Treatment with Imetelstat Provides Durable Transfusion Independence (TI) in Heavily Transfused Non-Del(5Q) Lower Risk MDS (LR-MDS) Relapsed/Refractory (R/R) to Erythropoiesis Stimulating Agents (ESAs)

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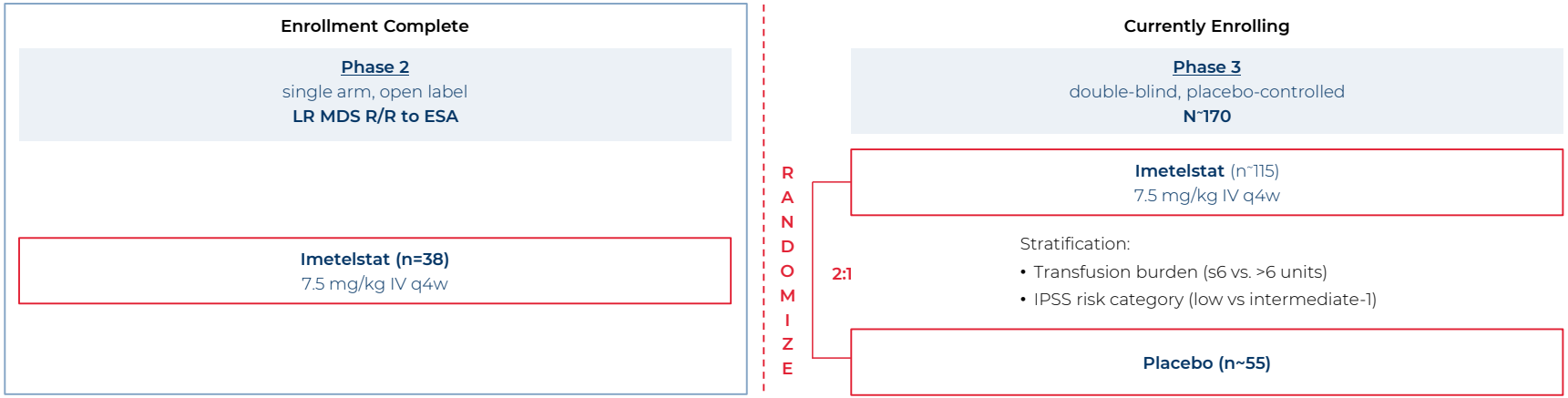
HEMA NEWS

Phase 2/3 Study Design



- **LR MDS patients:**
  - Non-del(5q), IPSS Low or Int-1
  - Relapsed/Refractory to ESA or EPO >500 mU/ml; HMA/Len naïve
  - Transfusion dependent: ≥ 4 units RBC/8 weeks over 16 week pre-study period
- **Primary Endpoint: 8-week RBC Transfusion Independence (TI)**
- **Key Secondary Endpoints: 24-week RBC TI/Duration of TI/HI-E**

EPO, erythropoletric, ESA, erythropoletric-stimulating agent; HI-E, hematologic improvement-erythroid; HMA, hypomethylating agents; IPSS, International Prognostic Scoring System; Len, lenalidomide; LR, low risk; RBC, red blood cell; R/R, relapsed/refractory

Meaningful and Durable Transfusion Independence (TI) with Imetelstat Treatment

Parameters	N = 38
8-week TI, n (%)	**16 (42)**
Time to onset of 8-week TI, weeks, median (range)	8.3 (0.1-40.7)
Duration of TI, weeks, median (95% CI)[a]	**88.0 (23.1 – 140.9*)**
Cumulative duration of TI ≥ 8 weeks[b], median (95% CI)[a]	92.3 (42.9, 140.9)
Hb rise ≥ 3.0 g/dL during TI[c], n (%)	12 (32)
24-week TI, n (%)	**12 (32)**
Hb rise ≥ 3.0 g/dL during TI[c], n (%)	11 (29)
1-year TI, n (%)	**11 (29)**

[a] Kaplan Meier method; [b] Cumulative Duration of TI ≥ 8 weeks is defined as the sum of all periods of TI ≥ 8 weeks during the treatment; [c] Maximum Hb rise of ≥ 3g/dL from pretreatment level (pretreatment level defined as mean Hb / 8 weeks).
CI, confidence interval; Hb, hemoglobin

***Longest TI > 2.7 years**

Hematologic Improvement and IWG Response with Imetelstat Treatment

Parameters	N = 38
HI-E per IWG 2006, n (%)	**26 (68)**
≥1.5 g/dL increase in Hb lasting ≥ 8 weeks[a], n (%)	13 (34)
Transfusion reduction by ≥ 4 units/8 weeks, n (%)	26 (68)
Duration of HI-E, weeks, median (95% CI)[b]	**92.7 (37.1, 149.4)**
Major and Minor Response per IWG 2018	
Major response: 16-week TI, n (%)	**14 (37)**
Minor response: ≥ 50% transfusion reduction/16 weeks, n (%)	21 (55)
CR + marrow CR, n (%)	9 (24)
CR, n (%)	4 (11)
marrow CR, n (%)	5 (13)

[a] All patients also achieved 8 week TI
[b] Kaplan Meier method
CI, confidence interval; CR, complete remission; Hb, hemoglobin; HI-E, hematologic improvement-erythroid; IWG 2006, International Working Group Response Criteria 2006; TI, Transfusion Independence

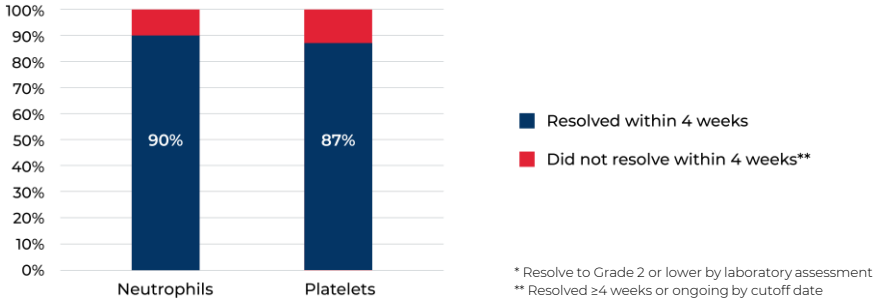
Reversible Grade 3/4 Cytopenias without Significant Clinical Consequences

Frequency of Hematologic AEs

AE	All Grades N=38 n (%)	Grade 3/4 N=38 n (%)
Thrombocytopenia	25 (66)	23 (61)
Neutropenia	22 (58)	21 (55)
Anemia	11 (29)	8 (21)

- 2/38 pts (5%) had febrile neutropenia (Gr3)
- 3/38 pts (8%) had Grade 3/4 bleeding

Reversibility of Grade 3/4 Cytopenias*



* Resolve to Grade 2 or lower by laboratory assessment
** Resolved ≥4 weeks or ongoing by cutoff date

Imetelstat in LR MDS Key Conclusions

- **Imetelstat treatment shows meaningful and durable transfusion independence:**
  - **High rates of TI and HI-E:** 42% 8-week TI rate and 68% HI-E rate
  - **Durable TI and HI-E:** Median duration of TI is 20 months and median duration of HI-E is 21 months
  - **TI across multiple patient subtypes:** RS+ and RS-, high and very high transfusion burden
- **Potential disease-modifying activity:**
  - 29% of patients transfusion free for ≥1 year
  - 75% of TI responders had hemoglobin rise of ≥ 3g/dL from pretreatment level
  - Reduction in SF3B1 mutation correlated with shorter onset time to achieve TI
- **No new safety signal** identified; reversable cytopenias were most frequent AEs, without significant clinical consequences
- **Phase 3 trial ongoing:** double-blind, placebo-controlled , 2:1 randomization