STATISTICAL ANALYSIS PLAN: CP-MGD007-02

26 July 2018

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STATISTICAL ANALYSIS PLAN

PROTOCOL CP-MGD007-02

A Phase 1b/2, Open Label, Dose Escalation Study of MGD007, a Humanized gpA33 × CD3 DART® Protein in Combination with MGA012, an Anti-PD-1 Antibody, in Patients with Relapsed or Refractory Metastatic Colorectal Carcinoma

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LIST OF ABBEVIATIONS

AE	Adverse event
ADA	Anti-drug antibodies
AESI	Adverse event of special interest
CI	Confidence interval
CR	Complete response
CTCAE	Common terminology criteria for adverse events
DART	Dual Affinity Retargeting
DLT	Dose limiting toxicity
DoR	Duration of response
ECG	Electrocardiogram
eCRF	Electronic case report form
gpA33	Glycoprotein A33
irCR	Immune-related complete response
irPD	Immune-related progressive disease
irPFS	Immune-related progression-free survival
irPR	Immune-related partial response
irRECIST	Immune-related Response Evaluation Criteria in Solid Tumors
irSD	Immune-related stable disease
IV	Intravenous(ly)
LID	Lead-in dose
MAD	Maximum administered dose
MedDRA	Medical Dictionary for Regulated Activities
MMR	Mismatch repair
MTD	Maximum tolerated dose

NCI	National Cancer Institute
ORR	Objective response rate
OS	Overall survival
PFS	Progression-free survival
PD	Progressive disease
PK	Pharmacokinetics
PT	Preferred term
PR	Partial response
QW	Once weekly
Q2W	Once every 2 weeks
RECIST	Response Evaluation Criteria in Solid Tumors
SAE	Serious adverse event
SAP	Statistical analysis plan
SOC	System organ class
TEAE	Treatment emergent adverse event

1 INTRODUCTION

This study is an open-label, Phase 1b/2, dose escalation and cohort expansion study designed to characterize the safety, tolerability, pharmacokinetics (PK), pharmacodynamics, immunogenicity, and preliminary antitumor activity of MGD007 and MGA012, administered in combination by intravenous (IV) infusion, in patients with histologically proven, relapsed/refractory metastatic colorectal carcinoma.

This statistical analysis plan (SAP) 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 Dose Escalation Phase

2.1.1 Primary Objectives

To characterize the safety, tolerability, dose-limiting toxicities (DLTs), and maximum tolerated dose (MTD) of MGD007 when combined with MGA012 in patients with relapsed/refractory metastatic colorectal carcinoma after at least 2 and up to 5 prior standard regimens of therapy in metastatic setting; or who did not tolerate fluoropyrimidines, oxaliplatin or irinotecan; or who are not good candidates for standard of care.

2.1.2 Secondary Objectives

- To characterize the pharmacokinetics (PK), pharmacodynamic activity, and immunogenicity of MGD007 and MGA012 in combination.
- To investigate the preliminary antitumor activity of MGD007 combined with MGA012 as measured by objective response rate, disease control rate, and progression-free survival (PFS) rate at 16 weeks in patients with relapsed/refractory metastatic colorectal carcinoma using both conventional Response Evaluation Criteria in Solid Tumors (RECIST 1.1) and immune-related response criteria (irRECIST).

2.1.3 Exploratory Objectives

- To explore the relationships between PK, pharmacodynamics of MGD007/MGA012, and antitumor activity.
- To explore the impact of this combination on PFS, immune-related PFS (irPFS), and overall survival (OS) in patients with relapsed/refractory metastatic colorectal carcinoma.
- To investigate the immunoregulatory activity of MGD007 combined with MGA012 in vivo, including various measures of T cell function in peripheral blood and/or tumor biopsy specimens.
- To assess potential biomarkers predictive of efficacy including but not limited to glycoprotein A33 (gpA33), CD3, TILs, PD-1, PD-L1, and immunosuppressive myeloid/lymphoid cells via immunohistochemistry and gene expression in archival tissue.

2.2 Cohort Expansion Phase

2.2.1 Primary Objective

To investigate antitumor activity of MGD007 combined with MGA012 when dosed at the MTD (or maximum administered dose [MAD] if no MTD is defined) as measured by objective response rate, disease control rate and PFS rate at 16 weeks in patients with relapsed/refractory metastatic colorectal carcinoma using both conventional Response Evaluation Criteria in Solid Tumors (RECIST 1.1) and immune-related response criteria (irRECIST).

2.2.2 Secondary Objectives

- To further characterize the safety and tolerability of MGD007 when combined with MGA012 in patients with relapsed/refractory metastatic colorectal carcinoma after at least 2 lines of therapy in a metastatic setting.
- To characterize the PK, pharmacodynamic activity, and immunogenicity of MGD007 and MGA012 in combination.
- To explore the impact of this combination on PFS, immune-related PFS (irPFS), and overall survival (OS) in patients with relapsed/refractory metastatic colorectal carcinoma.

2.2.3 Exploratory Objectives

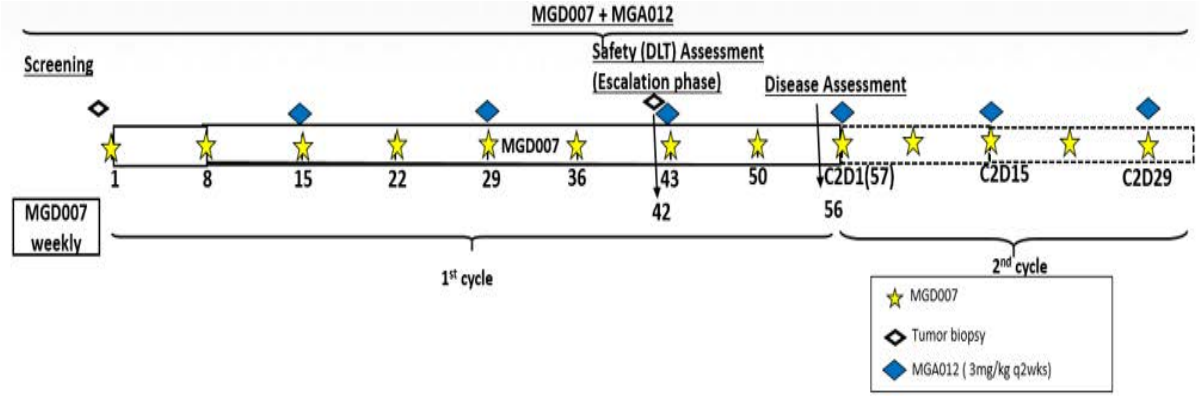
- To explore the relationships between PK and pharmacodynamics of MGD007/MGA012 and antitumor activity.
- To investigate the immunoregulatory activity of MGD007 combined with MGA012 in vivo, including various measures of T cell function in peripheral blood and/or tumor biopsy specimens.
- To assess potential biomarkers predictive of efficacy including but not limited to glycoprotein A33 (gpA33), CD3, TILs, PD-1, PD-L1, and immunosuppressive myeloid/lymphoid cells via immunohistochemistry and gene expression in archival tissue and assess the effect of the combination on tumor biomarkers, comparing initial and on treatment paired tumor biopsies.

3 STUDY DESIGN AND PLAN

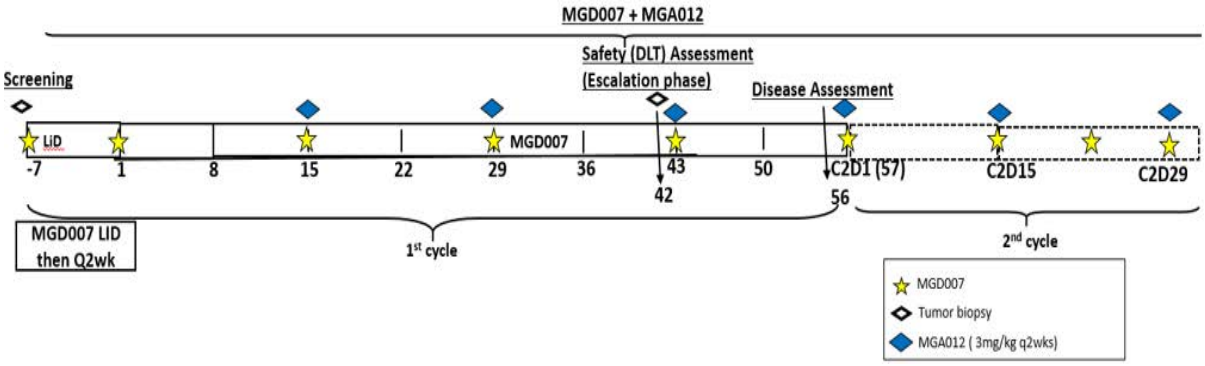
3.1 Overall Study Design and Plan

This study is an open-label, Phase 1b/2 dose escalation and cohort expansion study designed to characterize the safety, tolerability, PK, pharmacodynamics, immunogenicity, and preliminary antitumor activity of MGD007 and MGA012, administered in combination by IV infusion, in patients with histologically proven, relapsed/refractory metastatic colorectal carcinoma, irrespective of the KRAS and MMR status of their tumors. This study will enroll patients in 2 cohorts as described below.

QW Cohort: Overall Study Treatment Schema – MGD007 QW



Q2W Cohort: Overall Study Treatment Schema – MGD007 LID then Q2W



This study consists of two phases: a Dose Escalation Phase followed by a Cohort Expansion Phase. The Dose Escalation Phase will employ a 3+3+3 scheme to examine a series of increasing dose escalations in sequential cohorts of patients. Only the dose for MGD007 will be escalated; the dose for MGA012 will be kept constant at the dose of 3 mg/kg. For patients enrolled in QW cohort, 3 escalation doses of MGD007 (0.4, 0.6, and 0.8 µg/kg) are to be explored. For patients enrolled in Q2W cohort, 3 escalation doses of MGD007 (0.5, 0.8, and 1 µg/kg) are to be explored along with LID dose of 0.5 µg/kg. MGD007 will be given as 120-minute infusion and MGA012 IV will be given as 60-minute infusion. On days when both MGD007 and MGA012 will be administered, MGA012 will be administered first.

Intermediate dose levels may be explored selectively during the dose escalation portion of the study. Any escalation cohort, not exceeding the MTD, can be expanded to a maximum of 15 patients for further evaluation of safety and efficacy.

DLTs will be based on the occurrence of drug-related AEs that occur up to Cycle 1 Day 42 in both the QW and Q2W Cohort.

The Cohort Expansion Phase will include 25 patients in each of the 2 treatment cohorts to further define the safety and initial antitumor activity of the combination with the doses established in the Dose Escalation Phase; approximately 90% of these will be MSS patients and 10% MSI-H.

A full description of the study evaluations, including the number and timing of visits and the procedures to be performed at each visit can be found in Appendices 1 and 2 (Time and Events Schedule) of the protocol.

3.2 Sample Size

The study plans to treat approximately 104 patients: up to 27 in each of two treatment cohorts in Dose Escalation Phase and approximately 25 in the Cohort Expansion Phase in each of the two treatment cohorts.

The sample size of up to 27 patients for each cohort in the Dose Escalation Phase is based on 3+3+3 design with planned 3 dose cohorts. Additional patients may be enrolled to replace non-evaluable patients or if the enrollment to a dose cohort is expanded (up to 15 patients) or intermediate dose levels are evaluated in Dose Escalation Phase.

The Cohort Expansion Phase plans to treat approximately 25 patients in relapsed/refractory metastatic colorectal carcinoma in each cohort, approximately 90% of them are MSS patients, e.g., 22 MSS and 3 MSI-H patients. At the end of the Cohort Expansion Phase, 15 paired tumor biopsies will be required in each cohort, if tumor lesions are accessible with acceptable clinical risk. If 15 paired biopsies have not been collected in the initial 25 patients, additional patients with paired tumor biopsies will be enrolled, to ensure that the 15 paired biopsies are obtained.

The sample size in the Cohort Expansion Phase is primarily based on providing preliminary estimation of objective response rate and disease control rate. **Table 1** provides the 2-sided 95% confidence interval (CI) for a number of potential responses among 25 patients in each cohort.

Table 1 Response Rates and 95% Confidence Intervals

Sample Size	Number of Responses	Response Rate (%)	95% Confidence Interval (%)
25	2	8	1.0, 26.0
25	3	12	2.5, 31.2
25	4	16	4.5, 36.1
25	5	20	6.8, 40.7
25	6	24	9.4, 45.1
25	7	28	12.1, 49.4

During the Cohort Expansion Phase, patients who withdraw before completing the first tumor assessment for a reason other than clinically confirmed progressive disease or death is considered unevaluable for response. In these cases, replacement patients may be enrolled in the same dose level.

4 ANALYSIS POPULATIONS

4.1 Analysis Populations

The study analyses will be performed on the following populations:

- Safety Population: All patients who received at least one dose of any study drug. This population will be used for analyses of safety, PD, and immunogenicity. It will also be used for summary of baseline data and analyses of PFS and OS.
- Response Evaluable Population: All patients who received at least one dose of any study drug, had baseline measurable disease, and had at least one post-baseline radiographic tumor assessment or discontinued treatment due to clearly documented, clinically progressive disease or death. This population will be used for summary of tumor assessment data and analyses of response rates.

5 ENDPOINTS

5.1 Efficacy Endpoints

5.1.1 Response Endpoints

- Response by RECIST v1.1: The best overall response (BOR) will be categorized as CR, PR, SD, PD, or NE. To be qualified as BOR, CR and PR require confirmation at least 4 weeks after initial observation of such response, and SD requires to be observed at least once after 8 weeks (minus 3 days) from the start of MGD007 treatment.
- Immune related Response by irRECIST: The best overall response (BOR) will be categorized as irCR, irPR, irSD, irPD, or irNE. To be qualified as BOR, irCR, irPR, and irPD require confirmation at least 4 weeks after initial observation of such response, and irSD requires to be observed at least once after 8 weeks (minus 3 days) from the start of MGD007 treatment.

5.1.2 Time to Event Endpoints

- Progression-free survival (PFS): The PFS is defined as the time from the first dose date of MGD007 to the date of first documented progression or death from any cause, whichever occurs first. For patients who are not known to be dead or progressed at the time of data cut-off for PFS analysis, the PFS will be censored at the date of the last tumor assessment. The documented progression is determined by radiographic assessment using RECIST v1.1. PFS will be calculated as:

  PFS (months) = (date of event [documented progression or death] or date of censoring – first dose date +1) / (365.25/12)

- Immune related PFS (irPFS): The irPFS is defined as the time from the first dose date of MGD007 to the date of first documented immune related progression (irPD) or death from any cause, whichever occurs first. For patients who are not known to be dead or progressed at the time of data cut-off for irPFS analysis, the irPFS will be censored at the date of the last tumor assessment. The documented irPD is determined by radiographic assessment using irRECIST. The irPFS will be calculated as:

  irPFS (months) = (date of event [documented immune related progression or death] or date of censoring – first dose date +1) / (365.25/12)

- Duration of response (DoR): The DoR is 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. The documented progression is determined by radiographic assessment using RECIST v1.1. DoR will be calculated as:

  DoR (months) = (date of event [documented progression or death] or date of censoring – date of initial response+1) / (365.25/12)

  DoR may also be determined by irRECIST.

- Overall survival (OS): The OS is defined as the time from the first dose date of MGD007 to the date of death from any cause. For patients who are not known to be dead at the time of data cut-off for OS analysis, the OS will be censored at the time they are last known to be alive. OS will be calculated as:

  OS (months) = (date of death or last known alive – first dose date +1) / (365.25/12)

5.2 Safety Endpoints

5.2.1 Adverse Events

Adverse event (AE) means any untoward medical occurrence in a patient or clinical trial patient associated with the use of a drug in humans, whether or not considered drug related. An adverse event can therefore 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.

AEs will be captured starting from date of first study drug through end of treatment visit or 30 days following last dose of study drug (whichever is later). Only treatment-related serious AEs will be captured afterwards. These events will be recorded by the Investigators in the eCRFs. Verbatim terms will be coded to lower-level terms using the most recent version of the Medical Dictionary for Regulatory Activities (MedDRA). An assessment of severity grade will be made using National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 4.03.

AEs 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 medical history unless the AE is attributable to protocol-specified procedures that are not part of standard of care that occur during this time period, in which case the AE will be collected as AEs on the Adverse Event CRFs. Only treatment emergent adverse events (TEAEs) will be summarized in tables. 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.

5.2.2 Laboratory Evaluations

Standard safety laboratory parameters collected via a local laboratory will be summarized and graded according to CTCAE Version 4.03. A laboratory abnormality should be reported as an AE if it is associated with an intervention. An intervention includes, but is not limited to, discontinuation of treatment, dose reduction/delay, or concomitant therapy. In addition, any medical important laboratory abnormality may be reported as an AE at the discretion of the investigator.

5.2.3 Vital Signs and ECOG Performance Status

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

5.2.4 Electrocardiograms

All ECGs should be obtained in triplicate (3 ECGs per time point at approximately 1-minute intervals) according to the schedules outlined in the latest version of the protocol in order to evaluate the potential cardiac effects of study drug, including QT interval prolongation.

5.3 Pharmacokinetic, Pharmacodynamic, and Immunological Parameter Endpoints

PK samples, anti-drug antibody (ADA) samples and pharmacodynamic biomarker specimens will be collected according to the schedules outlined in the latest version of the protocol.

5.4 KRAS Mutation and MMR Status

Data regarding the KRAS and MMR mutational status (microsatellite instability [MSI-H] or microsatellite-stable [MSS]) will be collected for all patients; statuses for both must be formally documented for patients in the Cohort Expansion Phase.

6 STATISTICAL METHODOLOGY

6.1 General Considerations

This study is primarily observational and, thus, the majority of the statistical summaries will be descriptive. Safety and efficacy summaries will be provided for each dose level cohort during dose escalation and for all dose level cohorts combined, as well as for expansion cohorts where appropriate. Response rates will be calculated for the response evaluable population.

Unless otherwise specified, the following general considerations are applied in data analyses:

- The baseline value is defined as the latest value prior to the first dose of MGD007 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.
- 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 9.3 or higher.

6.2 Missing Data

Data that are reported as missing will be treated as missing in all data summaries. 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. Then the category of enrolled 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 patients will also be included. Duration of study, defined as time from the date of first dose of MGD007 to the date of withdraw of consent, lost to follow up, death, or the last contact date, will be summarized.

6.3.2 Patient Demographics and Baseline Characteristics

Patient demographics, baseline disease characteristics (e.g., KRAS mutation and MMR status), 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 actually administered as well as the total dose intended, and the dose intensity which is calculated as percentage of total dose actually administered divided by total dose intended during whole treatment period. Dose intensity by cycle may be summarized. Duration of study treatment exposure will also be summarized.

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

Critical 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 Analyses of Response Endpoints

Number and percent of patients with their best overall response will be summarized. The objective response rate (ORR) per RECIST v1.1 is estimated as the proportion of patients in response evaluable population who achieve BOR of CR or PR. Disease control rate is calculated as the proportion of patients who achieve a CR, PR, or SD. Progression-free survival rate at 16 weeks will be calculated by Kaplan-Meier method described in **Section 6.6.2.1**, based on response evaluable population and safety population, respectively. The 2-sided 95% exact binomial CI of the response rates will be calculated. The response rates per irRECIST will be estimated similarly. Subgroup analyses of these response rates by KRAS gene type (wild and mutant) and by MMR status (MSS and MSI-H) will be performed.

6.6.2 Analyses of Time to Event Endpoints

6.6.2.1 PFS and irPFS

The Kaplan-Meier method will be applied to estimate PFS curve, median PFS, and PFS rates at 4 (corresponding to 16 weeks), 6, and 12 months. The method of Brookmeyer and Crowley (1) will be used to construct 95% CI for median PFS. The 95% CIs for PFS rate at 4, 6, and 12 months will be calculated by normal approximation after log(-log) transformation.

For primary PFS analysis, the following table describes the censoring rules.

Table 2 Censoring Rules for Primary 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

PFS will be analyzed by MMR status and by KRAS gene type when sample size warrants. A sensitivity analyses for PFS may be performed to assess the robustness of above primary PFS analysis. For this sensitivity analysis, the censoring rules are the same as in **Table 2** except that the documented progression or death will be considered as an event, regardless of when it occurs during the study.

In addition, above analyses for PFS will also be repeated for irPFS.

6.6.2.2 Duration of Response

The Kaplan-Meier method will be applied to estimate DoR curve, median DoR, and DoR rates at 3 and 6 months. The last three situations described in **Table 2** will be applied for handling censorings. The method of Brookmeyer and Crowley (1) will be used to construct 95% CI for median DoR. The 95% CIs for DoR rate at 3 and 6 months will be calculated by

normal approximation after log(-log) transformation. These analyses will also be repeated for DoR based on irRECIST. The DoR analyses will be performed only if there are enough responders to render the analyses meaningful.

6.6.2.3 Overall Survival

The Kaplan-Meier method will be applied to estimate OS curve, median OS, and OS rates at 6, 12, and 24 months. The method of Brookmeyer and Crowley **(1)** will be used to construct 95% CI for median OS. The 95% CIs for OS rate at 6, 12, and 24 months will be calculated by normal approximation after log(-log) transformation. OS will be analyzed by MMR status and by KRAS gene type when sample size warrants.

6.6.3 Tumor Size Change Over Time

The tumor size is defined as the sum of diameters of the target lesions. The tumor size change from baseline over time will be summarized and presented by spider plot(s). The best percentage change from baseline will be presented by waterfall plot(s).

6.7 Safety Endpoint Analyses

6.7.1 Treatment Emergent Adverse Events

Only TEAEs will be summarized. All AEs will be presented in data listing format. The following TEAEs will be provided in summary tables as well as displayed in listings:

- All AEs
- AEs with CTCAE severity Grade ≥ 3
- Study drug related AEs
- Study drug related AEs with CTCAE severity Grade ≥ 3
- SAEs
- Study drug related SAEs
- AEs that result in discontinuation of study treatment
- AEs that led to interruption or withdrawal of individual study drug
- Fatal AEs
- Immediately reportable AEs (if applicable)
- AEs of special interest

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 order of overall PT

incidence within each SOC. An overall summary of AEs will display the number and percent of patients who experience at least one event of each of the above types.

6.7.2 Laboratory Values

Summaries of laboratory values will display descriptive statistics for numerically quantified labs. Summaries will be grouped by laboratory panel (hematology, blood chemistry, and urinalysis) and will be displayed by visit for each laboratory parameter. Number and percent of patients shifted from baseline to post-baseline maximum severity in CTCAE grade will be summarized. Graphs of mean values over time may also be generated.

6.7.3 Other Safety Endpoints

6.7.3.1 ECG

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

6.7.3.2 Vital Signs and ECOG Performance Status

Vital signs and ECOG performance status will be summarized with descriptive statistics at each visit and time point where they are collected. Vital sign shift tables may be produced to summarize changes in the following categories.

Systolic blood pressure (mmHg): < 90 (Low), 90-120 (Normal), > 120 (High)

Diastolic blood pressure (mmHg): < 60 (Low), 60-80 (Normal), > 80 (High)

Heart rate (Beats/min): < 60 (Low), 60-100 (Normal), > 100 (High)

Respiratory Rate (Breaths/min): < 12 (Low), 12-18 (Normal), > 18 (High)

Temperature (F): < 97.8 (Low), 97.8-99.1 (Normal), > 99.1 (High)

6.8 Pharmacokinetic, Pharmacodynamic, and Immunological Parameter Endpoint Analyses

Pharmacokinetic Analysis: Summary statistics will be tabulated separately for serum PK parameters by MGD007 and MGA012 dose. Geometric means and percent coefficients of variation will be reported for C_{max}, $AUC_{(0\text{-}T)}$, $AUC_{(TAU)}$, $AUC_{(INF)}$, and C_{trough}; arithmetic means and standard deviations will be reported for $t_{1/2}$, CL, and V_{ss}; and medians, minimum, and maximum will be reported for T_{max}. Separate scatter plots of C_{max} and AUC will be

provided versus dose to assess dose dependency. Dose proportionality may be assessed using a power model. Population PK analyses may be conducted using data from this study alone or combined with data from other studies.

Immunogenicity Analysis: The proportion of patients who are negative for ADA at baseline and become positive in this assay, the proportion of patients who are negative at baseline and remain negative, and those who have positive ADA at baseline that increases or decreases in titer over the course of treatment will be summarized. Analysis will be conducted separately for MGD007 and MGA012.

Pharmacodynamic Analysis: Summary statistics for pharmacodynamic parameters and corresponding changes from baseline will be summarized and/or may also be presented graphically as well as possible associations between changes in pharmacodynamic measures of interest and MGD007 in combination with MGA012 dose and exposure may be explored.

7 LIST OF TABLES, LISTINGS, AND FIGURES

The list of tables, listings, and figures (TLFs) and associated shells planned for the clinical study report 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. **Brookmeyer R and Crowley J.** A Confidence Interval for the Median Survival Time. Biometrics, 1982; 38:29-41.

CP-MGD007-02 Statistical Analysis Plan (Version 1.0, 26-Jul-2018)

This is the electronic signature page for the above referenced document.

User Task: eSignatories Approval	Jan Davidson Clinical – Research Approval (Intended or Designee) 26-Jul-2018 16:35:37 GMT+0000

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