**Aim:** Pazopanib is a multi-targeted tyrosine kinase inhibitor, blocking VEGF-A, B, C and FGF pathways and might suppress tumor angiogenesis and growth in HNSCC. In a phase II trial of pazopanib in R/M HNSCC, our group tried to point out some obstacles that maybe common in anti-angiogenesis treatments in this patient group.

**Methods:** We planned a single-arm phase II trial of pazopanib in patients with platinum-refractory recurrent or metastatic HNSCC. The screening process and follow-up images after pazopanib would be presented.

**Results:** We screened 43 patients in about 6 months. 30 (about 70%) were excluded due to easy bleeding and vessel contact. In the initial 10 patients, the objective response was seen in 1; 6 had clinical benefits just comparable with the outcomes of sorafenib or sunitinib. 2 patients experienced severe fatal bleeding; 2 suffered from grade 3 or 4 bleeding. The first enrolled patient had partial response initially but then soon suffered from fatal bleeding; therefore, this patient was finally not categorized as a partial response. Median progression-free survival was 70 days. Median overall survival was 129 days. The image pattern of tumor response was usually central cavity or necrosis formation, typical of the effect of anti-angiogenesis treatments in the literature. However, the rim of the cavity would extend outside and finally led to future resistance.

**Conclusions:** The risk of bleeding in our patient group (platinum-refractory R/M HNSCC) was very high (about 70%) in our enrollment screening process. The disease status was so advanced to cause unpredictable bleeding events & death and also too risky to receive anti-angiogenesis treatments. Besides, peripheral invasion phenomenon in our observation was one possible resistance pattern, maybe resulting from tumor invasion/migration signals and epithelial-mesenchymal transition (EMT). This phenomenon might further aggravate bleeding complications due to easy vessel rupture. Earlier combined blockage of angiogenesis and invasion (such as c-MET) is necessary for better tumor control and to prevent bleeding.

**Disclosure:** All authors have declared no conflicts of interest.