TRC105 is a human/murine chimeric IgG1 monoclonal antibody that inhibits angiogenesis and tumor growth. TRC105 binds human CD105, a proliferation-associated and hypoxia-inducible protein found on the surface of tumor vasculature. Preclinical in vitro and in vivo studies demonstrated the safety and tumor growth inhibitory effects of TRC105 in multiple tumor systems as monotherapy and in combination with cytotoxic chemotherapy. An ongoing phase 1 trial is evaluating the safety and tolerability of single-agent TRC105 in patients with solid cancers.

Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number of Patients (n=17)</th>
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<tbody>
<tr>
<td>Median Age</td>
<td>63</td>
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Methods

• Study patients were required to have advanced refractory cancer, ECOG 1, and adequate organ function.
• Patients with CNS or central nervous system cancers were excluded.
• TRC105 was administered by 30-minute IV infusion every 2 weeks until progression. Cohorts of 3 to 8 patients were planned at doses of 0.01, 0.05, 0.1, 0.3, and 1.0 mg/kg.

Results

• A total of 17 patients have been enrolled and treated at each of the planned doses. One patient at 0.01 mg/kg experienced Grade 4 bleeding from a gastric ulcer within 1 week of the first TRC105 infusion. The bleeding was considered possibly related to study treatment and a dose-limiting toxicity. The ulcer bleeding had resolved by the time of study entry after 2 units of packed red blood cells. No other Grade 3 or 4 adverse events related to TRC105 have been observed.

Patient #10012001 Ovarian Cancer

A metastatic ovarian cancer patient enrolled at 0.01 mg/kg was treated for 6 months with radiographically stable disease and a 16% decrease in plasma CA125. An ongoing phase 1 trial is evaluating the safety and tolerability of single-agent TRC105 in patients with solid cancers.

Summary of Safety Data – Related Events

• A single dose-limiting toxicity was observed at 0.05 mg/kg due to bleeding from an untreated asymptomatic gastric ulcer within 1 week of the first TRC105 infusion. The patient recovered completely; the time of adverse effect (AE) is 1 week post first dose, and the patient was removed from study. The protocol was amended to exclude patients with history of other active G1 or G2 AE.
• Grade 1 intermittent postural venous bleeding occurred in a premature-pausal woman treated at 0.01 mg/kg with therapy continued in combination with BEV.

Conclusions

• TRC105 is a human/murine IgG1 kappa monoclonal antibody that binds to ~2 ng/mL avidity to human CD105, signaling a membrane receptor required for angiogenesis and tumor growth inhibition. Preclinical studies of human cancer (Bockhorn et al, 2003; Davis et al, 2004), supplying a rationale for developing TRC105 in combination with VEGF antagonists.

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• TRC105 and a markedly improved bone scan.

• TRC105 is a candidate for further clinical development alone and in combination with other anticancer agents.

• TRC105 levels were detected in the first three cohorts at concentrations above the KD but below levels shown to saturate CD105 binding sites.

• HAMA data is available for the first 12 treated patients. One patient was positive at 0.03 mg/kg on Cycle 4 Day 1 (prior to dose 7).

• One of 12 patients treated in the first 3 cohorts developed HAMA after 3 months of treatment.

• One castrate-refractory metastatic prostate cancer patient remains on study at 11 months with a complete PSA response to TRC105 and a markedly improved bone scan.

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