

Transfusion Independence Achieved with Combination Fedratinib and Luspatercept in an Elderly Male with Heavily Pretreated INT-2 Primary Myelofibrosis



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Abstract

Myelofibrosis (MF)-associated anemia and transfusion dependency are associated with inferior quality of life and poor prognosis. We present the case of a 66-year-old male with a history of JAK-2 positive, transfusion-dependent PMF who achieved transfusion independence on combination fedratinib and luspatercept.

Background

Myelofibrosis (MF)-associated anemia and transfusion dependency are associated with inferior quality of life and poor prognosis. Combination JAK2 inhibitors and TGF- β superfamily ligand traps are being explored as treatment options for MF-associated anemia.

Objective

To demonstrate the efficacy and tolerability of combination fedratinib and luspatercept in transfusion-dependent MF.

Patient

66-year-old male was diagnosed with JAK2-positive PMF 8 years ago. At diagnosis, his spleen size was 25 cm below the costal margin. IPSS was 0. After 3 years of observation, he developed worsening anemia. Repeat bone marrow biopsy showed stable hypercellularity and reticulin fibrosis without increased myeloid blasts. DIPSS-PLUS score placed him in the INT-2 risk group.

Interventions

Ruxolitinib yielded a 50% reduction in spleen size. However, it resulted in worsening anemia and transfusion dependence, leading to dose reduction, followed by discontinuation. The patient declined evaluation for bone marrow transplantation. He was then enrolled in a clinical trial for pacritinib, which resulted in the stabilization of splenomegaly without improvement in transfusion requirements. Pacritinib was discontinued after the development of empyema and potential drug-induced pneumonitis.



Figure-1: CT of the abdomen and pelvis showing significant splenomegaly

Darbepoetin alfa was initiated without improvement in transfusion requirements. Ultimately, he was started on fedratinib 300 mg daily, then 400 mg daily. Periodic thiamine measurements were all normal and no adverse events were experienced. Four months later, luspatercept 1 mg/kg every 3 weeks was added to fedratinib.

Main Outcome Measures

- Hematological improvement/Transfusion independence.
- Reduction in splenomegaly.

Results

Spleen size decreased from 20 cm to 12 cm by palpation 5 months after starting fedratinib. Hemoglobin increased from a baseline of 6 g/dL to 8.9 g/dL 18 days after the first dose of luspatercept. He has remained transfusion-independent since that time. 8 months after the initiation of luspatercept, hemoglobin has stabilized around 11 g/dL. Luspatercept was held on several occasions due to hemoglobin >11.5 g/dL (highest 12.3 g/dL). The patient had significant improvement in his performance status and is now working full time.

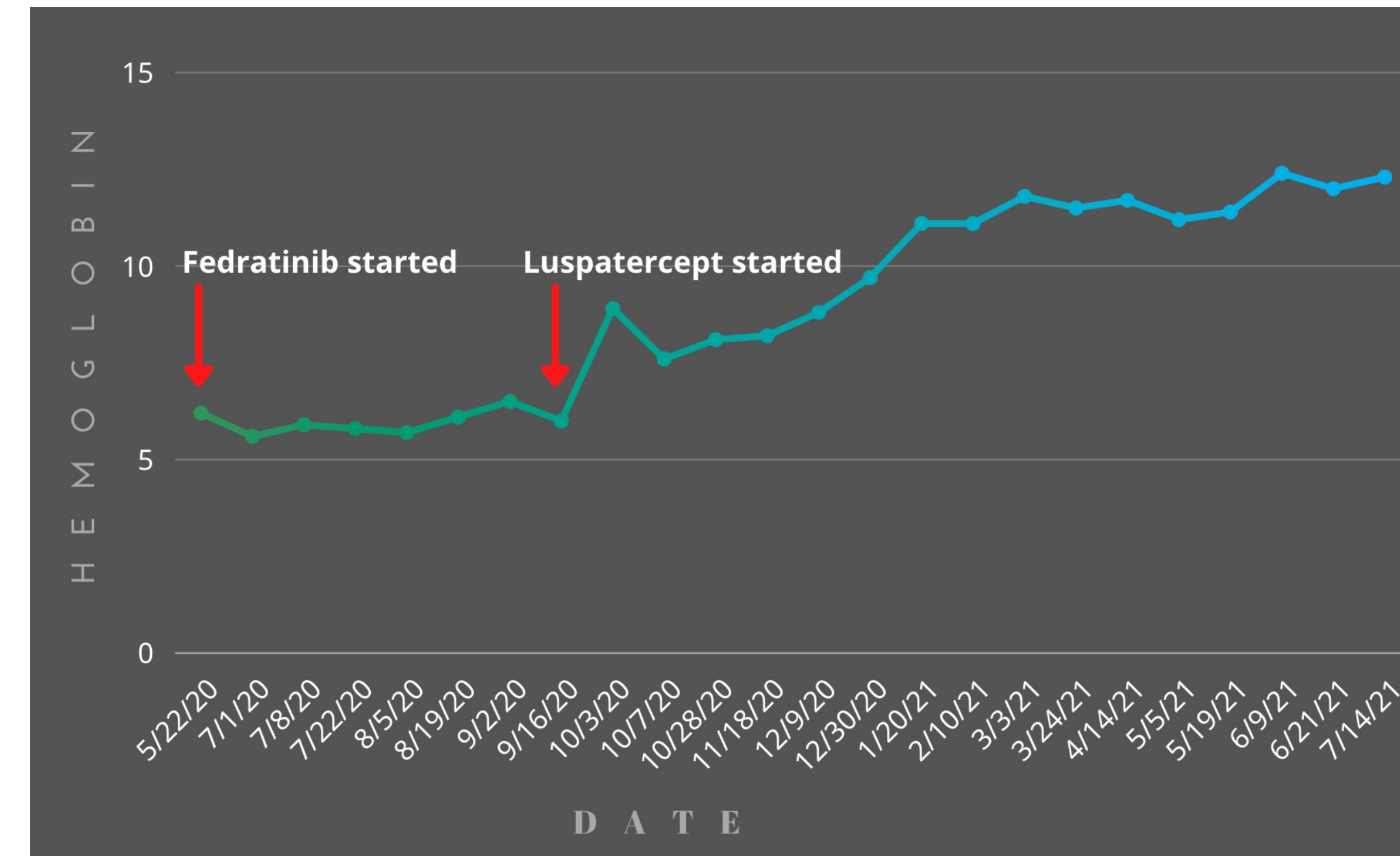


Figure-2: Graph demonstrating hemoglobin trend

Conclusions

Combination fedratinib and luspatercept is a promising therapy for anemia in patients with transfusion-dependent INT-2 MF. Currently, 3 clinical trials are evaluating luspatercept alone (NCT03194542) or in combination with a JAK2 inhibitor (NCT04717414 and NCT03755518) for the treatment of MF-associated anemia.