Epithelioid sarcoma (ES) is a rare soft tissue sarcoma (RTS); currently available treatments for metastatic ES have shown limited activity in terms of overall survival (OS) and progression-free survival (PFS). Loss of nuclear transcription factor (NTF), a subset of the INI1/SNF5/hSNF5-interacting nuclear (SWI/SNF) complex and a negative regulator of expression of many genes (SWI/SNF), appears to be a driving mechanism in ES. More specifically, EZH2, a histone methyltransferase in polycomb repressive complex 2 (PRC2), is a known driver of ES pathology. In this study, we report a phase 2 trial of tazemetostat, an EZH2 inhibitor, in ES, an aggressive, refractory RTS.

**Background**

**Stage I futility** was performed after the first 15 patients enrolled completed at least the 24-week treatment period. In cohort 5, tazemetostat was studied in adults (≥16 years of age) with ES in a 2-stage expansion design. All patients were required to have tumor INI1 loss confirmed by histology. Tazemetostat 800 mg was administered orally twice daily in continuous 28-day cycles until disease progression, leading to cell death or differentiation and subsequent tumor control and regression.

**Methods**

A Phase 2, Multicenter Study of the EZH2 Inhibitor Tazemetostat in Adults (Epithelioid Sarcoma Cohort) (NCT02601950) was initiated in November 2015. Tazemetostat (EMD 121974) is a small molecule, selective, and potent EZH2 inhibitor. Tazemetostat was orally administered in continuous 28-day cycles until disease progression, leading to cell death or differentiation and subsequent tumor control and regression.

**Results**

Of 62 patients enrolled, mean age was 37 years, 63% were male, and the median number of prior therapies was 4 (range, 2–9). Of 62 patients enrolled, mean age was 37 years, 63% were male, and the median number of prior therapies was 4 (range, 2–9). Patients with prior exposures to SWI/SNF target therapies were excluded. Prior malignancy other than the malignancies under study was not an exclusion criterion.

**Conclusion**

In this study, tazemetostat was well tolerated and showed antitumor activity in a subset of patients with ES. All patients were required to have tumor INI1 loss confirmed by histology. Tazemetostat 800 mg was administered orally twice daily in continuous 28-day cycles until disease progression, leading to cell death or differentiation and subsequent tumor control and regression.