Evaluation of the Spectrum Selective RTK Inhibitor Sitravatinib in Clear Cell Renal Cell Carcinoma (ccRCC) Refractory to Anti-Angiogenic Therapy

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METHODS

PHASE 1B ENTRY CRITERIA:

• Presence of sitravatinib targets or of RET, KDR, PDGFRA, KIT; IC50: 5-10nM.

METHODS

PARENCHYMAL LESIONS ASSESSED:

• Phs receive oral sitravatinib once daily (QD) at 150mg or 120mg in cycles of 21 days.

RESULTS

PATIENT CHARACTERISTICS AND DISPOSITION:

• As of 18 Apr 2016, 55 pts (71% SE/44) median age of 67 years; range 26-94 with advanced solid tumors were entered in Phase 1b cohorts.

RESULTS

PHASE 1B DOSING REGIMEN AND ASSESSMENTS:

• Treatment has been discontinued in 67 (64%) pts; primary reasons were disease progression (n=27), disease-related deterioration (n=5), and treatment failure (n=35).

RESULTS

SAFETY:

• Overall power of 83% with α of 0.028

RESULTS

PATIENT CHARACTERISTICS AND DISPOSITION:

• No symptomatic or uncontrolled brain metastases

RESULTS

SAFETY:

• Prior 5 weeks observed in a additional 3 pts (Figure 3).

RESULTS

SAFETY:

• Eighteen patients were evaluable for safety in the 150mg cohort and 14 pts were evaluable for efficacy (n=6).

RESULTS

SAFETY:

• All Grades AEs

RESULTS

CONCLUSIONS

• Sitravatinib (MGC516) is a potent inhibitor of multiple RTKs, VEGF2, PDGFRα, PDGFRβ, RET, and KIT with in vitro selectivity in ccRCC and is well tolerated in patients at all dose levels.

RESULTS

CONCLUSIONS

• Sitravatinib showed clinical activity with 4 confirmed PRs in a heavily pre-treated ccRCC patient population.

RESULTS

CONCLUSIONS

• Tolerable safety profile with manageable AEs.

RESULTS

CONCLUSIONS

• Sitravatinib treatment showed clinical activity with 4 confirmed PRs in a heavily pre-treated ccRCC patient population.

RESULTS

CONCLUSIONS

• Slow-escalating 3-stage Design with 10 evaluable pts per stage.

RESULTS

CONCLUSIONS

• Significant antitumor activity was observed in the ccRCC cohort with 4 confirmed PRs, 9 stable disease (SD) and 4 SD with objective response.

RESULTS

CONCLUSIONS

• Five patients continued on study for 82 weeks.

RESULTS

CONCLUSIONS

• Sitravatinib (MGC516) is an orally available, small molecule inhibitor of a spectrum of receptor tyrosine kinases (RTKs) including, but not limited to, VEGFR2, PDGFRα, PDGFRβ, and RET.

RESULTS

CONCLUSIONS

• Sitravatinib exhibited an overall safety profile with manageable adverse events (AEs).

RESULTS

CONCLUSIONS

• Increased MET activation in ccRCC patient-derived xenograft model following prolonged treatment and acquired resistance in murine.

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RESULTS

CONCLUSIONS

• Adapted with permission from Ciamporcero et al.

REFERENCES

• Inactivation of pVHL results in increased transcription of hypoxia inducible genes including VEGF, HIF-1α, and HIF-2α, which has been linked to increased tumor cell migration and invasion.

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• Increased MET activation in ccRCC patient-derived xenograft model following prolonged treatment and acquired resistance in murine.

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