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ORIGINAL RESEARCH REPORT

Evaluation of Eltrombopag in Thrombocytopenia Post Hematopoietic Cell Transplantation: Rertrospective Observational Trial

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Abstract

Background: **Thrombocytopenia remains a life-threatening late complication of HCT with an incidence of 5−20%. Currently, there is no approved drug for the treatment of persistent thrombocytopenia post HCT and platelet transfusion is the maintain stay of treatment. Eltrombopag is approved for the treatment of thrombocytopenia associated with different diseases, however; data on eltrombopag treatment post HCT are limited.**

Methods: **This is a retrospective cohort study evaluating the effect of eltrombopag on platelet recovery in patients with persistent thrombocytopenia post HCT. The primary endpoint was platelet recovery to ≥ 20,000/μL for 7 consecutive days without transfusion support after starting eltrombopag. Secondary endpoint was platelet recovery to ≥ 50,000/μL for 7 consecutive days.**

Results: **Twenty-one patients were included. Twelve (75%) of 16 patients became independent from platelet transfusions. Median time from starting eltrombopag to last transfusion was 60 days (range, 9−226 days). Ten (63%) of 16 transfusion dependent patients with platelet count < 20,000/μL achieved the primary endpoint. Seven (33%) patients of 21 included had successful platelet recovery (ie, ≥50,000/μL without transfusion support) and the median time to platelet recovery in patients who achieved it was 32 days (range, 13−265 days). Ten patients (48%) were able to successfully discontinue eltrombopag without recurrence of thrombocytopenia.**

Conclusion: **Our findings demonstrated that eltrombopag appears to have a clinically significant impact on platelet recovery in persistent thrombocytopenic patients post HCT.**

Keywords: Eltrombopag, Thrombocytopenia, Hematopoietic cell transplant

1. Introduction

Hematopoietic cell transplantation (HCT) is the primary curative treatment option for several hematologic malignancies and many other non-neoplastic hematologic disorders [1]. Although this procedure is effective and considered curative in treating certain diseases [2], a considerable number of complications occur during the HCT procedure. Persistent thrombocytopenia is one of the serious

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complications reported post HCT with an incidence of 5–20% [3–6]. Several mechanisms have been proposed as contributing factors for post-HCT thrombocytopenia including accelerated peripheral platelet destruction secondary to platelet antibodies, reduced number of marrow megakaryocytes, engraftment failure, infections, myelosuppressive effect of drugs, and disease relapse. Previous studies also showed that late-onset thrombocytopenia can be triggered by graft-versus-host disease [3–6]. Currently, there is no approved drug for the treatment of persistent thrombocytopenia post HCT, and platelet transfusion remains the mainstay treatment. Persistent thrombocytopenia post HCT increases the risk of bleeding which necessitates platelet transfusion. Although it is crucial, multiple platelet transfusions can be associated with serious complications including but not limited to hemolysis from ABO-mismatched transfusions, acute lung injury, bacterial sepsis, and thrombosis [7]. Post-HCT thrombocytopenia is also associated with a higher mortality rate, and its occurrence is considered as a poor prognosis [8]. Additionally, the need for multiple and repeated platelet transfusions exhausts the healthcare resources, thereby creating a significant cost burden on the healthcare system.

Two first-generation thrombopoietin agents were initially developed and used in the management of chemotherapy-related thrombocytopenia [9]. Despite their success in increasing the platelet production, they are no longer used due to autoantibody formation that leads to persistent thrombocytopenia. In the following years, second-generation thrombopoietin agents (e.g., romiplostim and eltrombopag) were developed and licensed for the treatment of patients with idiopathic (immune) thrombocytopenic purpura (ITP) [9]. Their unique properties have demonstrated potential for broader applications. Eltrombopag is an orally bioavailable, nonpeptide thrombopoietin receptor agonist (TPO-R) that induces differentiation and proliferation of megakaryocytes by activating the human TPO receptor. It is also approved in the treatment of idiopathic aplastic anemia, chronic hepatitis C infection-associated thrombocytopenia, and ITP. Eltrombopag also reportedly reduced the burden of thrombocytopenia and its associated complications [10–22]. Until now, there is no treatment for post-HCT thrombocytopenia and platelet transfusion remains the only treatment option available. Although the data is scarce regarding the use of eltrombopag for post-HCT thrombocytopenia, the possibility of a clinically significant platelet recovery has encouraged physicians to prescribe it in an attempt to improve platelets.

Prior studies that reported the use of eltrombopag comprised mainly case reports or small-sized prospective or retrospective studies [10–26]. In this study we aim to assess the safety and efficacy of eltrombopag for patients with post-HCT thrombocytopenia in a large tertiary care center.

2. Methods

2.1. Study design

Based on the earlier studies aforementioned, we hypothesized a reasonable efficacy of eltrombopag for patients with post-HCT thrombocytopenia, without any moderate or severe adverse effects. This retrospective cohort study was designed to evaluate the effect of eltrombopag on platelet recovery in patients with post-HCT thrombocytopenia. The study was conducted at a single center which is one of the largest HCT centers globally. Data were collected from adult and pediatric patients post HCT from 2014 to 2017. The study protocol was approved by the Research Ethics Committee (Institute Review Board at KFSH&RC, Riyadh). Informed consent was waived because of minimal risk associated with the retrospective study design.

2.2. Patients

All adult and pediatric patients who underwent HCT and received eltrombopag for thrombocytopenia were screened. Patients were included if they had post-HCT persistent thrombocytopenia as either prolonged isolated thrombocytopenia (PIT) or secondary failure of platelet recovery (SFPR). PIT was defined as dependence on platelet transfusion for 30 days or longer after HCT. SFPR was defined as a decline of platelet count $\leq$ 20,000/$\leq\mu$L lasting at least 7 consecutive days or requiring platelet transfusion within 7 days after achieving primary platelet recovery. Patients were excluded if they had secondary causes for thrombocytopenia such as chronic hepatitis C infection-associated thrombocytopenia, ITP, and drug-induced thrombocytopenia (e.g., ganciclovir-, valganciclovir-, and calcineurin inhibitor-induced thrombotic microangiopathy), or had persistent thrombocytopenia secondary to graft failure.

2.3. Endpoints

The primary endpoint was platelet recovery to $\geq$ 20,000/μL for 7 consecutive days without transfusion support after starting eltrombopag treatment. Secondary endpoints were platelet

transfusion independence, platelet recovery to ≥ 50,000/μL for 7 consecutive days, number of patients who tapered/stopped eltrombopag without recurrence of thrombocytopenia after successful platelet recovery, and platelet recovery based on thrombocytopenia type (i.e., PIT or SFPR) and based on the number of bone marrow megakaryocytes before starting eltrombopag treatment if available. Adverse events inducing hepatotoxicity defined by total bilirubin ≥ 1.5 × upper limit of the normal (ULN) or transaminase ≥ 3 × ULN and thromboembolism occurred after eltrombopag was started.

2.4. Statistical analysis

All statistical analyses were performed using SPSS Statistics for Mac version 22.0 (IBM, Armonk, NY, USA). Categorical variables were presented as *n* (%), whereas continuous variables were summarized as the mean ± standard deviation or medians, range and interquartile range when distributions were skewed. Paired *t* test was used to assess the means of platelets before and after eltrombopag. Categorical data were analyzed using Pearson's chi-square or Fisher exact tests were appropriate. A Kaplan–Meier curve was constructed to represent the time to achieve platelet recovery. The *p* value was set at 0.05 for all tests applied. Multivariate analysis was not applied due to small sample size and the possibility of underpowered estimates.

3. Results

3.1. Baseline characteristics

Out of 262 patients screened, 21 met the inclusion criteria. Indications for HCT were acute lymphoblastic leukemia ($n = 5$; 24%), acute myeloid leukemia ($n = 5$; 24%), chronic myeloid leukemia ($n = 3$; 14%), aplastic anemia ($n = 2$; 9.5%), Hodgkin lymphoma ($n = 2$; 9.5%), and other indications ($n = 4$; 19%). The median patient age was 27 years (range, 7–58 years). Fifteen (71%) patients had allogeneic HCT and six (29%) patients had autologous HCT. All allogeneic transplant patients had HCT from a related donor using peripheral blood stem cells with median CD34 + cells of 3.66 × $10^{(6)}$/kg, range 1.52–8 × $10^{(6)}$/kg.

Bone marrow aspiration was performed in 15 patients (71%) before starting eltrombopag treatment. Megakaryocytes were absent based on the average of 0–2 megakaryocytes/high-power microscopic field (HPF) in 3 (20%) patients and were adequate based on the average of 2–4 megakaryocytes/HPF in 12 (80%) patients. Eltrombopag was started in 16 patients with PIT and 5 patients with SFPR. At the time of the analysis, 15 (71%) patients were alive and 6 (29%) patients were deceased (Table 1).

Before starting eltrombopag treatment, 16 (76%) patients were dependent on platelet transfusions and 5 (24%) patients were independent of platelet transfusion. Eltrombopag was started at a median of 91 (31–787) days after HCT. The median administered dose of eltrombopag was 50 (25–150) mg daily.

Table 1. Characteristics of the cohort at baseline assessment.

Characteristic	*N* (%)
Age (y)	
Median (range)	27 (7–58)
Sex	
Male	15 (71)
Female	6 (29)
Diagnosis	
ALL	5 (24)
AML	5 (24)
CML	3 (14)
AA	2 (9)
HL	2 (10)
Others	4 (19)
Type of HCT	
Allogeneic	15 (71)
Autologous	6 (29)
Donor	
Related	15 (100)
Unrelated	0 (0)
Stem cell source	
Peripheral blood stem cells	21 (100)
Bone marrow	0 (0)
Type of thrombocytopenia	
PIT	16 (76)
SFPR	5 (24)
Prior Grade I–IV acute GvHD	9 (43)
Transfusion status pre eltrombopag	
Dependent	16 (76)
Independent	5 (24)
Platelet count pre eltrombopag	
Median ± SD	21 ± 17
Patient status at the time of data collection	
Alive	15 (71)
Deceased	6 (29)
Reason for death	
Infections	2 (34)
Disease relapse	2 (33)
GvHD	0 (0)
Others	2 (33)
Megakaryocyte in bone marrow pre eltrombopag	
Abundant	0 (0)
Adequate	12 (80)
Absent	3 (20)

Note. AA = aplastic anemia; ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia; CLL = chronic lymphocytic leukemia; CML = chronic myeloid leukemia; GvHD = graft-versus-host disease; HCT = hematopoietic cell transplantation; HL = Hodgkin lymphoma; PIT = prolonged isolated thrombocytopenia; SD = standard deviation; SFPR = secondary failure of platelet recovery.

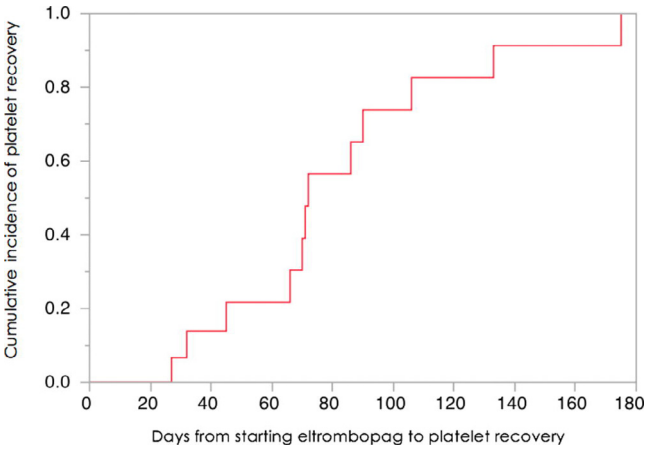

Fig. 1. A Kaplan–Meier curve of the time from starting eltrombopag to platelet recovery by days demonstrating the cumulative incidence of platelet recovery to either ≥ 20,000/μL or ≥ 50,000/μL for 7 days without platelet transfusion.

The median number of eltrombopag doses was 73 (11–594). Of the 16 transfusion-dependent patients, 12 (75%) became independent from platelet transfusions, whereas 4 (25%) patients remained dependent. The median time from starting eltrombopag to the last transfusion was 60 (9–226) days. Of the 16 transfusion-dependent patients, 10 (63%) patients with platelet count < 20,000/μL achieved the primary endpoint. Out of the 21 patients included, 7 (33%) had successful platelet recovery (i.e., ≥ 50,000/μL without transfusion support), and the median time to platelet recovery in patients who achieved it was 32 (13–265) days.

Ten patients (48%) were able to taper off eltrombopag without the recurrence of thrombocytopenia. Among the 20 patients who completed the course, the median total duration of treatment was 2.9 (0.7–19.9) months. The cumulative incidence of platelet recovery to either ≥ 20,000/μL or ≥ 50,000/μL for 7 days, without platelet transfusion, is 57% (95% confidence interval [CI] = 36–75%) as shown in Fig. 1. Platelet recovery occurred in 75% and 40% patients with PIT and SFPR, respectively. The results are shown in Table 2. The platelet count has been increased by 31 units (95% CI = 19–42.7) after using eltrombopag. A paired sample correlation was done that showed platelet recovery following eltrombopag. Mean platelet count was 21 ± 17 and 52 ± 30 before and after eltrombopag, respectively, which was statistically significant ($p = .003$; Fig. 2).

Eltrombopag was well tolerated, and no patient discontinued the drug because of adverse events. No patient developed liver toxicity or thrombosis.

4. Discussion

In our retrospective study, eltrombopag was shown to be effective and well tolerated in the

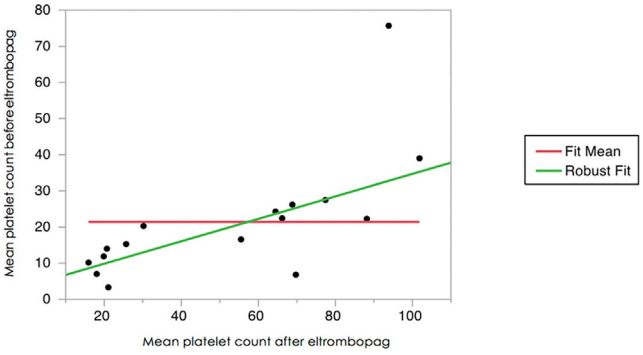

Fig. 2. Difference of means of platelet count before and after eltrombopag.

Table 2. Outcomes of the Cohort After Follow-up.

Characteristic	*n*
Maximum dose of eltrombopag, median (range)	
• 1st dose change	75 (50–100)
• 2nd dose change	50 (25–150)
• 3rd dose change	50 (25–100)
Platelet count post eltrombopag	
Median ± SD	52 ± 30
Duration from starting eltrombopag to platelet recovery (≥20,000/μL or ≥ 50,000/μL), median (range), d	68 (13–175)
Achievement of transfusion independence	
• Yes	12 (75)
• No	4 (25)
• Never transfusion dependent	5 (24)
Time from starting eltrombopag to last transfusion, median (range), d	60 (9–226)
Days from starting eltrombopag to platelet ≥ 50,000/μL, median (range), d	32 (13–265)
Status of thrombocytopenia at the last follow-up	
• Transfusion independent without eltrombopag	10 (48)
• Transfusion independent with eltrombopag	1 (4)
• Transfusion dependent	10 (48)

Note. SD = standard deviation.

Table 3. Literature Review.

Refs	Study design	Population	*N*	Transplant	Cause of thrombocytopenia	Transfusion independent	Treatment duration	Time from start of eltrombopag to platelet ≥ 50,000/μL
Reid et al. [19]	Case report	Adult	2	Allogeneic	Prolonged platelet recovery	Achieved ($n = 2$)	6 wk and 28 mo	Not achieved
Fujimi et al. [18]	Case report	Adult	1	Allogeneic	Prolonged platelet recovery	Achieved	30 mo	Not reported
Dyba et al. [11]	Case report	Adult	1	Allogeneic	Prolonged platelet recovery	Achieved	15 mo	Not reported
Ferrarini et al. [12]	Case report	Adults	1	Allogeneic	Secondary failure of platelet recovery	Achieved	3 mo	30 d
Ali et al. [13]	Case report	Child	1	Allogeneic	Prolonged platelet recovery	Achieved	10.7 mo	12 wk
Master et al. [14]	Case report	Adults	1	Allogeneic	Prolonged platelet recovery	Achieved	12 mo	18 d
Raut et al. [15]	Retrospective	Adult	12	Autologous/ Allogeneic	Prolonged platelet recovery	Achieved (n = 12)	Median, 29 d	Not reported
Ma et al. [20]	Retrospective	Adults	10	Allogeneic	Prolonged platelet recovery	Achieved ($n = 5$)	Not reported	Median, 16 d (range, 10−56 d)
Tanaka et al. [10]	Retrospective	Adult	12	Allogeneic	PIT/SFPR	Achieved ($n = 8$)	Median, 136 (range, 52−244) d	54 d
Mori et al. [16]	Retrospective	Adults	19	Autologous/ Allogeneic	Prolonged platelet recovery	Achieved ($n = 14$)	Not reported	Median, 41 d (range, 11−93 d)
Fu et al. [25]	Retrospective	Adults/ pediatrics	38	Allogeneic	PIT/SFPR	Achieved ($n = 23$)	Median, 64 (range 14−195) d	Median, 32 d (range, 7−127 d)
Yuan et al. [26]	Retrospective	Adults	13	Allogeneic	PIT/SFPR	Achieved ($n = 8$)	Not reported	Median, 33 d (range 11−68 d)
Rivera et al. [27]	Retrospective	Adults	467	Allogeneic	PIT/SFPR	Not reported	Median, 21 (9−93) d93 days)	Median, 91 d (8−206 d)

Note. PIT = prolonged isolated thrombocytopenia; SFPR = secondary failure of platelet recovery.

management of patients with persistent thrombocytopenia post HCT. Eltrombopag had a statistically significant impact on platelet count, with 48% patients remaining independent from platelet transfusion at their last follow-up visit without thrombocytopenia recurrence.

Post-HCT thrombocytopenia occurs in 5–20% of patients with more than 3 months' dependency on platelet transfusion [15–20]. The reason for low platelet count post HCT is still unclear, but increased platelet turnover, platelet destruction, and impaired thrombopoiesis are some of the proposed mechanisms [5]. The rationale behind using eltrombopag is to accelerate platelet recovery through stimulating hematopoiesis by mimicking natural TPO. Additionally, eltrombopag increases the platelet lifespan by preventing platelet apoptosis [21].

A Phase I dose-escalation study by Liesveld et al. [22] reported the use of eltrombopag in 19 patients who underwent HCT post total body irradiation. Eltrombopag was started prophylactically 24–48 hours post transplantation with escalating doses as tolerated [22]. No dose-limiting toxicities were reported. However, one episode of pulmonary embolism and one catheter-related clot was reported, whereas none were observed in our patient cohort. In a Phase II randomized, double-blind, placebo-controlled study by Popat et al. [23], the use of eltrombopag in post-HCT thrombocytopenia showed a probable superior response rate compared with placebo. However, the results were published in an abstract and the full article publication is eagerly awaited as it is the only randomized trial on the use of eltrombopag in this setting (ClinicalTrials.gov number, NCT01000051).

Table 3 provides a summary of the previously published reports regarding the use of eltrombopag in post-HCT thrombocytopenia. These reports have described a total of 578 patients who were treated with eltrombopag post HCT. Eltrombopag doses ranged from 12.5 mg to 100 mg daily. In total 77 patients responded and became platelet transfusion independent. Eltrombopag was well tolerated with no evidence of Grades 3–4 toxicities in most of the studies. A recently published review article gave an overview of TPO-Rs biology and summarized studies that used them to treat prolonged thrombocytopenia post HCT [24].

Reportedly, prolonged thrombocytopenia and slow platelet engraftment after allo-HCT may be related to a reduction in ploidy and immaturation of megakaryocytes [6]. Fu et al. [25] found that the presence of megakaryocytes in the bone marrow before starting eltrombopag better predicted the efficacy of eltrombopag than the type of thrombocytopenia after haplo-HCT.

Although the study demonstrated the efficacy of eltrombopag, it has several limitations. This was a retrospective observational study with no control arm, which may have influenced the accuracy of our findings. Second, the cohort size was small and therefore no associations could be analyzed. Further prospective randomized comparative studies are warranted to confirm the efficacy of eltrombopag.

In summary, eltrombopag resulted in the recovery of platelet count without transfusion support and reported side effects. Eltrombopag may be used successfully in the management of persistent thrombocytopenia post HCT. The results of this and other published prospective studies need to be validated in other larger studies optimally in a randomized controlled design.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Barriga F, Ramírez P, Wietstruck A, Rojas N. Hematopoietic stem cell transplantation: clinical use and perspectives. Biol Res 2012;45:307–16.
[2] Li D, Wang L, Zhu H, Dou L, Liu D, Fu L, et al. Efficacy of allogeneic hematopoietic stem cell transplantation in intermediate-risk acute myeloid leukemia adult patients in first complete remission: a meta-analysis of prospective studies. PLoS ONE 2015;10. e0132620.
[3] Bielski M, Yomtovian R, Lazarus HM, Rosenthal N. Prolonged isolated thrombocytopenia after hematopoietic stem cell transplantation: morphologic correlation. Bone Marrow Transplant 1998;22:1071–6.
[4] Ninan MJ, Flowers CR, Roback JD, Arellano ML, Waller EK. Posttransplant thrombopoiesis predicts survival in patients undergoing autologous hematopoietic progenitor cell transplantation. Biol Blood Marrow Transplant 2007;13:895–904.
[5] Yamazaki R, Kuwana M, Mori T, Okazaki Y, Kawakami Y, Ikeda Y, et al. Prolonged thrombocytopenia after allogeneic hematopoietic stem cell transplantation: associations with impaired platelet production and increased platelet turnover. Bone Marrow Transplantat 2006;38:377–84.
[6] Zhang X, Fu H, Xu L, Liu D, Wang J, Liu K, et al. Prolonged thrombocytopenia following allogeneic hematopoietic stem cell transplantation and its association with a reduction in ploidy and an immaturation of megakaryocytes. Biol Blood Marrow Transplant 2011;17:274–80.
[7] Blumberg N, Heal JM, Phillips GL. Platelet transfusions: trigger, dose, benefits, and risks. F1000 Med Rep 2010;2:5..
[8] Zaja F, Geromin A, Patriarca F, Puglisi S, Cerno M, Sperotto A, et al. Prognostic significance of delayed thrombocytopenia after allogeneic stem cell transplant. Am J Hematol 2011;86:790–2.
[9] Kuter DJ, Begley CG. Recombinant human thrombopoietin: basic biology and evaluation of clinical studies. Blood 2002; 100:3457–69.

[10] Tanaka T, Inamoto Y, Yamashita T, Fuji S, Okinaka K, Kurosawa S, et al. Eltrombopag for treatment of thrombocytopenia after allogeneic hematopoietic cell transplantation. Biol Blood Marrow Transplant 2016;22:919–24.
[11] Dyba J, Tinmouth A, Bredeson C, Matthews J, Allan DS. Eltrombopag after allogeneic haematopoietic cell transplantation in a case of poor graft function and systematic review of the literature. Transfus Med 2016;26:202–7.
[12] Ferrarini I, Turri G, Veneri D, Tecchio C, Ambrosetti A. Immune thrombocytopenia after allogeneic stem cell transplantation: case report and brief overview of treatment strategies. JHOR 2016;2:3.
[13] Ali S, Gassas A, Kirby-Allen M, Krueger J, Ali M, Schechter T. Eltrombopag for secondary failure of platelet recovery post-allogeneic hematopoietic stem cell transplant in children. Pediatr Transplant 2017;21:e1307.
[14] Master S, Dwary A, Mansour R, Mills GM, Koshy N. Use of eltrombopag in improving poor graft function after allogeneic hematopoietic stem cell transplantation. Case Rep Oncol 2018;11:191–5.
[15] Raut SS, Shah S, Sharanangat VV, Shah KM, Patel KA, Anand AS, et al. Safety and efficacy of eltrombopag in post-hematopoietic stem cell transplantation (HSCT) thrombocytopenia. Indian J Hematol Blood Transfus 2015;31:413–5.
[16] Mori S, Patel RD, Boyd A, Simon S, Nelson J, Goldstein SC. Eltrombopag treatment for primary and secondary thrombocytopenia post allogeneic and autologous stem cell transplantation is effective and safe. Biol Blood Marrow Transplant 2018;24:S343–4.
[17] Merli P, Strocchio L, Vinti L, Palumbo G, Locatelli F. Eltrombopag for treatment of thrombocytopenia- associated disorders. Expert Opin Pharmacother 2015;16:2243–56.
[18] Fujimi A, Kamihara Y, Hashimoto A, Kanisawa Y, Nakajima C, Hayasaka N, et al. Identification of anti-thrombopoietin receptor antibody in prolonged thrombocytopenia after allogeneic hematopoietic stem cell transplantation treated successfully with eltrombopag. Int J Hematol 2015; 102:471–6.
[19] Reid R, Bennett J, Becker M, Chen Y, Milner L, Phillips G, et al. Use of eltrombopag, a thrombopoietin receptor agonist, in post-transplantation thrombocytopenia. Am J Hematol 2012;87:743–5.
[20] Ma YR, Huang XJ, Mo XD, Han W, Yan CH, Chen Y, et al. Eltrombopag for refractory thrombocytopenia in patients with allogeneic hematopoietic stem cell transplantation. Zhonghua Xue Ye Xue Za Zhi 2016;37:1065–9.
[21] Polverelli N, Catani L, Sollazzo D, Vianelli N, Palandri F. Platelet fluctuations during thrombopoietin-receptor agonist treatment: correlation with platelet apoptosis. Ann Hematol 2015;94:339–41.
[22] Liesveld JL, Phillips II GL, Becker M, Constine LS, Friedberg J, Andolina JR, et al. A phase 1 trial of eltrombopag in patients undergoing stem cell transplantation after total body irradiation. Biol Blood Marrow Transplant 2013;19: 1745–52.
[23] Popat UR, Ray G, Bassett Jr RL, Poon MY, Valdez BC, Konoplev S, et al. Eltrombopag for post-transplant thrombocytopenia: results of phase II randomized double-blind placebo controlled trial. Blood 2015;126:738.
[24] Mahat U, Rotz SJ, Hanna R. Use of thrombopoietin receptor agonists in prolonged thrombocytopenia after hematopoietic stem cell transplantation. Biol Blood Marrow Transplant 2020;26:e65–73.
[25] Fu H, Zhang X, Han T, Mo X, Wang Y, Chen H, et al. Eltrombopag is an effective and safe therapy for refractory thrombocytopenia after haploidentical hematopoietic stem cell transplantation. Bone Marrow Transplant 2019;54:1310–8.
[26] Yuan C, Boyd AM, Nelson J, Patel RD, Varela JC, Goldstein SC, et al. Eltrombopag for the treatment of thrombocytopenia post-allogeneic stem cell transplantation. Biol Blood Marrow Transplant 2019;25:1320–4.
[27] Rivera D, Bastida JM, Lopez-Corral L, Sanchez-Guijo F, Cabrero M, Martin A, et al. Usefulness of eltrombopag for treating thrombocytopenia after allogeneic stem cell transplantation Bone Marrow Transplantation. Bone Marrow Transplant 2019;54:757–61.