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A PHASE 1 STUDY OF TRC105 (ANTI-CD105 ANTIBODY) IN PATIENTS WITH ADVANCED SOLID TUMORS

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Introduction

- High tumor microvessel density as measured by CD105 immunohistochemistry correlates with poor prognosis across more than 10 solid tumor types, including breast, colorectal, prostate and lung cancer
- In mouse models of human cancer, CD105 expression is upregulated by VEGF inhibitors (Bockhorn 2003, Davis 2004)
- TRC105 potentiates the activity of VEGF inhibitors in preclinical models
- CD105 is expressed on renal cell cancer stem cells (Bussolati 2008)

Methods

Key Inclusion Criteria

- Advanced incurable solid cancer
- ECOG PS of 0 or 1
- Adequate organ function
- Hemoglobin \geq 10 g/dL

Key Exclusion Criteria

- Lung cancer with central tumor
- CNS disease
- Clinically significant effusions
- Prior cancer therapy within 4 wks
- Major surgery within 4 wks
- Major bleeding within 4 wks

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Patient Demographics

Baseline Patient Characteristics (N=50)	
Age	Median: 64 Range: 25 - 84
Gender	Female: 15 Male: 35
Baseline ECOG Performance Status	ECOG PS 0: 15 ECOG PS 1: 35
Number of Prior Regimens	Median: 4 Range: 1-13
Cancer Type	Colorectal: 10 Prostate: 9 Renal: 5 Lung: 4 Ovarian: 3 Sarcoma: 3 Breast: 2 Pancreatic: 2 Other: 12

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Pharmacokinetics

- TRC105 concentrations that engage ADCC (1 ng/mL) were achieved at all dose levels
- The target concentration for maximum effect (200 ng/mL) was achieved at doses of 0.3 mg/kg and higher
- Serum concentrations expected to saturate CD105 binding sites (>200 ng/mL) were achieved continuously at 15 mg/kg q2 weeks and 10 mg/kg weekly.
- TRC105 accumulated with weekly dosing.

Safety

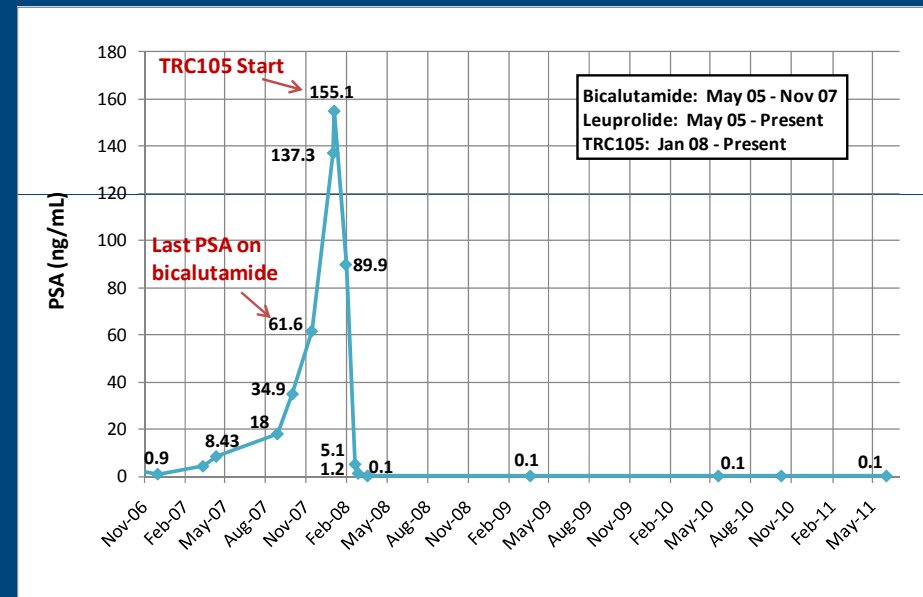
Possibly Related Adverse Events in >1 Patient or Grade 3/4 (N=50)

Drug Supply	TRC105 Dose	Schedule	Preferred Term	Grade 1	Grade 2	Grade 3	Grade 4
NS0	0.03 mg/kg	Every 2 Weeks	Fatigue		1		
NS0	0.1 mg/kg	Every 2 Weeks	Gastrointestinal hemorrhage				1
			Anemia		1		
			Diarrhea	1			
NS0	0.3 mg/kg	Every 2 Weeks	Flushing	1			
			Diarrhea	1			
NS0	1 mg/kg	Every 2 Weeks	Infusion related reaction		1	1	
			Fatigue		1		
			Nausea	1			
			Vomiting	1			
CHO	0.3 mg/kg	Every 2 Weeks	Infusion related reaction		2	1	
			Headache	1			
CHO	1 mg/kg	Every 2 Weeks	Infusion related reaction			1	
			Constipation	1			
			Flushing	1			
CHO	10 mg/kg	Every 2 Weeks	Infusion related reaction		2		
			Anemia		1		
			Epistaxis	1			
			Fatigue	1			
CHO	15 mg/kg	Every 2 Weeks	Anemia		1	1	
			Fatigue	1			
			Nausea	1			
			Vomiting	1			
CHO	10 mg/kg	Weekly	Epistaxis	1	1		
			Fatigue	1	1		
			Anemia		1		
			Headache	2			
			Pyrexia	2			
			Telangiectasia	1			
CHO	15 mg/kg	Weekly	Anemia			2	1
			Constipation		1		
			Fatigue		1		
			Headache		1		
			Infusion related reaction		1		
			Epistaxis	2			
			Telangiectasia	1			

Efficacy: Prostate Cancer

- A patient with metastatic castrate-resistant prostate cancer and multiple painful skeletal metastases has been on TRC105 therapy for over 3 years
- Complete PSA response
- Resolution of bone pain
- Bone scan normalization

PSA Results Before and During TRC105 Therapy



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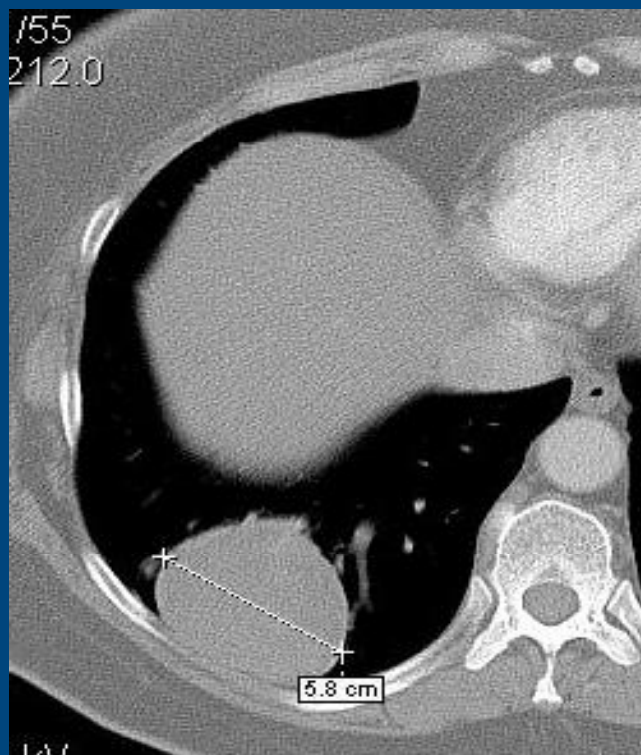
Efficacy: Endometrial Cancer

- A patient with lung metastases from endometrial cancer remains on study after 10+ months of treatment with a reduction in the maximum dimension of all 8 tumors including this 5.8 cm tumor
- Overall tumor burden reduction was 7%, 9%, 13%, and 8% at Month 2, 4, 6, and 8, respectively
- Progression-free survival on TRC105 exceeds that for all 3 prior systemic regimens including:
 - Carboplatin/paclitaxel (4 months)
 - Anastrozole (8 months)
 - Ifosfamide (2 months)

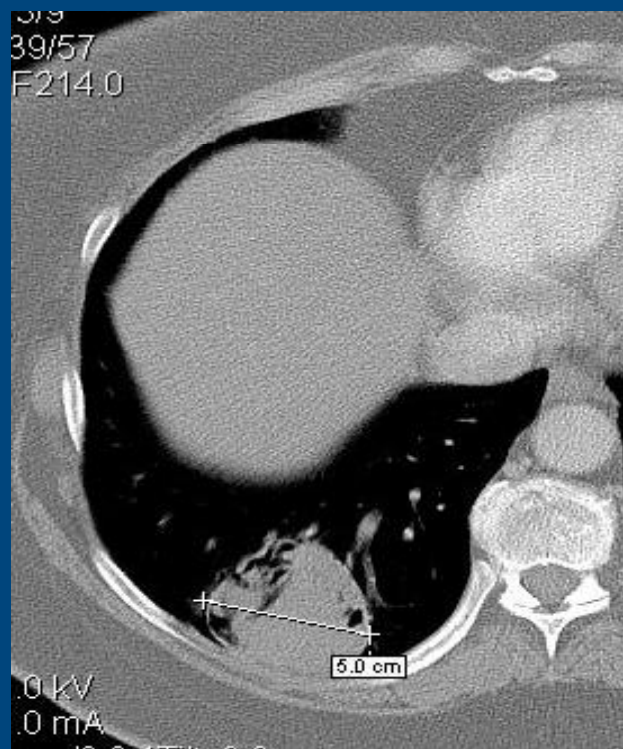
Efficacy: Endometrial Cancer

Chest CT Scan

Baseline



Month 2



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References

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- Bussolati B, FASEB 22:3696-3705, 2008
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- Li DY, Science 284:1534-1537, 1999
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