CONFIDENTIAL

Statistical Analysis Plan

A RANDOMIZED PHASE 2 TRIAL OF AXITINIB AND TRC105 VERSUS AXITINIB ALONE (INCLUDING A LEAD-IN PHASE 1B DOSE-ESCALATION PORTION) IN PATIENTS WITH ADVANCED OR METASTATIC RENAL CELL CARCINOMA

Protocol 105RC101

Version 4.0

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Approval Page

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STATISTICAL ANALYSIS PLAN

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1. Abbreviations and specialist terms

Abbreviation or specialist term	Explanation
AE	Adverse Event
AFP	Alpha Fetoprotein
APA	Anti-Product Antibody
AUC	Area Under the Curve
AUClast	Time of Last Measurable Concentration of Area Under the Curve
CA-125	Cancer Antigen-125
CEA	Carcinoembryonic Antigen
CI	Confidence Interval
CL	Clearance
C_{MAX}	Maximum Serum Concentration
CR	Complete Response
CRF	Case Report Form
CT	Computed Tomography
CTCAE	Common Terminology Criteria Adverse Events
DLT	Dose Limiting Toxicity
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EGFR	Epidermal Growth Factor Receptor
g	Gram
HR	Hazard Ratio
ID	Identification
IRB	Institutional Review Board
kg	Kilogram
LOQ	Limit of Quantification
mg	Milligram
mL	Milliliter
mm	Millimeter
MTD	Maximum Tolerated Dose
NCI	National Cancer Institute
OS	Overall Survival
PD	Progressive Disease
PDGF	Platelet Derived Growth Factor
PFS	Progression Free Survival
PlGF	Placental Growth Factor
PR	Partial Response
PSA	Prostate Specific Antigen
PT	Preferred Term
RECIST	Response Evaluation Criteria in Solid Tumors
SAE	Serious Adverse Event
sCD105	Soluble CD105/endoglin
SD	Stable Disease
SOC	System Organ Class
sVEGFR2	Soluble VEGF Receptor 2
t½	Half-Life
TGF-β	Transforming Growth Factor

Abbreviation or specialist term	Explanation
T_{max}	Time to Maximum Plasma Concentration
ULN	Upper Limit of Normal
VEGF	Vascular Endothelial Growth Factor

2. Objectives

2.1. Phase 1b

2.1.1. Primary Objective

To evaluate safety and tolerability and determine a recommended phase 2 dose for TRC105 when added to standard dose axitinib in patients with advanced renal cell carcinoma

2.1.2. Secondary Objective(s)

The secondary objectives are to evaluate pharmacokinetics (PK), immunogenicity and activity of the monoclonal antibody TRC105. The specific objectives of the efficacy analysis are:

- To look for preliminary evidence of antitumor activity when TRC105 is added to axitinib, by assessing response rate and progression-free survival
- To characterize the pharmacokinetic profile of TRC105 when given with axitinib
- To evaluate TRC105 immunogenicity by measuring anti-product antibody (APA) formation
- To explore the pharmacodynamic changes in circulating angiogenic biomarkers following treatment with TRC105 and axitinib

2.2. Phase 2

2.2.1. Primary Objective:

- To estimate the progression-free survival (PFS) of patients with advanced or metastatic RCC by RECIST 1.1 in patients treated with axitinib and TRC105 compared to those treated with axitinib alone, following failure of one prior VEGF inhibitor.

2.2.2. Secondary Objective(s):

- To estimate response rate by RECIST 1.1 and Choi criteria, including duration of response by RECIST 1.1 and Choi criteria
- To estimate the disease control rate (CR + PR + SD) at 16 weeks by RECIST1.1 and Choi criteria
- To determine the frequency and severity of adverse events as assessed by NCI CTCAE (Version 4.0)
- To evaluate TRC105 immunogenicity as measured by Anti-Product Antibody (APA) concentrations
- To explore the effects of TRC105 on circulating angiogenic protein biomarkers
- To characterize the pharmacokinetic profile of TRC105 and axitinib

3. Study Design

3.1. Phase 1

This is a multicenter, open-label, nonrandomized, phase 1b, dose-finding study of TRC105 in combination with standard dose axitinib in patients with advanced renal cell carcinoma. Escalating doses of i.v. TRC105 will be administered weekly beginning with Dose Level 1 in combination with oral axitinib given twice daily of each 28 day cycle. Additional intermediate doses (below the MTD established during the trial) may be explored based upon clinical, PK, and/or biomarker data.

Cohort	Number of Evaluable Subjects	Axitinib mg p.o., BID days 1-28	TRC105 mg/kg IV
-1	3-6	5	6[a]
1 (starting dose)	3-6	5	8[a]
2	3-6	5	10[a]
Expanded Cohort 1	9-12 (up to 15 total at the MTD)	5	10[a]
3	3-6	5	• 10 mg/kg weekly during cycle 1[b] • 15 mg/kg every two weeks beginning with cycle 2 day 1[b]
4	3-6	5	• 10 mg/kg weekly during cycle 1[b] • 20 mg/kg every two weeks beginning with cycle 2 day 1[b]
Expanded Cohort 2	At least 6 patients will be treated at the MTD (either cohort 3 or cohort 4 dose level)	5	• 10 mg/kg weekly during cycle 1[b] • Either 15 or 20 mg/kg every two weeks beginning cycle 2 day 1[b]

[a] In cohort -1, 1, 2 and expanded cohort 1 TRC105 will be given weekly.

[b] In cohorts 3 and 4 and Expanded Cohort 2, axitinib dosing will begin on cycle 1 day 1 and twice daily thereafter, and TRC105 will be administered weekly during cycle 1. The first weekly TRC105 dose will be split into two doses whereby 3 mg/kg is administered on cycle 1 day 1 and the balance is administered on cycle 1 day 4. Starting on cycle 2 day 1 and beyond, TRC105 will be administered every two weeks on days 1 and 15.

For cohorts 1 and 2, the DLT evaluation period, for purposes of dose expansion, will be the first 28 days of dosing axitinib and TRC105 together (e.g., from cycle 1 day 1 through cycle 1 day 28) . Cycles are 28 days in duration.

For cohorts 3 and 4, the DLT evaluation will be the first 28 days of dosing axitinib with TRC105 every 2 weeks (e.g., from cycle 2 day 1 through cycle 2 day 28). Cycles are 28 days in duration.

Three patients will be initially enrolled and treated at each dose level. If none of these 3 patients experiences a dose-limiting toxicity (DLT) during the 28-day evaluation period, dose escalation will proceed following review of safety data with appropriate site staff including the principal investigators at all sites.

Patients are eligible for additional treatment until progression.
Regular safety and toxicity assessments are performed. Toxicities will be graded according to the NCI Common Terminology Criteria for Adverse Events (CTCAE), Version 4.0.

Toxicity Category	**Drug-Related Toxicity/Grade**
Hematologic	Grade 4 neutropenia for ≥ 5 days
	Febrile neutropenia: grade 4 neutropenia with fever > 38.5 °C both sustained over a 24 hour period.
	Neutropenic infection: grade ≥ 3 neutropenia with grade ≥ 3 infection
	Anemia ≥ grade 3
	Grade > 4 thrombocytopenia or grade ≥ 3 thrombocytopenia and grade ≥ 3 hemorrhage
Nonhematologic	Grade 3 or 4 nonhematologic toxicity with the following exceptions: • Nausea, vomiting or diarrhea for < 48 hours[a] • Asymptomatic electrolyte abnormalities that are corrected to grade 1 or better in < 48 hours[b]

[a]Patients with related grade 3 or 4 diarrhea, nausea or vomiting for ≥ 48 hours despite optimal medical therapy will require a one-level dose-reduction of TRC105.
[b]Patients with related grade 3 or 4 electrolyte abnormalities that persist for ≥ 48 hours will require a one-level dose-reduction of TRC105.

Up to 15 patients with advanced renal cell carcinoma will be treated at the weekly dosing MTD (or top dose level if a MTD is not determined) to further characterize safety and tolerability. At

least 6 patients with advanced renal cell carcinoma will be treated at the every two week dosing MTD (or top dose level if a MTD is not determined).

Dose escalation will be according to the following dose escalation schema, based on the occurrence of DLT.

- If none of three patients in a cohort experiences a DLT after completing Cycle 1, dose escalation may be authorized by the medical monitor or designee.
- If one of three patients in a cohort experiences a DLT, three additional patients will be enrolled at the same dose level. If no additional DLT is reported, dose escalation may be authorized by the medical monitor or designee.
- If more than one of three or more than one of six patients at a dose level develop a DLT, the maximum tolerated dose (MTD) will be considered exceeded. Patient enrolment and treatment at that dose level will be stopped. There will be no further dose escalation and the previous lower dose will be designated as the MTD.
- Patients, who discontinue the study prior to completing the 28 day DLT evaluation period (Cycle 1), for reasons other than a DLT, will be replaced.

3.2. Phase 2

The study population for safety will include all patients receiving at least a portion of one dose of study drug (TRC105 or axitinib). The study population for efficacy will include all randomized patients (intention to treat). The primary endpoint is PFS and the primary analysis will compare the TRC105 and control groups using a one-sided, stratified (by the randomization stratification factor) log-rank test at the alpha=0.10 level of significance. The primary analyses of efficacy endpoints dependent on disease assessments (PFS, ORR and DR) will be performed in the intent-to-treat (ITT) population based on results of the central review of disease response and progression. Supportive analyses will be performed based on investigator assessments of disease response and progression. Pre-planned assessments of the primary endpoint will additionally be done based on number of prior therapies (one, two or three) and other known prognostic factors.

An interim analysis for futility will be conducted by the DMC when 55 events have occurred. At the interim analysis, the conditional power based on the observed hazard ratio (HR) will be estimated. If the conditional power is less than 25%, the DMC may recommend to the sponsor that the study be terminated for futility. However, this interim analysis will not consider the possibility of early termination on the basis of superior efficacy.

4. Sample Size Determination

4.1. Phase 1

The number of patients to be evaluated in this study is based primarily on sound clinical considerations established in dose-finding designs in Oncologic studies. This 3+3 dose escalation trial is expected to enroll approximately 18 patients. The final sample size will depend on the number of DLTs observed at the different dose levels.

4.2. Phase 2

A hazard ratio (HR) of 0.67 is considered to be clinically relevant. Based on 1:1 randomization and the use of a one-sided log-rank test at the alpha=0.10 level of significance, 115 events are required in order to have 80% power to detect a HR of 0.67. The expected PFS of patients treated with axitinib who have progressed following first line treatment with a VEGFR TKI is 4.8 months. Based on a planned accrual period of 12 months, and a minimum follow-up period of 4.3 months, approximately 150 patients will be required. Timing of the final analysis of PFS will be determined by the sponsor based on the expected total number of events that define PFS and the timing of these events, and may occur prior to the occurrence of 115 events.

5. Analysis Population

The safety population includes all patients who receive at least a portion of one dose of the study drug, TRC105 or axitinib (phase 2 portion).

The phase 2 study population for efficacy will include all randomized patients (intention to treat).

The Phase 1b study population for efficacy will include all patients who receive treatment with axitinib and TRC105.

6. General Analysis Comments

Summary statistics will include frequencies and percents of responses in each category for discrete measures; and may include means, medians, standard deviations, minimum and maximum values for continuous measures. Listings of data represented on the Case Report Form (CRF) will be provided.

SAS®, Version 9.0 or higher or R version 2.15 or higher, will be used to perform all statistical analyses.

7. Missing Data

All data collected, including unscheduled visits, will be presented in the data listings. Summary tables will generally be limited to planned visits.

In all analyses, except for partial dates, it is expected that only observed values will be presented; no imputation of missing data will be conducted. Partial dates will be imputed according to the following table. CRFs that are not listed below are not expected to contain partial dates. CRF versions may change. Only if a change impacts the imputation of a partial date will the SAP be amended.

Planned Imputation Methods for Partial Dates

CRF	Field	Planned Imputation Method	
		Month and Year Given	Year Given
Adverse Events	Date of Onset	First of Month	Jan 01 of Year
	Date of Resolution	Last day of Month	Dec 31 of Year
Concomitant Medications	Start Date	First of Month	Jan 01 of Year
	Stop Date	Last day of Month	Dec 31 of Year
Concomitant Treatment	Start Date	First of Month	Jan 01 of Year
	Stop Date	Last day of Month	Dec 31 of Year
Informed Consent Reconsent	Date of Consent/Reconsent	Last day of Month	Dec 31 of Year
Medical History and Baseline Emergent AE	Start Date	First of Month	Jan 01 of Year
	Stop Date	Last day of Month	Dec 31 of Year
Primary Diagnosis	Date of Diagnosis	Last day of Month	Dec 31 of Year
Prior Cancer Surgery	Date of Surgery	Last day of Month	Dec 31 of Year
Prior Cancer Therapy	Start Date	First of Month	Jan 01 of Year
	Stop Date	Last day of Month	Dec 31 of Year
	Date of Progression on Therapy	Last day of Month	Dec 31 of Year
Prior Radiation Therapy	Start Date	First of Month	Jan 01 of Year
	Stop Date	Last day of Month	Dec 31 of Year
Demography	Birth Date	15th of the Month	Jun 15 of Year

8. Patient Accountability and Patient Disposition

The number enrolled, the number of doses received and the number of cycles completed (per Section 12.1) will be presented for each dose level for the phase 1 portion and by treatment group for the phase 2 portion. A summary of reasons for withdrawal will be provided. The number of patients in the safety populations will also be presented. Patient disposition, including reasons for discontinuation, and number of cycles completed will be listed.

9. Demographics and Baseline Characteristics

Demographics and baseline characteristics will be summarized by dose level. Demographic variables, including age, gender, and race will be summarized in a tabular form.

Initial diagnosis, prior cancer surgery, prior radiotherapy, prior cancer therapy, and medical history will be listed. Initial diagnosis, prior cancer surgery, prior radiotherapy, and prior cancer therapy will also be summarized by dose level for the phase 1 portion and by treatment group for the phase 2 portion.

10. Concomitant Medications and Treatments

A listing of all concomitant medications and treatment will be provided by patient, drug name, start and stop dates, whether the medication or treatment was ongoing. Concomitant medications will be coded by using WHO Drug Dictionary version September 2012.

11. Efficacy Endpoints

11.1 Primary Endpoint

The primary endpoint for efficacy in Phase 2 will be PFS. For Phase 2, PFS is defined as time from randomization to either first disease progression (by RECIST 1.1) or death from any cause. For Phase 1, PFS is defined from the date of consent to either first disease progression by RECIST 1.1 or death from any cause.

For the purpose of analysis for patients who are alive at the time of analysis and have not had disease progression, the following rules will apply:

(1) The patient will be censored on the date of the last tumor assessment documenting absence of progressive disease
(2) If the patient was given antitumor treatment other than study drug treatment, the patient will be censored as of the date of the last tumor assessment prior to initiating that antitumor therapy
(3) If the patient was removed from study for toxicity or other reason, the patient will be censored as of the date of the last tumor assessment on study.

With regard to missed tumor assessments:

(1) In the event of one missed tumor assessment followed by a subsequent assessment of progressive disease (PD), the subsequent PD assessment qualifies as objective tumor progression.
(2) In the event of more than one consecutive missing tumor assessment followed by a subsequent assessment of PD, the patient will be censored at the last adequate tumor assessment. If individual scans are performed on different dates, but contribute to the same overall assessment, the date of the earliest scan will be used.

The PFS distributions in the two arms will be summarized using the Kaplan-Meier method. The distributions will be compared using a stratified (by the randomization stratification factor) log-rank test at the one-sided alpha=0.10 level of significance.

Additional exploratory analyses of PFS will be conducted in subgroups defined based on number of prior therapies (one, two or three), ECOG performance status, and the biomarkers TGF-β receptor III and osteopontin. The same methods are for the primary analysis (Kaplan-Meier

survival estimation, log rank tests) will be used. The effects of these covariates may also be assessed using Cox proportional hazards regression models.

The best response (CR, PR, SD or PD according to RECIST 1.1 and according to Choi criteria) for each patient with measurable disease who received at least one dose of study drug will be listed by cohort and response rate (CR or PR) between the two arms will be compared using Pearson's chi-square test or Fisher's exact test. Stable disease will be defined as lack of tumor progression lasting for 2 cycles or longer. Additional analysis will be conducted based on duration of response, defined from the time to first response (CR or PR) to disease progression and will be compared between arms using Kaplan Meier methods. Other secondary analysis would include disease stability rate (DSR) defined as the percent of subjects in ITT population with CR, PR and SD at 16 weeks, and will be compared using Pearson's chi-square test or Fisher's exact test.

The primary Phase 2 endpoint of PFS will be determined based on objective tumor assessments made by Central Radiographic Review according to RECIST version 1.1. PFS will also be determined based on investigator assessment. Treatment decisions will be made by the investigator based on application of RECIST 1.1. Supportive analyses will be performed based on investigator assessments of disease response and progression. In cases where Central Radiographic Review assessment of response conflict with investigator assessment the data will be censored as it related to the endpoint.

The clinical response of the study treatment will be assessed by a comparative evaluation of computed tomography (CT) or magnetic resonance imaging (MRI) scans prior to enrollment into the study and every 8 weeks using RECIST 1.1 (primary endpoint) or Choi criteria (secondary endpoint).

A listing will be provided for best overall response, i.e., CR, PR, SD, PD or NA (not assessable due to missing or incomplete assessments or inconsistent assessment methods) for each patient. A listing or figure will also be provided for duration of PFS and sum of the diameters for target lesions over time in patients. The listings for best overall response and PFS will compare to overall response and PFS of treatments received prior to study entry, including the most recent treatment that included a VEGF inhibitor.

12. Safety Analyses

Safety will be assessed by examining vital signs, physical exams, clinical laboratory tests, and adverse events (AEs). These analyses will be conducted on the safety population. Descriptive statistics will be provided for safety variables.

Baseline will be defined as the last available measurement prior to First Dose. Where this definition does not apply, the definition for that analysis will be specified.

12.1. Extent of Exposure

The extent of exposure will be summarized by the number of doses received, the number of cycles completed, and dose received in milligram/kilogram. A cycle is considered completed if the patient received all treatment infusions required during a given cycle.

12.2. Adverse Events

All AEs with an onset after initiation of treatment will be considered as treatment-emergent AEs. A preexisting condition that worsens during the treatment period will also be considered as a treatment emergent AE. All AEs will be coded by system organ class (SOC) and preferred term using NCI CTCAE (MedDRA) version 4.0.

The number and percentage of patients with the following types of treatment-emergent AEs will be summarized for each study arm: common and serious AEs, AEs related to study medication, AEs resulting in study discontinuation, and clinically significant laboratory abnormalities. Laboratory data will be summarized for baseline, treatment visits and change from baseline as appropriate for each arm. Non-treatment-emergent serious AEs will be described separately. Deaths will be reported with demographic information. Comparison of categorical values will be made by Chi-square or Fisher exact test and of continuous variables will be made by Student t test.

For the phase 1b portion treatment-emergent AEs will be summarized by dose level. For the phase 2 portion treatment emergent AEs will be summarized by treatment group. Treatment-emergent is defined as all events starting during or after the first dose of study drug (or axitinib) until 28 days following the last dose of study drug or axitinib, whichever is later. The number and percentage of patients with AEs will be displayed by SOC and PT. Summaries will be provided of AEs by grade and of AEs by relationship to study medication. Serious AEs, AEs leading to study discontinuation, AEs resulting in dose delay, and AEs with an outcome of death will be summarized and listed.

For the phase 1b portion, a summary table and listing will also be provided for DLTs.

12.3. Laboratory Evaluations

Quantitative laboratory test results and changes from baseline will be summarized at each visit for hematology, coagulation, serum chemistry panel, and urinalysis.

The Investigator will determine whether abnormal lab values are clinically significant. Such results are to be reported as adverse events and CTCAE grading will be assigned (except for urinalysis) where applicable.

Laboratory results that are abnormal and clinically significant will be flagged by the investigator. Abnormal and clinically significant results will be presented in listings with Investigator comments.

The number and percentage of patients who exhibit clinically significant abnormal laboratory results will be produced at each visit.

12.4. Physical Examination

The physical examination results will be displayed at each cycle. Listing of results of examinations will be provided by anatomical sites, assessment dates, and description of physical abnormalities. The number and percent of patients with abnormalities will be displayed by body system.

12.5. Vital Signs

Vital signs will be summarized at each visit for systolic blood pressure, diastolic blood pressure, pulse, respiratory rate, temperature, and weight. Actual values and change from baseline will be summarized. Listing of vital sign values will be provided.

12.6. Electrocardiogram

ECG results including ECG time, heart rate (bpm), PR interval (ms), QRS interval (ms), and QT interval (ms) (normal; abnormal, not clinically significant; abnormal, clinically significant) and comments for clinically significant abnormalities will be reported for each patient and compared to baseline. In addition, RR interval will be reported for each patient and compared to baseline and will be calculated using the following formula: 60 seconds/Heart Rate. QTc interval will also be calculated and reported for each patient and compared to baseline using Bazett's Formula as follows:

$$QT_C = \frac{QT}{\sqrt{RR}}$$

12.7. ECOG Performance Status

The Eastern Cooperative Oncology Group (ECOG) performance grade scale will be used to measure patient ECOG performance status. The number and percent of patients in each grade category will be summarized at each visit for each dose level with individual patient data displayed in a listing.

13. Pharmacokinetic Analysis

Serum samples will be assayed to measure the concentration of TRC105 and axitinib. Only concentrations greater than or equal to the limit of qualification (LOQ) from the assay will be used. The following parameters will be determined:

- C_{max} (ng/mL) [Maximal TRC105 concentration]
- C_{min} (ng/mL) [Minimal TRC105 concentration]

Descriptive statistics of C_{max}, C_{min} , following drug administrations will be calculated by dose level and time of treatment (baseline versus patient withdrawal). Gender specific analysis will be performed if adequate data are available for each gender within a given dose cohort, e.g. the

expanded cohort at MTD. Summary PK analyses will include all patients and also include only those patients who develop positive titers for APA.

Listings of individual patient serum concentrations, actual blood sampling times, and pharmacokinetic parameters will be provided.

14. Additional Analysis

A listing of serum sample collections for anti-product antibody (APA) testing and the APA assay results will be provided. Also, the number and proportion of APA responses and changes in responses over time will be summarized. APA responses (Immunogenicity) will be measured utilizing a 3-tiered validated screening approach (screening, confirmatory, and titer) using a highly sensitive electrochemiluminescent bridging assay format.

Plasma levels of soluble angiogenic biomarkers will be listed by patient. Biomarker levels will be log-transformed before analysis, and analyses will be performed using baseline data from all available patients with continuous values for the protein analytes. PFS determined using univariate Cox proportional hazards models independent of treatment arm, and the resulting hazard ratios (HR), 95% confidence intervals (CI), and asymptotic P-values based on the score test will be reported. Multivariate Cox regression models will then test for interaction between marker level and treatment arm to identify markers predictive of benefit from axitinib or TRC105 and asymptotic P-values based on the Wald test for the interaction term will be reported. Biomarker levels will also be tested for interaction with each treatment arm separately. P-values will not be adjusted for multiple testing, and the results will be considered exploratory and hypothesis-generating. However, because high baseline levels of transforming growth factor-beta (TGF-β) receptor 3 and low baseline levels of osteopontin correlated with PFS and response rate in the Phase 1b study of TRC105 and axitinib, each of these biomarkers will be formally tested for correlation with PFS at the two-sided alpha level 0.05.

Hierachical agglomerative clustering, using Euclidean distance and complete linkage, will be used to identify groupings among protein markers based on their baseline levels. The results will be illustrated using dendrograms. Forest plots will be created as illustrations of prognostic effect sizes (HRs and corresponding 95% CIs) with markers dichotomized as "high" or "low" relative to the median. Kaplan–Meier plots of PFS will also be created, with separate curves for each combination of treatment group by biomarker level. It has previously been shown in the Phase 1b study of axitinib and TRC105 that high baseline levels of TGF-β receptor 3 and low baseline levels of osteopontin correlated with PFS and response rate in the Phase 1b study of TRC105 and axitinib, so we will consider these biomarker levels dichotomized at the first quartile.

15. Changes from the Protocol-Specified Analysis

The details of analysis as indicated in this plan are based on the specifications of the 22Feb2016 version of the study protocol. Any later changes to the protocol may require consequential revision of this plan.

16. Programming Considerations

The format of listing and table shells should be followed as closely as possible during SAS or R programming, however, changes in format may be made due to space considerations and abbreviation of labels etc. The number of decimal places for presentation of the data should be based on the actual data, not the format presented in the shells (i.e., xx.xx is only a place holder.)

17. Appendices

Appendix 1: Planned 105RC101 Tables
Appendix 2: Planned 105RC101 Listings
Separate tables and listings will be generated for the phase 1b and phase 2 portion of the study.

18. References

1. Therasse P, Arbuck SG, Eisenhauer EA, et al. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. J Natl Cancer Inst 2000; 92:205-16.
2. NCI Common Terminology Criteria for Adverse Events (CTCAE), Version 4.0. http://www.acrin.org/Portals/0/Administration/Regulatory/CTCAE_4.02_2009-09-15_QuickReference_5x7.pdf
3. MedDRA: Medical Dictionary for Regulatory Activities terminology. Version 14.1. Reston, VA: Northrop Grumman, MedDRA MSSO.

19. Appendix 1 Tables

19.1. Tables in Text Phase 1b:

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- Incidence of Protocol Deviations by Treatment Group
- Demographics and Baseline Characteristics
- Screening ECOG Performance Status
- Past Cancer Treatment
- Primary Cancer Diagnoses by Dose Group
- Disease Present at Screening
- Best Overall Response and Duration of Response
- Summary of Serum TRC105 Pharmacokinetic Parameters Following Multiple Intravenous Infusions of TRC105
- Most Common (n > 1) and all Grade 3 and 4 Adverse Events by System Organ Class, by Preferred Term and by Grade and Dose Level
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19.3. Tables in Text Phase 2 (by treatment group) :

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Enrollment by country by Treatment Group

- Disposition of Patients by Treatment Group
- Incidence of Protocol Deviations by Treatment Group
- Demographics and Baseline Characteristics
- Screening ECOG Performance Status
- Past Cancer Treatment
- Primary Cancer Diagnoses by Treatment Group
- Disease Present at Screening
- Best Overall Response and Duration of Response
- Summary of Serum TRC105 Pharmacokinetic Parameters Following Multiple Intravenous Infusions of TRC105
- Most Common (n > 1) and all Grade 3 and 4 Adverse Events by System Organ Class, by Preferred Term and by Grade
- Most Common (N >1) and all Drug-Related Grade 3 and 4 Adverse Events by System Organ Class, by Preferred Term and by Graded Full Analysis Population
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