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Eltrombopag Improves Platelet Engraftment After Haploidentical Bone Marrow Transplantation: Results of a Phase II Study

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Authorship Contributions:

SA and URP conceptualized the study, oversaw its regulatory compliance, enrolled patients on the study, provided care to the patients enrolled on the study, interpreted data, and wrote the manuscript. RLB analyzed the data, completed the statistical analyses, and wrote the statistical analysis section of the manuscript. QB, FU, FA, AMM, CH, PK, IK, DM, YN, AO, BO, MHQ, KR, RM, EJS, and SC enrolled patients on the study and provided care for the patients enrolled on the study. BV completed laboratory studies. BSA and REC enrolled patients on the study, provided care for the patients, and conceptualized the study design. All authors had access to the data of the study and approve of the manuscript.

Ethics Approval Statement: This study was approved by the University of Texas MD Anderson Cancer Center Institutional Review Board and was conducted in accordance with the Declaration of Helsinki.

Permission to Reproduce Material from Other Sources: n/a

Clinical Trial Registration: The study was registered with clinicaltrials.gov (NCT01927731).

Conflict of Interest Disclosure:

SA has received research support to institution for clinical trials from Nektar, Merck, Xencor, Chimagen and Genmab; has membership on Chimagen scientific advisory committee; serves on Data Safety Monitoring Board for Myeloid Therapeutics; is a consultant for ADC therapeutics, KITE/Gilead. EJS has license agreements with Takeda, Affimed, and Syena, receives honoraria from the University of Chicago, Banner MD Anderson Cancer Center, and Penn Medicine Abramson Cancer Center; has received travel support for meetings from MD Anderson Cancer Center Office for Training Mentoring of Scientists and the CSO, NMDP, ASTCT, and DAVA Oncology; and is on scientific advisory boards for Synthego Corporation, Bayer, ASC Therapeutics, Novartis, Cimeio Therapeutics AG, NY Blood Center, Adaptimmune, Navan, Celaid Therapeutics, Zelluna Immunotherapy, FibroBiologics, and Axio. QB is on scientific advisory boards for Purdue Pharma, Spectrum Pharma, Kite, Takeda, and Amgen and has grant support from Takeda, Stemline, and Acrotech. KR has consulting fees from Takeda, Affimed, Pharmacyclics, GemoAb, AvengeBio, Virogin, GSK, Bayer, Navan Technologies, Caribou, Jannsen Allogeneic Cell Therapy, and Innate Pharma; and royalties or licenses from Takeda and Affimed. MHQ has research funding from Janssen, Bioline, Angiocrine, Amgen, and NexImmune. PK has consulting fees from Kite, Pfizer, and Jazz Pharmaceuticals. URP has received research support from Bayer, Abbvie, Incyte, and Novartis. All other authors have not declared a conflict of interest.

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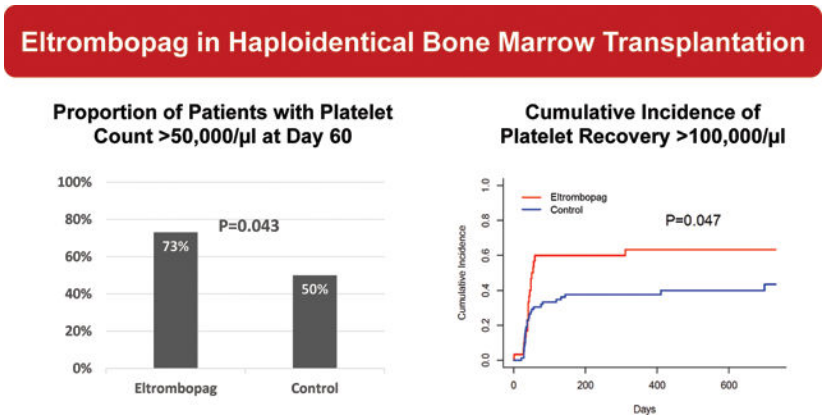
Abstract

Slow platelet recovery frequently occurs after haploidentical hematopoietic stem cell transplantation (haplo-HSCT) with bone marrow graft and post-transplant cyclophosphamide (PCy)-based graft-versus-host disease (GVHD) prophylaxis. Improved platelet recovery may reduce the need for transfusions and improve outcomes. We investigated the safety and efficacy of eltrombopag, a thrombopoietin receptor agonist, at enhancing platelet recovery post-haplo-HSCT. The prospective study included patients ≥18 years of age who received haplo-HSCT with bone marrow graft and PCy. Patients received eltrombopag 300mg/day starting on day +5. The primary objective was to estimate platelet engraftment (>50,000/μl by day 60). In a post hoc analysis, they were compared to a contemporary matched control group who did not receive eltrombopag. One-hundred-ten patients were included in the analysis (30 eltrombopag and 80 control). Seventy-three percent and 50% of patients in the eltrombopag group and control group, respectively, attained >50,000/μl platelet count by day 60 (P=0.043). No eltrombopag-related grade ≥4 adverse events were observed. Median time to platelet recovery (>20,000/μl) was 29 days with eltrombopag and 31 days for controls (P=0.022), while its cumulative incidence was 90% (95%CI: 78%−100%) with eltrombopag versus 67.5% (95%CI: 57%−78%) for controls (P=0.014). Number of platelet transfusions received, overall survival, progression-free survival, GVHD rate, relapse rate, and non-relapse mortality were similar between groups. Overall, eltrombopag is safe and improves platelet recovery in patients undergoing haplo-HSCT with bone marrow graft and PCy.

Graphical Abstract



Eltrombopag increases the proportion of patients with platelet count >50,000/μl at day 60 and the cumulative incidence of platelet recovery >100,000/μl at day 100 post-haploidentical stem cell transplant. The results of this study indicate that eltrombopag improves platelet recovery in the setting of haploidentical stem cell transplantation with bone marrow graft and post-transplant cyclophosphamide.

Keywords

Eltrombopag; haploidentical hematopoietic stem cell transplantation; thrombocytopenia; platelet

Introduction

Poor graft function is a serious complication following allogeneic hematopoietic stem cell transplantation (HSCT), with post-HSCT thrombocytopenia correlating with increased morbidity and mortality. Prolonged isolated thrombocytopenia (PT) is observed in 5–20% of cases and is characterized by persistent thrombocytopenia (<20,000/μl) with normal counts of other blood cell lines or need for transfusion within 60 days after HSCT.[1–3] The underlying mechanisms of thrombocytopenia are often multifactorial and poorly understood. Standard treatment guidelines for post-HSCT thrombocytopenia are lacking, though management generally relies on transfusion support. However, the decision to transfuse platelets depends on several factors, including platelet refractoriness, infusion reactions, acute lung and cardiac injury, as well as a heavy financial burden.

Thrombopoietin (TPO) regulates platelet production through binding to the receptor c-MPL (myeloproliferative leukemia virus) expressed on megakaryocytes, promoting platelet maturation and release.[4] Eltrombopag, an oral TPO mimetic, is approved for use in aplastic anemia and refractory chronic immune thrombocytopenic purpura. Our group previously reported a phase II study where patients were adaptively randomized to receive either placebo or eltrombopag starting at least 35 days post-HSCT. The study demonstrated safety and improved platelet count (>50,000/μl) in patients with persistent thrombocytopenia after HSCT.[5] Several studies have also demonstrated the safety of eltrombopag early after matched-donor HSCT.[6–8] However, there is sparse data about the efficacy and safety of eltrombopag for thrombocytopenia after haploidentical HSCT (haplo-HSCT). Moreover, no published data exists on the pre-emptive use of eltrombopag to prevent prolonged thrombocytopenia in this patient population. This knowledge gap is noteworthy, particularly since use of haplo-HSCT is increasing, and patients receiving haplo-HSCT with a bone marrow graft and post-transplant cyclophosphamide face a higher risk of prolonged post-HSCT thrombocytopenia.[9–11]

In this study, we report the results of a prospective, open-label phase II trial examining the safety and efficacy of eltrombopag in enhancing platelet recovery in patients undergoing haplo-HSCT. We then compare these results to a concurrent cohort of matched patients who also received haplo-HSCT but did not receive eltrombopag treatment.

Methods

Phase II Trial Design and Oversight

This investigator-initiated, open-label phase II study aimed to assess eltrombopag's safety and efficacy in patients undergoing allogeneic HSCT who were at risk for prolonged thrombocytopenia. The study included two arms: one for patients receiving a cord blood transplant (CBT) and the other for patients undergoing haplo-HSCT and post-transplant cyclophosphamide (PCy)-based graft-versus-host disease (GVHD) prophylaxis. The primary objective was to estimate the rate of platelet engraftment (>50,000/μl) by day 60 in patients undergoing CBT or haplo-HSCT and treated with eltrombopag. Patients who were eligible

for analysis, as defined by having received at least 10 consecutive doses of eltrombopag, were then matched to control patients as above.

The trial was originally planned to enroll 20–30 patients in each arm, with a total accrual of no more than 60 patients for the entire study. In October 2015, the study was modified to allow for up to 20 additional patients (for a total of 50) in the haplo-HSCT arm, since most patients accrued by that date had been enrolled on the haplo-HSCT arm. At the conclusion of the study, the total enrollment was six CBT patients and 39 haplo-HSCT patients. Thirty-seven of the haplo-HSCT patients had received at least one dose of eltrombopag and 30 were considered evaluable. Here, we report results of the patients treated in the haplo-HSCT arm.

The trial was registered with clinicaltrials.gov (NCT01927731) and approved by the University of Texas MD Anderson Institutional Review Board. Written informed consent was obtained for all study participants and was conducted in compliance with the Declaration of Helsinki.

Post Hoc Analysis

To put the results of prospective trial in context, the patients included in the phase II study's haplo-HSCT arm were compared to control patients who received a similar conditioning regimen and stem cell source, but did not receive a TPO mimetic, including eltrombopag. This retrospective analysis was approved by the University of Texas MD Anderson Institutional Review Board.

Patients

Eligible patients for the study were aged 18 years or older, had an indication to receive a haplo-HSCT for treatment of a hematologic disorder, and met standard institutional criteria to undergo haplo-HSCT and PCy-based GVHD prophylaxis. Exclusion criteria included recurrence or progression of the primary malignancy after HSCT; abnormal liver function tests such as alanine aminotransferase (ALT) ≥2.5 times the upper limit of normal or serum bilirubin >1mg/dl, except Gilbert's syndrome or hemolysis; documented deep vein thrombosis within one year of enrollment, except catheter-related thrombosis, which was excluded within three months of study enrollment; and Eastern Cooperative Oncology Group (ECOG) performance status >2. Bone marrow biopsy and aspiration was performed as part of the diagnostic or routine pre-transplant evaluations, per departmental standards. Chimerism, cytogenetics, immunohistochemistry, and molecular markers were assessed on these bone marrow biopsies to determine status of the primary malignancy. Patients undergoing haplo-HSCT received a minimum target of 2×10^8/kg total nucleated cells (TNC), per departmental standards.

Interventions and Treatments

In this study, eligible patients were given eltrombopag at a daily dose of 300mg, taken orally starting on day +5 after transplant and continuing for 60 days. Patients had to receive eltrombopag continuously for at least 10 days to be considered evaluable. As a safety rule, if a patient's platelet count reached or exceeded 400,000/μl at any point during treatment, eltrombopag was to be discontinued and the patient removed from the study. However, no

patients on this study met this threshold. The graft source used in this study was exclusively bone marrow-derived stem cells.

Statistical Analysis and Outcomes

The primary objective of this study was to estimate the rate of platelet engraftment by day 60 in patients undergoing haplo-HSCT treated with eltrombopag. Secondary endpoints were assessment of overall survival (OS), progression-free survival (PFS), non-relapse mortality (NRM), time to neutrophil engraftment, characterization of immune reconstitution and to assess incidence of acute graft-versus-host disease (aGVHD). Evaluable patients were those who received eltrombopag for a minimum of 10 consecutive days and the control patients were selected based upon these and other criteria, and thus all were considered evaluable. Control patients were matched to trial patients across the following categorical parameters: sex, age, race, diagnosis, intensity of preparative regimen (myeloablative versus nonmyeloablative), preparative regimen, donor relation, and final disease response post-transplant.

Wilcoxon rank-sum tests were used to compare the distribution of categorical variables between trial and control patients. Fisher's exact tests were used to compare the distribution of categorical variables between the studies. The distribution of OS, PFS, time to neutrophil engraftment, and time to platelet engraftment were estimated using the Kaplan-Meier method. Distributions were compared using the log-rank test. The cumulative incidences of aGVHD grades 2–4 and 3–4 were assessed in a competing risks framework with competing risks of disease relapse and death without relapse. The cumulative incidence of platelet recovery at the levels of 20,000/μl, 50,000/μl, and 100,000/μl were assessed in a competing risks framework with competing risks of death without relapse and disease relapse. The cumulative incidence of non-relapse mortality was assessed in a competing risks framework with relapse as the competing risk. All statistical analyses were performed using R version 3.4.3. All statistical tests used a significance level of 5%.

Role of the Funding Source

The analyses of this work were supported in part by a Cancer Center Support Grant (NCI Grant P30 CA016672). GlaxoSmithKline (GSK) and Novartis provided eltrombopag free of charge, supported the study, and did not play any role in the study's conduct. The authors were solely responsible for the design and conduct of the study, as well as the analyses and interpretation of results. All authors had complete access to the data and assured the integrity and completeness of the reported data.

Results

Patients and Treatment

Thirty-nine of the patients were in the phase II study examining the safety and efficacy of eltrombopag. Patients in the study were considered evaluable for analysis if they received at least 10 consecutive doses of eltrombopag starting on day +5 post-haplo-HSCT. Two patients in the study did not receive any dose of eltrombopag, and an additional seven patients received less than the minimum of 10 consecutive days of eltrombopag. (Reasons

for not receiving dose are as follows: 2 patients did not receive drug due to significant complications associated with transplant, one had a catastrophic CNS bleed and the other had graft failure and sepsis. Of the 7 patients who were not evaluable, 3 patients withdrew consent prior to receiving 10 doses, 3 had issues swallowing pills due to either GVHD or intubation which precluded treatment and 1 had early progressive disease and the treating physician recommended discontinuing trial and the patient did not receive at least 10 doses of eltrombopag.) This resulted in 30 evaluable patients in the eltrombopag-treated haplo-HSCT group. Eighty patients were in a matched control group that did not receive eltrombopag. There were no significant differences in patient characteristics between the eltrombopag group and the control group, including sex, race, diagnosis, intensity or type of preparative regimen, donor relation, or disease response post-transplant and prior to initiation of eltrombopag. The presence of anti HLA antibodies was evaluated for patients on study and the control cohort and there was no statistically significant difference in either group. Patient characteristics for the evaluable patients are summarized in Table 1, and patient characteristics for all patients who received at least one dose of eltrombopag are summarized in Supplementary Table 1.

Efficacy

We assessed measures of efficacy and outcomes in the eltrombopag-treated haplo-HSCT patients of the phase II study and then compared these results with that of the matched control group. The primary endpoint of attaining a platelet count of >50,000/μl by day 60 was achieved in 73% of the eltrombopag-treated patients compared to 50% of patients in the matched control group (P=0.043) [Figure 1]. The median time to reach a platelet count >20,000/μl was 29 days for the eltrombopag group and 31 days for the control group (P=0.022). The cumulative incidence of platelet recovery >20,000/μl was 90% (95% confidence interval (CI): 78%−100%) in the eltrombopag group compared to 67.5% (95% CI: 57%−78%) for the control group (P=0.014) [Figure 2A]. The cumulative incidence of platelet recovery >50,000/μl was 76.7% (95% CI: 61–93%) in the eltrombopag group and 64% (95% CI: 53–75%) in the control group (P=0.11). The cumulative incidence of platelet recovery at the level of >100,000/μl was significantly higher in patients who received eltrombopag, with 63% (95%CI: 46–81%) of the eltrombopag-treated group and 44% (95% CI: 31–56%) of the control group achieving this level (P=0.047) [Figure 2B].

The median time to achieve an absolute neutrophil count (ANC) above 500/μl was 19 days for both the eltrombopag and control groups (P=0.17). Additionally, there was no significant difference in the number of platelet transfusions received by patients in the eltrombopag group (median: 12; range: 4–72) compared to those in the control group (median: 19; range: 2–116) (P=0.27).

Relapse, GVHD, and Survival

Patients in the eltrombopag group had a relapse incidence of 36.7% (95% CI: 19.0% −54.3%) versus 32.1% (95% CI: 18.9%−45.3%) in the control group (P=0.62). Time point for evaluation of relapse, non-relapse mortality, and chronic GVHD was cumulative incidence at the end of the study while for acute GVHD, it is day 100. At 100 days, the cumulative incidence of aGVHD grades 2–4 was 43.3% (95% CI: 25.2%−61.5%) in

the eltrombopag group and 40.1% (95% CI: 28.8%−51.4%) in the control group (P=0.57). The incidence of grades 3–4 aGVHD at day 100 was also similar between groups, with 10.0% (95% CI: 0%−20.9%) in the eltrombopag group and 5.2% (95% CI: 0.2%−10.3%) in the control group (P=0.36). No significant difference in the cumulative incidence of chronic GVHD was observed between groups. The eltrombopag group had a chronic GVHD incidence of 6.7% (95% CI: 0%−16%), while the control group had an incidence of 20.7% (95% CI: 10%−31%) (P=0.15).

There were also no significant differences in OS, PFS, and NRM between groups. The 100-day NRM was 3.3% (95% CI: 0.0%−9.9%) in the eltrombopag group and 17% (95% CI: 8.5%−25.5%) in the control group (P=0.33). Among the evaluable patients, the median OS was 19.8 months (95% CI: 11.5-not reached) in the eltrombopag group and 11.2 months (95% CI: 6.6-not reached) in the control group (P=0.26). The median PFS was also similar between groups, at 10.8 months (95% CI: 6.5-not reached) for the eltrombopag group and 8.7 months (95% CI: 5.5–23.8) for the control group (P=0.44).

Toxicity

No eltrombopag-related clinically meaningful side effects were observed. No grades 3–4 toxicities, cataract, thrombosis, or bone marrow fibrosis occurred, and no patient required discontinuation of eltrombopag due to side effects (Table 2).

Discussion

Prolonged thrombocytopenia commonly occurs after allogeneic HSCT and is a strong risk factor for transplant-related morbidity and mortality.[2, 12–16] Poor graft function is a severe complication after allo-HSCT, but occurs more frequently in patients receiving haplo-HSCT compared to other donor types, as well as in those using bone marrow graft and post-transplant cyclophosphamide as GVHD prophylaxis.[17–19] TPO receptor agonists (TRAs) are increasingly being studied as a method to increase platelet production post-HSCT, though there are currently no standard treatment guidelines for their use in this setting.[20]

In this study, we demonstrate that eltrombopag post-haplo-HSCT is well-tolerated and results in enhanced platelet engraftment compared to patients who do not receive a TRA. Patients had a statistically significant improvement in platelet counts at the threshold of both >20,000/μl and >100,000/μl, as well as quicker engraftment to a platelet count of 20,000/μl in comparison to patients who did not receive eltrombopag. Eltrombopag was well-tolerated, with low toxicity and without any increase in thromboembolic complications, bone marrow fibrosis, or other clinically meaningful side effects. These results indicate that eltrombopag is a safe and effective therapy to improve platelet recovery after haplo-HSCT.

The use of oral TRAs for prolonged thrombocytopenia has been explored in a number of studies.[5, 20] However, there is limited data regarding their use in enhancing platelet engraftment. TPO regulates platelet production through binding to the receptor c-MPL (myeloproliferative leukemia virus) on megakaryocytes, resulting in platelet maturation and release. Two such agents, romiplostim and eltrombopag, are currently approved by the US Food and Drug Administration (FDA) for treating chronic refractory immune

thrombocytopenia (ITP) in adults and children age >1 year, while eltrombopag is also approved for the upfront treatment of severe aplastic anemia along with standard immunosuppressive therapy. In addition, avatrombopag and lusutrombopag are two newer orally bioavailable small molecules with reportedly better safety profiles than romiplostim and eltrombopag, and are currently FDA-approved for use in adults with thrombocytopenia and liver disease undergoing invasive procedures.[21, 22] Furthermore, the FDA recently expanded the approval for avatrombopag for use in adults with chronic ITP refractory to previous treatments. Although the use of these agents to treat other thrombocytopenic states is currently being investigated, their safety and efficacy in the post-HSCT thrombocytopenia setting is limited. Zhou et al. reported on the use of avatrombopag for delayed platelet engraftment or secondary failure of platelet recovery post-HSCT.[23] In their cohort, the overall response rate to avatrombopag was 68.9%, attainment of platelet count >50,000/μl for 7 days without transfusion was 39.3%, and the median days from avatrombopag initiation to platelet count >50,000/μl was 25 days. Interestingly, they found that the presence of an adequate number of megakaryocytes in the bone marrow prior to initiation of avatrombopag was an independent prognostic factor of its efficacy.

The use of TRAs for enhancing platelet engraftment, as opposed to treating delayed engraftment or secondary failure of platelet recovery, has been reported on in small studies in the setting of CBT. Pasvolsky et al. described their experience with eltrombopag administration early post-CBT to enhance platelet recovery in a cohort of 12 adult and pediatric patients with hematologic malignancies. In their study, patients were given oral eltrombopag from day +1 of CBT until platelet count exceeded 50,000/μl for 14 consecutive days without platelet transfusion.[24] Starting doses were 100mg/day and were escalated every 2 weeks if platelet recovery did not meet 20,000/μl, with a maximum dose of 300mg/day. The median time to neutrophil engraftment was 23 (range 16–40) days and median time to platelet count >20,000/μl and >50,000/μl was 55 (range 25–199) and 66 (range 31–230) days, respectively. While this phase II study demonstrated safety even at higher dose levels, it did not reveal a statistically significant improvement in platelet or neutrophil engraftment times between the experimental cohort and a historical cohort of 16 patients who received CBT at their center. The authors did mention their interpretation of data and results may be limited due to the study population being quite heterogenous, which included both adult and pediatric patients, multiple conditioning regimens, and transplants with single and double umbilical cord blood units. In another phase I study, Christakopoulos and colleagues examined romiplostom and its effects on accelerated platelet recovery post-CBT.[25] In their single center analysis they administered romiplostim beginning on day +28–42 and continued until day +100 to find the maximum tolerated dose. In their cohort of 20 patients, 100% of romiplostim-treated patients achieved platelet engraftment to 20,000/μl at a median of 45 (range 35–68) days post-CBT, compared to 90% of controls who achieved platelet engraftment at a median of 45 (range 28–168) days (P=0.08). Similarly, 90% of romiplostim-treated patients achieved platelet engraftment to 50,000/μl at a median of 48 (range 38–66) days compared to 75% of historical controls, who achieved platelet engraftment at a median of 52 (range 33–157) days (P=0.09).

There are several limitations in our study. First, although our study's cohort was larger than that of most previous studies using eltrombopag and is the first to demonstrate activity of

eltrombopag to improve platelet engraftment in the setting of haplo-HSCT, it included a retrospective control cohort. Second, our study had strict inclusion and exclusion criteria and was limited to patients who were at least 18 years old. Therefore, our results may not be generalized to pediatric patients. Third, our study was limited to patients undergoing haplo-HSCT with post-transplant cyclophosphamide, which often exhibits delayed engraftment. Therefore, this effect may not be seen in matched-donor transplants that do not utilize post-transplant cyclophosphamide. Fourth, we did not see any differences in transfusion requirements or NRM between groups, although this may be associated with the fact that treatment occurred over a limited duration of time, and extended therapy may therefore yield improved outcomes. Finally, eltrombopag is a relatively expensive drug and further studies are needed to identify patient populations for whom it is most beneficial.

To our knowledge, this is the first trial demonstrating eltrombopag's efficacy at enhancing platelet recovery after haplo-HSCT, and our findings provide clinical evidence of its safety and efficacy in this setting. Patients will inherently experience cytopenia after haplo-HSCT using bone marrow stem cells with post-transplant cyclophosphamide, and interventions to mitigate cytopenia can improve quality of life and decrease resource utilization. These data pave the way for additional studies to explore TPO mimetics to reduce the duration of thrombocytopenia after HSCT and potentially other cellular therapy-related cytopenias.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The analyses of this work were supported in part by the Cancer Center Support Grant (NCI Grant P30 CA016672). GlaxoSmithKline (GSK) and Novartis provided eltrombopag free of charge, supported the study, and did not play any role in the conduct of this study.

Patient Consent Statement:

All patients provided written informed consent prior to enrollment on the prospective study.

Data Availability Statement:

The data presented in this study is available upon request to the corresponding author.

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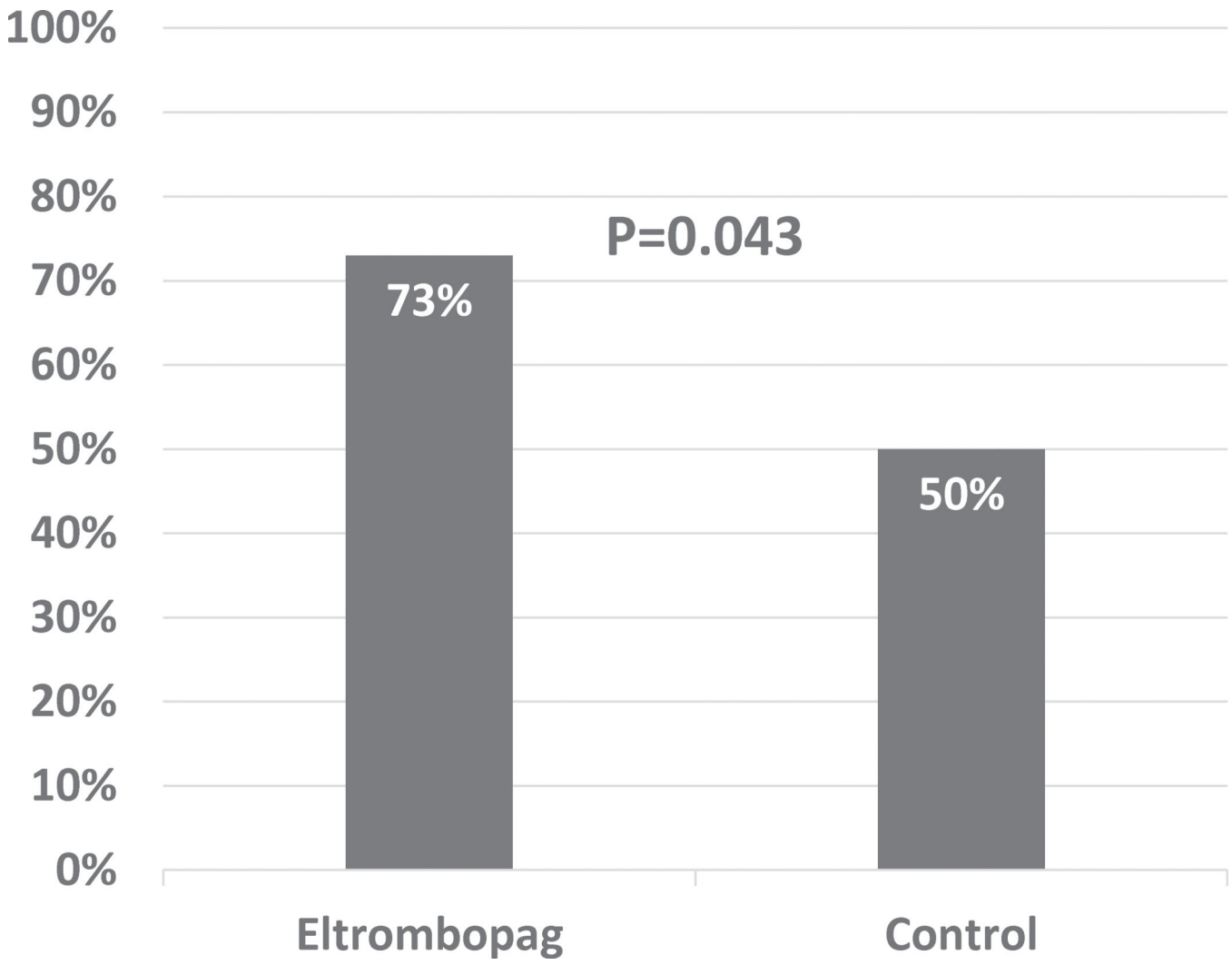

Figure 1.
Primary endpoint: Proportion of patients with platelet count >50,000/μl at day 60.

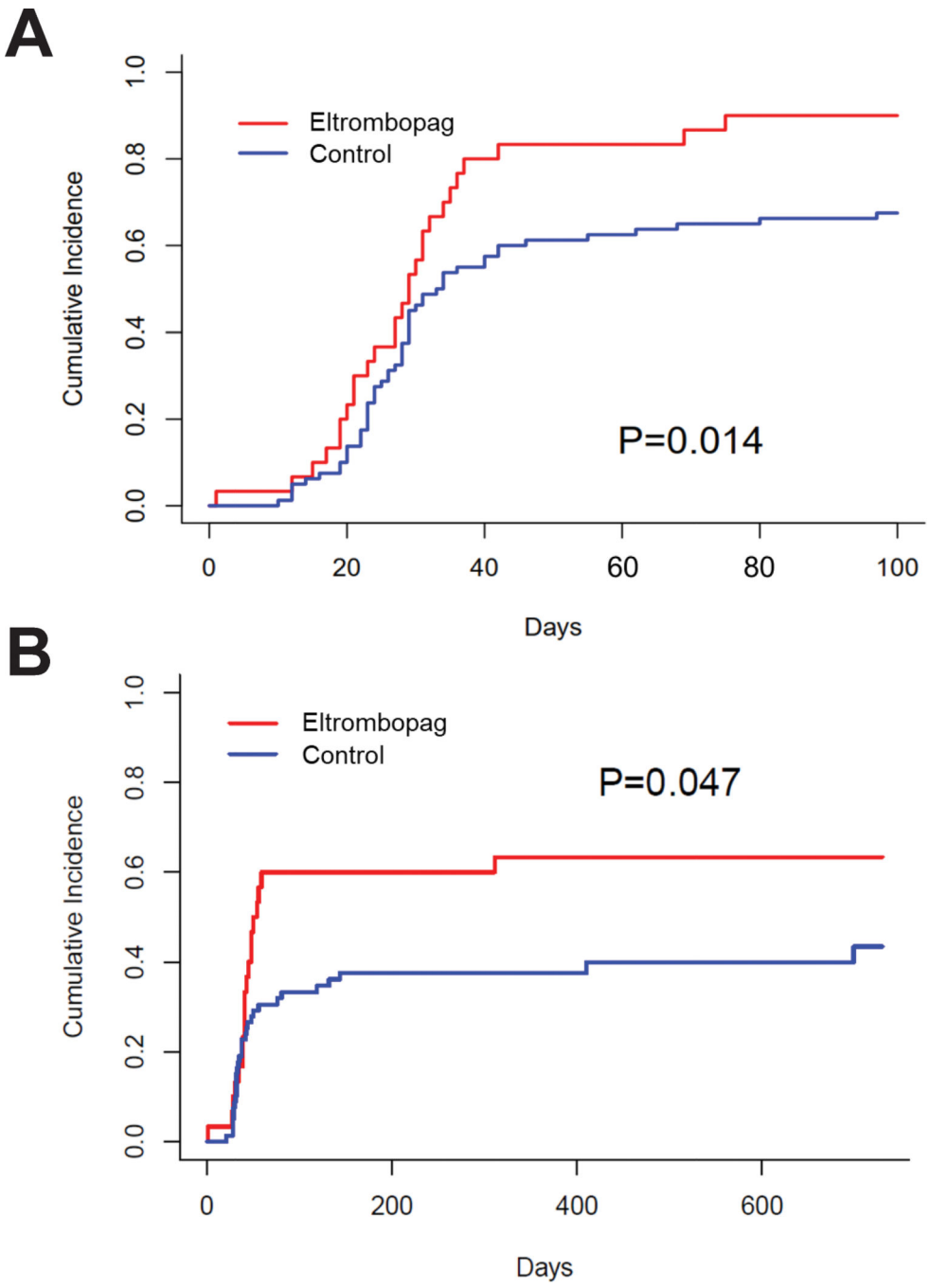

Figure 2.
Cumulative incidence of platelet recovery >20,000/μl (**A**) and >100,000/μl (**B**) in evaluable patients.

Table 1:

Patient Characteristics.

Variable	Characteristic	Eltrombopag	Matched Control	p-value
Gender	Female	12 (40.0%)	33 (41.0%)	1.00
	Male	18 (60.0%)	47 (59.0%)	
Race/Ethnicity	Asian	0 (0%)	4 (6.1%)	0.66
	Black	5 (16.7%)	9 (13.4%)	
	Hispanic	4 (10%)	16 (17)	
	White	19 (70.0%)	44 (58.5%)	
	Unknown	2 (3.3%)	6 (6.1%)	
Cell Type	HPC-M	30 (100%)	79 (100%)	
Diagnosis	ALL	5 (16.7%)	21 (26.5%)	0.49
	AML/MDS	19 (63.3%)	49 (59.0%)	
	CLL	1 (3.3%)	0 (0%)	
	CML/MPD	2 (6.7%)	4 (4.8%)	
	Lymphoma	3 (10.0%)	6 (9.6%)	
Prep Regimen	Fludarabine/Melphalan +/− Rituximab	10 (33.4%)	16 (16.9%)	0.20
	Fludarabine/Melphalan/TBI +/− Rituximab	6 (20.0%)	19(32.5%)	
	Fludarabine/Melphalan/Thiotepa	14 (46.7%)	45 (50.6%)	
Donor Relation	Child	15 (53.3%)	32 (44.6%)	0.48
	Parent	2 (6.7%)	12 (10.8%)	
	Sibling	13 (40.0%)	36 (44.6%)	
Donor Age	Median	37 years	38 years	0.68
	Range	12–66 yrs	12–65 yrs	
Anti-HLA Antibodies	Anti HLA Class I Ab detected	3	11	0.93
	Anti HLA Class I and II Ab detected	4	6	
	Anti HLA Class II Ab detected	2	6	
	No Donor Specific Ab detected	21	57	
	all	30	80	
Final Response	CCR/CR	28 (93%)	68 (87%)	0.38
	ED	0 (0%)	5 (6.0%)	
	NE	0 (0%)	3 (3.6%)	
	NR	1 (3.3%)	0 (0%)	
	PR/SD	1 (3.3%)	1 (1.2%)	

HPC-M – hematopoietic progenitor cells-bone marrow; ALL – acute lymphoblastic lymphoma; CLL – chronic lymphocytic leukemia; CML-chronic myeloid leukemia; AML/MDS – acute myeloid leukemia/myelodysplastic disease; MPD – myeloproliferative disease; CCR – complete cytogenetic response; CR – complete response; PR – partial response; SD – stable disease; NR – no response; NE – not evaluable; ED- early death (prior to day 30); Ab – antibodies; HLA – Human Leukocyte Antigen

Table 2:

Toxicity associated with eltrombopag.

Parameter	Grade	n=37
Pain, n (%)	Grade 1 possibly related	1 (2.7%)
Blood bilirubin increase, n (%)		
	Grade 1 probably related	1 (2.7%)
	Grade 2 possibly related	1 (2.7%)
Diarrhea, n (%)	Grade 1 possibly related	1 (2.7%)
Headache, n (%)	Grade 2 possibly related	1 (2.7%)