Safety and Efficacy of Eltrombopag in Post-hematopoietic Stem Cell Transplantation (HSCT) Thrombocytopenia

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Abstract Twelve adult patients (median age 29.5 years) were started on Eltrombopag 25–50 mg/day for post-hematopoietic stem cell transplantation (HSCT) thrombocytopenia. All patients were having primary thrombocytopenia after HSCT. No patient had other secondary cause for thrombocytopenia. Two patients were allogenic subsets (1 acute myeloid leukemia i.e., AML and 1 aplastic anemia), and 10 were autologous transplants (3 multiple myeloma, 6 lymphoma and 1 AML). Nine patients were males, three were females. The median time of starting Eltrombopag was 21 days post-stem cell infusion (range day +17 to +60) at a median platelet count of 9,000/cmm (range 3,000–11,000/cmm). The median duration for treatment was 29 days. Median total dose of 812.5 mg was received by patients and they had a median platelet increment of 36,000/cmm. We observed that there were no adverse effects in these patients and there was a gradual increase in platelet count so that none of the patients had any complication due to thrombocytopenia. The cost of treatment was less than the cost of extended hospitalization and irradiated single donor platelet transfusion.

Keywords Eltrombopag · Post-hematopoietic stem cell transplantation thrombocytopenia

Introduction

Delayed recovery from thrombocytopenia is common after stem cell transplantation, and platelet transfusion is just temporary measure to tide over the high risk interval for bleeding before engraftment. Eltrombopag is a small-molecule, nonpeptide oral agent which is an agonist of the thrombopoietin receptor. It is approved by the FDA for chronic idiopathic thrombocytopenic purpura and is now being evaluated in thrombocytopenia of other etiologies.

Patients and Methods

Design

Retrospective.

Setting

Bone marrow transplantation unit, GCRI, Ahmedabad.

Period

January 2012–July 2014.

Inclusions

All patients satisfied the following: (1) patients who have undergone hematopoietic stem cell transplantation (HSCT), (2) improved total leucocyte counts (post-engraftment), (3) thrombocytopenia needing platelet transfusion with unavailability of donors for platelet transfusion OR ineffective platelet transfusion.

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Patients receiving either an autologous (Auto) or allogeneic (Allo) stem cell transplantation from a sibling, related donor, or matched unrelated donor were included. All had stem cells from peripheral blood. However, cord blood stem cell transplantation were not included.

Exclusions

Other secondary causes of thrombocytopenia e.g., drugs, cytomegalovirus and infection.

Patients at risk of thromboembolism or with a history of thromboembolic disease in the preceding 6 months were not included in this study. Lactating females, pre-existing cardiovascular disease were also not included.

End Points

Primary End Point(s)

- Safety and tolerability of Eltrombopag as assessed by evaluating adverse events reporting, and changes from baseline in other safety parameters including clinical laboratory values.
- Transfusion independence.

Results

Twelve adult patients (median age 29.5 years) were started on Eltrombopag 25–50 mg/day for post-HSCT thrombocytopenia. Minimum age was 18 years and maximum of 57 years. Nine patients were males, three were females. All 12 patients were having primary thrombocytopenia after HSCT in which 11 patients had problem of unavailability

of donors for platelet transfusion and in 1 patient there was no rise of platelet count even above 3,000/cmm in spite of adequate daily single donor platelet transfusions suggesting alloimmunisation. All patients had improved total leucocyte counts at the time of starting Eltrombopag. No patient had other secondary cause for thrombocytopenia like drugs, cytomegalovirus or infection. Two patients were Allo subsets (1 acute myeloid leukemia i.e., AML and 1 aplastic anemia), and 10 were Auto transplants (4 multiple myeloma, 6 lymphoma and 1 AML). The median time of starting Eltrombopag was 21 days post-stem cell infusion (range day +17 to +60) at a median platelet count of 9,000/cmm (range 3,000–11,000/cmm). No patient had active bleeding at the time of start of Eltrombopag but they were at high risk of bleeding. Eltrombopag was given to tide over the thrombocytopenia with high risk of bleeding without active bleeding when there was lack of availability of platelet units for transfusion or with ineffective platelet unit transfusion. The median duration for treatment was 29 days. Definition of safe platelet count recovery was single value if platelet count more than 30,000/cmm or 2 values set 3 days apart if platelet count more than 20,000/cmm. Median total dose of 812.5 mg was received by patients and they had a median platelet increment of 36,000/cmm. There was a mild fall in platelet count after stopping Eltrombopag suggesting the rise was due to Eltrombopag. We observed that there were no possible drug related adverse effects in these patients and there was a gradual increase in platelet count so that none of the patients had any complication due to thrombocytopenia. Also the platelet count increments achieved for the total dose of Eltrombopag received were variable (Fig. 1). The cost of treatment was less than the cost of extended hospitalization and irradiated single donor platelet transfusion. Daily cost of Eltrombopag 25 mg treatment at our institute being 900 rupees, that of bed charges at bone marrow

Fig. 1 Eltrombopag total dose and platelet increment

transplant unit being 3,000 rupees/day and that of single donor platelet unit being 9,000 rupees.

As of July 2014, a total of 12 subjects were prescribed Eltrombopag and all completed the Eltrombopag treatment and stopped it on earliest outpatient visit with safe platelet count recovery. 10 subjects were given Eltrombopag 25 mg once a day and 2 were given 50 mg once a day. The duration ranged from 13 to 114 days (median 29 days). The drug compliance was 100 %. To date, all patients are alive and in remission. No dose limiting toxicities have been observed. There was a safe transfusion independence while on the Eltrombopag therapy.

Discussion

The rationale for Eltrombopag use in patients with post-hematopoietic stem cell transplant thrombocytopenia is that there is already damage to platelet-producing cells in the bone marrow. Secondly, Eltrombopag is already been evaluated in the immune thrombocytopenia where there is in fact more platelet destruction than decreased production. It is recommended when there is increased risk of bleeding and not for normalising the platelet count. This should encourage its use in the condition where there is delayed thrombopoiesis like post-HSCT thrombocytopenia. Stimulating megakaryocyte growth and differentiation within the patient's own bone marrow should lead to a rise in the patient's own platelets, thereby avoiding exposure to

donated platelets which is not completely safe. Safety and tolerability of Eltrombopag has also been evaluated in other similar settings with thrombocytopenia prospectively with similar good results [1–3].

Conclusions

25–50 mg once daily dosing of Eltrombopag to enhance platelet recovery for post-HSCT thrombocytopenia is well tolerated, appears efficacious and offers transfusion independence.

Conflict of interest None.

References

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