Profound and Rapid Symptomatic Relief and Sustained Red Blood Cell Transfusion Independence With Imetelstat: a Case Report of a Patient With Lower-Risk Myelodysplastic Syndromes

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Background

- Anemia is common in patients with lower-risk myelodysplastic syndromes (LR-MDS) and is often associated with fatigue[1]
- About 50% of patients with LR-MDS depend on red blood cell (RBC) transfusions to manage anemia, which are associated with deterioration of quality of life (QOL)[2,3]
- Improving QOL and achieving RBC transfusion independence (TI) are primary treatment goals in LR-MDS[3]

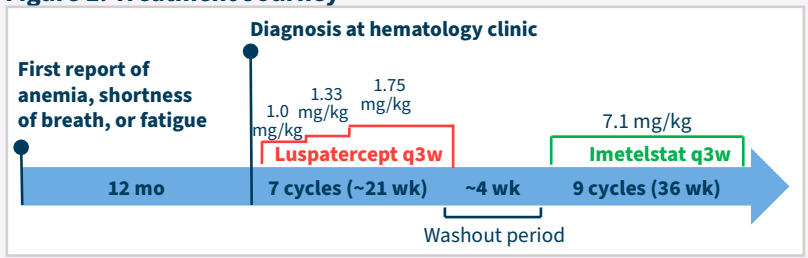
Clinical Presentation and Diagnosis

- Male, 66-year-old, history of tobacco dependency and diabetes
- Significant shortness of breath and fatigue severely affecting his QOL and limiting his ability to perform his job as a farmer
- Serum erythropoietin level: 7,201
- **Diagnosis:** Ring sideroblast–negative LR-MDS with multilineage dysplasia (*ASXL1*, *STAG2*, *TET2*, and *ZRSR2* mutations)
- Pretreatment baseline hemoglobin (Hb): 6.9 g/dL
- Revised International Prognostic Scoring System (IPSS) score of 2.0 (age adjusted: 1.86) and mutational IPSS score of −0.30

Treatment Course (Figure 1)

- Patient initiated first-line luspatercept but remained RBC transfusion-dependent despite stepwise dose increases, with 6 transfusions (8 units total) over the course of 5 months
  - He discontinued luspatercept after 7 cycles
- He initiated 7.1 mg/kg imetelstat by intravenous infusion every 4 weeks for 9 cycles, discontinuing due to worsening cytopenias and disease progression

Figure 1. Treatment Journey



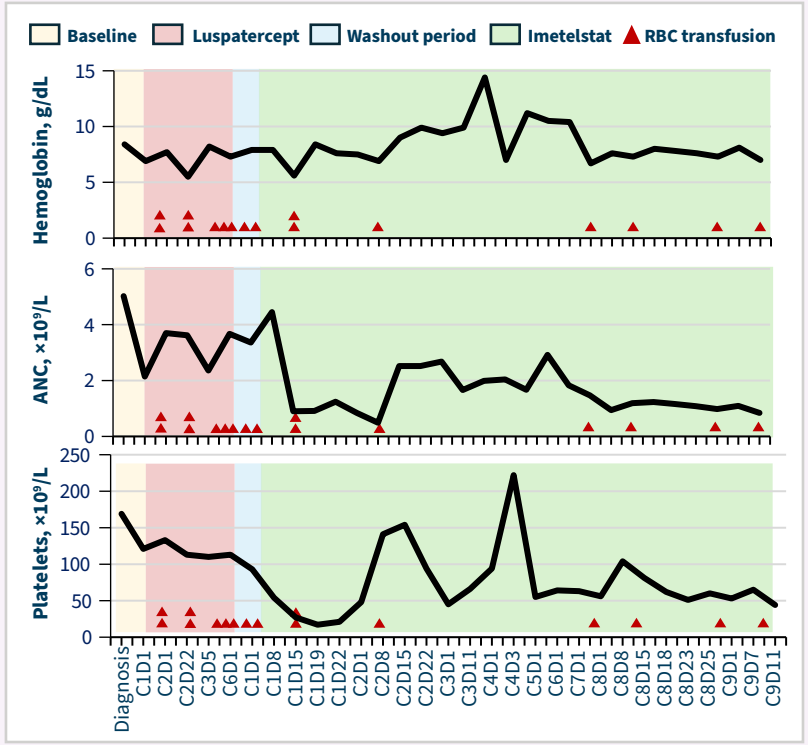
q3w, every 3 weeks; q4w, every 4 weeks.

Outcomes With Imetelstat

Efficacy (Figure 2)

- 2 RBC transfusions early in his treatment (2 units during cycle 1, and 1 unit during cycle 2)
- Hb levels increased shortly after starting imetelstat, peaking at 14.4 g/dL on cycle 4. Improvement was sustained thereafter, with an Hb mean (range) of 8.2 g/dL (6.7-8.1). Results were maintained in the absence of RBC transfusions
- Treatment duration was ~36 weeks

Figure 2. Hematology Levels Over Time and by Treatment



ANC, absolute neutrophil count; C, cycle; D, day.

QOL

- Within 1 month of starting imetelstat, the patient reported substantial relief from his fatigue and was able to resume his occupational activities

Safety

- The patient tolerated imetelstat well and generally became asymptomatic up until cycle 9, with grade 3/4 thrombocytopenia and neutropenia observed early in the treatment course. These events were temporary, resolving to grade ≤2 without intervention (no platelet transfusions or imetelstat dose delays or reductions were needed)

Cytogenetics (Table 1)

- Variant allelic frequency changes were observed, with *STAG2* showing the greatest decline, followed by *ZRSR2* and *TET2*

Table 1. Change From Baseline in VAF With Imetelstat Treatment

Gene	Baseline VAF, %	C9D23 VAF, %	Difference[a]
ASXL1	32.6	32.5	−0.1
STAG2	76.6	7.2	−69.4
TET2 (Gly1154Asp)	40.3	3.1	−37.1
TET2 (Ser1369Leu)	44.3	21.2	−23.1
ZRSR2	87.1	43.0	−44.1

C, cycle; D, day; VAF, variant allele frequency.
[a]Change between baseline and C9D23 VAF assessment for each mutation.

Discussion

- Within 1 month of starting imetelstat after luspatercept failure, this patient had a positive, robust, and rapid improvement in Hb and QOL
- This single-patient case report highlights the importance of symptom assessment, patient-reported outcomes, and patient-centered care alongside RBC-TI when evaluating treatment success in LR-MDS

References

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3. Balducci L. *Cancer*. 2006;106(10):2087-2094.

Disclosure

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