# STATISTICAL ANALYSIS PLAN ADDENDUM

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| **Protocol Title:** | MOUNTAINEER: A Phase 2, Open Label Study of Tucatinib Combined with Trastuzumab in Patients with HER2+ Metastatic Colorectal Cancer |
| **Protocol Number:** | ACCRU-GI-1617, SGNTUC-017 |
| **Sponsor:** | Seagen Inc.<br>21823 30th Drive SE<br>Bothell, WA 98021, USA |
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## SPONSOR APPROVAL PAGE

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The individuals signing below have reviewed and approve of this statistical analysis plan addendum.

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## LIST OF ABBREVIATIONS

| | |
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| AE | Adverse Event(s) |
| ATC | Anatomical Therapeutic Chemical |
| BICR | Blinded Independent Central Review |
| CSR | Clinical Study Report |
| DoR | Duration of Response |
| EOS | End of Study |
| ITT | Intent-to-treat |
| MedDRA | Medical Dictionary for Regulatory Activities |
| OS | Overall Survival |
| PFS | Progression Free Survival |
| PT | Preferred Term |
| RECIST | Response Evaluation Criteria in Solid Tumors |
| SAE | Serious Adverse Event |
| SAP | Statistical Analysis Plan |
| SMQ | standard MedDRA query |
| sSAP | Supplemental Statistical Analysis Plan |
| SSQ | Sponsor Specific Query |
| TEAE | Treatment Emergent Adverse Event |
| WHO | World Health Organization |

# 1 INTRODUCTION

The primary analysis for this trial was conducted based on a data cut-off date of 28 March 2022. As the primary objective was met, the decision was made to close the trial. For subjects remaining on study, a last visit contact will occur and subjects who are still receiving treatment will revert to physician care. When applicable, the Sponsor will assist with post-trial access to tucatinib and trastuzumab. The protocol version Amendment 12.0 provided "End of Study" rationale and procedure, and this SAP addendum is to provide guidelines for "End of Study" analyses.

All planned analyses specified in this document will be performed. Any changes will either be reflected in amendments to this plan or specifically documented in the final clinical study report. Any changes to this plan, in the form of "post hoc" or "data driven" analyses will be identified as such in the final clinical study report.

# 2 STUDY ENDPOINTS

The following endpoints will be analyzed for the final study report.

Efficacy

- Duration of Response (DOR) per BICR, in Cohorts A+B, and Cohort C post-crossover.
- DOR per Investigator, in Cohorts A+B, and Cohort C post-crossover.
- PFS per BICR, in Cohorts A+B.
- PFS per Investigator, in Cohorts A+B.
- OS, in Cohorts A+B, and Cohort C.

Safety

- Frequency and severity, according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 criteria or higher, of all treatment-emergent adverse events (TEAEs) and treatment-related TEAEs, in Cohorts A+B, and Cohort C post-crossover
- Frequency of serious adverse events (SAEs) and deaths due to adverse events (AEs), in Cohorts A+B, and Cohort C post-crossover
- Frequency of treatment modifications and permanent treatment discontinuations due to AEs, in Cohorts A+B, and Cohort C post-crossover
- Frequency and severity of laboratory abnormalities, in Cohorts A+B, and Cohort C post-crossover
- Vital signs and other relevant safety variables, in Cohorts A+B, and Cohort C post-crossover

# 3 GENERAL STATISTICAL CONSIDERATIONS

The general statistical considerations (for instance, analysis sets, definition of endpoint and subgroup, censoring rules, handling of missing data, data conventions and definitions) should follow the study SAP and sSAP unless otherwise specified in this document.

## 3.1 Analysis Sets

The analysis sets follow the study SAP unless otherwise specified in this document.

## 3.2 Timing of Analyses

The "End of Study" analyses will be conducted after the final database lock of this study.

# 4 STATISTICAL METHODOLOGY

## 4.1 Trial Details

### 4.1.1 Subject Disposition

Patient enrollment and disposition will be summarized by cohort and total. The table will present the number and percentage of patients who were enrolled or randomized in each cohort, received study drug, and participated in long-term follow-up. The number and percentage of patients who discontinued treatment will be summarized by the reason for treatment discontinuation. The number and percentage of patients who discontinued the study will be summarized by the primary reason for study discontinuation. The summary of disposition will be conducted for ITT analysis set.

### 4.1.2 Protocol Deviations

Important protocol deviations are a subset of protocol deviations that may represent a divergence from the protocol that could have a significant effect on the integrity of the study data, or on the subject's rights, safety, or welfare. Important protocol deviations also include exemptions to the study inclusion/exclusion criteria and will be summarized by category. A list of subjects with important protocol deviations will be presented.

### 4.1.3 Concomitant Therapy

Concomitant medications will be summarized by the WHO Drug ATC class and preferred name. The number and percentage of subjects who take concomitant medications will be tabulated. Multiple occurrences of the same medication within a subject will be summarized only once. Concomitant medications will be listed by subject. Concomitant medications will be coded using World Health Organization (WHO) Drug Dictionary (version: WHODrug Global 2023Mar B3 or higher).

### 4.1.4 Extent of Exposure

All the analyses for treatment exposure specified in the SAP will be conducted for Cohorts A+B and Cohort C post-crossover.

### 4.1.5 Subsequent Anti-Cancer Treatment

The number and percentage of subjects who receive subsequent anticancer therapies will be summarized for the FAS.

## 4.2 Analysis of Efficacy

PFS by investigator and by BICR will be summarized per study SAP for Cohorts A+B. DoR by investigator and by BICR will be summarized per study SAP for Cohorts A+B and Cohort C post-crossover. OS will be summarized for Cohorts A+B and Cohort C per study SAP.

## 4.3 Analysis of Safety

The safety analyses at the end of study will be the same as for the primary CSR, except for the following changes:

1. Adverse events will be coded using Medical Dictionary for Regulatory Activities (MedDRA, Version 26.0 or higher).
2. The preferred term " Suspected drug-induced liver injury" will be added to the hepatotoxicity SSQ list used in the primary CSR. This preferred term was newly added in MedDRA 26.
3. Summary tables, figures and listings will not be updated for Cohort C pre-crossover because all patients in Cohort C either crossed over or had EOS by the primary database lock.

## 4.4 Changes in the Planned Analysis

There following analyses were not specified in the protocol for this trial.

Summary of duration of response (DoR) per BICR and per INV for Cohort C post-crossover.

Summary of additional risk categories hepatotoxicity (SMQ), hepatotoxicity (SMQ), Diarrhea (PT), serum creatinine by lab, blood urea nitrogen by lab, infusion related reactions/Infusion related hypersensitivity reactions

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