Statistical Analysis Plan Addendum I6T-MC-AMBG (1)

# Statistical Analysis Plan for Maximum Extended Enrollment Addendum for I6T-MC-AMBG: A Phase 3, Multicenter, Randomized, Double-Blind, Parallel, Placebo-Controlled Maintenance Study of Mirikizumab in Patients with Moderately to Severely Active Ulcerative Colitis

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# 1. Statistical Analysis Plan for Maximum Extended Enrollment Addendum for I6T-MC-AMBG: A Phase 3, Multicenter, Randomized, Double-Blind, Parallel, Placebo-Controlled Maintenance Study of Mirikizumab in Patients with Moderately to Severely Active Ulcerative Colitis



Mirikizumab (LY3074828) Ulcerative Colitis


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Indianapolis, Indiana USA 46285


Protocol I6T-MC-AMBG
Phase 3

Statistical Analysis Plan Addendum Version 1 electronically signed and approved by Lilly on date provided below.



Approved on 04 Dec 2021 GMT

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# 3. Revision History

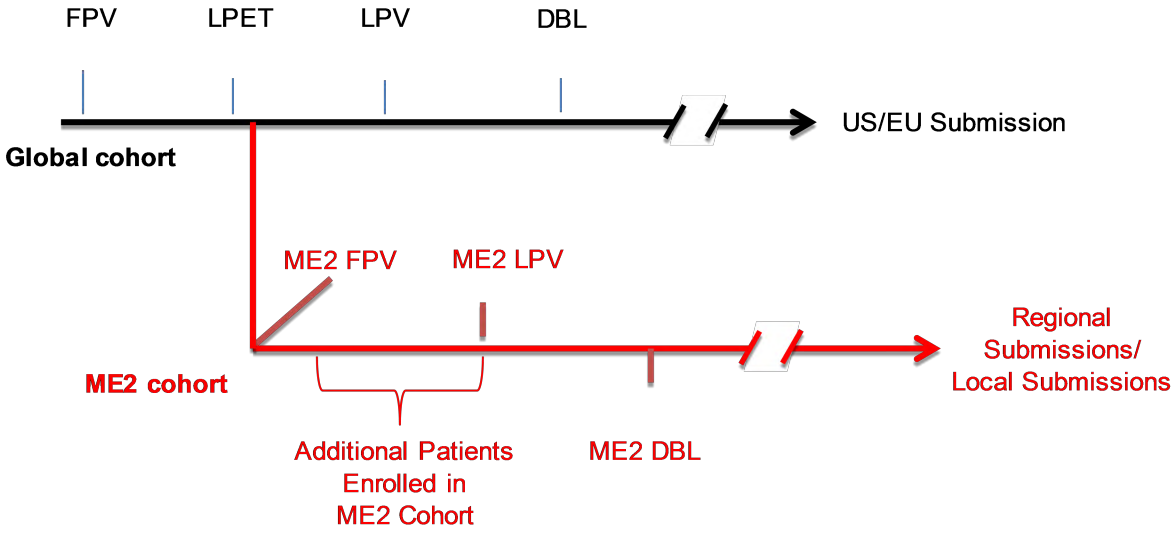
I6T-MC-AMBG (AMBG) ME2 Statistical Analysis Plan (SAP) Addendum Version 1 was approved prior to the Week 40 database lock of patients for Study I6T-MC-AMBG (AMBG) Global cohort.

# 4. Study Design of Protocol Addendum

The detailed rationale and description for the study design of the protocol Maximum Extended Enrollment (ME2) addendum for Study AMBG is described in the Protocol Addendum I6T-MC-AMBG(4).

Once the protocol milestone of last-patient-enters-treatment (LPET) for the Global Cohort is reached, enrollment will continue for those countries participating in the ME2 cohort, if needed, until sufficient numbers of patients are enrolled to meet the regulatory needs for those countries. Enrollment in the Global Cohort from the respective country is required before enrolling patients in the ME2 Cohort from the same country.

Figure AMBG.5.1 shows the milestones for enrollment in Study AMBG (Global Cohort and ME2 Cohort) through global and local submissions.




Abbreviations: DBL = database lock; EU = European Union; FPV = first patient visit; LPET = last patient entered treatment; LPV = last patient visit; ME2 = Maximized Extended Enrollment; US = United States.

**Figure AMBG.5.1. Milestones for Global and ME2 Cohort enrollment through global and local submissions.**

In the countries relevant to the ME2 addendum (i.e., China), in order to enroll in the Global Cohort of Study AMBG, patients must have completed Study I6T-MC-AMAN (AMAN) in the Global Cohort. Similarly, in order to enroll in the ME2 Cohort of Study AMBG, patients must have completed Study AMAN in the AMAN ME2 Cohort. Approximately 184 patients from China (from the primary study cohort and ME2 cohort combined) were planned to be enrolled into Study AMAN. It is expected that approximately 165 patients from China will enroll in AMBG based on a 10% dropout rate.

# 5. A Priori Statistical Methods

## 5.1. General Considerations

As described in the Study AMBG ME2 protocol addendum, the Global Cohort includes all patients who are enrolled for the purpose of primary study Week 40 database lock. The ME2 cohort includes additional patients from sites in China enrolled to meet country-specific sample size requirements. Patients from sites in China who are randomized in Study AMAN on or after the date 28 October 2020 will comprise the China ME2 cohort for Study AMAN. Patients in the China ME2 cohort for AMAN who complete the study and enroll in AMBG will comprise the China ME2 cohort for Study AMBG.

The analyses for the Study AMBG protocol will be conducted on the Global Cohort. The details of the analyses are described in the global AMBG SAP. This China ME2 SAP addendum describes the efficacy and safety analyses based on the China patients, defined as all randomized patients from sites in China for both the Global Cohort and the ME2 cohort. The analysis of this China population will be based upon statistical considerations provided in the global AMBG SAP. The China ME2 SAP addendum will not need to be updated solely to change which subset of tables, figures, and listings will be produced for the China population. Additional displays/analyses may be performed as deemed necessary.

## 5.2. Analysis Methods

All analysis endpoint definitions, data handling, analysis population definitions and statistical analysis methods will be the same as in the global AMBG SAP unless otherwise specified. Descriptive summary statistics such as means and proportions will be reported. Analysis considerations such as those presented in the Global Cohort SAP will be used. For binary efficacy endpoints, the common risk differences (i.e., adjusted for baseline stratification factors) will be estimated. All analyses will be for descriptive purpose only. P-values for between-treatment comparisons may not be displayed for all analysis, and multiplicity adjustment will not be applied.

The analyses of patient disposition, important protocol deviations, patient characteristics, prior and concomitant therapy will be as described in the global AMBG SAP. The efficacy analysis will be as described in the global AMBG SAP, except that country or region will be excluded from the analysis model. The safety analysis will be the same as described in the global AMBG SAP. The subgroup analysis will be as described in global AMBG SAP except that the racial origin, ethnicity, and geographical region will not be included. The sensitivity analysis, if conducted, will be the same as in AMBG SAP. No interim analyses are planned for the patients enrolled in ME2 cohort.

# 6. Unblinding Plan

Patients and site personnel in ME2 sites will remain blinded to the treatment assignment of ME2 patients until the ME2 database lock is conducted. Any information released in the public domain from the AMBG Global Cohort will be available to the investigators and sites in China. Details will be provided in a separate document titled “Blinding and Unblinding Plan for I6T-MC-AMBG.”

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