NCT04082364


# STATISTICAL ANALYSIS PLAN
# VERSION 3.0

## CLINICAL STUDY PROTOCOL: CP-MGAH22-06

## PROTOCOL AMENDMENT 5 (06 JUNE 2022)

# A PHASE 2/3 TRIAL TO EVALUATE MARGETUXIMAB IN COMBINATION WITH INCMGA00012 AND CHEMOTHERAPY OR MGD013 AND CHEMOTHERAPY IN PATIENTS WITH METASTATIC OR LOCALLY ADVANCED, TREATMENT-NAÏVE, HER2-POSITIVE GASTRIC OR GASTROESOPHAGEAL JUNCTION CANCER

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# LIST OF ABBREVIATIONS

| | |
|---|---|
| ADA | Anti-drug antibodies |
| ADaM | Analysis Data Model |
| AE | Adverse event |
| AESI | Adverse event of special interest |
| BOR | Best overall response |
| CDISC | Clinical Data Interchange Standards Consortium |
| CI | Confidence Interval |
| $C_{max}$ | Maximum concentration |
| CPI | Checkpoint inhibitor |
| CPS | Combined positive score |
| CR | Complete response |
| CRF | Case report form |
| CSR | Clinical Study Report |
| CT | Computed tomography |
| $C_{trough}$ | Trough concentration |
| DCR | Disease control rate |
| DoR | Duration of response |
| ECG | Electrocardiogram |
| ECOG | Eastern Cooperative Oncology Group |
| FISH | Fluorescent in situ hybridization |
| GC | Gastric cancer |
| GEJ | Gastroesophageal junction |
| HR | Hazard ratio |
| HER2 | Human epidermal growth factor receptor 2 |
| ICF | Informed consent form |
| IDMC | Independent data monitoring committee |
| IHC | Immunohistochemistry |
| IRT | Interactive response technology |

| | |
|---|---|
| ITT | Intent-to-treat |
| LVEF | Left ventricular ejection fraction |
| MedDRA | Medical dictionary for regulatory activities |
| MSI | Microsatellite instability |
| MSI-H | Microsatellite instability-High |
| MUGA | Multigated acquisition ventriculography scanning |
| mFOLFOX-6 | modified 5-fluorouracil, leucovorin and oxaliplatin |
| NE | Not evaluable |
| ORR | Objective response rate |
| OS | Overall survival |
| PD | Progressive disease |
| PD-L1 | Programmed death ligand 1 |
| PFS | Progression-free survival |
| PK | Pharmacokinetics |
| PR | Partial response |
| RECIST v1.1 | Response Evaluation Criteria in Solid Tumors version 1.1 |
| REP | Response Evaluable Population |
| SAE | Serious adverse event |
| SAP | Statistical analysis plan |
| SD | Stable disease |
| SOC | System organ class |
| TEAE | Treatment-emergent adverse event |
| TRAE | Treatment-related adverse event |
| XELOX | Capecitabine and oxaliplatin |

# 1 INTRODUCTION

This SAP provides a detailed and comprehensive description for the analysis of Study CP-MGAH22-06 entitled "A Phase 2/3 Trial to Evaluate Margetuximab in Combination with INCMGA00012 and Chemotherapy or MGD013 and Chemotherapy in Patients with Metastatic or Locally Advanced, Treatment-naïve, HER2-Positive Gastric or Gastroesophageal Junction Cancer". This SAP Version 3.0 applies to Protocol Amendment 5 of this study and describes in detail the statistical methods to be used for analysis of the primary and secondary efficacy endpoints, the safety endpoints, and the PK parameters to be collected from this study.

# 2 STUDY OBJECTIVES

## 2.1 Primary Objectives

**Cohort A:**

- To evaluate the safety and tolerability of margetuximab + INCMGA00012 in patients with untreated locally advanced or metastatic GC or gastroesophageal junction (GEJ) cancer that is HER2 IHC 3+ and PD-L1+ by IHC staining.
- To evaluate the ORR of margetuximab plus INCMGA00012 for non-MSI-H patients in the response evaluable population (REP) using investigator-assessed radiology review.

## 2.2 Secondary Objectives

**Cohort A:**

- To determine DoR, DCR, and PFS for non-MSI-H patients using investigator-assessed radiology review.
- To evaluate the number of patients with anti-drug antibodies (ADA) to margetuximab or INCMGA00012, or both.

**Cohort B Part 1:**

- To evaluate ORR and DCR of each treatment arm.
- To evaluate the number of patients with ADA to margetuximab, MGD013, or INCMGA00012.

# 3 STUDY DESIGN AND PLAN

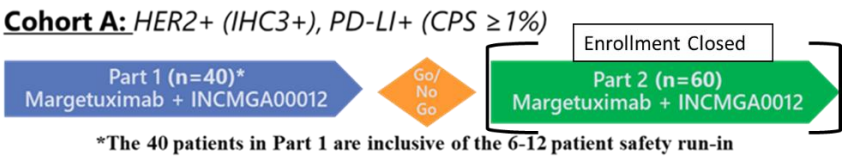
## 3.1 Overall Study Design and Plan

This is a Phase 2/3, randomized, open-label study for the treatment of patients with HER2+ GC or GEJ cancer. This study will determine the efficacy of margetuximab combined with a checkpoint inhibitor (CPI) INCMGA00012 in patients who are positive for both HER2 and PD-L1, excluding MSI-H (Cohort A), and a margetuximab plus CPI (INCMGA00012 or MGD013) plus chemotherapy compared to trastuzumab plus chemotherapy in patients who are HER2 positive, irrespective of PD-L1 status (Cohort B). Patients will be treated in 3-week (21-day) cycles. Cohort A and Cohort B will not be opened simultaneously at the same institution.

**Cohort A (Single Arm)**

Cohort A was closed prior to completing enrollment target. There were 48 patients enrolled in Cohort A.

The combination of INCMGA00012 plus margetuximab will be evaluated in up to 100 patients that are HER2 IHC3+, PD-L1+, and non-MSI-H. After approximately 40 patients have enrolled and are evaluable for response, data will be analyzed for ORR, as determined by central imaging review, and safety. Additional 60 patients will be enrolled in Part 2 of the cohort if the threshold for study continuation is met. Decision rules that govern the analysis of the ORR from Part 1 and continuation of Part 2 of Cohort A are outlined in **Section 6.10**.



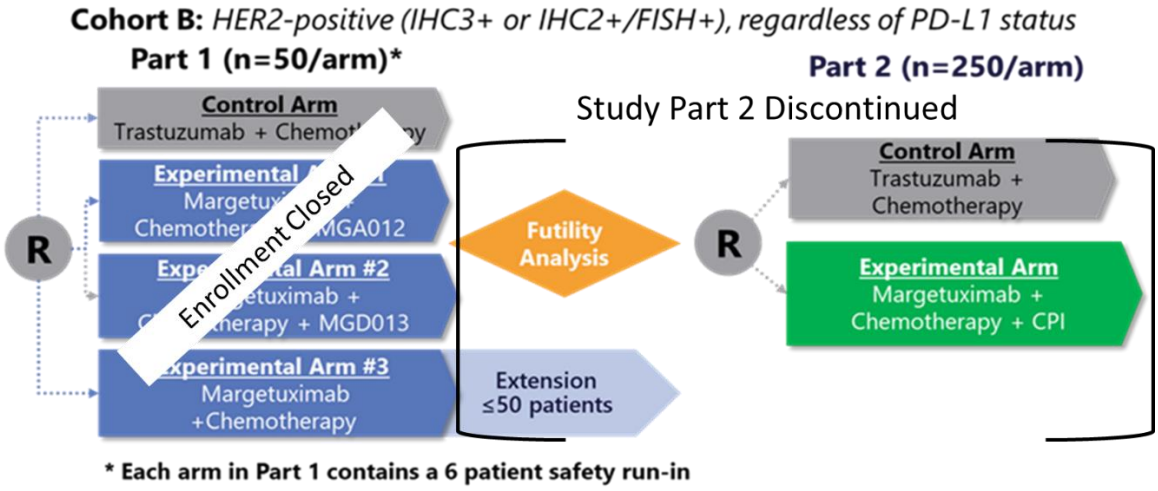

**CPS = combined positive score; IHC = immunohistochemistry; ORR = objective response rate**

**Cohort B (Randomized, Open-label)**

Cohort B was closed prior to completing enrollment target. There were 34 patients randomized of which 33 were treated in Cohort B, Part 1. No patients were enrolled in Cohort B, Part 2.

Cohort B Part 1 consists of 4 arms: 1 control arm of trastuzumab plus chemotherapy and 3 experimental arms of margetuximab-containing regimens. Experimental Arms 1 and 2 will combine margetuximab plus a CPI plus chemotherapy. The CPI for Experimental Arm 1 is INCMGA00012, and the CPI for Experimental Arm 2 is MGD013. Experimental Arm 3 will evaluate margetuximab alone in combination with chemotherapy. Chemotherapy will be modified 5-fluorouracil, leucovorin and oxaliplatin (mFOLFOX-6) or capecitabine and oxaliplatin (XELOX), according to the investigator's choice based on local approval and availability. The schema is displayed below.

First, approximately 200 patients will be randomized in a 1:1:1:1 ratio of 4 arms. The randomization will be stratified by two stratification factors: chemotherapy regimen (XELOX vs mFOLFOX-6) and results of local HER2 testing (IHC2+/FISH+ vs IHC3+). An interactive response technology (IRT) system will be used to register and randomize patients.




In addition to regular Sponsor medical oversight, an independent data monitoring committee (IDMC) will oversee the ongoing monitoring and interpretation of the safety and efficacy data from this study. When approximately 40 patients (Cohort A) have at least one CT scan to evaluate response, the IDMC will be asked to make a recommendation regarding continuation of full enrollment for the cohort or suspending enrollment pending Sponsor final decision. The committee will be provided with safety and efficacy tables and data listings for these reviews. Additional details on the IDMC monitoring, and administration can be found in the IDMC Charter, which will be created, reviewed, and approved by the committee prior to study initiation.

## 3.2 Sample Size

Planned sample sizes are described below. Study enrollment was closed prior to completion. Forty-eight patients were treated in Cohort A. Thirty-four patients were randomized, of which 33 patients were treated, in Cohort B Part 1. Cohort B Part 2 never started.

**Cohort A**

The sample size of approximately 100 non-MSI-H is based on a Simon two-stage design to provide approximately 83% power to test ORR of at a 2-sided alpha level of 0.05. The first stage (Part 1) will enroll and treat non-MSI-H 40 response evaluable patients. If at least 21 (53%) responders [CR or partial response (PR)] are observed, the study will move to the second stage (Part 2) with enrollment of approximately 60 additional response evaluable non-MSI-H patients. Other efficacy data such as DoR and PFS will be considered as well in enrollment decision-making. If the study continues to enroll an additional 60 patients, the null hypothesis $H_0$: ORR = would be rejected at 1-sided alpha level of 0.025 (or equivalently, 2-sided 0.05) if the observed ORR from all 100 response evaluable

non-MSI-H patients is ≥ . The totality of the data will be assessed to determine not only statistical significance but a clinically meaningful effect. The total number of patients to be enrolled in Cohort A is expected to be approximately 110 in order to obtain approximately 100 non-MSI-H patients.

**Cohort B**

The sample size for Cohort B is determined based on a Phase 2/3 design. The sample size will consist of patients that are HER2+ by central confirmation. Entry criteria for HER2 may be based on a local test, however, enrollment will continue until the sample size is accrued based on central confirmation. The total planned sample size for Cohort B is approximately 750, consisting of two parts:

- In the Cohort B Part 1, a total of approximately 250 patients with centrally confirmed HER2+ will be enrolled as follows. First, approximately 200 patients will be randomized in a 1:1:1:1 ratio to 1 of 4 arms (one control arm and three margetuximab-containing arms). The randomization will be stratified by two stratification factors: chemotherapy regimen (XELOX vs mFOLFOX-6) and results of local HER2 testing (IHC2+/FISH+ vs IHC3+). Selection of which of 2 margetuximab and CPI-containing arms to move to the Phase 3 part of the study (Cohort B Part 2) for further testing will be primarily based on ORR but will also take into consideration PFS and safety. After this randomization portion of enrollment is complete, enrollment of up to approximately 50 additional non-randomized patients will continue into the margetuximab + chemotherapy arm only.
- In Cohort B Part 2, approximately 500 patients with centrally-confirmed HER2+ will be randomized in a 1:1 ratio between the control arm and the selected margetuximab and CPI-containing arm. The randomization will be stratified by the same two stratification factors in Cohort B Part 1.

By applying the closed testing procedure (**1**) and the inverse normal p-value combining method (**2**) to test primary endpoint OS at the end of Cohort B Part 2, the sample size of approximately 650 patients planned enrollment [Cohort B Part 1: control arm (50 patients), 2 margetuximab and CPI-containing arms (100 patients) and 500 patients from Cohort B Part 2] will provide approximately 80% power to detect OS HR = (median OS increase from months for control arm to months for either margetuximab and CPI-containing arm) at 2-sided alpha level of 0.05.

# 4 ANALYSIS POPULATIONS

The study analyses will be performed on the following populations:

- **Safety Population:** All patients who receive at least one dose of study drug. The safety population will be used to summarize safety data for Cohort A and Cohort B of the study, respectively. Patients enrolled in Cohort B will be analyzed according to the actual treatment received rather than the treatment group they were assigned. This population will also be used to summarize baseline data for Cohort A.
- **PK Evaluable Population**: All patients who received at least one dose of study drug, date and time of dose administration and relative PK sample collection are known and have sufficient concentration data to derive at least one PK parameter.
- **ADA Evaluable Population**: All patients who received at least one dose of study treatment, date and time of dose administration and relative ADA sample collection are known and have a reportable ADA result.
- **ITT Population:** All patients who are assigned to treatment in Cohort A and all patients who are randomized into Cohort B of the study. Patients will be analyzed according to the treatment assigned. This population will be used to summarize baseline data for Cohort B and evaluate PFS for Cohort A.
- **Response Evaluable Population (REP):** All patients who received at least one dose of study treatment and had baseline radiographic tumor assessment. This population will be used for objective response related efficacy analyses for Cohort A and Cohort B, respectively, and will be analyzed according to the actual treatment received.

# 5 ENDPOINTS

## 5.1 Efficacy Endpoints

Efficacy evaluations will be based on tumor response and time to event measures.

### 5.1.1 Primary Efficacy Endpoints for Cohort A

The primary efficacy endpoint for Cohort A is ORR per RECIST v1.1, defined as the proportion of non-MSI-H patients in REP who achieve the BOR of CR or PR (called responders) per RECIST v1.1. ORR will be calculated based on investigator-assessed response data. Available data on centrally reviewed response data will also be summarized.

For RECIST v1.1, the BOR will be categorized as CR, PR, stable disease (SD), PD, or NE. To be qualified as an objective response, CR and PR require confirmation at least 4 weeks after initial observation of such response, and SD requires an observation at least once after 6 weeks. BOR will be evaluated from the start of study treatment.

### 5.1.2 Secondary Efficacy Endpoints for Cohort A

The secondary efficacy endpoints for non-MSI-H patients in Cohort A are:

- PFS, defined as the time from start of study treatment to the first documented disease progression per RECIST v1.1 or death due to any cause, whichever occurs first. For patients who are not known to be dead or progressed at time of data cutoff for PFS analysis, the PFS will be censored at the last tumor assessment. Specifically, the following censoring rules will be applied as the analysis of PFS (**Table 1**).

**Table 1 Censoring Rules for PFS Analysis**

| Situation | Date | Outcome |
|---|---|---|
| No baseline tumor assessments | First dose date | Censored |
| Death prior to first scheduled tumor assessment | Date of death | Progressed |
| No post-baseline tumor assessments in absence of death prior to first scheduled tumor assessment | First dose date | Censored |
| Documented progression | Date of progression | Progressed |
| Initiation of alternative anti-cancer treatments in absence of documented progression | Date of last tumor assessment prior to initiation of such treatment | Censored |
| Death or documented progression immediately after missing two or more consecutive scheduled tumor assessments | Date of last tumor assessment prior to missed assessments | Censored |

- DoR, defined as the time from the date of initial response (CR or PR) to the date of first documented progression or death from any cause, whichever occurs first. The DoR is calculated only for the responders. For responders who are not known to be dead or progressed at the time of data cut-off for DoR analysis, the DoR will be censored at the date of the last tumor assessment. Specifically, the last 3 situations described in **Table 1** will be applied.
- DCR, defined as the percentage of response evaluable patients who experienced response of CR, PR, or SD for at least 3 months from start of treatment.

### 5.1.3 Efficacy Endpoints for Cohort B Part 1

The efficacy endpoints include ORR and DCR defined in the same way as for Cohort A, based on investigator assessments.

## 5.2 Tumor Size Change Over Time

The tumor size is defined as the sum of diameters of the target lesions.

## 5.3 Safety Endpoints

### 5.3.1 Adverse Events

Safety will primarily be addressed by evaluations of the adverse events (AEs). An AE is defined as any untoward medical occurrence in a patient or clinical trial patient associated with use of a drug in humans, whether or not considered drug related. An AE can be

- any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.
- Any occurrence that is new in onset or aggravated in severity or frequency from baseline, or abnormal results of diagnostic procedures, including laboratory test abnormalities.

All AEs, whether serious or nonserious, will be captured starting with signing of the informed consent form until 30 days following the last dose of study drug or until the start of a subsequent systemic anticancer therapy, if earlier. Verbatim terms will be coded to lower-level terms in the Medical Dictionary for Regulatory Activities (MedDRA). AEs will be coded to MedDRA. An assessment of severity grade will be made using NCI-CTCAE v5.0.

Protocol-related AEs and SAEs will be collected from the time the patient has consented to study participation. AEs and SAEs reported between the time the patient signs the informed consent form and the administration of the first dose of study drug will be captured as concurrent medical history unless the events are attributed to protocol-specified procedures. Events attributed to protocol-specified procedures will be collected on the AE eCRFs and SAE Report Form, as appropriate.

Only treatment emergent adverse events (TEAEs) will be summarized as safety endpoints. A TEAE is defined as any event that is newly occurring on or after the administration of study drug or an event that existed before but increased in severity on or after study drug administration.

### 5.3.2 Laboratory Evaluations

Standard safety laboratory parameters collected via a local laboratory will be graded according to CTCAE v5.0 and will be summarized. A laboratory abnormality is reported as an AE if it is associated with an intervention including, but is not limited to, discontinuation of treatment, dose reduction/delay, or concomitant therapy. Also, any laboratory abnormality may be reported as an AE at the investigator's discretion, based on clinical significance.

### 5.3.3 Other Safety Endpoints

Physical examination will be performed (including weight and height) of all patients according to the schedules outlined in the latest version protocol.

Vital signs (include temperature, pulse, blood pressure, and respiratory rate) and ECOG performance status will be performed according to the schedules outlined in the latest version protocol.

Twelve-lead ECGs will be obtained according to the latest version of the protocol to evaluate the potential cardiac effect.

MUGA scans or echocardiograms will be obtained and analyzed locally in all patients according to the schedules outlined in the latest protocol.

## 5.4 Pharmacokinetic, Pharmacodynamic/Biomarker, and Immunological Parameter Endpoints

PK samples, ADA samples and pharmacodynamic biomarker specimens will be collected according to the schedules outlined in the latest version protocol.

# 6 STATISTICAL METHODOLOGY

## 6.1 General Considerations

The baseline value is defined as the most recent value collected prior to the start of study drugs.

Study Day 1 is defined as the first day of study drug administration. For Cohort B, a 3-day window is allowed between randomization and dosing. If randomization and dosing do occur on separate days, randomization day will be defined as: Study Day -2, -1, 0. For Cohort A, endpoints that are time related such as PFS will be determined from time of start study treatment.

Categorical data will be summarized by the number and percent of patients falling within each category. Continuous variables will be summarized by descriptive statistics, including mean, standard deviation, median, minimum, and maximum.

Unless otherwise noted, continuous variable summaries will be summarized with one more significant digit than the original values.

Time-to-event endpoints will be summarized by the number and percent of the event, median time and corresponding 95% confidence interval (CI), and event free rate and corresponding 95% CI at the specified time points of interest.

All data summaries and tabulations will be conducted using SAS® software Version 9.4 or higher.

## 6.2 Missing Data

Data that are reported as missing will be treated as missing in all data. Imputation rules for partially recorded dates, in case that the complete dates are required to carry out an analysis, will be provided in the Statistical Programming Plan (SPP). In descriptive summaries for safety, observations that are spurious (extreme relative to the majority of the data) will not be altered or removed from the summary.

## 6.3 Patient Disposition and Baseline Characteristics

### 6.3.1 Patient Disposition

For patient disposition, the number and percentage of patients who reach various study milestones are summarized. All screened patients are broken down by screen failures (with reasons if collected) and enrolled (Cohort A) or randomized (Cohort B). Then the category of enrolled/randomized is broken down by never treated (with reasons if collected) and treated. The category of treated will further be broken down by treatment ongoing and treatment discontinuation (with reasons for discontinuation, which also include protocol-defined treatment completion, if any). The end of study status for all enrolled/randomized patients will also be included.

### 6.3.2 Patient Demographics and Baseline Characteristics

Patient demographics, baseline disease characteristics, disease history, medical history, prior cancer therapy, and other collected baseline data will be summarized using descriptive statistics.

## 6.4 Study Drug Exposures and Concomitant Medications

Study drug exposure and concomitant medications will be summarized by descriptive statistics.

The summary of study drug exposure will include descriptive statistics as well as frequency counts for the number of doses or cycles received, the total dose administrated as well as the total dose intended, and the dose intensity which is calculated as percentage of total dose administrated divided by total dose intended while patients on treatment exposure.

The summary of concomitant medications will include the number and percentage of patients who receive any concomitant medications as well as each concomitant medication by drug class.

## 6.5 Protocol Deviations

Major protocol deviations will be identified prior to database lock for final analysis and will be listed and summarized.

## 6.6 Efficacy Endpoint Analyses

### 6.6.1 Primary Efficacy Endpoints Analyses for Cohort A

The number and percentage of patients with BOR and ORR for non-MSI-H patients in the REP will be summarized. The 2-sided 95% exact binomial CI of ORR will be calculated. At the end of Part 1, that is, enroll and treat 40 non-MSI-H patients in REP, if at least 21 (53%) responders (CR or PR) are observed, the study will move to Part 2. For Part 1 interim

analysis, the primary analysis of ORR will be based on centrally reviewed response data. Sensitivity analysis of ORR will be performed using investigator assessed response data.

### 6.6.2 Secondary Efficacy Endpoints Analyses for Cohort A

The 2-sided 95% exact binomial CI of DCR for non-MSI-H patients in REP will be calculated. The Kaplan-Meier method will be applied to estimate PFS and DoR curves; their median times; PFS rates at 6, 9, and 12 months. The method of Brookmeyer and Crowley (**3**) will be used to construct 95% CIs for median times of time-to-event endpoints. The 95% CIs for PFS rates at each time point of interest will be calculated by normal approximation after log(-log) transformation. The analyses of PFS and DoR will be performed using investigator assessed response data. Available data from independent review will also be provided.

The DoR analyses will be performed only if there are enough responders to render the analyses meaningful in the REP. The PFS analysis will be performed in the ITT population.

Note that all primary and secondary efficacy endpoints in Cohort A will be analyzed only for non-MSI-H patients.

### 6.6.3 Efficacy Endpoints Analyses for Cohort B Part 1

The number and percentage of patients with BOR, ORR, and DCR will be summarized in the REP.

## 6.7 Tumor Size Change Over Time Analyses

The tumor size percent change and absolute change from baseline over time will be summarized in tables and percent change from baseline will also be presented by spider plot. For Cohort A, both the independent and investigator assessed tumor size change will be analyzed for non-MSI-H patients in REP. For Cohort B, the investigator assessed tumor size change will be analyzed by treatment arm.

The best tumor size percent change from baseline on or prior to first PD will be presented by waterfall plot.

## 6.8 Safety Endpoint Analyses

### 6.8.1 Adverse Events Analyses

All AEs will be presented in data listing format in safety population. Only TEAEs will be summarized. The following TEAEs will be provided in summary tables:

- All TEAEs
- TEAEs with CTCAE ≥ 3
- Treatment related AEs (TRAEs)

- TRAEs with CTCAE ≥3
- TEAE related to study drug
- Any SAEs
- Treatment-related SAEs
- SAEs related to study drug
- TEAEs that result in study treatment discontinuation
- TRAEs that result in study treatment discontinuation
- TEAEs which lead to interruption of each individual study drug
- TEAEs which lead to withdrawal of each individual study drug
- Fatal AEs
- AESIs

All of these tables will display the number and percent of patients that experience the given event and will display events by MedDRA. System Organ Class (SOC) and Preferred Term (PT). Events will be displayed alphabetically for SOC and in descending incidence order of PT. An overall summary of AEs will display the number and percent of patient/patients who experience at least one event of each of the above types.

### 6.8.2 Laboratory Values Analyses

Laboratory values will be based on central lab results unless they are done only locally. Summaries of laboratory values will display descriptive statistics for numerically quantified labs. Summaries will be grouped by laboratory panel (hematology, blood chemistry, and urinalysis if collected) and will be displayed by visit for each laboratory parameter. A listing of abnormal values will be provided, and a normal-abnormal shift table between baseline and worst post-baseline values will be summarized. Graphs of mean values over time may also be generated.

### 6.8.3 Other Safety Endpoints Analyses

Physical examination data will not be summarized explicitly. Abnormal physical examination findings discovered or becoming progressively abnormal after enrollment are to be noted as adverse events and will be summarized as such. Further, physical examination results from tumor evaluations will be reflected in the efficacy (tumor evaluation) data.

ECGs will be collected and analyzed for evidence of cardiac toxicity, especially prolongation of QT interval. The following categories for QTcF interval and maximum post dose change from baseline QTcF interval (ΔQTcF) may be used in summary and shift tables:

QTcF: ≤ 450 msec, >450 to 480 msec, >480 to 500 msec, and >500 msec

ΔQTcF: ≤ 30 msec, >30 to 60 msec, and >60 msec

Vital signs and ECOG performance status will be summarized with descriptive statistics at each visit and time point where they are collected.

All MUGA scans or echocardiography performed will be evaluated for the change in LVEF from baseline. A graph of LVEF change from baseline will be generated. In addition, time to >15% reduction in LVEF value may be summarized using the Kaplan-Meier approach.

## 6.9 Pharmacokinetic, Pharmacodynamic, and Immunological Parameter Endpoints

**PK Analysis:** Serum samples from patients with positive ADA results will be analyzed for concentrations of relevant study treatments. Concentration data will be summarized accordingly to evaluate the relationship between study drug exposure and ADA positivity.

**Pharmacodynamic Analysis:** Summary statistics for pharmacodynamic parameters, such as, but not limited to, those listed in latest version protocol (Section 10.2 Pharmacodynamic/ Biomarker Assessments) and corresponding changes from baseline, will be summarized and/or may also be presented graphically as will possible associations between changes in pharmacodynamic measures of interest and study drug and exposure may be explored.

**Immunogenicity Analysis:** The proportion of patients who are negative for study-drug specific ADA (i.e., margetuximab, INCMGA00012, or MGD013) at baseline and have a study drug-specific ADA-positive after administration of study treatment(s), the proportion of patients who are ADA-negative at baseline and remain negative, and the proportion of patients who have a positive ADA result at baseline that increases or decreases in titer over the course of treatment will be summarized.

## 6.10 Interim Analyses

**Cohort A**

There is a planned interim analysis after 40 non-MSI-H patients in the REP have been enrolled and their responses have been assessed by central review. As described in **Section 3.2**, if at least 21 (53%) responders (CR or PR) per independent review are observed, then enrollment will continue. The investigator assessed response, PFS based on both independent review and investigator assessment, and safety data will also be summarized to assist in decision making.

## 6.11 Final Analyses

The final analysis will occur after all patients have completed treatment and the 30-day follow-up.

## 6.12 Data Standards

Analysis datasets similar to Analysis Dataset Model (ADaM) datasets will be created from EDC data.

# 7 LIST OF TABLES, LISTINGS AND FIGURES

The list of tables, listings, and figures (TLFs) and associated shells planned for CSR based on the analyses described in this SAP will be provided in a separate statistical programming plan (SPP), which will also include data reporting conventions and programming specifications for the development of these TLFs.

# 8 REFERENCES

1. **Henning KS and Westfall PH**, Closed Testing in Pharmaceutical Research: Historical and Recent Developments. Stat Biopharm Res, 2015. 7(2): p. 126-147.

2. **Bauer P and Kohne K**, Evaluation of experiments with adaptive interim analyses. Biometrics, 1994. 50(4): p. 1029-41.

3. **Brookmeyer, R. and Crowley, J. (1982)**, A Confidence Interval for the Median Survival Time, Biometrics, 38, 29-41.