TRAXAR Study: A Randomized Phase 2 Trial of Axitinib and TRC105 versus Axitinib Alone in Patients with Advanced or Metastatic Renal Cell Carcinoma (mRCC)


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INTRODUCTION

• TRC105 is a chimeric IgG1 anti-endoglin monoclonal antibody with high avidity (K_D = 5 pM) that inhibits angiogenesis by competitively inhibiting bone morphogenic protein (BMP) binding to endoglin (Nolan-Stevaux 2012) that also mediates ADCC.

• Endoglin is a membrane receptor required for angiogenesis (Li 1999) that is highly expressed by proliferating endothelial cells in solid tumors (Seon 2011) and also expressed on renal carcinoma stem cells (Bussolati 2008).

• Endoglin heterozygosity is a cause of the Osler-Weber-Rendu syndrome that results in telangiectasia and is associated with improved cancer survival (Duarte 2013).

• Endoglin expression is up-regulated by hypoxia in response to VEGF inhibition (Bockhorn 2003, Davis 2004) and TRC105 potentiates the activity of VEGF inhibitors in preclinical models.

• The recommended phase 2 dose (RP2D) of TRC105 given as a single agent or when given with bevacizumab is 10 mg/kg by weekly intravenous infusion. TRC105 treatment is not associated with hypertension or proteinuria.

• Telangiectasia, a characteristic finding of the Osler-Weber-Rendu syndrome, is observed routinely at the recommended phase 2 dose and immunogenicity is rare (Rosen 2012, Gordon 2014).

PHASE 2 METHODS

• Randomized (1:1), multicenter study in patients with advanced or metastatic clear cell renal cell carcinoma.

• Approximately 150 patients will be enrolled at approximately 30 sites.

• Patients receive axitinib at a starting dose of 5 mg Bid on a 28 day cycle with or without TRC105 at 10 mg/kg weekly.

• Titrations of axitinib is permitted after cycle 1.

• Primary Objective: To estimate PFS by RECIST 1.1

• Secondary Objectives: To evaluate overall response, disease control rate, PK, immunogenicity, and circulating angiogenic biomarkers.

PHASE 2 ELIGIBILITY

• Advanced or metastatic renal cell carcinoma with a clear cell component.

• Progression on treatment with one and only one VEGF inhibitor (prior axitinib not allowed).

• Prior mTORi allowed.

• Prior immunotherapy allowed.

• ECOG ≤ 1.

PHASE 2 STUDY DESIGN

PHASE 2: ENROLLING

• Randomized (N=150)

• 1° Endpoint: PFS

• Advanced or metastatic clear cell RCC

• Progression on 1 prior VEGF inhibitor

• 1 prior mTORi inhibitor allowed

• 1 prior immunotherapy allowed

SUMMARY

• TRC105 inhibits angiogenesis by competitively inhibiting BMP binding to endoglin.

• Based on the results from Phase 1b, the combination of TRC105 and axitinib was well tolerated in patients with advanced renal cell carcinoma.

• The combination of TRC105 and axitinib demonstrated encouraging preliminary signs of activity including RECIST 1.1 partial responses in patients that were prior non-responders and doubling of the PFS expected with axitinib as a single agent.

• Enrollment into Phase 1b is complete and the Phase 2 TRAXAR Study is actively enrolling at approximately 30 sites in the US.

• TRAXAR study design details are at https://clinicaltrials.gov/show/NCT01806064

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