Introduction

- Osteosarcoma (OS) is the most common primary bone malignancy in adolescents and young adults
- Overall survival rate for patients with metastatic or recurrent disease is <30%
- Survival outcomes have remained stagnant for the past 3 decades and new agents are needed to improve outcomes

- Eltrombopag (EP) is a small molecule thrombopoietin receptor (TPO-R) agonist and polyclonal cation chelator
- FDA-approved to treat chronic immune thrombocytopenia purpura (ITP) and severe aplastic anemia
- EP reduces leukemia cell proliferation via the depletion of intracellular iron levels, independent of TPO-R binding
- EP’s inhibits osteosarcoma cell growth in vitro in a dose-dependent manner
- The PPTC sought to evaluate the potential anti-cancer efficacy of EP against in vivo osteosarcoma models

Methods

EP Administration:
- 5 mg/kg/day (low-dose) via oral gavage for 5 days per week over 4 weeks
- 50 mg/kg/day (high-dose) administered to 2 models (OS2, OS9) per the same schedule

Study Design and Analysis:
- Six OS patient-derived xenograft (PDX) models (OS-2, OS-9, OS-31, OS-33, OS-36, and OS-60-SJ) were heterotopically injected into the flanks of CB17SC id mice
- A control cohort that received vehicle was included for each PDX model
- Tumor volume was monitored in all cohorts
- Events defined as 4x initial tumor growth
- Tumor growth, Event Free Survival (EFS) compared between treatment and control groups
- p-values were two-sided and considered statistically significant if p < 0.05

Results

- No toxic deaths with either dose of EP
- EP dose 5 mg/kg/day:
  - No significant prolongation of time to event observed
  - No objective responses observed
  - All mice met criteria for PD1 (Table 1)
- EP dose 50 mg/kg/day:
  - Resulted in a small, but significant prolongation in time to event for both models tested
  - No objective responses observed
  - All mice met criteria for PD1 (Table 1)

Results: Response to Low-Dose and High-Dose EP (EFS)

Discussion and Conclusions

- EP failed to exhibit significant anti-tumor activity in the osteosarcoma PDX models
- EP did not enhance tumor growth in any of the models tested
- Lack of meaningful EP anti-tumor activity suggests that leukemia and osteosarcoma may exhibit different dependencies on intracellular polyvalent cations
- EP may be considered as a potential supportive care agent in stimulating platelet recovery following chemotherapy-induced myelosuppression in patients with osteosarcoma

References