Background: Angiosarcoma has a particularly poor prognosis with 5 year overall survival rates of approximately 30–40%. Treatment of locally advanced and metastatic angiosarcoma is inadequate. Data strongly suggest concurrent, potent inhibition of VEGFR and Tie2 represents an attractive therapeutic strategy in angiosarcoma. Regorafenib displays potent VEGFR and Tie2 receptor inhibition and also possesses activity against additional potential targets in angiosarcoma including PDGFRA, RAF, KIT and FGFR.

Methods: A multicenter phase II study of regorafenib in patients with locally advanced or metastatic angiosarcoma was conducted through the Midwest Sarcoma Trials Partnership. Adequate performance status, organ function, measurable disease (RECIST 1.1) and 1–4 prior therapies were required. Regorafenib 160 mg PO daily was given in 28 day cycles (21 days on, 7 days off) until disease progression (PD) or unacceptable toxicity. The primary endpoint was progression-free survival (PFS), assessed at 16 weeks. Secondary endpoints include overall response rate (ORR), clinical benefit rate (CBR), OS, and safety and tolerability. A Simon 2-stage design was used.

Results: A total of 18 pts were enrolled at 5 sites, 14 are evaluable for response. Median age was 55.6 (range 21–82); 61% were female; 72% metastatic disease. PFS at 4 months is 46% with a median PFS and OS of 2.7 and 15 months, median follow-up 7.9 months (0.4–23). 1 confirmed CR and PR, 5 SD and 7 PD were observed. ORR and CBR are 14 and 30%, respectively. Common grade 3–4 adverse events were as expected.

Conclusions: Regorafenib was well tolerated in this study of pretreated patients with angiosarcomas. Median PFS and OS at 4 months are promising. Regorafenib will continue to be explored in this two-stage optimal Simon design, for a total of 31 patients.

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