

FINAL RESULTS FROM A PHASE 1 STUDY OF TRC093 (HUMANIZED ANTI- CLEAVED COLLAGEN ANTIBODY) IN PATIENTS WITH SOLID CANCER

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Presentation Outline

- TRC093 Mechanism of Action
- Phase 1 study objectives
- Phase 1 study methods
- Phase 1 study results
- Summary and conclusions

TRC093 Background

- TRC093 is a humanized IgG1 monoclonal antibody to cryptic collagen epitopes that are exposed during angiogenesis and tumor growth
- Cleaved collagen epitopes are selectively expressed on proliferating vasculature, including tumor vasculature and developing retinal vasculature
- TRC093 has been shown to inhibit angiogenesis and tumor growth in mouse models of cancer and has also been shown to inhibit choroidal neovascularization in mouse models of age-related macular degeneration
- Studies also indicate TRC093 potentiates the activity of approved anticancer therapies in preclinical xenograft models including paclitaxel and bevacizumab

Objectives

- Evaluate the safety and tolerability of TRC093 when administered intravenously every two weeks to patients with solid tumors
- Evaluate pharmacokinetics, tumor response, human antihuman antibody (HAHA) formation, and change in protein biomarkers after treatment

Methods

- Phase 1, non-randomized, open-label, dose-finding, first-in-human study conducted at 3 institutions in the U.S.
- TRC093 was administered i.v. on Days 1 and 15 of each 28-day cycle
- All patients were treated until progression with efficacy evaluations performed every 4 doses (2 months)

Methods

- Key Inclusion Criteria
 - Adults (age ≥ 18 years) with advanced or metastatic solid tumors refractory to standard treatment or for which no effective treatment exists
 - ECOG performance status 0, 1 or 2
 - Adequate organ function
- Key Exclusion Criteria
 - Receipt of cancer treatment within 4 weeks
 - CNS malignancy
 - Major surgery within 4 weeks
 - Unhealed wounds, ulcers or bone fractures
 - Screening proteinuria or hematuria $> 1+$

Results – Baseline Characteristics

Characteristic	Number of Patients (N=19)
Age	Mean: 59 years
Gender	Female: 8 Male: 11
Screening ECOG Performance Status	ECOG 0: 6 ECOG 1: 13
Number of Prior Chemotherapies	Median: 5 Range: 2-14
Race	Caucasian: 17 Black/African American : 1 Native Hawaiian/Other Pacific Islander : 1

Results - Safety

- No dose-limiting toxicity was reported in 19 patients treated at TRC093 doses up to 24 mg/kg every 2 weeks
- The maximum feasible dose was 12 mg/kg due to limited drug supply
 - 9 patients were treated at 12 mg/kg every 2 weeks
 - 1 patient was treated at 24 mg/kg
- Human ant-human antibody formation was not detected

Results - Safety

- Related Adverse Events

# Patients Out of 19 Total Treated		
Preferred Term	Grade 1	Grade 2
Anemia		1
Palpitations	1	
Lacrimation Increased	1	
Photophobia	1	
Abdominal Discomfort	1	
Gastritis	1	
Nausea	2	
Asthenia	1	
Fatigue	2	5
Pain	1	
Drug Hypersensitivity	1	

Results - Safety

- Related Adverse Events (Continued)

# Patients Out of 19 Total Treated		
Preferred Term	Grade 1	Grade 2
Anorexia/Decreased Appetite	1	1
Hyponatremia	1	
Arthralgia		1
Joint Stiffness		1
Muscle Spasms	1	
Musculoskeletal Stiffness	1	1
Pain in Extremity	2	
Dizziness	1	
Dysarthria	1	
Dysgeusia	1	
Rhinorrhea	1	
Pruritus	1	

Results - PK

Summary of Serum TRC093 Exposure Parameters Following Multiple Intravenous Infusions of TRC093¹

TRC093 Dose (mg/kg)	n	Cmax (µg/mL)	AUC _{0-n} (hr*µg/mL) ²	Half-life, hr
0.5	2	8.9 (0.4)	1090 ³	369
1.5	3	43.3 (9.5)	3349 (1150)	488 (159)
5.0	3	131 (58.7)	14069 (8354)	302 (123)
12.0	6	467 (111)	35336 (4374)	262 (71)
24.0	1	1475 ³	- ⁴	- ⁵

¹Mean (SD)

²AUC_{0-n} = Serum TRC093 AUC during the fourth dose interval

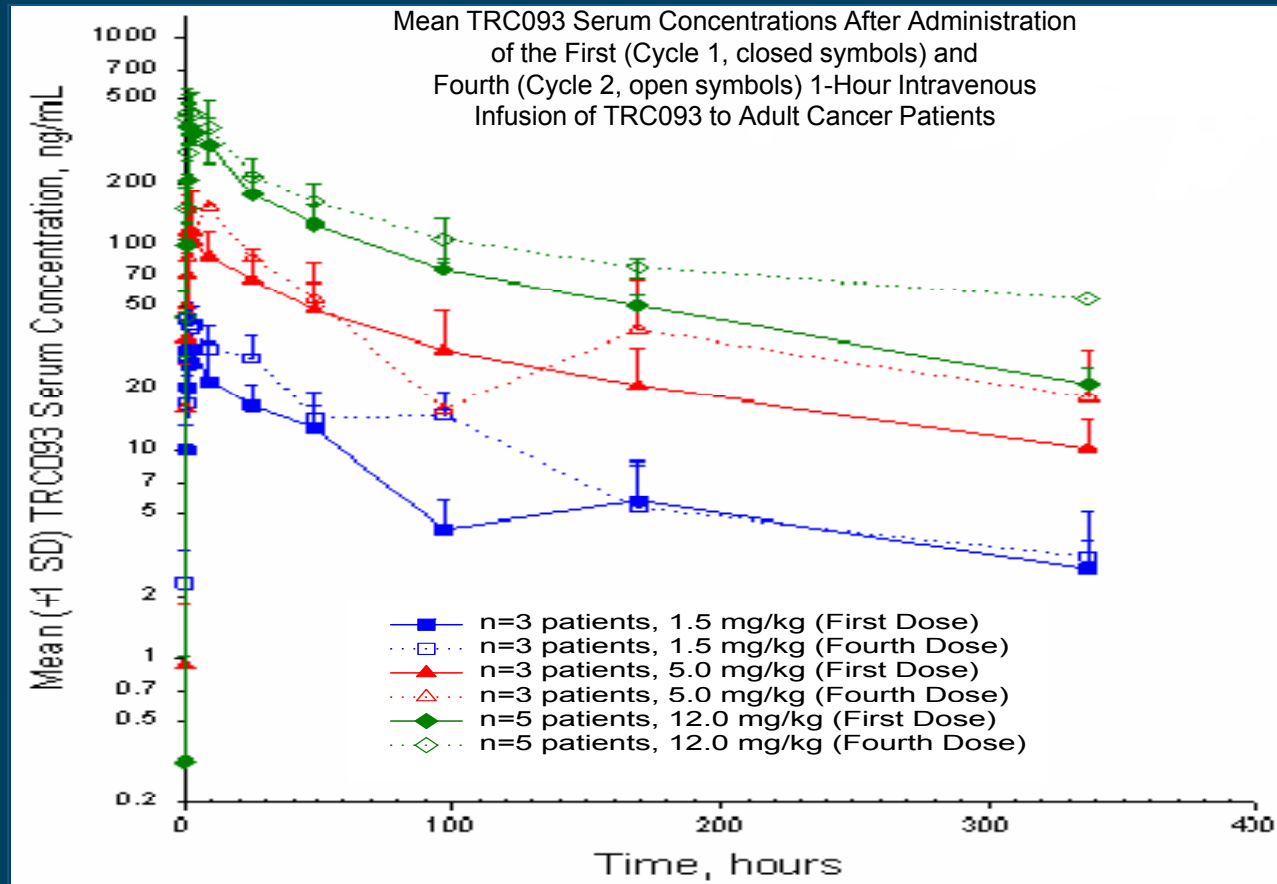
³S.D. could not be calculated, n=1

⁴Insufficient serum concentration data to calculate AUC_{0-n}

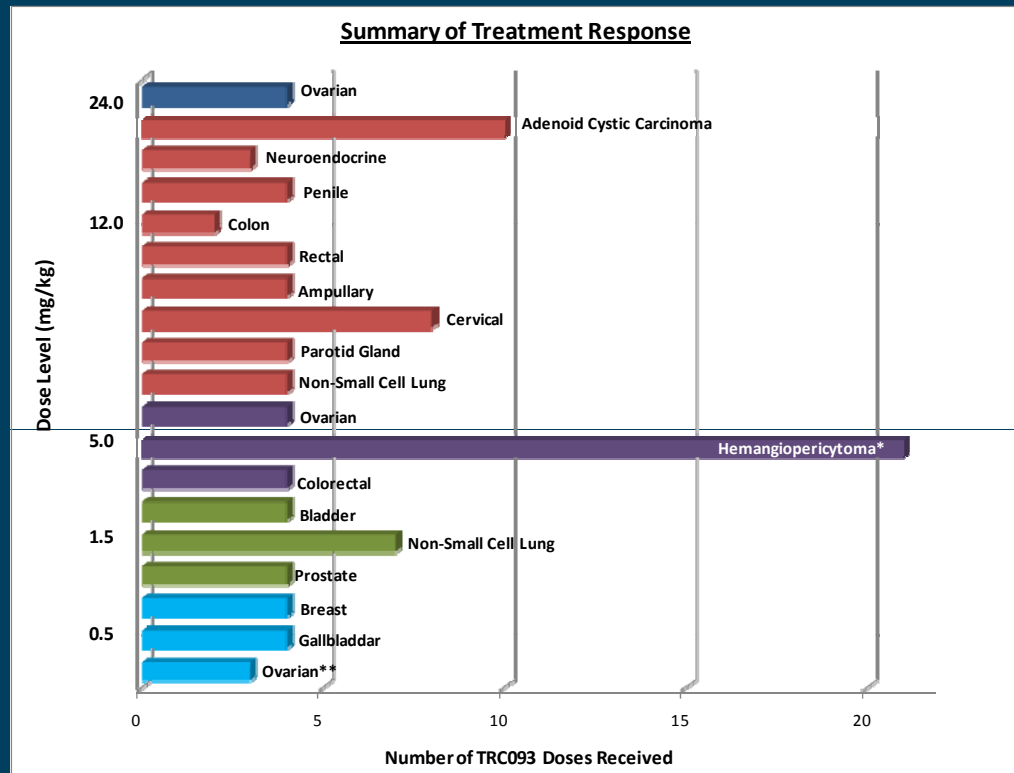
⁵PK parameters could not be reliably estimated using a linear 2-compartment PK model

Pharmacokinetic evaluation demonstrated linear dose-dependent exposures characteristic of a humanized monoclonal antibody.

Results – PK



Results - Efficacy



* A patient with metastatic hemangiopericytoma had stable disease for 9 months prior to progressing at Month 11. Sites of disease included the chest wall, malignant pleural effusion, malignant ascites, lymph nodes and pancreas.

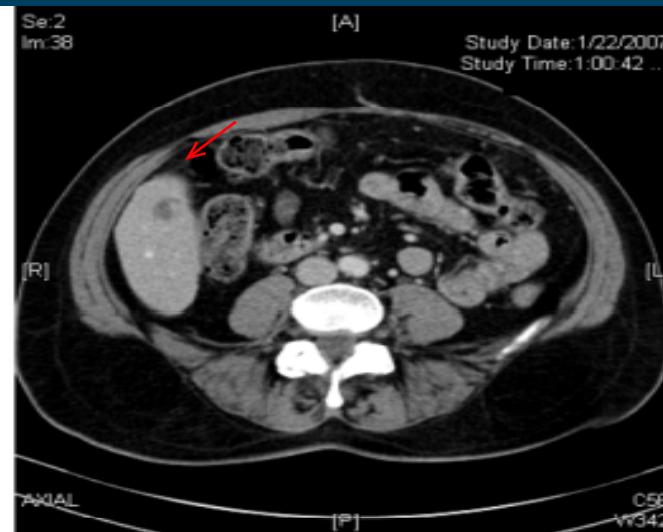
** An ovarian cancer patient demonstrated a mixed response in her liver after 3 doses of TRC093 at 5 mg/kg but demonstrated disease progression overall.

Results - Efficacy

Baseline CT Scan



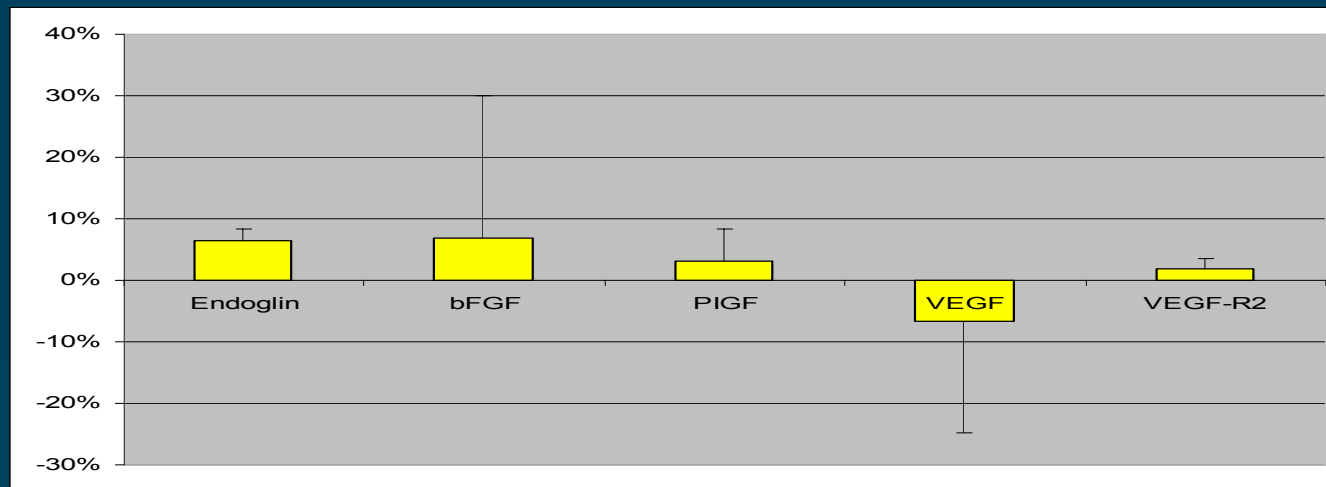
CT Scan After 2 Months of TRC093



- Mixed Response
 - After receiving 7 prior cancer therapies, a 56 year old patient with granulosa cell ovarian cancer demonstrated a mixed response in her liver (two lesions regressed, including the right lobar lesion indicated above) although the presence of a new lesion indicated disease progression overall.

Results – Protein Biomarkers

- This figure presents the mean change in protein biomarker values between Cycle 1 Day 1 and Cycle 1 Day 22 for 16 treated patients across all dose levels
- Results are expressed as mean percent change +/- standard error



Summary and Conclusions

- TRC093 was well-tolerated at doses up to 24 mg/kg every 2 weeks without dose-limiting toxicity
- Human antihuman antibody (HAHA) formation was not observed
- Pharmacokinetic evaluation demonstrated linear dose-dependent exposure
- Early evidence of efficacy included stable disease for up to 9 months and a mixed response at 2 months
- 26% of patients demonstrated stable disease \geq 2 months
- Mean circulating VEGF levels declined with treatment
- These results support further development of TRC093 in combination with standard of care agents