**Abstract/Poster No: 354**

**Introduction**

- Tivozanib hydrochloride (tivozanib) is a potent, selective inhibitor of angiogenic vascular endothelial growth factors (VEGFs) 1, 2, and 3 with a long half-life that allows for once-daily administration while minimizing antifibrotic effects.
- Tivozanib is a tumor-specific (PO) active at 1.5 mg for 3 weeks followed by 1 week off and is excreted primarily via renal clearance.
- A Phase III trial evaluated tivozanib in previously untreated or metastatic RCC patients met its primary endpoint of radiographic progression-free survival (PFS). For patients who had ESA therapy for hematologic disease, the median PFS was 12.7 months versus 9.1 months with sorafenib.

**Methods**

- **Study Design**: A monotherapy, Phase III, randomized, controlled, multinational, multi-center, placebo-controlled study comparing tivozanib with sorafenib in patients with mRCC who had a prior response to targeted therapy or were not candidates for targeted therapy and had no prior VEGF-targeted therapy or mandatory maintenance of targeted therapy (mITT), and final Eastern Cooperative Oncology Group (ECOG) performance status of ≤1. Patients were randomized (1:1) to receive a 1.5 mg dose daily for 3 weeks followed by 1 week off, or placebo 400 mg twice daily in a double-blind (dual) design (Figure 1).

**Results**

- Of 337 patients enrolled, 330 were evaluable for efficacy and 325 for safety.
- In the modified intention-to-treat (mITT) population, the median PFS for tivozanib was 12.7 months versus 9.1 months for sorafenib.
- In addition, the 1-year PFS rates were 62% and 39% for tivozanib versus sorafenib, respectively.
- In patients with favorable MSKCC risk, the median PFS was 21.8 months with tivozanib versus 9.2 months with sorafenib.
- In patients with an ECOG 0 performance status, the median PFS was 18.7 months with tivozanib versus 10.8 months with sorafenib.
- In patients with North America/Western Europe region and clear cell histology, the median PFS was 19.8 months with tivozanib versus 9.2 months with sorafenib.
- In patients with ≥3 organs involved, the median PFS was 15.7 months with tivozanib versus 10.8 months with sorafenib.
- In patients with ≥3 risk factors, the median PFS was 15.7 months with tivozanib versus 10.8 months with sorafenib.

**Discussion and Conclusion**

- The results demonstrated a statistically significant improvement in PFS for patients treated with tivozanib compared to sorafenib, meeting the primary endpoint of radiographic progression-free survival.
- **Table 1**: Baseline Characteristics

**Table 2**: On study OR and PFS

- **Table 3**: On-study OR and PFS

- **Table 4**: On-study OR and PFS

- **Table 5**: On-study OR and PFS

- **Figure 1**: Tivozanib and placebo study design for treatment of mRCC.

- **Figure 2**: Forest plot of PFS hazard ratios.

- **Figure 3**: PFS in North America/Western Europe and Central Europe.

- **Figure 4**: PFS by ECOG performance status.

- **Figure 5**: PFS by prior treatment history.

- **Figure 6**: PFS by Heng intermediate or favorable score.

- **Figure 7**: PFS by Heng favorable or intermediate score.

- **Figure 8**: PFS by organ involvement.

- **Figure 9**: PFS by prior treatment history.

- **Figure 10**: PFS by ECOG performance status.

- **Figure 11**: PFS by prior treatment history.

- **Figure 12**: PFS by organ involvement.

**References**