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Trial in Progress
Abstract #3113

IMerge
63935937MDS3001

IMerge: A Phase 3 Study to Evaluate Imetelstat in Transfusion-Dependent Subjects with IPSS Low or Intermediate-1 Risk Myelodysplastic Syndromes (MDS) that is Relapsed/Refractory to Erythropoiesis-Stimulating Agent (ESA) Treatment

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Disclosure

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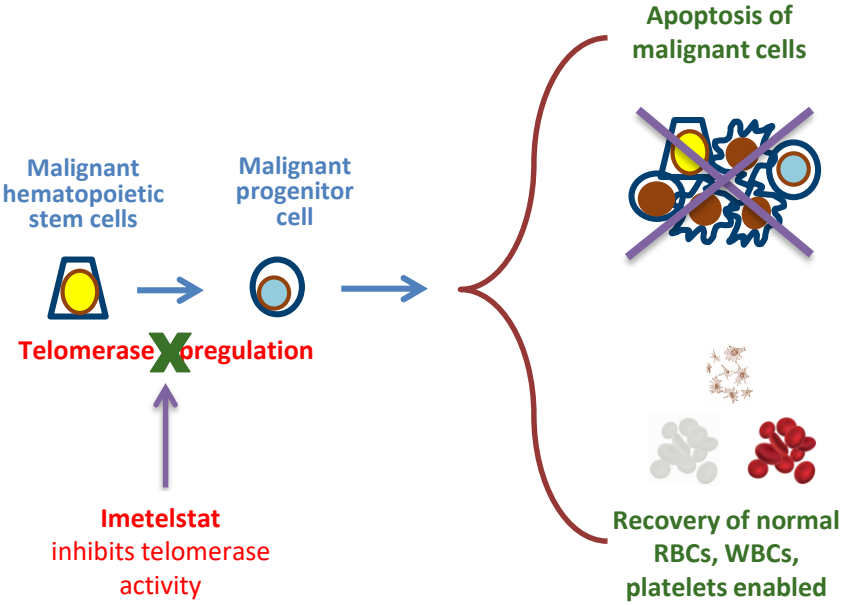
Introduction

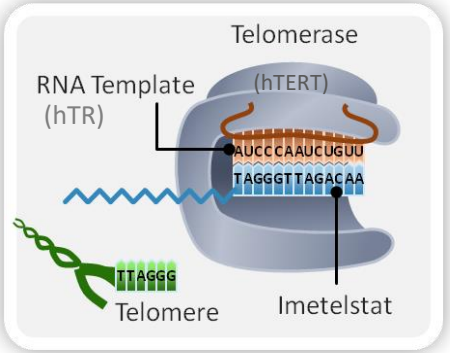
- Myelodysplastic syndromes (MDS) are characterized by clonal myeloproliferation arising from malignant progenitor cell clones that have multiple genetic abnormalities.[1]
- Patients with red blood cell (RBC) transfusion-dependent (TD), lower risk MDS (LR-MDS) that has relapsed or is refractory to erythropoiesis-stimulating agents (ESAs) have limited treatment options. New approaches are needed.
- Higher telomerase activity, overexpression of human telomerase reverse transcriptase (hTERT) and shorter telomeres predict for shorter overall survival in LR-MDS.[2, 3]

1. Sperling AS, et al, Nat Rev Cancer 2017; 17(1): 5–19.
2. Gurkan E, et al , Leuk Res 2005; 29:1131-9.
3. Mittelman M, et al, Leukemia Research 34 (2010) 1551–1555.

Imetelstat: First-in-Class Telomerase Inhibitor with Disease-Modifying Potential



Imetelstat binds to RNA template, preventing maintenance of telomeres

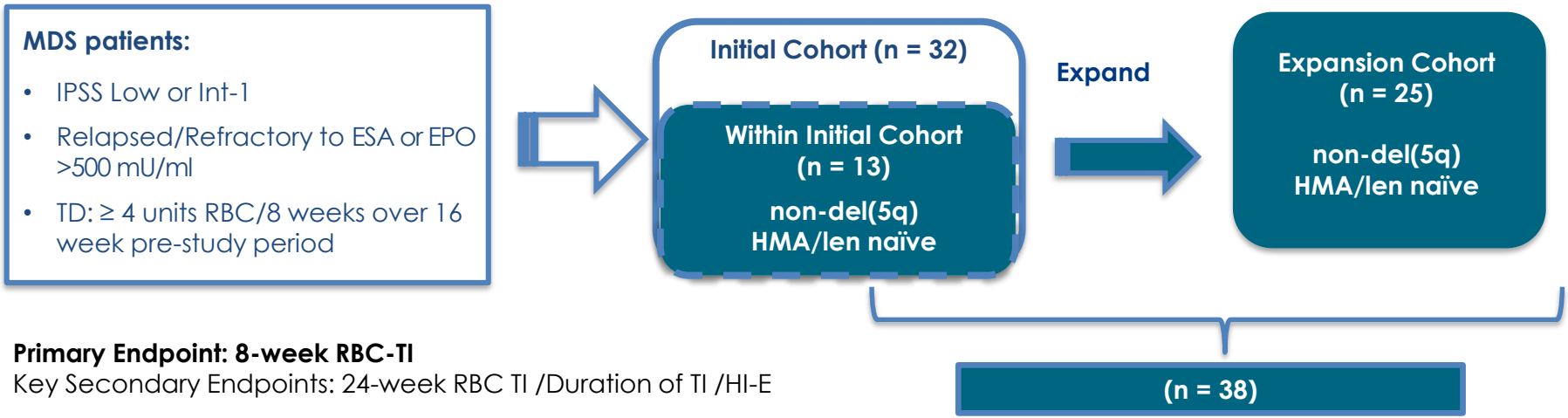


Mechanism of Action

- **Potent competitive inhibitor of telomerase activity**
- **Structure:** Proprietary 13-mer thio-phosphoramidate (NPS) oligonucleotide, with covalently-bound lipid tail to increase cell permeability
- **Disease-modifying potential: selective killing** of malignant stem and progenitor cells enabling normal blood cell production

IMerge Part 1/Phase 2 of Study

- IMerge is an ongoing global two-part, Phase 2/3 study of imetelstat in RBC TD patients with LR-MDS with a primary endpoint of 8-week RBC Transfusion Independence (TI). Patients in Phase 2 received open-label treatment with imetelstat at 7.5 mg/kg IV q 4 weeks.
- Phase 2 enrolled 57 patients: an initial cohort of 32 patients and an expansion cohort of 25 lenalidomide (len) and hypomethylating agent (HMA) naïve patients without del(5q) based on the results from the initial cohort.



Primary Endpoint: 8-week RBC-TI
Key Secondary Endpoints: 24-week RBC TI /Duration of TI /HI-E

Result from IMerge Part 1/Phase 2 of Study

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)**
HI-E per IWG 2006, n (%)	26 (68)
≥1.5 g/dL increase in Hb lasting ≥ 8 weeks, n (%)	13 (34)
Transfusion reduction by ≥ 4 units/8 weeks, n (%)	26 (68)
Duration of HI-E, weeks, median (95% CI)[a]	92.7 (37.1, 149.4)

[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**

Platzbecker et al, EHA 2020, S183
Platzbecker et al, ASH 2020, Abstract #658

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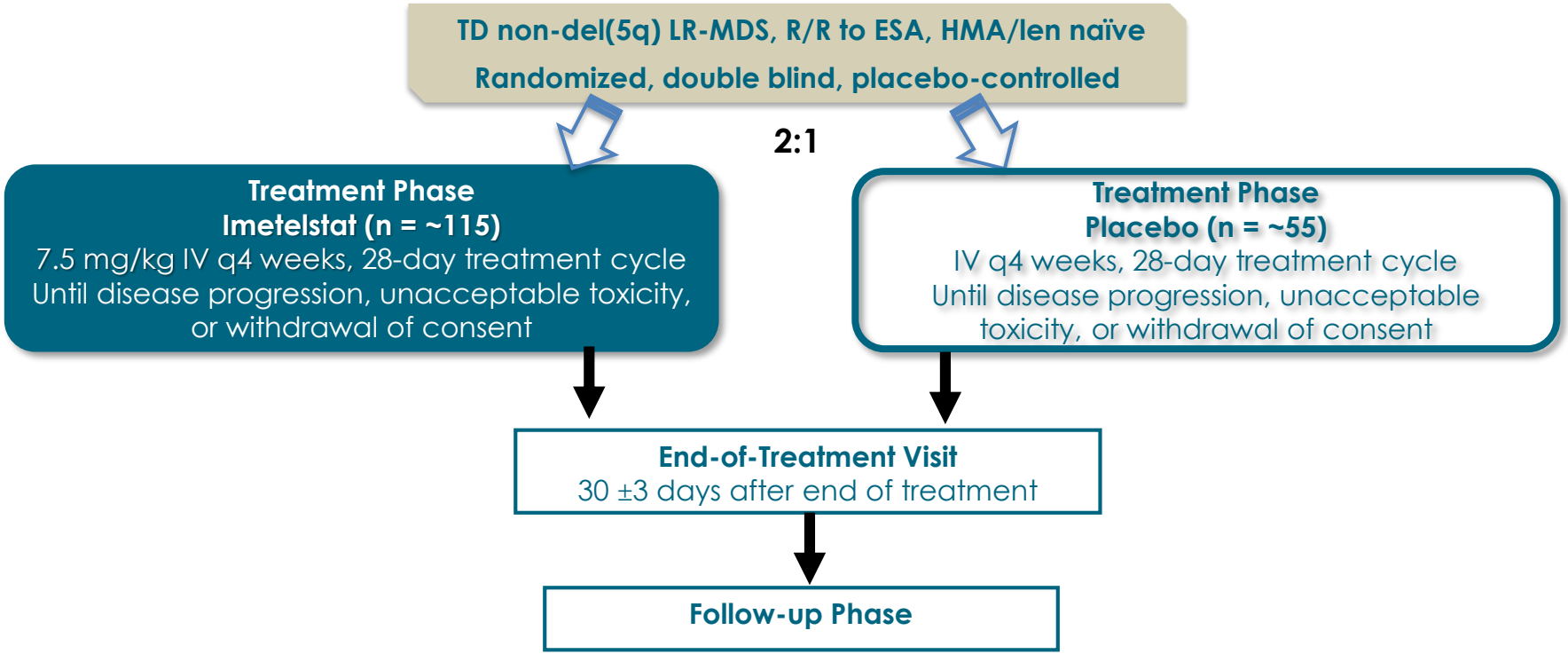
Part 2/Phase 3 Study Design



Primary endpoint: 8-week RBC TI

Phase 3 Inclusion And Exclusion Criteria

Inclusion Criteria

- Man or woman >=18 years of age.
- International Prognostic Scoring System (IPSS) low risk or intermediate-1 risk MDS; non-del(5q).
- RBC transfusion dependent, defined as requiring at least 4 RBC units transfused over an 8-week period during the 16 weeks prior to Study Entry; pre-transfusion hemoglobin (Hb) should be less than or equal to 9.0 gram per deciliter (g/dL) to count towards the 4 units total.
- Relapsed/Refractory to ESA or EPO.
- Eastern Cooperative Oncology Group (ECOG) performance status 0, 1 or 2.

Exclusion Criteria

- Participant has known allergies, hypersensitivity, or intolerance to imetelstat or its excipients.
- Participant has received an investigational drug or used an invasive investigational medical device within 30 days prior to Study Entry or is currently enrolled in an investigational study.
- Prior treatment with imetelstat.
- Have received corticosteroids greater than 30 milligram per day (mg/day) prednisone or equivalent, or growth factor treatment within 4 weeks prior to study entry.
- Prior treatment with a hypomethylating agent [e.g. azacitidine, decitabine).
- Prior treatment with lenalidomide.
- Has received an erythropoiesis-stimulating agent (ESA) or any chemotherapy, immunomodulatory, or immunosuppressive therapy within 4 weeks prior to study entry (8 weeks for long-acting ESAs).

Study End Points

Primary endpoint:

- 8-week RBC TI.

Secondary endpoints:

- 24-week RBC TI; Duration of TI; Time to 8-week RBC TI.
- HI-E per IWG 2006; MDS response per IWG.
- Overall survival, progression free survival.
- Time to progression to acute myeloid leukemia.
- Safety.
- Pharmacokinetics and immunogenicity.
- QT interval in a subset of subjects.
- Patient-Reported Outcomes.

Exploratory endpoints

- Biomarkers: Telomerase activity, Telomere length, hTERT.
- Cytogenetic responses.
- Baseline mutation status and change of mutation burden.

Study Status

Trial Enrollment

- Approximately 130 sites are planned across North America, Europe, Middle East and Asia.
- Enrollment of the Phase 3 study was opened in August 2019; the study is currently enrolling.

Trial registration

- This study is registered at ClinicalTrials.gov (NCT02598661).

Contact information

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