STATISTICAL ANALYSIS PLAN

NCT Number: NCT04159805

Study Title: A Phase 2, Randomized, Placebo-Controlled Study to Evaluate Safety, Tolerability, and Efficacy of TAK-079 in Patients With Generalized Myasthenia Gravis

Study Number: TAK-079-1005

SAP Version and Date:

Version 1.0: 14-Apr-2022

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Phase: 2

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REVISION HISTORY

Version	Approval Date	Primary Rationale for Revision
Original version	18-FEB-2021	Not applicable
Amendment 1.0	14-APR-2022	To clarify statistical analysis methods as outlined in Section 9.1

TABLE OF CONTENTS

LIST OF IN-TEXT TABLES

ABBREVIATIONS

Abbreviation	Term
AChR	acetylcholine receptor
ADA	antidrug antibody
AE	adverse event
AUC	area under the plasma concentration-time curve
C_{max}	maximum observed plasma concentration
CRO	contract research organization
CRS	cytokine release syndrome
CSR	clinical study report
C_{trough}	trough concentration
DSMB	data safety monitoring board
ECG	electrocardiogram
eCRF	electronic case report form
EDC	electronic data capture
FcRn	neonatal Fc receptor
FDA	Food and Drug Administration (US)
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
IB	investigator brochure
ICF	informed consent form
ICH	International Council for Harmonisation
IEC	independent ethics committee
Ig	immunoglobulin
IRB	institutional review board
IRR	infusion-related reaction
ISR	injection site reaction
IV	intravenous(ly)
IVIg	intravenous immunoglobulin
IXRS	interactive voice/web response system
LFP	long-term follow-up period
MedDRA	Medical Dictionary for Regulatory Activities
MG	myasthenia gravis
MG-ADL	Myasthenia Gravis Activities of Daily Living
MGC	Myasthenia Gravis Composite
MGFA	Myasthenia Gravis Foundation of America
MGII	Myasthenia Gravis Impairment Index
MG-QoL15r	revised 15-item Myasthenia Gravis Quality of Life scale
MHRA	Medicines and Healthcare products Regulatory Agency
MMRM	Mixed model for repeated measures
MuSK	muscle-specific tyrosine kinase

Abbreviation	Term
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NK	natural killer
NMJ	neuromuscular junction
NOAEL	no-observed-adverse-effect level
PD	pharmacodynamic
PGIC	Patient Global Impression of Change
PGIS	Patient Global Impression of Severity
PK	pharmacokinetic(s)
PMDA	Pharmaceuticals and Medical Devices Agency
PPD	purified protein derivative
PT	Preferred term
PTE	pretreatment event
QMG	Quantitative Myasthenia Gravis
RBC	red blood cell
RRMM	relapsed and/or refractory multiple myeloma
SAE	serious adverse event
SC	subcutaneous(ly)
SFP	safety follow-up period
SLE	systemic lupus erythematosus
SOC	system Organ Class
SOE	schedule of events
SUSAR	suspected unexpected serious adverse reaction
TB	tuberculosis
TEAE	treatment-emergent adverse event
TIGRA	T-cell interferon-γ release assay
TNF-α	tumor necrosis factor alpha
UK	United Kingdom
ULN	upper limit of the normal range
US	United States

1.0 OBJECTIVES, ENDPOINTS AND ESTIMANDS

1.1 Objectives

1.1.1 Primary Objective

To evaluate the safety and tolerability of TAK-079 in patients with generalized MG who are receiving stable background therapy for MG.

1.1.2 Secondary Objective(s)

To assess the effects of TAK-079 on MG disease activity using clinical rating scales and autoantibody levels.

1.1.3 Exploratory Objective(s)

1. *To determine the pharmacokinetics (PK) of TAK-079.*
2. *To determine the pharmacodynamic (PD) profile of TAK-079.*
3. *To explore the effects of repeated administration of TAK-079 on MG disease activity using a novel clinical disease assessment scale.*
4. *To explore the duration of a clinically meaningful effect on MG disease severity (using at least 1 MG clinical rating scale).*
5. *To explore the frequency and proportion of patients requiring rescue therapy.*
6. *To explore vaccine-induced protective antibodies.*
7. *To explore the effects of repeated administration of TAK-079 on exploratory biomarkers of disease activity.*

1.2 Endpoints

1.2.1 Primary Endpoint(s)

Percentage of patients with TEAEs, including Grade 3 or higher events, SAEs, and AEs leading to TAK-079 discontinuation.

1.2.2 Secondary Endpoint(s)

1. *Score change from baseline in the following:*
   a) *MG Activities of Daily Living (MG-ADL) score.*
   b) *Quantitative Myasthenia Gravis (QMG) score.*
   c) *Myasthenia Gravis Composite (MGC) score.*
   d) *Revised 15-item Myasthenia Gravis Quality of Life scale (MG-QoL15r).*
2. *Change from baseline in anti-AChR antibody or anti-MuSK antibody levels.*

3. *The percentage of patients meeting minimal clinically important difference criteria in the respective MG clinical impairment scales (MG-ADL, QMG, MGC).*

1.2.3 Exploratory Endpoint(s)

1. *Serum concentration-time profile of TAK-079 PK parameters will include, but are not limited to observed concentration at the end of a dosing interval (C_{trough}) over time.*
2. *Change in serum immunoglobulin levels.*
3. *Pharmacodynamic analysis of the presence and changes of* CD38+ *immune cells in peripheral blood before and during therapy.*
4. *Score change from baseline in Myasthenia Gravis Impairment Index (MGII) scores.*
5. *Duration of a clinically meaningful effect on MG disease severity (in all of the clinical disease impairment scales: MG-ADL, QMG, MGC, MGII).*
6. *Percentage of patients meeting minimal clinically important difference criteria in the MGII scale.*
7. *Frequency and proportion of patients requiring rescue therapy.*
8. *Immunogenicity assessment of TAK-079 in serum, including antidrug antibody (ADA).*
9. *Biomarkers of disease activity such as complement levels (C3, C4, complement split products); specific markers of CD38 pathway modulation may also be evaluated.*
10. *Change in levels of the following vaccine-protective antibodies: measles, mumps, rubella, diphtheria, and tetanus.*

2.0 STUDY DESIGN

This is a phase 2, randomized, double-blind, placebo-controlled study designed to assess the safety, tolerability, and efficacy of TAK-079 in patients with generalized MG in combination with standard background therapy.

It is expected that approximately 36 patients will be randomized into the study. After a screening period of up to 28 days, eligible patients will be randomized in a 1:1:1 ratio to one of the following treatment groups:

- *TAK-079 300 mg added to stable standard background therapy.*
- *TAK-079 600 mg added to stable standard background therapy.*
- *Matching placebo added to stable standard background therapy.*

Evaluation of intermediate doses and expansion of an existing dose level are all permissible after discussions between the sponsor and the investigators, if such measures are needed for patient safety or for a better understanding of the dose-related toxicity, clinical activity, exposure, or pharmacodynamics of TAK-079.

The study will be divided into 3 sequential periods: a dosing period (8 weeks), a safety follow-up period (SFP; 8 weeks), and a long-term follow-up period (LFP; 16 weeks).

During the 8-week dosing period, TAK-079/matching placebo will be administered via SC injection once weekly for 8 weeks.

Safety assessment, including safety laboratory tests (as listed in Protocol Appendix A), will be performed each week before subsequent dosing. Patients may have study drug (TAK-079/placebo) doses modified (eg, withheld or delayed) for safety reasons

After completing the 8-week dosing period, patients will enter an 8-week blinded SFP, completing safety and efficacy assessments every 2 weeks. After completion of the Week 16 visit in the SFP, patients will be unblinded before entering the LFP visit at Week 20.

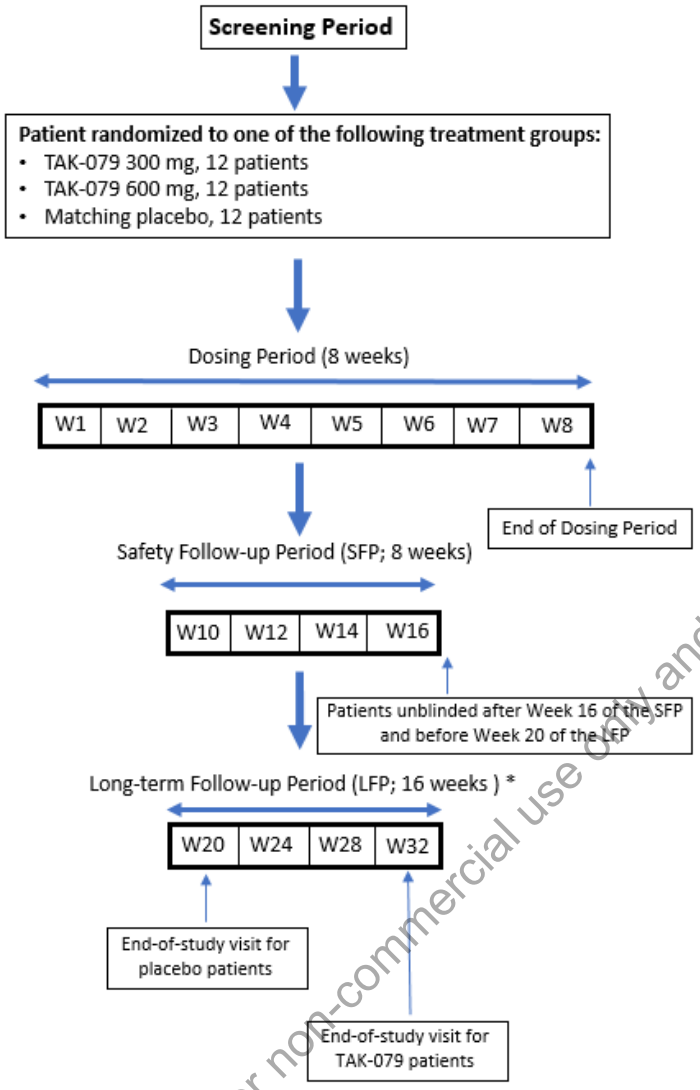
Patients randomized to TAK-079 will be followed every 4 weeks from Week 20 through Week 32 of the LFP for MG clinical activity scores and autoantibody levels; the end-of-study visit will take place at Week 32 of the LFP. For patients randomized to placebo, the end-of-study visit will take place at Week 20 of the LFP. The study schematic diagram is outlined in Protocol Figure 6.a.

AEs ongoing at the Week 16 visit of the SFP (including unresolved clinical/laboratory parameters [see Protocol Section 9.6]) should be monitored through the LFP until they are resolved, return to baseline, or are clearly determined to be due to a patient's stable or chronic condition or intercurrent illness(es). Study drug–related AEs/SAEs with onset after the SFP will be collected through the LFP.

Overall, the maximum follow-up period is approximately 24 weeks after the last dose of study drug. Patients will be permitted to receive rescue medication (eg, IVIg, high dose corticosteroids, or plasmapheresis/plasma exchange) as determined by the investigator and described in Protocol Section 8.1.3. If the patient receives rescue therapy, they will automatically enter the SFP. Rescue therapy is defined as additional dosing of concomitant medications in accordance with institutional practices or the physician's best medical judgment to control and manage underlying MG conditions.

Study procedures and assessments, with associated time points, are presented in the schedule of events (SOE) table in Protocol Appendix A.

Protocol Figure 6.a Study Schematic



AE: adverse event; LFP: SAE: serious adverse event; W: week.
* Unresolved AEs as of Week 16 and related AEs/SAEs with onset after SFP will be collected through the LFP.

3.0 STATISTICAL HYPOTHESES AND DECISION RULES

3.1 Statistical Hypotheses

No tests of statistical hypotheses are planned.

3.2 Multiplicity Adjustment

No multiplicity adjustments are planned.

4.0 SAMPLE-SIZE DETERMINATION

Approximately 36 patients are planned to be randomized to treatment in a ratio of 1:1:1 (TAK-079 300 mg, TAK-079 600 mg, or placebo). This study is exploratory and not powered to address any predefined hypothesis.

5.0 ANALYSIS SETS

The analysis sets will include the following.

5.1 Safety Analysis Set

Patients who have received at least 1 dose of study drug.

5.2 Full Analysis Set

All enrolled patients. In efficacy analyses, only patients with both baseline and at least 1 valid postbaseline value will be included.

In this study, a subject is considered enrolled if and only if the subject was randomized.

5.3 Pharmacokinetic Analysis Set

Patients who have received at least 1 dose and have at least 1 measurable TAK-079 serum concentration.

5.4 Pharmacodynamic Analysis Set

Patients who have a baseline and at least 1 postbaseline PD *sample assessment.*

5.5 Immunogenicity Analysis Set

Patients from the safety population who have a baseline and at least 1 postbaseline immunogenicity sample assessment.

6.0 STATISTICAL ANALYSIS

6.1 General Considerations

6.1.1 General Principles

Continuous data will be summarized using number of subjects (N), mean, standard deviation (SD), median, minimum, and maximum, where appropriate. Where indicated, the coefficient of variation (%CV) and geometric mean may also be included in the summary of continuous data. Arithmetic means, geometric means, and medians will be presented to 1 more decimal place than the recorded data, and SDs will be presented to 2 more decimal places than the recorded data, where appropriate.

Categorical data will be summarized using the number and percent of subjects for each category, where appropriate. Percentages will be reported to 1 decimal place.

Confidence intervals (CIs) will be 2-sided at the 95% level. P-values will be 2-sided, and values that are less than 5% may be noted as statistically significant.

Summaries will be presented by treatment group (placebo, TAK-079 300 mg, TAK-079 600 mg) and by visit where applicable. An additional "TAK-079 Combined" category combining the TAK-079 300 mg and 600 mg treatment groups may be displayed in selected summaries.

6.1.2 Longitudinal Analysis of Change from Baseline for Efficacy Endpoints

- ***Statistical model.*** Analyses of change from baseline or percent change from baseline (where indicated) for efficacy endpoints – i.e., MG impairment scales or anti-AChR/anti-MuSK antibodies – will use only data up to Week 16 (last blinded visit) and will be performed using a mixed model for repeated measures (MMRM) analysis, which will include treatment, visit, and treatment-by-visit interaction terms as the factors and adjusted by baseline value and baseline-by-visit interaction. The Kenward-Roger method for calculating denominator degrees of freedom will be used. The unstructured covariance will be used as the default structure for the model. If there are convergence issues, a first order autoregressive (AR(1)) covariance structure will be used.
- ***Intercurrent events and missing data.*** If a subject receives rescue therapy or prematurely discontinues from study drug, any assessments obtained thereafter will be excluded from the MMRM analysis. This approach allows estimation of the treatment effect under the hypothetical situation in which the dosing schedule is adhered to without use of rescue therapy. Based on the missing at random assumption, the MMRM analysis will be performed using observed case data only, except where otherwise indicated. If an MG impairment scale has partially missing data, i.e., missing scores for certain items in the questionnaire, the scale will be considered missing at that timepoint, except where otherwise indicated.
- ***Analysis set.*** For efficacy analyses, only subjects with a non-missing baseline value and at least one non-missing post baseline value will be included in the model.
- ***Tables, listings, and figures.*** The MMRM estimated mean change from baseline or mean percent change from baseline (where indicated) along with standard error and CI, will be presented for each visit up to Week 16 by treatment group. Comparisons of means between different TAK-079 arms and the placebo arm will be performed for all scheduled post-baseline assessment timepoints up to Week 16. Estimated differences of means as well as standard errors and CIs for the differences will be provided; p-values will be provided for descriptive purposes. Observed values, change from baseline, and percent change from baseline (where indicated) by visit up to Week 32 for TAK-079 subjects and up to Week 20 for placebo subjects will be summarized descriptively. Observed values will also be provided in the listings. The MMRM estimated mean change from baseline and mean percent change from baseline (where indicated) at each scheduled visit up to Week 16 by treatment group will be plotted. The observed mean change from baseline and observed mean percent change from baseline (where applicable) will be plotted.

6.1.3 Analysis of Binary Efficacy Endpoints

Binary efficacy endpoints will be presented using frequencies, percentages, and CIs by treatment group. CIs for percentages will be calculated using the Clopper-Pearson method. CIs for differences of percentages will be calculated using the Miettinen-Nurminen method. Details regarding handling of intercurrent events, missing data, and presentation of results will be described in later sections when the specific endpoint is discussed.

6.1.4 Handling of Treatment Misallocations

For analyses of safety, efficacy, PK, PD, and immunogenicity, subjects will be analyzed according to actual treatment received.

6.2 Disposition of Subjects

Screen failures will be summarized, including number of subjects, demographics, and primary reason for failed screening. Screen failures are defined as subjects who signed ICF but were not randomized.

Additional summaries and listings, based on all randomized subjects, will include:

- Summary of disposition in terms of subjects who prematurely discontinued from study drug, subjects who completed study drug treatment phase, subjects who prematurely discontinued from the study, and subjects who completed the study, as well as primary reason for discontinuation from study or study drug.
- Listing of subject disposition including date of first dose, date of last dose, duration of treatment, the reason for premature discontinuation of study drug, and the reason for premature discontinuation of study.
- Summary of number of subjects in each analysis set.
- Summary by country and site.
- Summary and listing of significant and critical protocol deviations.
- Listing of deviations from inclusion/exclusion criteria.
- Listing of protocol deviations related to COVID-19, including visits impacted by COVID-19.

6.3 Demographic and Other Baseline Characteristics

6.3.1 Demographic Characteristics

Demographic characteristics will be summarized and listed using the safety analysis set. Variables to be presented include age, sex, ethnicity, and race.

6.3.2 Baseline Characteristics

Baseline characteristics including disease characteristics related to MG will be summarized and listed using the safety analysis set. Variables to be presented include:

- Weight, height, body mass index (BMI)
- ECG findings and reproductive system findings.
- Disease characteristics and medical history related to MG, including:
  - MGFA classification
  - Prior autoantibody type (AChR or MuSK)
  - Time since MG diagnosis (years) (as defined in Section 9.5)
  - History of MG crisis, hospital admissions for MG, ventilator support, plasma exchanges, thymectomy, or diagnosis of thymoma or thymic neoplasm
  - Use of feeding tube
  - Prior MG medications and MG medication categories
  - Baseline values for scores on disease activity assessment tools (MG-ADL, QMG, MGC, MG-QoL15r, MGII).

All medical history data related to MG will be included in listings. Medications will be coded using the World Health Organization (WHO) Drug Dictionary.

6.3.3 Medical History

Medical history refers to significant conditions or diseases that stopped at or prior to informed consent or are ongoing at informed consent. Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA, version 24.0 or higher) and will be summarized using System Organ Class (SOC) and MedDRA preferred term (PT). The table will be sorted in alphabetical order by SOC. Within a SOC, PTs are sorted in decreasing frequency based on the total number of subjects. The number and percentage of subjects with any significant medical history will be summarized for each SOC and PT. The denominator used for calculating the percentages will be the total number of subjects included in each treatment group. For the tables, if a subject reports the same PT multiple times, then that PT will be counted only once for that subject. Similarly, if a subject reports multiple conditions within the same SOC, then that SOC will be counted only once for that subject. All medical history data will be presented in listings. Summaries and listings will use the safety analysis set.

Medical history related to MG will be presented as part of baseline characteristics (see Section 6.3.2).

6.4 Concomitant Medications and Procedures

Medications used by subjects and therapeutic procedures completed by subjects, from within 28 days before the first dose of study drug through the end of the subject's participation in the study

as recorded in the eCRF, are referred to as concomitant medications and concomitant procedures and will be summarized and listed using the safety analysis set. Medications will be coded using the WHO Drug Dictionary.

Missing or partial dates will not be imputed. Conservatively, a medication or procedure will be classified as concomitant if the available information about the end date is insufficient to determine whether it occurred during the reporting period.

A separate summary for COVID-19 related medications and procedures may be provided.

6.5 Efficacy Analysis

6.5.1 Primary Endpoint(s) Analysis

The study has no primary efficacy endpoints.

6.5.2 Secondary Endpoint(s) Analysis

6.5.2.1 Derivation of Endpoint(s)

The secondary efficacy endpoints are defined as follows:

- Change from baseline at each scheduled assessment up to Week 32 for TAK-079 subjects and up to Week 20 for placebo subjects for the following endpoints. Additionally, MMRM modeling (as described in Section 6.1.2) at each scheduled assessment up to Week 16 will be performed for the following endpoints.
    - MG-ADL total score
    - QMG total score
    - MGC total score
    - MG-QoL15r total score

  Change from baseline is calculated as the post-baseline score minus baseline score.
- Change from baseline at each scheduled assessment up to Week 32 for TAK-079 subjects and up to Week 20 for placebo subjects for the following endpoints. Additionally, MMRM modeling (as described in Section 6.1.2) at each scheduled assessment up to Week 16 will be performed for the following endpoints.
    - Anti-AChR antibody levels for subjects who are positive for anti-AChR antibodies at baseline.
    - Anti-MuSK antibody levels for subjects who are positive for anti-MuSK antibodies at baseline.

  Both absolute change and percent change from baseline will be analyzed and are defined as follows:
    - Absolute change = post-baseline value – baseline value

- Percent change = [(post-baseline value – baseline value)/baseline value] × 100

- Percentage of subjects attaining the minimal clinically important difference criteria (also considered as responder criteria) defined as in Table 1 in each of the following scales at each scheduled assessment up to Week 32 for TAK-079 subjects and up to Week 20 for placebo subjects:
  - MG-ADL
  - QMG
  - MGC
  - MGII

Table 1 Minimal Clinically Important Difference Criteria (Responder Criteria) in MG-ADL, QMG, MGC, and MGII

Clinical Rating Scale	Minimal Clinically Important Difference
MG-ADL	2-point reduction in MG-ADL total score from baseline
QMG	3-point reduction in QMG total score from baseline
MGC	3-point reduction in MGC total score from baseline
MGII	8-point reduction in MGII total score from baseline

6.5.2.2 Main Analytical Approach

The full analysis set is used for efficacy analyses of secondary endpoints.

Change from Baseline Analyses

Change from baseline in MG impairment scales (MG-ADL, QMG, MGC, MG-QoL15r) and antibody levels (anti-AChR, anti-MuSK), and percent change from baseline in antibody levels, will be analyzed and summarized using the approach described in Section 6.1.2. For analysis of QMG, the following imputations will be done prior to MMRM analysis:

- **Baseline imputation for missing item on the QMG.** If the baseline assessment of the Forced Vital Capacity (FVC) item in the QMG scale for a subject is missing and no other items in the QMG scale are missing for that subject, the missing FVC item score will be imputed as the mean of all non-missing baseline FVC values from the set of randomized subjects.
- **Post baseline imputation of missing item on QMG.** If the FVC item on any post baseline QMG assessment is missing, this missing item will be imputed using last observation carried forward (LOCF) for that subject for that item only.

Responder Analyses

Subjects meeting the minimal clinically important difference from baseline criteria in the MG impairment scales (MG-ADL, QMG, MGC, MGII), as defined in Table 1, at a given visit will be referred to as *responders* on the respective scale at that visit.

To estimate the treatment effect, the analysis will account for intercurrent events and missing data as follows.

- If a subject receives rescue therapy or prematurely discontinues from study drug, the subject is considered not a responder for visits thereafter.
- If an assessment for a subject is missing at a visit, but the subject is a responder at the scheduled visit occurring directly before and the one occurring directly after the missing assessment, then the subject is considered a responder at the visit with the missing assessment.
- QMG scores that have been imputed because of missing FVC, as described previously, are not considered missing, and the imputed scores will be used for responder analysis.
- An assessment that is missing for any other reason not described in the above scenarios will be imputed as not a response. With this imputation strategy, comparisons of responder percentages between different TAK-079 arms and the placebo arm will be performed for all scheduled post-baseline assessment timepoints up to Week 16 (last blinded visit). Differences of percentages and CIs for the differences will be provided. The frequency, percentage, and CI for percentage will also be presented for each visit by treatment group up to Week 16. The percentages at each scheduled visit will be plotted by treatment group. Refer to Section 6.1.3 for additional details.
- Observed frequencies and percentages by visit up to Week 32 for TAK-079 subjects and up to Week 20 for placebo subjects will also be summarized descriptively.

Sensitivity analyses to responder analyses: Additional sensitivity analyses will be performed for responder analyses. In these sensitivity analyses, subjects who prematurely discontinued from study drug due to reasons other than 'Symptomatic Deterioration' or 'Unsatisfactory Therapeutic Response' will be excluded from responder analyses thereafter, rather than being considered as non-responders thereafter.

6.5.3 Exploratory Endpoints Analysis

The exploratory efficacy endpoints are defined and analyzed as follows:

- ***Change from baseline at each scheduled assessment up to Week 32 for TAK-079 subjects and up to Week 20 for placebo subjects in the MGII total score, the MGII ocular subscore (sum of items 1-6), and the MGII generalized symptoms subscore (sum of items 17-22).*** This endpoint is analyzed in the same manner as the analysis of change from baseline for the other MG scales (MG-ADL, QMG, MGC, MG-QoL15r) as described in Section 6.5.2.2.

- ***Duration of a clinically meaningful effect on MG disease severity in the following clinical disease impairment scales: MG-ADL, QMG, MGC, MGII.***

Both maximum duration and cumulative duration will be analyzed. *Maximum duration* is defined as the longest sustained period during which the minimal clinically important difference from baseline is attained (see Table 1). *Cumulative duration* is defined as the sum of all time periods during which the minimal clinically important difference from baseline is attained. The following rules are used for calculating time periods:

- If the minimal clinically important difference is attained at a visit, then it is assumed to have been attained starting 1 or 2 weeks prior to the visit and sustained until 1 or 2 weeks after the visit. Due to collection schedule shift during the study, the exact number of weeks a visit covers will be different. Refer to Table 2 for the exact number of weeks each visit covers.

Table 2 Number of Weeks Each Visit Covers in Calculating Duration of a Clinically Meaningful Effect

Collection Week	# of Weeks Covered Prior - for First 16 Weeks	# of Weeks Covered After - for First 16 Weeks	# of Weeks Covered Prior - for First 32 Weeks	# of Weeks Covered After - for First 32 Weeks
4	1	1	1	1
6	1	1	1	1
8	1	1	1	1
10	1	1	1	1
12	1	1	1	1
14	1	1	1	1
16	1	0	1	2
20	0	0	2	2
24	0	0	2	2
28	0	0	2	2
32	0	0	2	0

- If the minimal clinically important difference is attained at two consecutive visits, or at two visits separated by only one missing assessment, then it is assumed that the minimal clinically important difference was attained and sustained for the entire time period between the two visits.
- If an assessment is missing, then the minimal clinically important difference is considered not attained at that visit, except as described in the previous paragraph.
- If an assessment occurs after rescue therapy or premature discontinuation of study drug, then the minimal clinically important difference is considered not attained at that visit.

- QMG scores that have been imputed per Section 6.5.2.2 are not considered missing, and the imputed scores will be used for all calculations of duration.
- Calculations are based on nominal visit weeks as defined in Schedule of Events (Protocol Appendix A).

For example, if a subject attains the minimal clinically important difference at weeks 4, 8, 12, and 16 but not at weeks 6 and 14, and the assessment is missing at week 10, then the maximum duration at week 16 is 6 weeks (longest period occurs from weeks 7 to 13), and the cumulative duration at week 16 is 9 weeks, calculated as 2 (weeks 3-5) + 6 (weeks 7-13) + 1 (weeks 15-16).

Maximum duration and cumulative duration at week 16 and week 32 (TAK-079 subjects only) will be calculated. Differences in mean duration at week 16 will be presented for each TAK-079 arm vs placebo, along with standard errors and CIs for the differences that are derived from a Student's t-test assuming common standard deviation. Descriptive statistics along with standard errors and CIs will also be presented by treatment group at week 16 and at week 32 (for TAK-079 subjects only).

Number and percentage of subjects who have ≥4-, 6-, 8-, 10-, or 12-weeks maximum duration or cumulative duration by week 16 (TAK079 subjects and placebo subjects) and week 32 (TAK-079 subjects only) will be summarized for each treatment group. Risk difference at visits up to Week 16 comparing each TAK-079 arm vs. placebo, and corresponding exact 95% confidence interval will be provided.

- ***Percentage of subjects meeting minimal clinically important difference criteria in the MGII scale.***
  The number and percentage of subjects who achieve the minimal clinically important difference criteria for MGII per Table 1 will be analyzed in the same manner as for MG-ADL, QMG, and MGC as described in Section 6.5.2.2.

- ***Percentage of subjects requiring rescue therapy.***
  The number and percentage of subjects requiring rescue therapy by Week 16 will be summarized by treatment group and compared between different TAK-079 arms and the placebo arm. In addition, the number and percentage of subjects requiring rescue therapy by Week 32 will be summarized for TAK-079 subjects only. Differences in percentages at Week 16 and CIs for the differences between each TAK-079 arm and placebo will be presented, along with percentages for each treatment group. Numbers and percentages will also be presented for TAK-079 subjects at Week 32. The summaries will also include the number and percentage of subjects in each treatment group who prematurely discontinued from study drug but did not require rescue therapy. All rescue therapies will be listed.

The Patient Global Impression of Change (PGIC) and Patient Global Impression of Severity (PGIS) may be explored in post hoc analyses of meaningful change and other psychometric properties and performance characteristics of MG disease assessment scales. Data on PGIC and PGIS will be presented in listings.

Alternative criteria for minimal clinically meaningful difference (Table 1) maybe explored.

The full analysis set is used for efficacy analyses of exploratory endpoints.

6.5.4 Subgroup Analyses

Subgroup analyses are not planned.

6.6 Safety Analysis

Safety will be evaluated by the frequency of AEs, severity and types of AEs, and by changes from baseline in vital signs, weight, and clinical laboratory results using the safety analysis set.

Exposure to study drug and reasons for discontinuation will be tabulated.

To assess the impact of contingency measures taken on safety results of participating subjects during the COVID-19 pandemic, the alternative method(s) of safety assessments (e.g., laboratory evaluations, vital signs, and/or ECG) due to COVID-19 may be listed or summarized if data permits.

6.6.1 Adverse Events

All pretreatment events (PTEs) and AEs will be coded by SOC and PT using MedDRA (version 24.0 or later) and will be listed for subjects in the safety analysis set. AE severity is determined by the CTCAE scale version 4.03.

A pretreatment event (PTE) is any untoward medical occurrence in a subject who has signed informed consent to participate in a study but before administration of any study medication; it does not necessarily have to have a causal relationship with study participation.

A treatment-emergent adverse event (TEAE) is defined as an AE having a start date and time equal to or later than the start date and time of the first dose of study drug. If the start date of the AE equals the start date of the first treatment and either the start time of the AE or the start time of the treatment is missing, then the AE will count as a TEAE. AEs with partially missing onset dates will be counted as TEAEs if the month (if available) and the year are equal to or later than the month and year of the date of first dose. AEs with a completely missing start date will be counted as TEAEs.

The following summaries for TEAEs will be presented by treatment group for the dosing and SFP period. If not otherwise specified, TEAEs occurred during the LFP period will be presented by listings only. Dosing and SFP period TEAEs and LFP period TEAEs are defined in Section 9.9.

- Overall TEAEs including summaries of any TEAE, any TEAEs related to study drug, any serious TEAEs, any serious TEAEs related to study drug, any Grade 3 or higher TEAE, any Grade 3 or higher TEAE related to study drug, any ISR TEAE, any IRR TEAE, death due to TEAE, hospitalizations due to TEAE, and discontinuation from study drug due to TEAE will be presented for dosing and SFP period and LFP period separately.
- TEAEs by SOC and PT.
- TEAEs by maximum toxicity grade, SOC, and PT.
- TEAEs by relationship to study drug (i.e., causality), SOC, and PT.

- TEAEs considered related to the study drug by SOC and PT.
- TEAEs leading to discontinuation of study drug by SOC and PT.
- Serious TEAEs by SOC and PT.
- Most frequent (occurring in ≥10% of all subjects) TEAEs by PT

SOCs will be sorted in descending order of total number of subjects with the SOC in the combined TAK-079 group. Within an SOC, adverse events will be sorted in descending order of total number of subjects with the preferred term in the combined TAK-079 group.

In the high-level adverse event summary tables, TEAEs will be summarized regardless of severity and relationship to study drug. Within each subject, multiple reports of events that map to a common MedDRA preferred term will be counted only once.

At the adverse event level, the summary tables will present the number of subjects reporting each of these MedDRA events, i.e., the number of subjects reporting 1 or more events that map to the given MedDRA preferred term.

At the SOC level, the summary tables will present the number of subjects reporting 1 or more events that map to the given SOC. That is, the number of subjects reported at the SOC level will be less than or equal to the sum of the subject counts across all adverse events within that SOC.

For the summary of TEAEs by SOC, PT, and maximum severity, if a subject experiences more than 1 episode of a particular coded adverse event, the subject will be counted only once by the maximum severity of the episode (preferred term). Similarly, if a subject has more than 1 adverse event within an SOC, the subject will be counted only once by the maximum severity in that SOC. Missing toxicity grades will be imputed as grade 3 (severe).

AEs with missing causal relationship will be classified as related to study drug.

All AEs will be listed by treatment, subject identifier and onset date of the adverse event. The listing will contain: subject identifier, age, sex, race, study period, adverse event (preferred term and reported term), relationship to study drug, onset date, end date or whether the event was ongoing, duration, severity, action taken concerning study drug, the outcome, study period, and whether the adverse event was an SAE.

Special listings for SAEs, IRRs, ISRs, TEAEs leading to discontinuation of study drug, Grade 3 or higher TEAEs, related TEAEs, and TEAEs leading to death will also be presented.

TEAEs with start dates that are completely or partially missing will be imputed as follows:

- If month and year are known but day is missing
    - If month and year are the same as month and year of first dose date, then first dose date will be used.
    - If month and year are later than first dose date, then first day of the month will be used.
- If year is known but day and month are missing

  - If year equals year of first dose date, then first dose date will be used.
  - If year is greater than year of first dose date, then 1st of January of the year will be used.
- If all are missing then the first dose date will be used.

After imputation, if the stop dates are complete, all imputed dates are checked against the stop dates to ensure that start dates do not occur after stop dates. If an imputed start date occurs after the stop date, then change the imputed start date to be the same as the stop date. When the start date and the stop date are both incomplete for a subject, the start date will be imputed first.

Adverse events with stop dates that are completely or partially missing will be imputed as follows:

- If "ongoing" is checked, no imputation is necessary.
- If month and year are known but day is missing, the last day of the month will be used.
- If year is known, but day and month are missing
  - If the year is equal to or less than the year of last dose, then 31st of December will be used.
  - If the year is greater than the year of last dose, then 1st of January will be used.
- If all are missing then 31st of December of the year of last dose will be used.

If a subject dies, then use death date for AE stop date. After imputation, all imputed dates are checked against start dates to ensure that stop dates do not occur before start dates. If an imputed stop date occurs prior to the start date, then change the imputed stop date to be the same as the start date.

To assess of the impact of COVID-19 on the safety of participating subjects, a listing of COVID-19 related TEAEs will be provided.

6.6.2 Clinical Laboratory Evaluations

All laboratory values will be converted to standardized units and summarized in tables and listings by treatment groups. If a lab value is reported using a non-numeric qualifier (e.g., less than (<) a certain value, or greater than (>) a certain value), the given numeric value will be used in the summary statistics, ignoring the non-numeric qualifier.

The following summaries for laboratory test results will be presented by treatment group:

- Actual value and change from baseline values at each scheduled assessment.
- Shift tables for the change from Baseline to each post-baseline time point will be presented. For these tables, each subject will be categorized as low, normal, or high for the baseline value, and low, normal, or high for each post-baseline time point, according to the local laboratory reference ranges. The number of subjects as well as percentages in each of the combinations of shifts will be presented.

- Markedly abnormal values (MAVs) as defined by the criteria in Section 9.4 will be summarized by treatment group. The number and percentage of subjects with MAVs observed post-baseline in each of the applicable laboratory parameters will be presented.

All clinical laboratory data will be presented in SI units in data listings.

6.6.3 Vital Signs

The actual values and changes from baseline of vital sign parameters and weight at each scheduled visit will be summarized by treatment group. Vital sign values will also be presented in listings.

Post-dose vital sign MAVs as defined in Section 9.4 will be tabulated. If a subject has a post-dose MAV for a particular vital sign parameter, all visits for that subject for that parameter will be listed. The number and percentage of subjects with at least 1 post-dose markedly abnormal vital signs measurement will be summarized. The mapping of the subjects who meet the MAV criteria will be listed as a table. All observations, including ones at unscheduled visits, will be included in the MAV evaluation and summaries if MAV criteria are satisfied.

6.6.4 12-Lead ECGs

A single 12-lead ECG is to be performed at the screening visit (for assessment of eligibility) and at Weeks 10 and 16 of the SFP, and 32 of the LFP and will be read locally. Additional ECGs may be done per investigator discretion.

ECG variables at scheduled visits and their changes from baseline will be summarized by treatment group. A shift table for the investigator's ECG interpretation will provide the number and percentage of subjects in each of the appropriate categories (Normal; Abnormal, Not Clinically Significant; Abnormal, Clinically Significant) at the scheduled visit relative to the baseline status. All ECG results will be presented in listings.

6.6.5 Pregnancy Test

Clinical laboratory sample collection and results for pregnancy tests will be presented in a separate listing.

6.6.6 Extent of Exposure and Compliance

The total number of doses taken and the total amount of doses taken will be summarized descriptively by treatment group.

Treatment compliance will be summarized in terms of the percent of scheduled doses received, defined for each subject as: [(Actual total number of doses taken) ÷ (Planed number of doses taken)] *100.

The date and time of each dose for each subject will be reported in a data listing.

The impact of the COVID-19 on exposure and compliance will be summarized in terms of the percent of scheduled doses missed for each subject due to each of the following reason:

- Subject diagnosed with COVID-19
- Subject discretion due to COVID-19
- Travel restrictions due to COVID-19
- Investigative site accessibility (site closure, site visit restrictions, or site staff unavailability) due to COVID-19

All COVID-19 impacts on dose administration are included in the COVID-19 impact listing.

6.7 Pharmacokinetic, Pharmacodynamic, and Biomarker Analyses

6.7.1 Pharmacokinetic Analysis

The PK analysis set will be used for presentations of PK data.

Due to sparse PK sampling, no noncompartmental analysis will be conducted. Individual TAK-079 concentration data will be presented in listings and summarized by treatment group and nominal timepoint using descriptive statistics (including n, mean (SD), min, max, median, geometric mean, and geometric CV%). Mean concentration-time profiles will be plotted by treatment group using box-plot and line plot. Individual concentration-time profiles using both linear and log scales will be generated with subjects in the same treatment group plotted in the same graph. Concentration values below the lower limit of quantitation (LLOQ) will be assigned a value of zero for calculation of summary statistics and plots.

Additionally, TAK-079 concentration data will be analyzed by immunogenicity status category of (1) ADA negative, (2) pre-existing ADA positive, and (3) treatment-emergent or treatment-boosted ADA positive (see Section 6.8 for details) for each treatment group. TAK-079 concentration data will be summarized using descriptive statistics by immunogenicity status category, treatment group, and nominal timepoint. A plot showing mean TAK-079 concentration over time by treatment group and immunogenicity status category will also be provided.

A population PK model may be developed. If developed, the population PK model may be reported separately. The analysis plan for the population PK analysis may be separately defined, and the results of these analyses may be reported separately.

6.7.2 Pharmacodynamic and Biomarker Analysis

For the pharmacodynamic measures listed in Appendix Section 9.9 and biomarker measures listed below, if not otherwise specified, observed values, change from baseline and percent change from baseline values at different timepoints will be summarized by treatment group.

- Serum immunoglobulin levels.
- Serum levels of complement proteins.
- Additional biomarker parameters, if available.
- Anti-AChR autoantibody.

- Vaccine-protective antibodies for measles, mumps, rubella, diphtheria, and tetanus.

Figures of mean values and mean percent change from baseline over time will be generated for some PD/biomarker parameters as indicated in Appendix Section 9.9. Individual subject profiles over time for the following parameters will be plotted:

- IgG and AChR individual plots with each treatment group on a separate plot
  - Absolute value on linear scale
  - % change from baseline on linear scale
- MuSK plot for individual data combined into 1 plot with each treatment group a different color:
  - Absolute values on semi-log scale
  - Fold change from baseline on linear scale

For anti-MuSK autoantibody titer results, observed values and fold change from baseline anti-MuSK titer values will be reported and summarized by visit and treatment group. Mean observed values will be presented by treatment group on semi-log scale plot and mean fold change from baseline over time will be presented by treatment group on linear scale plots.

All PD/biomarker data will be presented in listings. The PD analysis set will be used for all presentations of PD/biomarker data.

Data allowing, PK/PD models may be developed to explore the relationship between TAK-079 serum concentrations and PD markers. The analysis plan for the population PK/PD analysis may be separately defined, and the results of these analyses may be reported separately. Additional PD analysis to evaluate the dose effect may be performed if appropriate.

6.8 Immunogenicity Analysis

Number and percentage of subjects with ADA response (confirmed positive vs. negative) will be summarized by treatment group and nominal timepoint. Number and percentage of subjects with immunogenicity status, as defined in Table 3, will be summarized by treatment group. All results will be listed using the Immunogenicity Analysis Set. The relationship between immunogenicity and PK, PD, efficacy, and safety may be explored.

Table 3 Immunogenicity Status Definition

Immunogenicity Status	Definition
ADA Negative	subject who does not have positive ADA response at baseline and all postbaseline assessments
Pre-existing ADA Positive	• Subject who has positive ADA response in the baseline sample and none of the postbaseline samples, **or** • Subject who has positive ADA response in both baseline and postbaseline samples but

	the maximum titer of the postbaseline ADA is <4 times the baseline titer value.
Treatment-boosted ADA Positive	• Subject who has positive ADA response in both baseline and postbaseline samples, **and** • The titer of the maximum postbaseline ADA is ≥4 times that of the baseline titer value.
Treatment Emergent ADA positive	• Subject who has negative ADA in baseline sample, **and** • Subject who has positive ADA response in any postbaseline assessment.
Transiently ADA Positive	Subject who has positive ADA response in 3 or less than 3 postbaseline assessment(s).
Persistently ADA Positive	Subject who has positive ADA response in more than 3 postbaseline assessments.
High ADA Titer	subject who has at least one postbaseline ADA titer >320
Low ADA Titer	subject who has at least one postbaseline ADA titer ≤320

6.9 Interim Analyses

No interim analyses are planned. However, preliminary unblinded analyses on safety and efficacy outcomes to support internal review purposes will be performed after all subjects are unblinded individually.

7.0 REFERENCES

Not applicable.

8.0 CHANGES TO PROTOCOL PLANNED ANALYSES

Not applicable.

9.0 APPENDIX

9.1 Changes from the Previous Version of the SAP

Changes made from the previous version of the SAP that have an impact to the planned statistical analysis methods are described in Table 4. In addition, there were textual changes purely to improve the flow, organization, and clarity. As these represent cosmetic changes with no impact to the planned statistical analyses, they are not included in the table below.

Table 4 Changes from the Previous Version of the SAP

SAP Section	Change	Rationale for Change
6.3.2 Baseline Characteristics	Added summary on 'Time since MG Diagnosis (years)'. Added summary on 'Prior MG medication categories'	For additional clarity of presenting the baseline characteristics.
6.5.2.2 Main Analytical Approach	Changed imputation method for missing item on the QMG by allowing all missing FVC item to be imputed	To resolve an issue that some missing FVC items were not imputed.
6.5.2.2 Main Analytical Approach	Added sensitivity analyses to responder analyses	To assess the robustness of responder analyses
6.5.3 Exploratory Endpoints Analysis	Redefined number of weeks each visit covers in the duration of clinical meaningful effect analysis	To resolve an issue that not all visits are covered in the previous definition.
6.6.1 Adverse Events	Added more AE summaries to the overall TEAE summaries	For additional clarity of presenting TEAEs
6.6.1 Adverse Events	Defined that dosing and SFP period TEAEs will be analyzed separately from LFP period TEAEs	For a fair comparison of TEAEs occurred during dosing and SFP period
6.6.2 Clinical Laboratory Evaluations	Removed listings in conventional units.	For brevity of results presentation
6.7 Pharmacokinetic, Pharmacodynamic and Biomarker Analyses	Added additional analyses to PK, PD, and ADA analyses. Provided more details to analysis methods.	For additional clarity of defining PK, PD, and ADA analyses.

9.2 Data Handling Conventions

9.2.1 Definition of Baseline

Unless otherwise stated, baseline value is defined as the last observed value before the first dose of study drug.

9.2.2 Definition of Study Days

Study Day 1 is defined as the day on which a subject is administered their first full dose of the medication. Other study days are defined relative to Study Day 1 with Day 1 being Study Day 1

and Day -1 being the day prior to Study Day 1. Study days prior to the first dose of study drug will be calculated as: [date of interest – date of first dose of study drug]. Study days on or after the first dose of study drug will be calculated as: [date of interest – date of first dose of study drug + 1].

9.2.3 Definition of Visit Windows

Visit designators are predefined values that appear as part of the visit tab in the electronic case report form (eCRF). The detailed study visit windows can be found in Protocol Appendix A. Summaries by visit in tables and plots will use the nominal week associated with each visit as recorded on the eCRF.

9.3 Analysis Software

All statistical analyses will be conducted using SAS® Version 9.4 or higher.

9.4 Criteria for Identification of Markedly Abnormal Values

Hematology

Parameter	Low Abnormal	High Abnormal
Hemoglobin	<8 g/dl	>1.2 × ULN
Hematocrit	<24 percent	>1.2 × ULN
WBC	<1500/mm3	>1.5 × ULN
Platelet count	<50,000/mm3	>600,000/mm3
Total lymphocyte count	<500/mm3	>1.5 × ULN

LLN=lower limit of normal, ULN=upper limit of normal, WBC=white blood cell.

Serum Chemistry

Parameter	Low Abnormal	High Abnormal
ALT	--	>3 × ULN
AST	--	>3 × ULN
Alkaline phosphatase	--	>3 × ULN
Total bilirubin	--	>34.2 µmol/L
ALT and Total Bilirubin	--	ALT>3 × ULN and TB>2 × ULN
AST and Total Bilirubin		AST>3 × ULN and TB>2 × ULN
Albumin	<25 g/L	--
Creatinine	--	>177 µmol/L
Glucose	<2.8 mmol/L	>19.4 mmol/L
Chloride	<75 mmol/L	>126 mmol/L
Sodium	<130 mmol/L	>6.0 mmol/L

Potassium	<3.0 mmol/L	>6.0 mmol/L
Blood Urea Nitrogen	--	>10.7 mmol/L
Calcium	<1.75 mmol/L	>2.88 mmol/L
Carbon dioxide	<23 mmol/L	>29 mmol/L
Lactate dehydrogenase	<105 IU/L	>333 IU/L

ALT=alanine aminotransferase, AST=aspartate aminotransferase, LLN=lower limit of normal, ULN=upper limit of normal.

Vital Signs

Parameter	Unit	Low Abnormal	High Abnormal
Pulse	bpm	<50	>120
Systolic blood pressure	mm Hg	<85	>180
Diastolic blood pressure	mm Hg	<50	>110
Body temperature	°C	<35.6	>37.7

9.5 Time Since MG Diagnosis

Time since diagnosis will be derived as:

(Date of informed consent – Date of MG diagnosis) /365.25 years

For date of diagnosis with missing month and day, July 1st will be used in this derivation; for date of diagnosis with missing day, the first day of the month will be used in this derivation.

9.6 Rescue Therapies

Rescue therapies will be identified by concomitant medications or concomitant procedures with the 'indication' field containing 'rescue'.

9.7 Prior MG Medications

Prior medications are further classified according to the categories in Table 5. In the table below, other medications that are reported as free text are shown in *italic* to differentiate from pre-specified medications. All prior MG medications were reviewed by clinicians prior to DBL and classified. In table summaries, the number and percentage of subjects in each prior MG medication category, as well as the number and percentage of subjects receiving each prior MG medication will be summarized by treatment group. In this summary, the 'Other' category will not be included.

Table 5 Prior MG Medications and Category

Medication Category	Medication Name
Immunosuppressants	Azathioprine Cyclosporine Methotrexate Mycophenolate Tacrolimus Cyclophosphamide
Corticosteroids	Methylprednisolone Cortisone Dexamethasone *Calcort/Deflazacort* Prednisolone Prednisone
Acetylcholinesterase Inhibitors	Pyridostigmine *Pyridostigmine SR* Ambenonium Neostigmine
Rituximab	Rituximab
IVIG	Intravenous Immunoglobulin Subcutaneous Immunoglobin
Eculizumab	Eculizumab

9.8 COVID-19 Related Medications

COVID-19 related medications are defined as concomitant medications with verbatim terms or indication containing 'COVID'.

9.9 TEAEs Occurring during Dosing and SFP Period vs. LFP period

TEAEs occurring during Dosing and SFP period are defined as TEAEs with a start date on or before the date of Week 16 visit date.

TEAEs occurring during LFP period are defined as TEAEs with a start date after the date of Week 16 visit date.

9.10 Pharmacodynamic Parameters

Table 6 Pharmacodynamic Parameters to be Presented in TFLs

Q Test Code	Mapped Test Name	Name to Include in TFLs
FCT23693	B Cell ABS Tube 3	B Cells/ul
FCT23694	B Cell (%Lymphocyte) Tube 3	B Cells %Lymphocytes
FCT23770	CD27++ HLA-DR++ PB (% PB) Tube 3	CD27++ HLADR++ PB %PB
FCT23775	CD27++ HLA-DR-Lo/- PB (% PB) Tube 3	CD27++ HLA-DR-Lo/- PB %PB
FCT23739	Grans ABS Tube 3	Granulocytes/ul
FCT23740	Grans (%Leuk) Tube 3	Granulocytes %Leukocytes
FCT23729	Lymph ABS Tube 3	Lymphocytes/ul
FCT23730	Lymph (%Leuk) Tube 3	Lymphocytes %Leukocytes
FCT23673	Mono ABS Tube 3	Monocytes/ul
FCT23673	Mono (%Leukocyte) Tube 3	Monocytes %Leukocytes
FCT23683	NK ABS Tube 3	NK Cells/ul
FCT23684	NK (%Lymphocyte) Tube 3	NK Cells %Lymphocytes
FCT23709	Plasmablast (%B Cell) Tube 3	Plasmablasts %B cells
FCT23714	Plasma cell ABS Tube 3	Plasma Cells/ul
FCT23716	Plasma cell (%CD138+ B-cells) Tube 3	Plasma Cells %CD138+ B cells
FCT23708	Plasmablast ABS Tube 3	Plasmablasts/ul
FCT23828	Plasma Cell RO (Percent)	Receptor Occupancy %Calculation Plasma Cells (%)
FCT23827	Plasmablast RO (Percent)	Receptor Occupancy %Calculation Plasmablasts (%)
FCT23793	B Cell RO (Percent)	Receptor Occupancy %Calculation CD38+ B Cells (%)
FCT23817	Granulocyte RO (%)	Receptor Occupancy %Calculation CD38+ Granulocytes (%)
FCT23812	Lymphocyte RO (%)	Receptor Occupancy %Calculation CD38+ Lymphocytes (%)
FCT23788	Monocyte RO (Percent)	Receptor Occupancy %Calculation CD38+ Monocytes (%)
FCT23798	NK Cell RO (Percent)	Receptor Occupancy %Calculation CD38+ NK Cells (%)
FCT23778	T Cell RO (Percent)	Receptor Occupancy %Calculation CD38+ T Cells (%)
FCT23643	T Cell ABS Tube 3	T Cells/ul
FCT23644	T cells (%Lymphocytes) Tube 3	T Cells %Lymphocytes
FCT23698	TSF19+ B Cell ABS Tube 3	CD38+ B Cells/ul
FCT23699	TSF19+ B Cell (%B Cell) Tube 3	CD38+ B Cells %B cells
FCT23744	TSF19+ Grans ABS Tube 3	CD38+ Granulocytes/ul

FCT23745	TSF19+ Grans (%Gran) Tube 3	CD38+ Granulocytes %Granulocytes
FCT23734	TSF19+ Lymph ABS Tube 3	CD38+ Lymphocytes/ul
FCT23735	TSF19+ Lymph (%Lymph) Tube 3	CD38+ Lymphocytes %Lymphocytes
FCT23678	TSF19+ Mono ABS Tube 3	CD38+ Monocytes/ul
FCT23679	TSF19+ Mono (%Mono) Tube 3	CD38+ Monocytes %Monocytes
FCT23688	TSF19+ NK ABS Tube 3	CD38+ NK Cells/ul
FCT23689	TSF19+ NK (%NK) Tube 3	CD38+ NK Cells %NK cells
FCT23648	TSF19+ T Cell ABS Tube 3	CD38+ T Cells/ul
FCT23649	TSF19+ T cells (%T Cells) Tube 3	CD38+ T Cells %T cells
FCT23731	Lymph Tube 3_AF647 MFI	Lymphocytes CD38 Mean MFI
FCT23675	Mono Tube 3_AF647 MFI	Monocytes CD38 Mean MFI
FCT23741	Grans Tube 3_AF647 MFI	Granulocytes CD38 Mean MFI
FCT23751	T Cell Tube 3_AF647 MFI	T Cells CD38 Mean MFI
FCT23685	NK Tube 3_AF647 MFI	NK Cells CD38 Mean MFI
FCT23695	B Cell Tube 3_AF647 MFI	B Cells CD38 Mean MFI
FCT23711	Plasmablast Tube 3_AF647 MFI	Plasmablasts CD38 Mean MFI
FCT23771	CD27++ HLA-DR++ PB Tube 3_AF647 MFI	CD27++ HLA-DR++ PB CD38 Mean MFI
FCT23776	CD27++ HLA-DR-Lo/- PB Tube 3_AF647 MFI	CD27++ HLA-DR-Lo/- PB CD38 Mean MFI
FCT23717	Plasma cell Tube 3_AF647 MFI	Plasma Cells CD38 Mean MFI

STATISTICAL ANALYSIS PLAN APPROVAL FORM

Drug: TAK-079	Protocol Number: TAK-079-1005
Protocol Name:	A Phase 2, Randomized, Placebo-Controlled Study to Evaluate Safety, Tolerability, and Efficacy of TAK-079 in Patients With Generalized Myasthenia Gravis
Statistical Analysis Plan (SAP) Version Number: 2.0	Date: 13 APR 2022

I confirm the final SAP for above noted study and approve the content for submission to the SAP approval team.

Biostatistics Author	[redacted], Ph.D. [redacted] Statistics Rare Disease TAU Statistics
	Print Name and Title
	DocuSigned by: [redacted] Signer Name: [redacted] Signing Reason: I approve this document Signing Time: 14-Apr-2022 | 01:08:44 JST 02A32628C89F40C88A2476724AEC1F31
	Signature and Date (DD/MM/YYYY)

Statistical Analysis Plan Approval by SAP Approval Team Members
I approve the final SAP for the above study as it pertains to my area of expertise.
Note: An approver may delegate the review and approval of this document to an appropriately qualified and clearly identified (by name and title) designee.

SAP Signatory	[redacted] Ph.D. [redacted] Rare Disease TAU Statistics Statistics and Quantitative Sciiences
	Print Name and Title
	DocuSigned by: [redacted] Signer Name: [redacted] Signing Reason: I approve this document Signing Time: 14-Apr-2022 | 01:16:07 JST 68371897F4A94B66BEB9F045DEF271BA
	Signature and Date (DD/MM/YYYY)