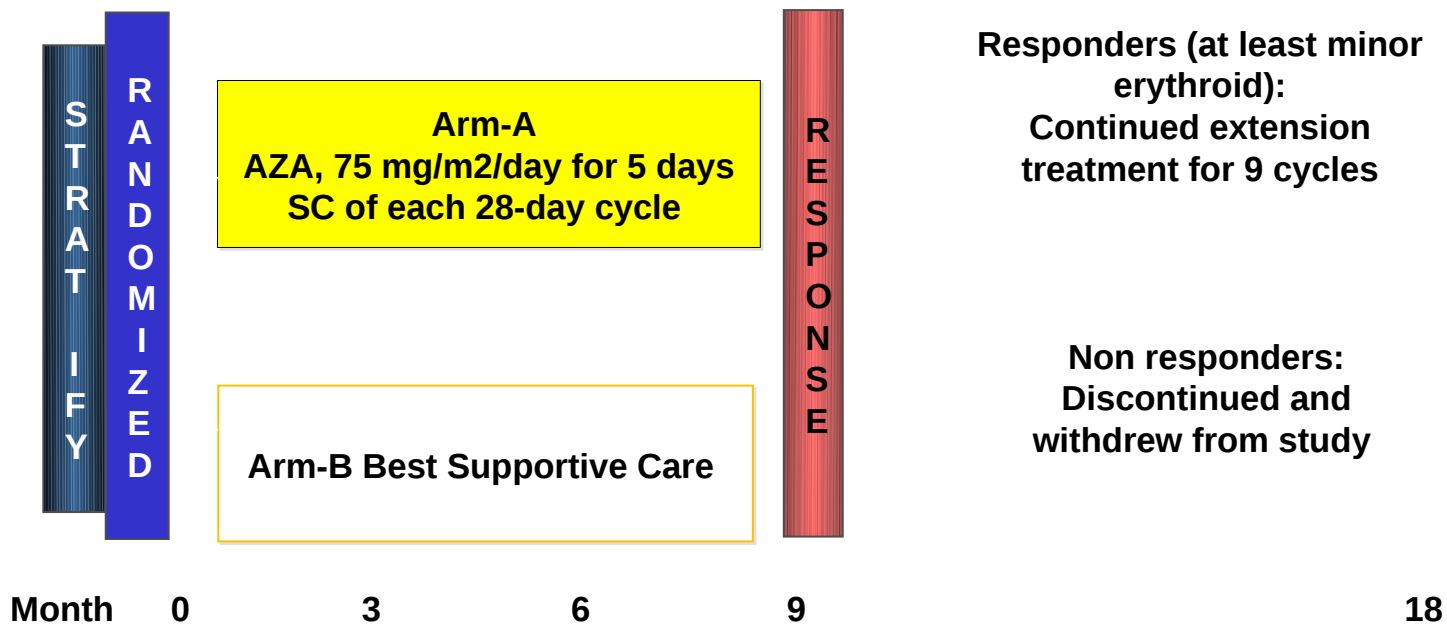
La toxicidad hematológica podría ser menor que en los pacientes con del5q.

Son necesarios factores predictivos biológicos que identifiquen pacientes con SMD de bajo riesgo sin del5q respondedores a lenalidomida.

En esta serie del RESMD el uso de AZA es preferentemente posterior a lenalidomida.

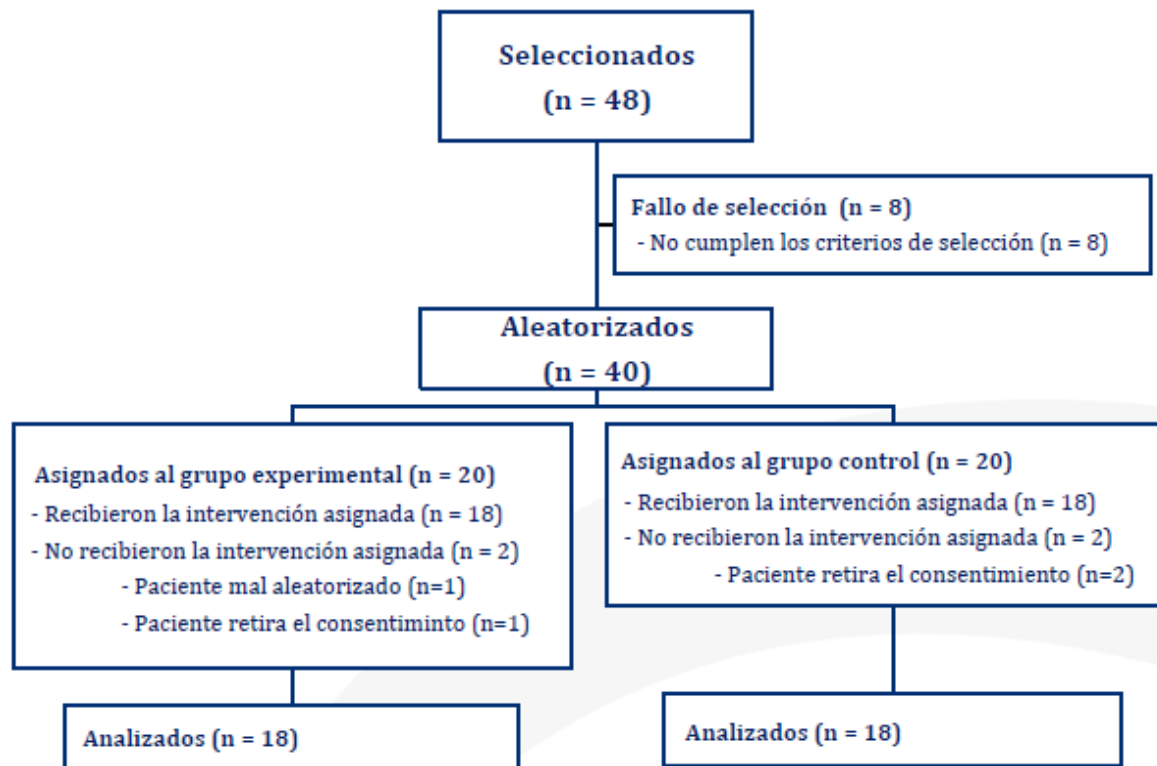
FINAL RESULTS OF PHASE II RANDOMIZED TRIAL OF AZACITIDINE VERSUS SUPPORT TREATMENT IN PATIENTS WITH LOW RISK MDS WITHOUT 5Q DELETION

Open-label phase II : AZA 75 mg/m²/5 days vs BSC



VI Reunión

GESMID

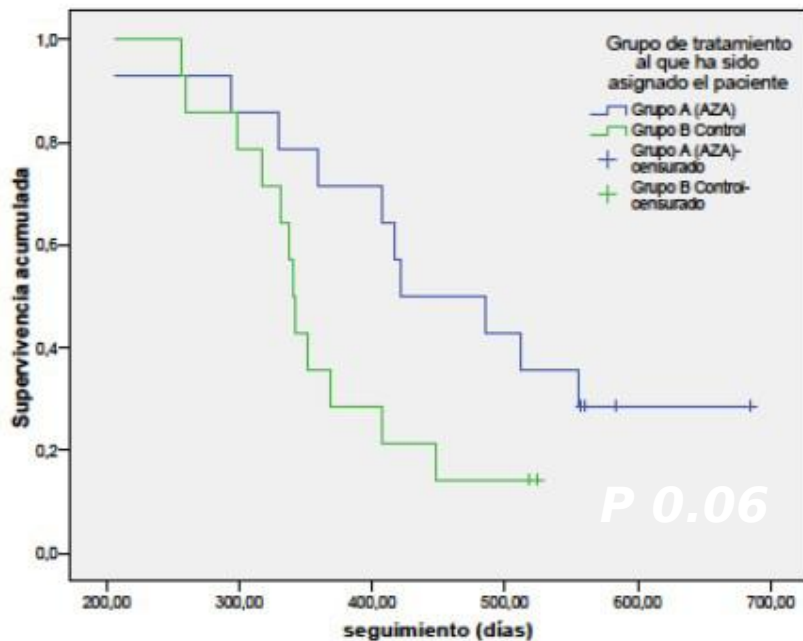


**44 % (31% TI) vs 5.5%. Mediana de 50 semanas IQ 17-121
Neutropenia III-IV 53%**

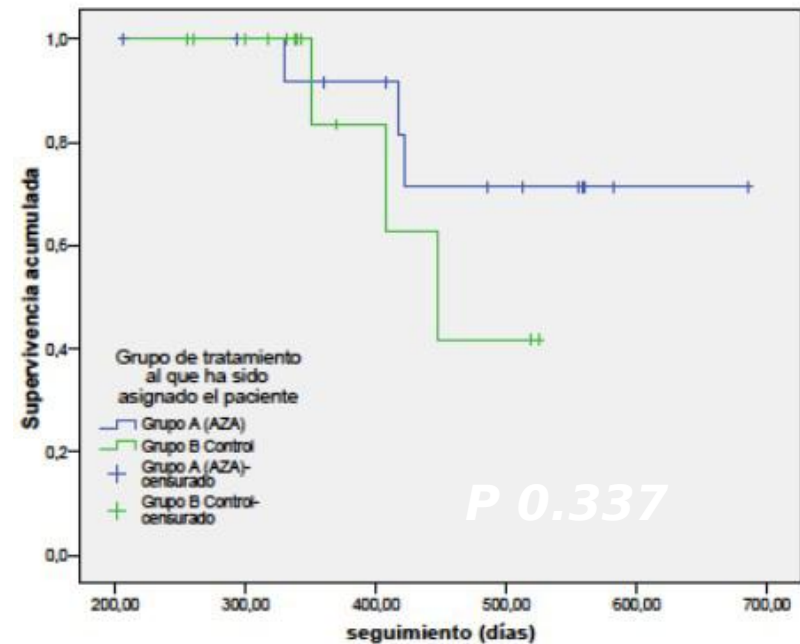
VI Reunión

GESMD

Supervivencia Global



Supervivencia Libre Transformacion



Mutaciones en SF3B1 (54%), TET2 (36%), STAG2 (18%) KMT2D (18%)

Low-Dose HMAs in LR-MDS: Study Design

Adults with de novo or secondary IPSS low- or int-1-risk MDS or CMML, ECOG PS ≤ 3 , adequate organ function, no prior HMAs (N = 91) →

Azacitidine 75 mg/m² IV/SC (n = 34)
OR
Decitabine 20 mg/m² IV (n = 57)
Days 1-3 q4w

Open-label phase II trial

Between 11/2012 and 10/2015, 91 pts with LR-MDS were treated

At least 2 cycles of therapy

Evaluable for response (modified IWG 2006)

Endpoints: ORR, response duration, transfusion independence, cytogenetic response, event-free survival, OS, safety

Low-Dose HMAs in LR-MDS: Conclusions

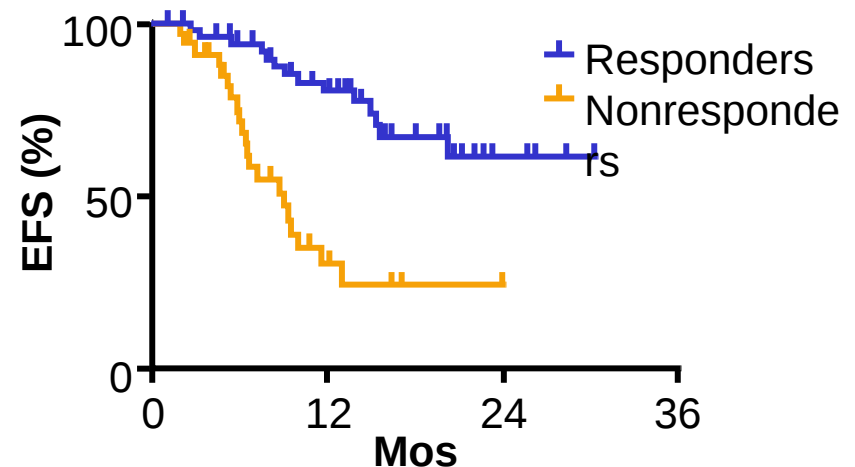
**Low-dose HMA therapy appears safe, effective in LR-MDS,
according to investigators^[1]**

ORR: 59%

Transfusion independence: 32%

1-yr OS: 86%

1-yr event-free survival: 62%



**Randomized phase II trial evaluating low-dose azacitidine vs
decitabine vs best supportive care in progress^[2]**

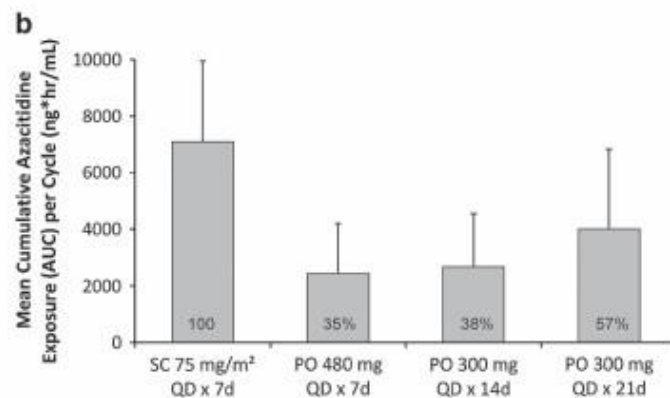
1. Short N, et al. ASH 2015.
Abstract 94.

2. ClinicalTrials.gov.
NCT02269280.

ORIGINAL ARTICLE

Efficacy and safety of extended dosing schedules of CC-486 (oral azacitidine) in patients with lower-risk myelodysplastic syndromes

G Garcia-Manero¹, SD Gore², S Kambhampati³, B Scott⁴, A Tefferi⁵, CR Cogle⁶, WJ Edenfield⁷, J Hetzer^B, K Kumar^B, E Laille^B, T Shi^B, KJ MacBeth^B and B Skikne^B



*Percentage cumulative exposure/cycle relative to subcutaneous (SC) azacitidine 75 mg/m² x 7 days.

Table 2. Hematologic response and transfusion independence

Parameter	Treatment schedule n responders/N evaluable (%)		
	CC-486 300 mg once daily 14 days/cycle (n=28)	CC-486 300 mg once daily 21 days/cycle (n=27)	Total (N=55)
Overall response (CR, PR, any HI, TI) ^a	10/28 (36)	11/27 (41)	21/55 (38)
CR ^b	1/7 (14)	0/5	1/12 (8.3)
PR	0/5	0/3	0/7
Any HI	7/28 (25)	10/27 (37)	17/55 (31)
HI-E	4/25 (16)	8/25 (32)	12/50 (24)
HI-P	4/18 (22)	3/15 (20)	7/33 (21)
HI-N	3/10 (30)	0/6	3/16 (19)
Marrow CR	0/7	3/5 (60)	3/12 (25)
RBC TI ^c			
Sustained for 56 days	5/16 (31)	6/16 (38)	11/32 (34)
Sustained for 84 days	2/16 (13)	5/16 (31)	7/32 (22)
Platelet TI ^d	0/4	0/2	0/6

VI Reunión

GESMD

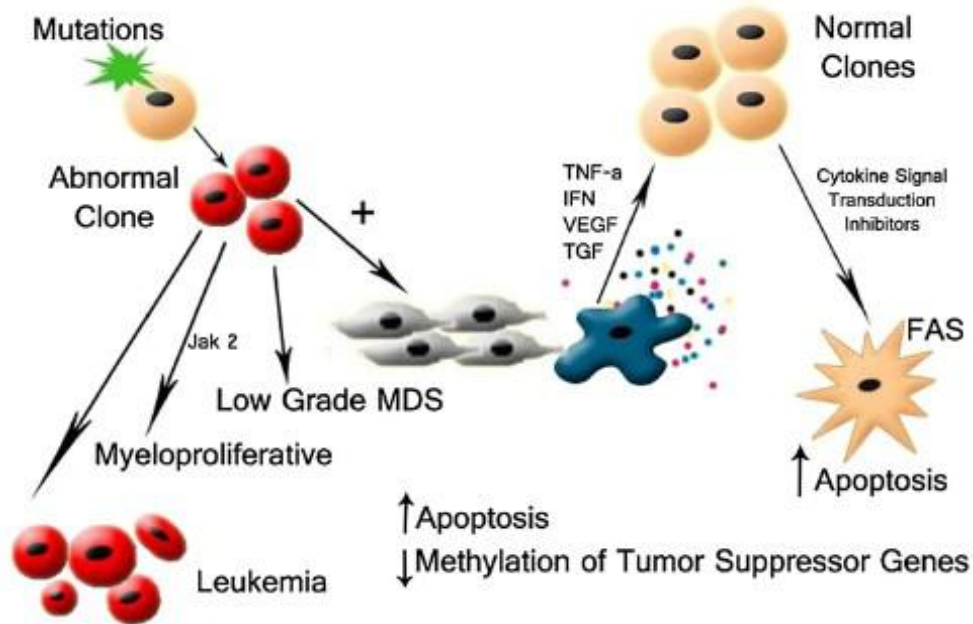
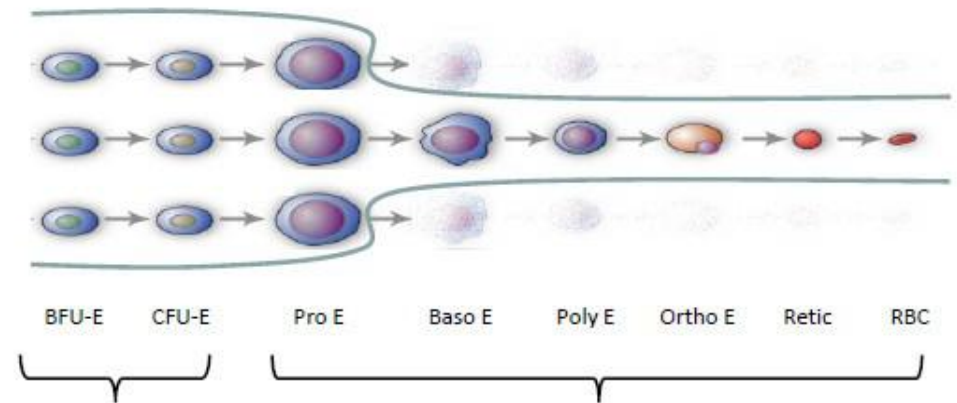
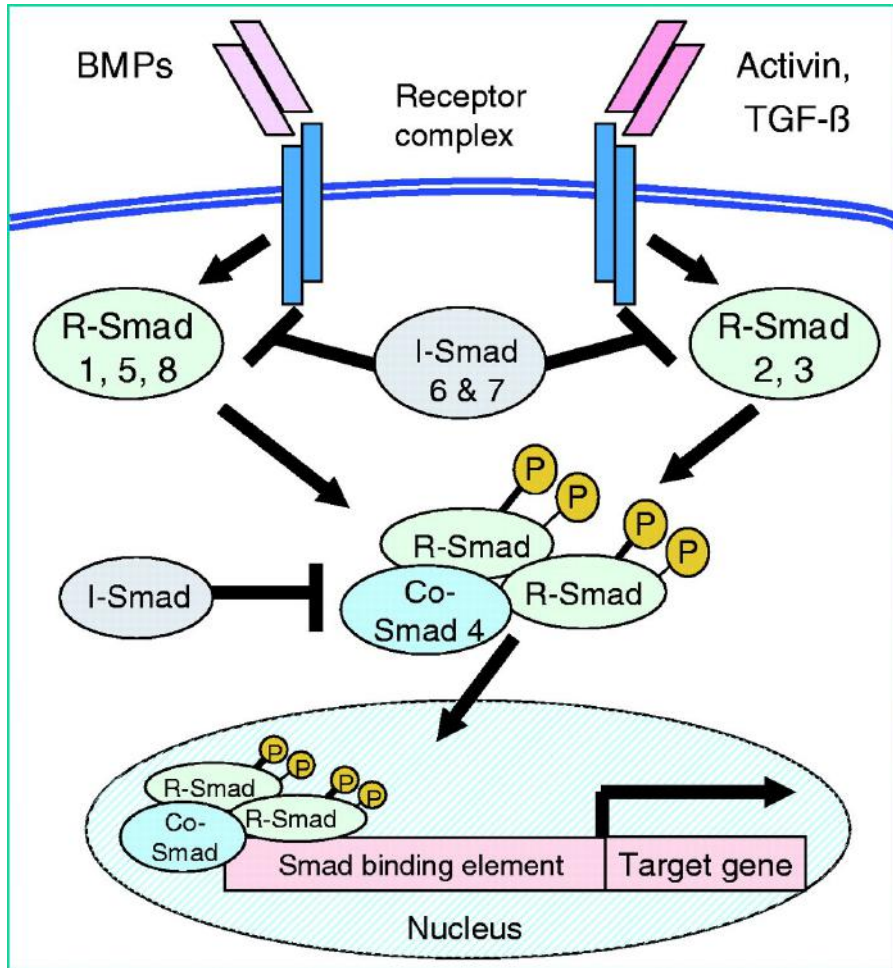


Figure 2 Model for pathogenesis of MDS. A mutation or epigenetic alteration in hematopoietic stem cells (HSC), leads to generation of pro-inflammatory milieu in marrow microenvironment that can result in apoptotic cell death of normal HSCs. Inhibition of myelo-suppressive cytokine signaling cascades can stimulate hematopoietic activity in HSCs.

VI Reunión

GESMMD



High EPO levels drive proliferation

Excessive GDF-induced Smad2/3 signaling inhibits RBC maturation

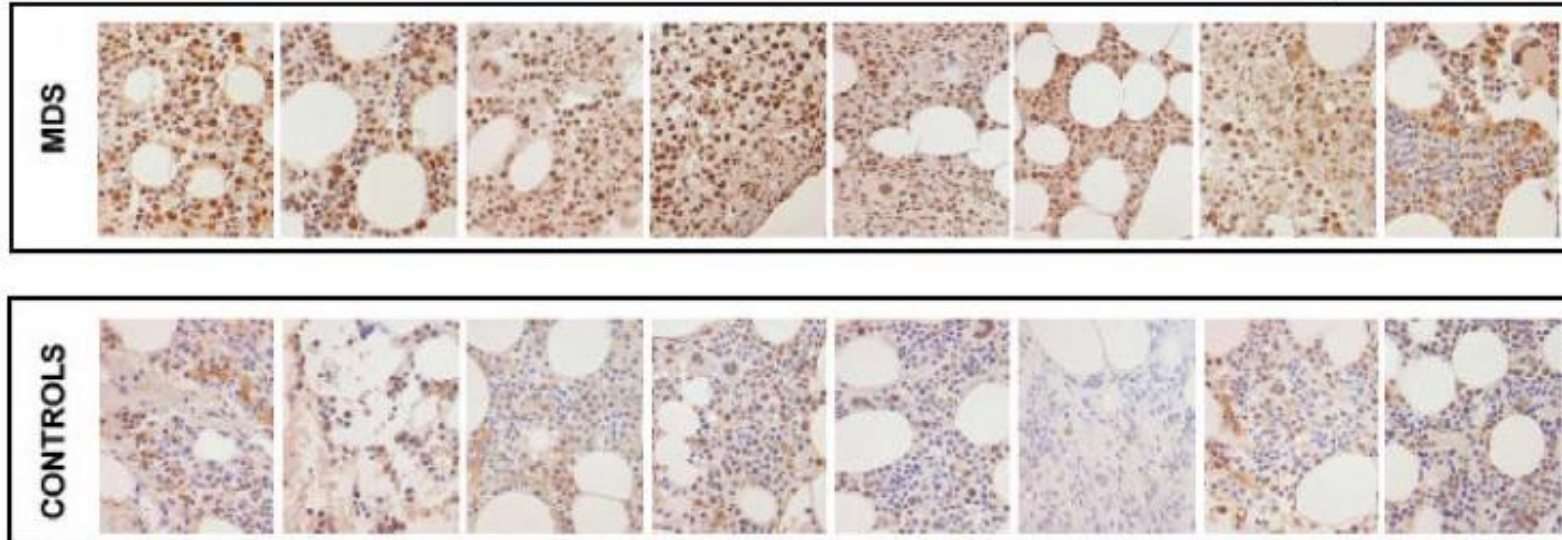
→ GDF-11
Growth Differentiation Factor 11

VI Reunión

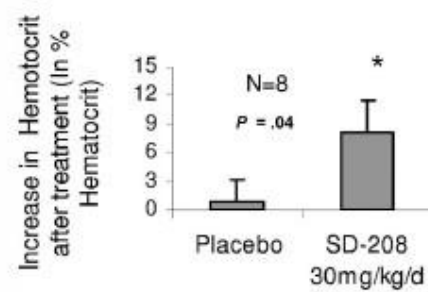
GESMD

A

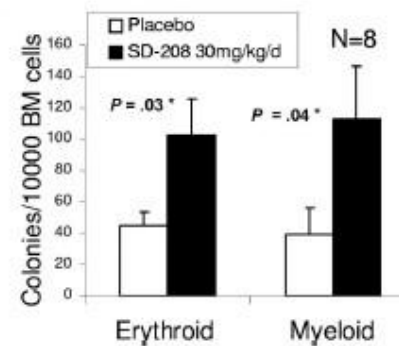
Phospho-Smad2 IHC



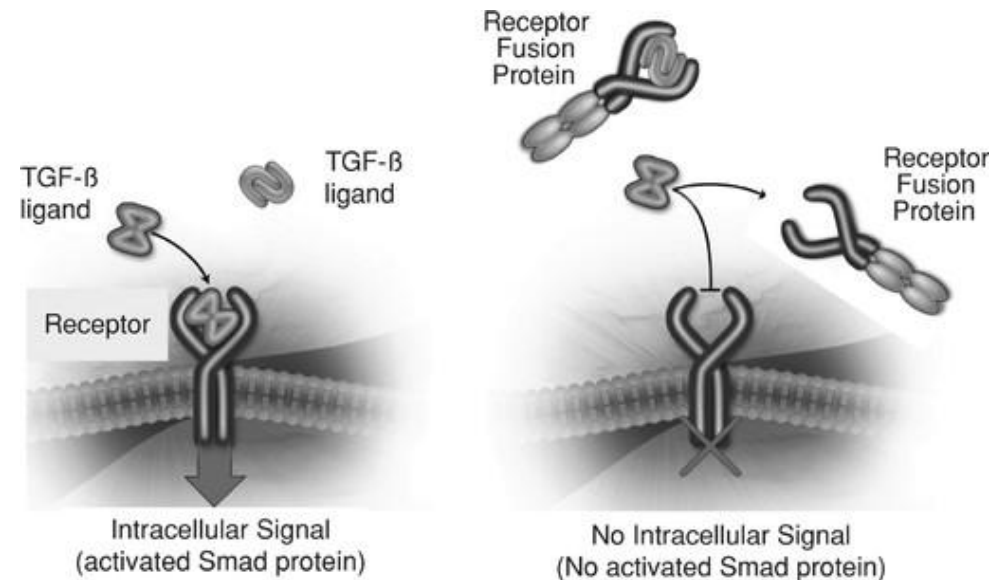
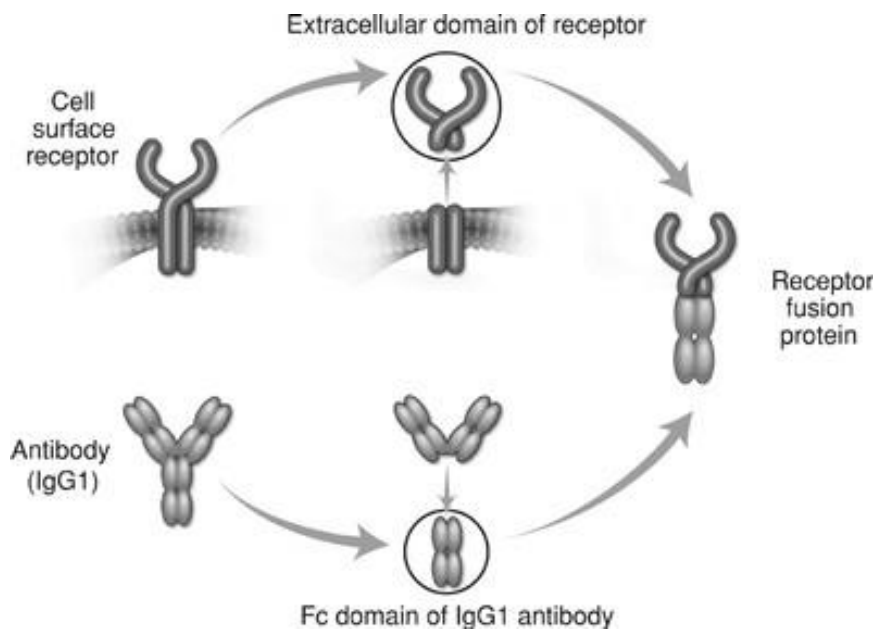
C



D



PROTEINAS DE FUSION LIGAND-TRAP



Modified ECD of ActRIIB receptor

Fc domain of human IgG₁ antibody

ACE-011 SOTATERCEPT- Receptor Activina tipo IIA
ACE-536 LUSPATERCEPT-Receptor Activina tipo IIB
Subcutáneo cada 21 días

**A Phase 2, Dose-Finding Study of
Sotatercept (ACE-011) in Patients With
Lower-Risk Myelodysplastic Syndromes or
Non-Proliferative Chronic Myelomonocytic
Leukemia and Anemia Requiring
Transfusion**

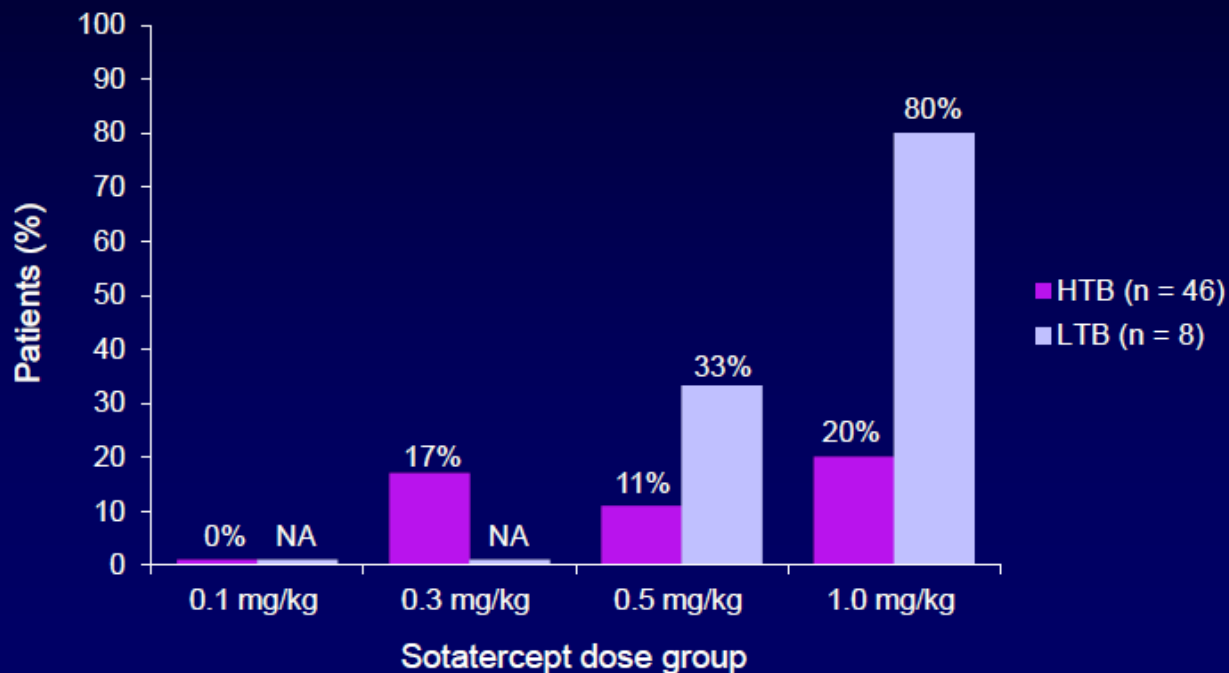
Rami Komrokji¹, Guillermo Garcia-Manero², Lionel Ades³, Abderrahmane Laadem⁴,
Bond Vo⁴, Thomas Prebet⁵, Aspasia Stamatoullas⁶, Thomas Boyd⁷, Jacques Delaunay⁸,
David P. Steensma⁹, Mikkael A. Sekeres¹⁰, Odile Beyne-Rauzy¹¹, Jun Zou⁴,
Kenneth M. Attie¹², Matthew L. Sherman¹², Pierre Fenaux³, Alan F. List¹

Results: Baseline Characteristics

Characteristic	Sotatercept dose group					Overall (N = 59)
	0.1 mg/kg (n = 7)	0.3 mg/kg (n = 6)	0.5 mg/kg (n = 21)	1.0 mg/kg (n = 20)	2.0 mg/kg (n = 5)	
Serum EPO level, n (%)						
≤ 500 mIU/mL	4 (57)	5 (83)	11 (52)	13 (65)	2 (40)	35 (59)
> 500 mIU/mL	3 (43)	1 (17)	8 (38)	6 (30)	1 (20)	19 (32)
Missing	0	0	2 (10)	1 (5)	2 (40)	5 (9)
Prior use of ESA, n (%)	6 (86)	6 (100)	20 (95)	20 (100)	4 (80)	56 (95)
Prior use of hypomethylating agents, n (%)	6 (86)	6 (100)	13 (62)	6 (30)	0	31 (53)
Prior use of lenalidomide, n (%)	5 (71)	5 (83)	10 (48)	6 (30)	1 (20)	27 (46)
Prior use of other MDS treatments, n (%)	6 (86)	5 (83)	8 (38)	7 (35)	0	26 (44)

Results: Overall

Achievement of RBC-TI in HTB patients or RBC-TI with mean Hb increase ≥ 1.5 g/dL in LTB patients over any 8-week period



NA, not applicable.

Results: Common Adverse Events

	Sotatercept dose group					Overall (N = 59)
	0.1 mg/kg (n = 7)	0.3 mg/kg (n = 6)	0.5 mg/kg (n = 21)	1.0 mg/kg (n = 20)	2.0 mg/kg (n = 5)	
Patients with ≥ 1 TEAE	6 (86)	3 (50)	20 (95)	19 (95)	4 (80)	52 (88)
TEAEs $\geq 10\%$ of patients						
Fatigue/asthenia ^a	0	1 (17)	10 (48)	12 (60)	1 (20)	24 (41)
Peripheral edema	2 (29)	2 (33)	4 (19)	4 (20)	0	12 (20)
Diarrhea	0	2 (33)	5 (24)	3 (15)	2 (40)	12 (20)
Nausea	0	1 (17)	4 (19)	4 (20)	1 (20)	10 (17)
Constipation	0	1 (17)	6 (29)	2 (10)	0	9 (15)
Vomiting	0	1 (17)	2 (10)	3 (15)	0	6 (10)
Decreased appetite	0	0	3 (14)	3 (15)	0	6 (10)
Pain in extremity	0	1 (17)	2 (10)	3 (15)	0	6 (10)
Headache	3 (43)	1 (17)	2 (10)	2 (10)	1 (20)	9 (15)
Dizziness	1 (14)	2 (33)	1 (5)	1 (5)	1 (20)	6 (10)
Cough	1 (14)	1 (17)	2 (10)	5 (25)	0	9 (15)
Dyspnea	0	1 (17)	4 (19)	2 (10)	0	7 (12)
Grade 3–4 TEAEs ^b	1 (14)	1 (17)	9 (43)	5 (25)	2 (40)	18 (31)

^aPooled incidence of fatigue and asthenia. ^bTreatment-related AEs were reported in 3 patients: 1 patient with grade 3 pain in extremity, 1 patient with grade 3 hypertension, and 1 patient with grade 4 acute myeloid leukemia.
TEAE, treatment-emergent adverse event.



LUSPATERCEPT INCREASES HEMOGLOBIN AND REDUCES TRANSFUSION BURDEN IN PATIENTS WITH LOW OR INTERMEDIATE-1 RISK MYELODYSPLASTIC SYNDROMES (MDS): PRELIMINARY RESULTS FROM A PHASE 2 STUDY

Uwe Platzbecker, MD

U Platzbecker¹, U Germing², A Giagounidis³, K Goetze⁴, P Kiewe⁵, K Mayer⁶, O Ottman⁷, M Radsak⁸,
T Wolff⁹, D Haase¹⁰, M Hankin¹¹, D Wilson¹¹, A Laadem¹², M Sherman¹¹ and K Attie¹¹

¹Universitätsklinikum Carl Gustav Carus, Dresden; ²Universitätsklinikum Düsseldorf;

³Marien Hospital Düsseldorf; ⁴Technical University of Munich; ⁵Onkologischer Schwerpunkt

am Oskar-Helene-Heim, Berlin; ⁶Universitätsklinikum Bonn; ⁷Klinikum der J.W. Goethe-Universität Frankfurt;

⁸University Medical Center - Johannes Gutenberg-Universität, Mainz; ⁹OncoResearch Lerchenfeld UG, Hamburg;

¹⁰Department of Hematology and Medical Oncology, University Medicine of Göttingen, Germany;

¹¹Acceleron Pharma, Cambridge, MA; ¹²Celgene Corporation, Summit, NJ, USA



Dosing Cohorts

- **Enrollment complete (N=58)**
 - **Dose Escalation, N=27, completed**
 - 7 sequential cohorts, n=3-6 each, luspatercept dose ranging from 0.125 to 1.75 mg/kg
 - **Expansion Cohort, N=31, ongoing**
 - Starting dose 1.0 mg/kg, individual dose titration up to 1.75 mg/kg
 - 17 patients had at least 4 cycles of treatment or discontinued early, and were included in the analysis as of 23 Feb 2015
- **Preliminary results for 44 patients are presented**

	Dose Escalation							Expansion
Dose Level (mg/kg)	0.125	0.25	0.50	0.75	1.0	1.33	1.75	1.0 ^a
No. of patients	3	3	3	6	3	6	3	17

^aStarting dose level; dose level increased to 1.33 mg/kg in 5 patients and to 1.75 mg/kg in 1 patient

Erythroid Response and Transfusion Independence

Response Criteria	Lower Dose Groups 0.125-0.5 mg/kg N=9 n (%)	Higher Dose Groups 0.75-1.75 mg/kg N=35 n (%)
	Primary efficacy endpoint	3 (33%)
IWG HI-E	2 (22%)	19 (54%)
Transfusion independence (Patients who received at least one transfusion)	1/7 (14%)	10/28 (36%) <u>LTB</u> <u>HTB</u> 4/6 6/22

Primary efficacy endpoint:

For LTB patients: Hemoglobin increase ≥ 1.5 g/dL for ≥ 2 weeks
For HTB patients: ≥ 4 Unit or $\geq 50\%$ reduction in transfusions over 8 weeks

IWG HI-E:

International Working Group, Hematologic Improvement – Erythroid Response

For LTB patients: Hemoglobin increase ≥ 1.5 g/dL for ≥ 8 weeks
For HTB patients: ≥ 4 Unit reduction in transfusions over 8 weeks

Transfusion Independence:

Transfusion-free for ≥ 8 weeks on treatment

Erythroid Response in RS+, mSF3B1 Patients Higher Dose Groups (0.75-1.75 mg/kg)

Patient Population	IWG HI-E
All Patients (n=35)	19 (54%)
RS positive (n=30)	19 (63%)
RS negative (n=4)	0 (0%)
SF3B1 mutation present (n=22)	16 (73%)
SF3B1 mutation absent (n=13)	3 (23%)

IWG HI-E: For LTB patients: Hemoglobin increase ≥ 1.5 g/dL for ≥ 8 weeks
For HTB patients: ≥ 4 Unit reduction in transfusions over 8 weeks

- 39% (9/23) of RS positive patients achieved transfusion independence (TI)

Safety Summary

Adverse events (all grades) reported in ≥ 4 patients, regardless of causality

Preferred Term n (%)	0.125 mg/kg (N=3)	0.25 mg/kg (N=3)	0.50 mg/kg (N=3)	0.75 mg/kg (N=6)	1.0 mg/kg (N=3)	1.33 mg/kg (N=6)	1.75 mg/kg (N=3)	Exp 1.0 mg/kg (N=17)	Overall (N=44)
Diarrhea	0	1 (33)	1 (33)	1 (17)	0	1 (17)	0	2 (12)	6 (14)
Nasopharyngitis	0	1 (33)	0	2 (33)	0	0	0	3 (18)	6 (14)
Myalgia	0	1 (33)	1 (33)	0	1 (33)	0	0	2 (12)	5 (11)
Bone pain	0	0	1 (33)	0	2 (67)	0	0	1 (6)	4 (9)
Bronchitis	0	0	0	0	1 (33)	0	0	3 (18)	4 (9)
Headache	0	0	0	1 (17)	0	1 (17)	0	2 (12)	4 (9)
Muscle spasms	0	0	2 (67)	0	1 (33)	0	1 (33)	0	4 (9)

- Majority of adverse events (AEs) were grade 1 or 2
- Two possibly related serious adverse events (SAEs): grade 3 muscle pain (onset day 90); grade 3 worsening of general condition (onset day 46, recurred day 66, unrelated)
- One possibly related non-serious grade 3 AE of blast cell count increase

Luspatercept PACE-MDS Study: Conclusions

- In this 3 month study, lower risk MDS patients treated with luspatercept ≥ 0.75 mg/kg demonstrated a robust hematologic improvement (54% achieved IWG HI-E)
- A greater response rate was achieved in RS positive patients in the higher dose groups
 - 63% achieved IWG HI-E
 - 39% achieved transfusion independence
- Luspatercept was generally safe and well-tolerated
- These results support pivotal, controlled studies of luspatercept in patients with lower-risk MDS

A Study of Luspatercept (ACE-536) to Treat Anemia Due to Very Low, Low, or Intermediate Risk Myelodysplastic Syndromes (MEDALIST)

This study is currently recruiting participants. (see [Contacts and Locations](#))

Verified February 2016 by Celgene Corporation

Sponsor:

Celgene Corporation

Collaborator:

Acceleron Pharma, Inc.

Information provided by (Responsible Party):

Celgene Corporation

ClinicalTrials.gov Identifier:

NCT02631070

First received: November 10, 2015

Last updated: February 11, 2016

Last verified: February 2016

[History of Changes](#)

Full Text View

Tabular View

No Study Results Posted

[Disclaimer](#)

[? How to Read a Study Record](#)

Purpose

The study will be conducted in compliance with the International Council on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use/Good Clinical Practice (GCP) and applicable regulatory requirements.

This is a Phase 3, double-blind, randomized, placebo-controlled, multicenter study to determine the efficacy and safety of luspatercept (ACE-536) versus placebo in subjects with anemia due to International Prognostic Scoring System-Revised (IPSS-R) very low, low, or intermediate Myelodysplastic syndrome (MDS) with ring sideroblasts ($\geq 15\%$) who require Red blood cell (RBC) transfusions.

Condition	Intervention	Phase
Myelodysplastic Syndromes	Drug: Luspatercept Other: Placebo	Phase 3

Imetelstat in RARS and RARS-T: Background

Imetelstat: a potent telomerase inhibitor used to target malignant progenitor cells with a high level of telomerase activity^[1]

Spliceosome mutations are common in refractory anemia,^[2] suggesting that imetelstat could be clinically beneficial in pts with RARS/RARS-T

Imetelstat produced CRs and PRs in pts with ET and MF, as well as molecular responsiveness in a substantial subset of pts with spliceosome mutations^[3,4]

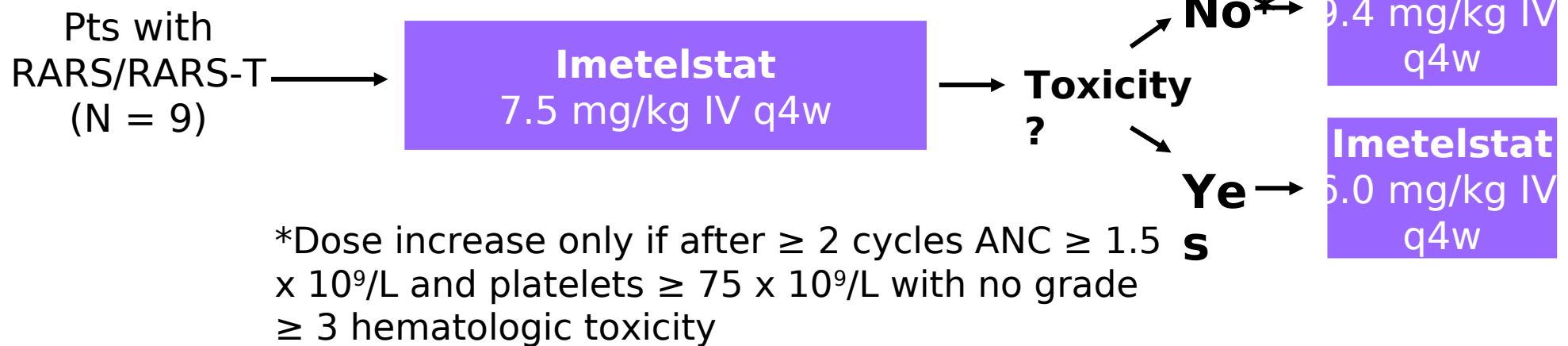
1. Joseph I, et al. Cancer Res. 2010;70:9894-9504.

2. Broséus J, et al. Leukemia. 2013;27:1826-1831.

3. Baerlocher G, et al. N Engl J Med. 2015;373:920-928.

4. Tefferi A, et al. N Engl J Med. 2015;373:908-919.

Imetelstat in RARS and RARS-T: Study Design



Assessments: efficacy (IWG response), effects on spleen size, thrombosis, leukocytosis, safety

Exploratory assessment: mutational analysis

Imetelstat in RARS and RARS-T: Results

Result

RARS/RARS-T (N = 9)

Transfusion independent (of 8 transfusion-dependent pts at study entry),* n (%)	3 (38)
Resolution of leukocytosis and thrombocytosis, n (%)	1 (11)
> 50% reduction in spleen size, n (%)	1 (11)
Normalization of neutrophil and platelet counts, n (%)	2 (22)
*Median duration: 28 wks. Erythroid Improvement (Hb ↑ 1.5 mg/dL), n (%)	1 (11)

Posttreatment analysis: no effect on mutations

JAK2 (n = 3); SF3B1 (n = 7)

OTRAS DIANAS

Farmaco	Diana	Fase-N	Resultados
Biltuximab vs Plac. 15 mg/Kg/4wks	IL-6	II	12% HI-E NS
Galusertib	ALK5-TGFbeta	//	Pendiente
ARRY-614 400 a 1200 mg	P38 MAPK/Tie2	I-45 pts	12% TI
APG 101	CD95	<i>In vitro</i>	

VI Reunión

GESMD

- *La anemia transfusión dependiente en los SMD de Bajo riesgo impacta negativamente en la calidad de vida y en la supervivencia global*
- *Tras el fallo de AEEs las alternativas disponibles sin autorización en pacientes sin de5q incluyen lenalidomida y agentes hipometilantes con IT 25-45 % de duración 30-45 semanas*
- *Nuevos agentes estimulantes de eritropoyesis inhibidores de vía TGF muestran datos prometedores para pacientes previamente muy tratados*
- *Es necesario establecer herramientas predictoras de respuesta a cada uno de los agentes (CRB-Metilación etc,..) para optimizar y establecer las líneas de tratamiento efectivas para alcanzar IT de la máxima duración posible.*

MUCHAS GRACIAS