



# Imetelstat in RBC Transfusion-Dependent Lower Risk MDS Relapsed/Refractory to Erythropoiesis-Stimulating Agents (IMerge): Updated Efficacy and Safety

Pierre Fenaux<sup>1</sup>, Azra Raza<sup>2</sup>, Edo Vellenga<sup>3</sup>, Uwe Platzbecker<sup>4</sup>, Valeria Santini<sup>5</sup>, Irina Samarina<sup>6</sup>, Koen Van Eygen<sup>7</sup>, María Díez-Campelo<sup>8</sup>, Mrinal M. Patnaik<sup>9</sup>, Laurie Jill Sherman<sup>10</sup>, Libo Sun<sup>11</sup>, Helen Varsos<sup>11</sup>, Esther Rose<sup>11</sup>, Aleksandra Rizo<sup>11</sup>, **David P. Steensma**<sup>12</sup>

<sup>1</sup>Hôpital St Louis, Paris, France; <sup>2</sup>Columbia Presbyterian, New York, NY, USA; <sup>3</sup>UMCG, Groningen, Netherlands; <sup>4</sup>Universitätsklinikum Carl Gustav Carus Dresden, Germany; <sup>5</sup>AOU Careggi, University of Florence, Italy; <sup>6</sup>Emergency Hospital of Dzerzhinsk, Nizhny Novgorod, Russia; <sup>7</sup>AZ Groeninge – Oncology Centre, Kortrijk, Belgium; <sup>8</sup>Hosp. Clinico Univ. De Salamanca, Spain; <sup>9</sup>Mayo Clinic Rochester, Rochester, MN, USA; <sup>10</sup>Janssen Research & Development, LLC, Spring House, PA, USA; <sup>11</sup>Janssen Research & Development, LLC, Raritan, NJ, USA; <sup>12</sup>Dana-Farber Cancer Institute, Boston, MA, USA

*This study was funded by Janssen Research & Development LLC and Geron Corporation*



EUROPEAN  
HEMATOLOGY  
ASSOCIATION

## Disclosures: David P. Steensma

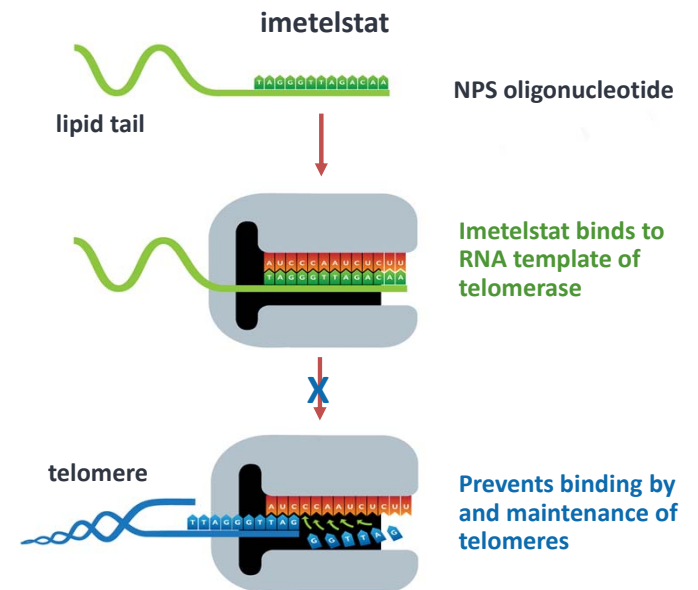
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Acceleron			√				
Amphivena						√	
Celgene	√						
H3 Biosciences	√						
Janssen	√		√				
Kura	√						
Novartis						√	
Onconova			√				
Otsuka						√	
Syros	√						
Takeda			√				



# Myelodysplastic Syndromes (MDS) and Imetelstat

- ❑ MDS are associated with multiple somatic genetic abnormalities and on average shorter telomeres than age-matched controls
- ❑ Limited treatment options are available for anemia in lower risk MDS relapsed or refractory to ESA therapy
- ❑ Higher telomerase activity, expression of hTERT and shorter telomeres predict for shorter overall survival in lower risk MDS
- ❑ Imetelstat is a first-in-class telomerase inhibitor, targets cells with short telomere lengths and active telomerase, and has clinical activity in myeloid malignancies<sup>1-3</sup>

ESA, erythropoiesis-stimulating agent; hTERT, human telomerase reverse transcriptase.



1. Baerlocher GM, et al. *N Engl J Med* 2015;373:920-928
2. Tefferi A, et al. *N Engl J Med* 2015;373:908-919
3. Tefferi A, et al. *Blood Cancer J* 2016;6:e405



EUROPEAN  
HEMATOLOGY  
ASSOCIATION

## IMerge Study Design: Part 1

### Patients with MDS (N=32)

- IPSS Low or Int-1
- Relapsed / refractory to ESA or ineligible for ESA
- Transfusion dependent ( $\geq 4$ u RBC/8 wks)
- Prior therapy with lenalidomide or HMA permitted
- Del(5q) karyotype permitted

single arm  
→  
open label

### Imetelstat Treatment

7.5 mg/kg IV q4w  
(2-hr infusion)  
increase to 9.4 mg/kg  
allowed after 3 cycles

**1° Endpoint:** 8-Week RBC TI

**2° Endpoints:** 24-Week RBC TI / Time to TI / TI duration / TR (HI-E: Transfusion Reduction by  $\geq 4$  RBC units over 8 weeks) / MDS response per IWG / OS / Incidence of AML / Safety

**Pre-medication:** diphenhydramine, hydrocortisone 100-200 mg (or equivalent)

**Supportive care:** RBC transfusions, myeloid growth factors per local guidelines



# IMerge: Baseline Characteristics and Prior Treatment

Parameters	N=32
Median age (range), year	68.5 (46-83)
Male, n (%)	16 (50)
ECOG PS 0-1, n (%)	29 (91)
IPSS risk, n (%) Low / intermediate-1	19 (59) / 13 (41)
Baseline median (range) RBC transfusion burden, units/8 weeks	6 (4-14)
Karyotype <sup>a</sup> , n (%) Normal Any abnormality / del(5q)	17 (53) 11 (34) / 7 (22)
WHO 2001 category, n (%) RARS or RCMD-RS / All others	16 (50) / 16 (50)
sEPO > 500 mU/mL, n (%)	13 <sup>b</sup> (43)
Prior ESA / lenalidomide / decitabine or azacitidine, n (%)	28 (88) / 12 (38) / 8 (25)
Naïve to lenalidomide and HMA and non-del(5q), n (%)	13 (41)

<sup>a</sup>Results were missing from the central laboratory for 4 patients. <sup>b</sup>Of the 30 patients with sEPO levels reported.



EUROPEAN  
HEMATOLOGY  
ASSOCIATION

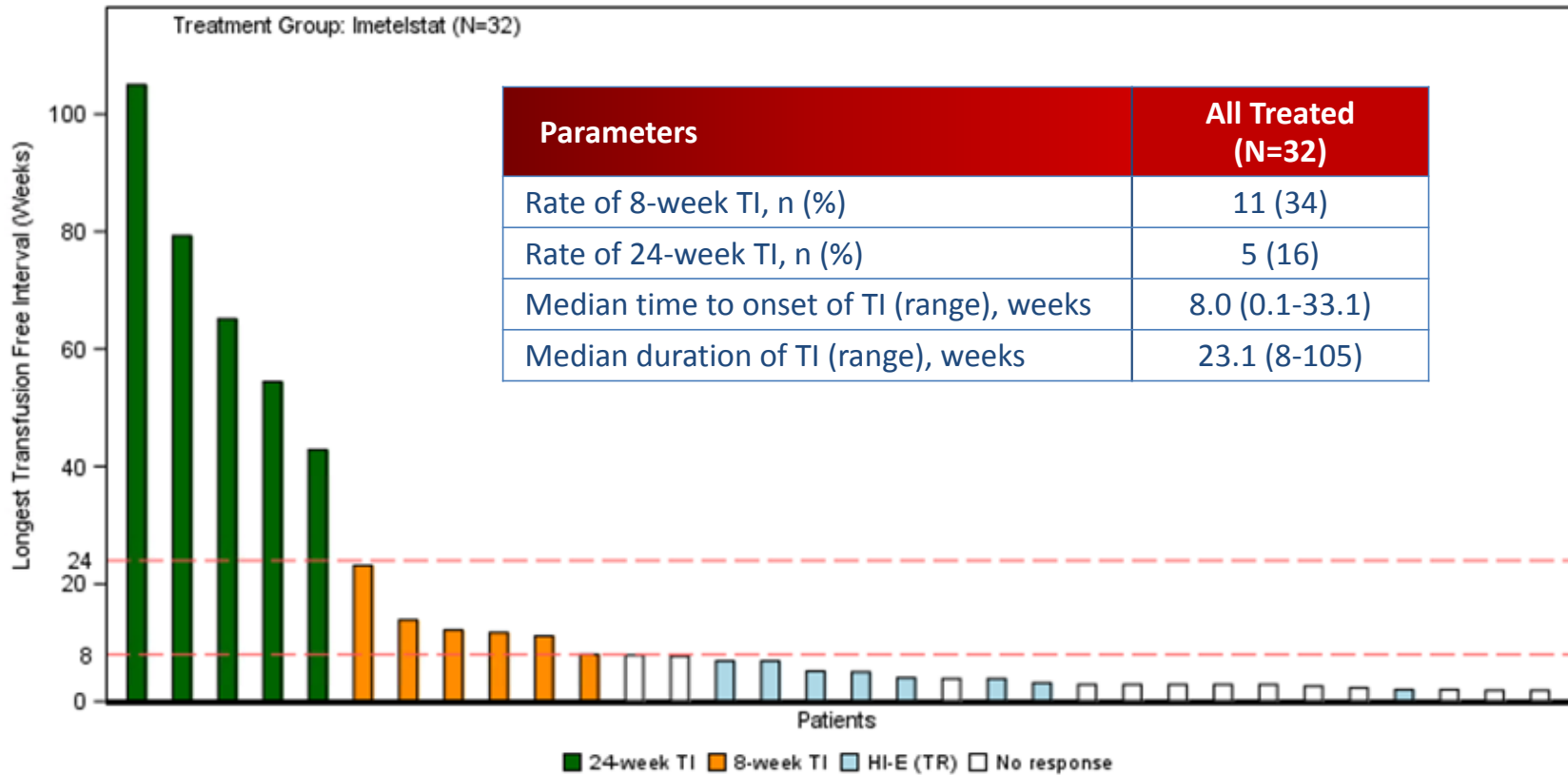
## IMerge: Treatment Exposure

- ❑ Median follow-up for this analysis: 95 weeks
  - Clinical Cutoff: 10-May-2018
- ❑ Median number of treatment cycles: 6.5 (range: 1–28) cycles
- ❑ 7 patients had imetelstat dose escalation to 9.4 mg/kg
- ❑ 16 patients (50%) had dose reductions and 19 patients (59%) had cycle delays



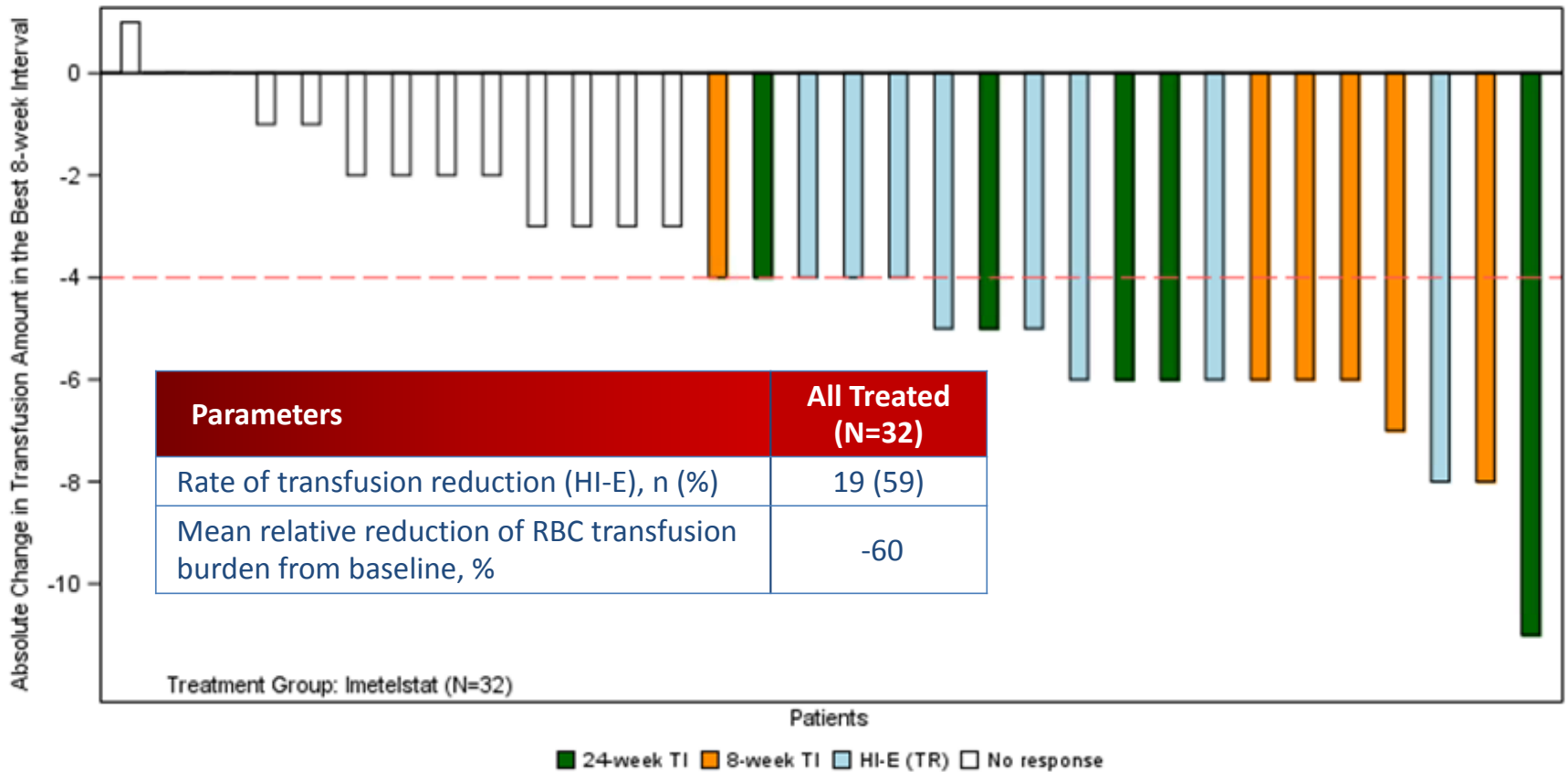
EUROPEAN  
HEMATOLOGY  
ASSOCIATION

# IMerge: Longest Transfusion-Free Interval





# IMerge: Absolute Change in Transfusion Amount in the Best 8-Week Interval







EUROPEAN  
HEMATOLOGY  
ASSOCIATION

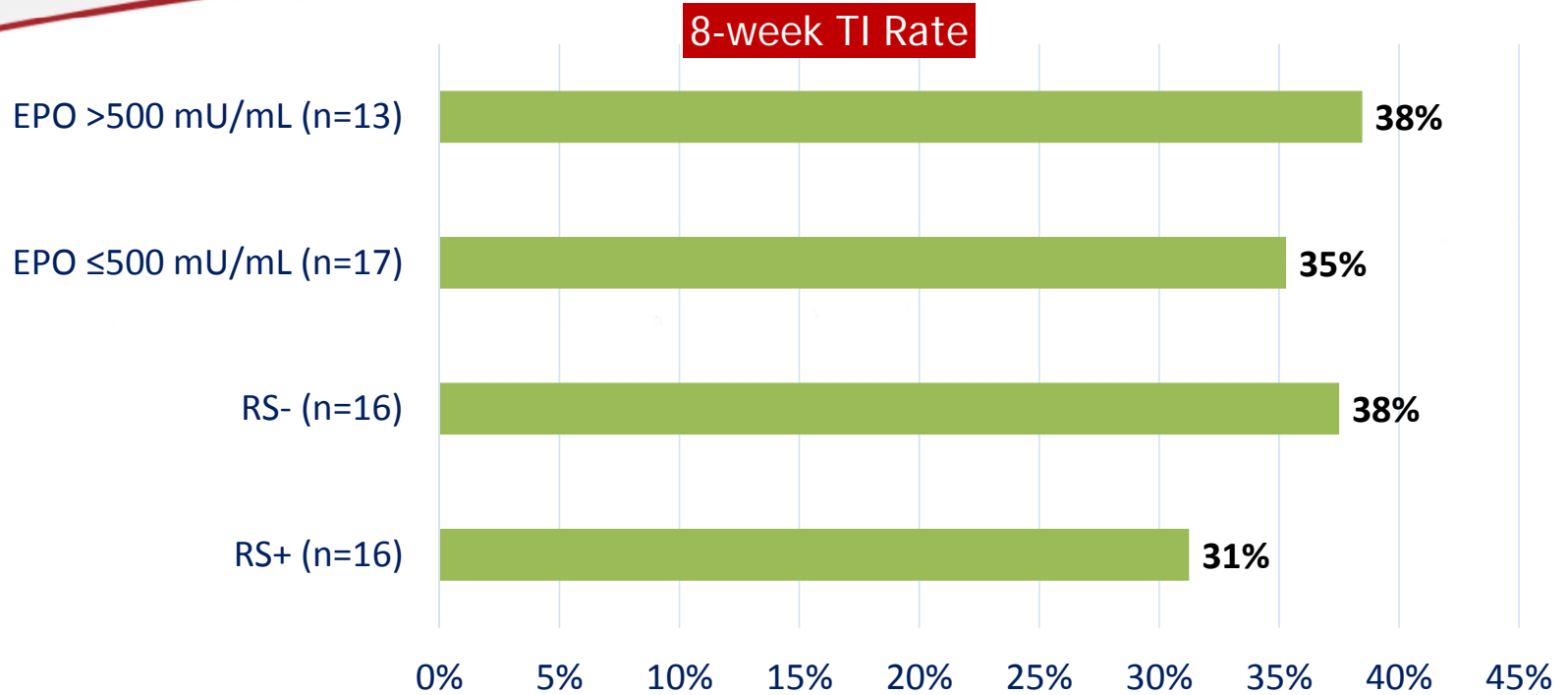
## IMerge: Key Efficacy Outcomes

Parameters	All Treated (N=32)	Lenalidomide and HMA naïve and Non-del(5q) (n=13)
Rate of 8-week TI, n (%)	11 (34)	7 (54)
Rate of 24-week TI, n (%)	5 (16)	4 (31)
Median time to onset of TI (range), weeks	8.0 (0.1-33.1)	8.3 (0.1-33.1)
Median duration of TI (range), weeks	23.1 (8-105)	42.9 (8-105)
Rate of transfusion reduction (HI-E), n (%)	19 (59)	9 (69)
Mean relative reduction of RBC transfusion burden from baseline, %	-60	-71
CR + marrow CR + PR (per IWG), n (%)	6 (19)	4 (31)



EUROPEAN  
HEMATOLOGY  
ASSOCIATION

# IMerge: Efficacy Results in EPO and RS Subgroups



Similar efficacy was observed across these subgroups



EUROPEAN HEMATOLOGY ASSOCIATION

# IMerge: Hemoglobin and Imetelstat Dosing Among Patients with Durable TI

Prior RBC Transfusion Burden

6 units/8 weeks

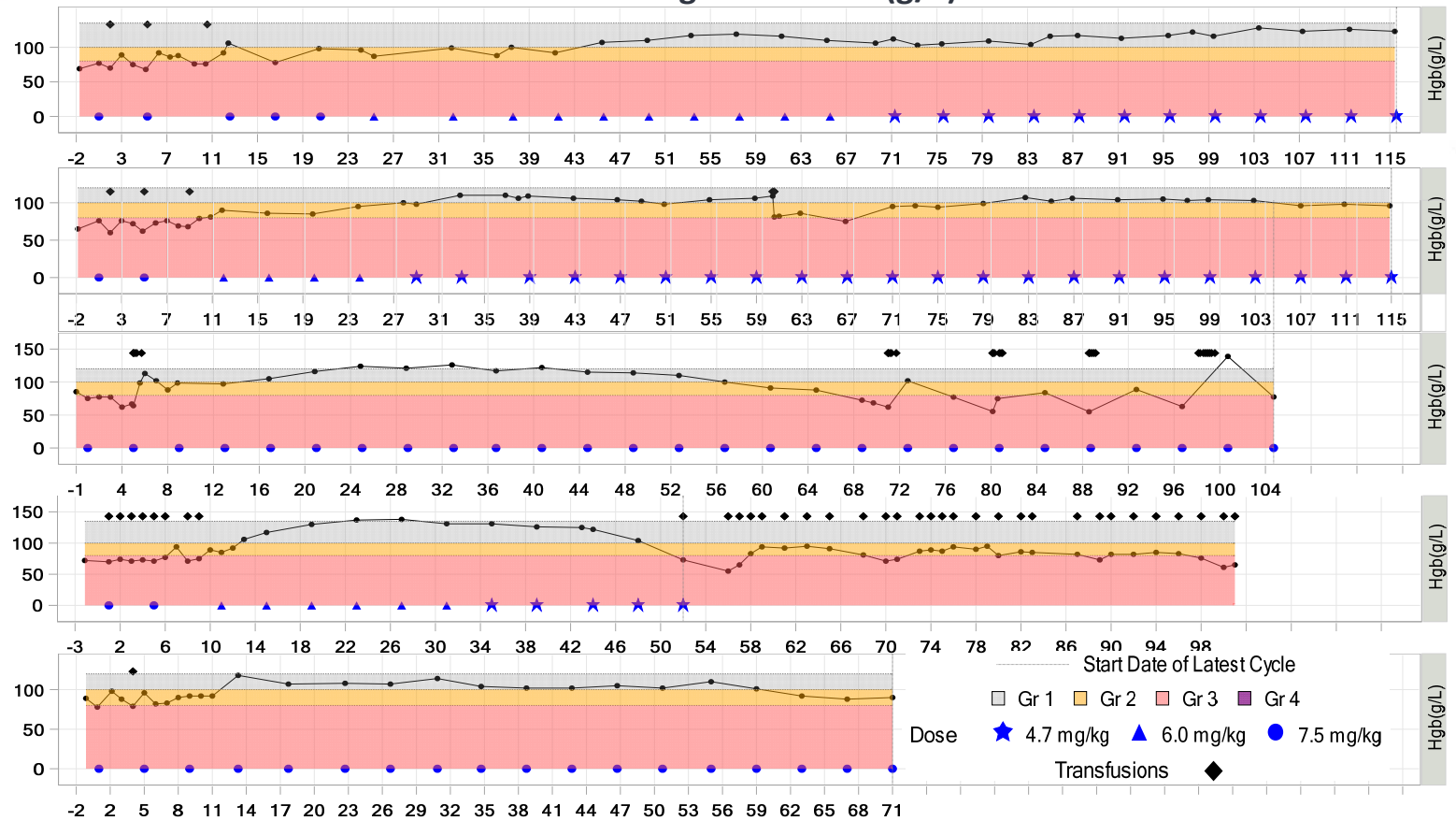
6 units/8 weeks

5 units/8 weeks

11 units/8 weeks

4 units/8 weeks

Hemoglobin Levels (g/L)





EUROPEAN  
HEMATOLOGY  
ASSOCIATION

## IMerge: Most Common Adverse Events (All Grades)

Safety findings for those who were lenalidomide/HMA-naïve/non-del(5q) were similar to the overall study population

≥10% of Patients in All Treated Patients	All Treated (N=32)	Lenalidomide and HMA naïve and Non-del(5q) (n=13)
Patients with ≥1 treatment-emergent AEs, n (%)	31 (97)	12 (92)
Neutropenia	23 (72)	7 (54)
Thrombocytopenia	18 (56)	8 (62)
Headache	8 (25)	2 (15)
ALT increased	6 (19)	3 (23)
AST increased	5 (16)	3 (23)
Leukopenia	5 (16)	2 (15)
Muscle spasms	5 (16)	2 (15)
Diarrhea	5 (16)	2 (15)
Anemia	4 (13)	2 (15)
Asthenia	4 (13)	4 (31)
Back pain	4 (13)	2 (15)
Constipation	4 (13)	2 (15)
Cough	4 (13)	1 (8)
Dyspnea	4 (13)	2 (15)
Influenza like illness	4 (13)	1 (8)
Nausea	4 (13)	2 (15)
Peripheral edema	4 (13)	2 (15)
Viral URI	4 (13)	4 (31)



## IMerge: Occurrence and Reversibility of Gr 3/4 Cytopenias

	All Treated (N=32)	Lenalidomide and HMA naïve and Non-del(5q) (n=13)
Neutrophils, n (%)		
Grade 3	8 (25)	2 (15)
Recovered < 4 weeks	4 (50)	1 (50)
Grade 4	13 (41)	5 (38)
Recovered < 4 weeks	12 (92)	5 (100)
Platelets, n (%)		
Grade 3	10 (31)	5 (38)
Recovered < 4 weeks	9 (90)	5 (100)
Grade 4	8 (25)	3 (23)
Recovered < 4 weeks	6 (75)	3 (100)



## Conclusions (1)

- ❑ Overall, 8-week TI observed in 34% of all patients, with a 24-week TI rate of 16%
  - Median time to TI: 8.0 weeks
  - Median duration of TI: 23.1 weeks
- ❑ For those who were lenalidomide/HMA-naive and non-del(5q), the 8-week and 24-week TI rates were 54% and 31%, respectively
  - Median duration of TI: 42.9 weeks
- ❑ TR (HI-E) observed in 59% of all patients
  - Mean relative reduction of RBC transfusion burden from baseline = 60%



## Conclusions (2)

- ❑ AEs (mostly cytopenias) were predictable and reversible
- ❑ These results support further study of imetelstat (7.5 mg/kg /4 weeks) in IPSS Low/Int-1, TD, ESA-relapsed/refractory MDS
- ❑ In RBC TD patients with LR-MDS (median: 6 U/8 weeks), imetelstat treatment resulted in erythroid improvement in a majority of patients
- ❑ Based on improved efficacy in the cohort who were naïve to lenalidomide and HMA and non-del(5q), a new cohort of 25 additional patients have been fully enrolled



EUROPEAN  
HEMATOLOGY  
ASSOCIATION

## Acknowledgements

The authors thank all the patients for their participation in this study and acknowledge the collaboration and commitment of all investigators and their staff



Mazure, Dominiek



Jang, Jun Ho  
Kim, Inho



Langemeijer, Saskia  
van de Loosdrecht, Arjan



Oliva, Esther



Gourin, Marie-Pierre  
Gyan, Emmanuel  
Legros, Laurence  
Thepot, Sylvain



Alexander, Pristupa  
Samoilova, Olga  
Udovitsa, Dmitry



De Paz, Raquel  
Esteve, Jordi  
Font, Patricia  
Valcarcel, David  
Xicoy, Blanca



Boccia, Ralph  
Grunwald, Michael  
Jacoby, Megan  
Miller, Carole  
Schiller, Gary  
Silverman, Lewis  
Stevens, Don



Germing, Ulrich