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Randomized, Placebo-Controlled, Phase I/II Trial Of The Thrombopoietin Receptor Agonist Eltrombopag In Thrombocytopenic Patients With Advanced Myelodysplastic Syndromes Or Acute Myeloid Leukemia — A Subgroup Analysis Of Patients Receiving Concomitant Anticancer Therapy

Uwe Platzbecker, MD, PhD[1], Raymond S.M. Wong[2], Amit Verma, MD[3], Camille N. Abboud, MD[4], Sergio Araujo[*,5], Tzeon-Jye Chiou, MD[*,6], John Feigert, MD[7], Su-Peng Yeh, MD[*,8], Katharina Götze, M.D.[*,9], Norbert Claude Gorin, MD, PhD[10], Peter L. Greenberg, MD[11], Suman Kambhampati, MD[*,12], Yoo Jin Kim, MD[*,13], Je-Hwan Lee[14], Roger M. Lyons, MD[15], Marco Ruggeri, MD[16], Valeria Santini, MD[*,17], Gregory Cheng[*,18], Jun Ho Jang[*,19], Chien-Yuan Chen[*,20], Souria Hasan Dougherty[*,21], Frank Mannino[*,21], Yasser Mostafa Kamel[*,22], Geoffrey W. Chan, MD[*,21], Nicole L. Stone, PhD[21], and Aristoteles Giagounidis, MD[*,23]

+ Author Affiliations

Abstract

Background In a randomized study of single-agent eltrombopag (EPAG; n=64) versus placebo (PBO; n=34) in thrombocytopenic patients with advanced myelodysplastic syndromes or acute myeloid leukemia (AML), median overall survival (OS) was 27 weeks for EPAG versus 15.7 weeks for PBO (hazard ratio [HR]: 0.73). In addition to standard supportive care, disease-modifying treatments were generally permitted at any time at the investigator's discretion. To explore the role of concomitant anticancer therapy in this study population, a post hoc subgroup analysis was conducted in patients in each treatment group who received anticancer treatment.

Methods Anticancer treatment was grouped post hoc into the following categories: palliative treatment (eg, hydroxyurea, low-dose cytarabine), hypomethylating agents (HMAs; eg, azacitidine and decitabine), induction chemotherapy (eg, 7 + 3; mitoxantrone, etoposide, and cytarabine, etc), and other (eg, lenalidomide). Baseline characteristics and safety/efficacy parameters were examined in this subgroup of patients.

Results While on study treatment, a similar proportion of patients in both treatment arms of the trial received anticancer therapy (EPAG, n=28 [44%]; PBO, n=13 [38%]). The majority of patients receiving anticancer therapy in both the EPAG (64%) and PBO (54%) arms received palliative treatments (primarily hydroxyurea and low-dose cytarabine) followed by HMAs (*Table*). Induction chemotherapy was received by 11% of patients in the EPAG subgroup, compared with no patients in the PBO subgroup. For the subgroup of patients who received anticancer therapy, EPAG patients had higher baseline median platelet counts and absolute neutrophil counts, and a lower incidence of poor prognosis karyotype (*Table*). The percentage of patients with AML and those who were platelet transfusion dependent were similar between treatment arms at baseline (*Table*).

All patients in both treatment groups experienced ≥1 adverse event (AE) while on study treatment. A lower proportion of EPAG patients experienced a serious AE (SAE) on therapy compared with PBO patients, and proportionately fewer infection-related SAEs were reported in EPAG versus PBO patients (*Table*).

Pyrexia SAEs were higher in the EPAG (5 [18%]) arm versus the PBO (1 [8%]) arm. In the subgroup of patients receiving anticancer therapy, a similar proportion of EPAG and PBO patients experienced Grade ≥3 hepatobiliary events (3 [11%] vs 1 [8%]). Three (11%) EPAG patients experienced Grade ≥3 renal and 2 (7%) thromboembolic events on study drug, whereas no PBO patients experienced these events. A lower proportion of patients on EPAG (18%) experienced AEs that led to discontinuation of study treatment compared with those on PBO (46%). A lower proportion of EPAG patients (32%) died on therapy compared with PBO (69%); the primary cause of death in both arms was the underlying disease.

Median platelet counts for EPAG patients receiving anticancer treatment increased above baseline, whereas median platelet counts remained stable at baseline levels for PBO patients. A higher proportion of EPAG patients than PBO patients achieved platelet (50% vs 31%) and red blood cell (RBC; 29% vs 8%) transfusion independence for ≥8 weeks (*Table*). Bleeding events (Grade ≥3) were reported in fewer EPAG patients (11%) versus PBO patients (38%). When censoring patients at the start of anticancer treatment, no apparent difference in OS was observed between treatment arms (HR: 0.97).

Summary/conclusion In the subgroup who received anticancer therapy, EPAG patients had higher incidences of platelet and RBC transfusion independence, higher median platelet counts, and lower incidences of bleeding and infectious complications compared with PBO patients, with selected SAEs occurring at higher rates. These results support the safety profile of EPAG in combination with a variety of anticancer agents. In addition, these data suggest a possible beneficial supportive care effect in patients receiving concomitant therapy with EPAG and anticancer treatment. Further studies of EPAG in combination with anticancer therapy are warranted to confirm these hypotheses.

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Disclosures: Platzbecker: *GlaxoSmithKline:* Honoraria. **Off Label Use:** Eltrombopag is a TPO receptor agonist that is used for the treatment of thrombocytopenia due to various diseases. It is approved in cITP and now being evaluated for the correction of thrombocytopenia in subjects with MDS/AML. **Wong:** *GlaxoSmithKline:* Consultancy, Honoraria, Research Funding, Speakers Bureau. **Verma:** *GlaxoSmithKline:* Research Funding. **Abboud:** *Alexion:* Honoraria; *Ariad:* Honoraria; *Novartis:* Honoraria; *Teva:* Speakers Bureau. **Greenberg:** *Amgen:* Research Funding; *GlaxoSmithKline:* Research Funding; *KaloBios:* Research Funding; *Novartis:* Research Funding; *Onconova:* Research Funding. **Lyons:** *Novartis:* Research Funding; *GlaxoSmithKline:* Research Funding; *Amgen:* Honoraria, Research Funding. **Santini:** *Novartis:* Honoraria; *Janssen:* Honoraria; *GlaxoSmithKline:* Honoraria; *Celgene:* Honoraria. **Cheng:** *GlaxoSmithKline:* Speakers Bureau. Dougherty: *GlaxoSmithKline:* Employment. **Mannino:** *GlaxoSmithKline:* Employment. **Mostafa Kamel:** *GlaxoSmithKline:* Employment, Equity Ownership. **Chan:** *GlaxoSmithKline:* Employment. **Stone:** *GlaxoSmithKline:* Employment. **Giagounidis:** *GlaxoSmithKline:* Honoraria.

↵* Asterisk with author names denotes non-ASH members.