Statistical Analysis Plan (China) I6T-MC-AMAN

A Phase 3, Multicenter, Randomized, Double-Blind, Parallel, Placebo-Controlled Induction Study of Mirikizumab in Conventional-Failed and Biologic-Failed Patients with Moderately to Severely Active Ulcerative Colitis (LUCENT 1)

NCT03518086

Approval Date: 02-MAR-2021

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

Mirikizumab (LY3074828) Ulcerative Colitis

Study I6T-MC-AMAN is a Phase 3, multicenter, randomized, double-blind, parallel, placebo-controlled induction study of Mirikizumab in conventional-failed and biologic-failed patients with moderately to severely active ulcerative colitis. The study consists of a 12-week induction period where subjects will receive 1 of 2 treatment arms (300-mg mirikizumab or placebo) every 4 weeks.

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Protocol I6T-MC-AMAN
Phase 3

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

Approval Date: 02-Mar-2021 GMT

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3. Revision History

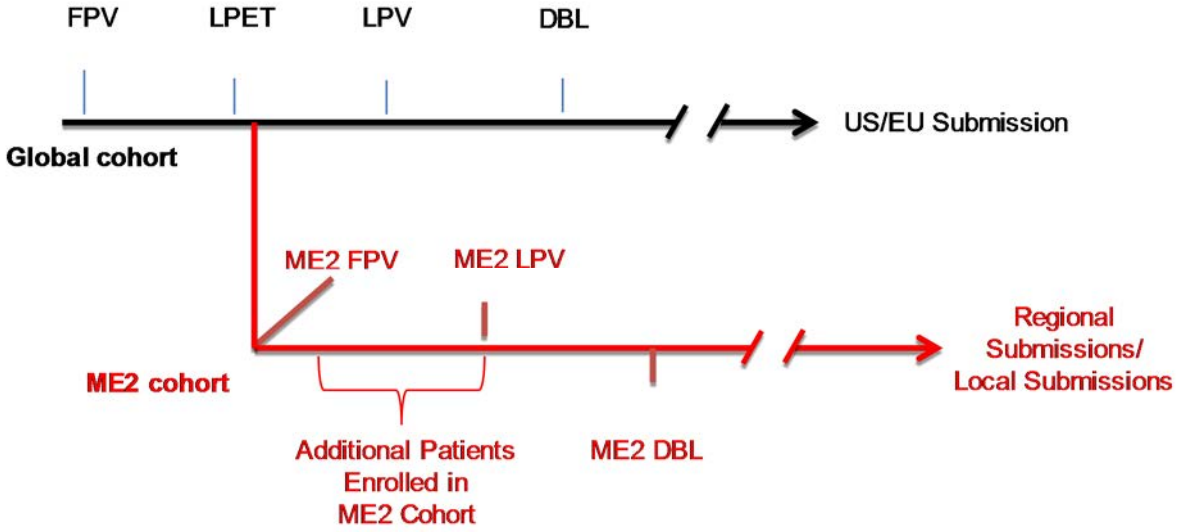
I6T-MC-AMAN (AMAN) ME2 Statistical Analysis Plan (SAP) Addendum Version 1 was approved prior to the Week 12 database lock of patients for Study I6T-MC-AMAN (AMAN) primary study cohort.

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 AMAN is described in the Protocol Addendum I6T-MC-AMAN(5).

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 AMAN.5.1 shows the milestones for enrollment in Study AMAN (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 AMAN.5.1. Milestones for Global and ME2 Cohort enrollment through global and local submissions.

Approximately 184 patients from China (from the primary study cohort and ME2 cohort combined) were planned to be enrolled.

5. A Priori Statistical Methods

5.1. General Considerations

As described in the Study AMAN ME2 protocol addendum, the global cohort includes all patients who are enrolled for the purpose of primary study Week 12 database lock. The ME2 cohort includes additional Chinese patients enrolled to meet country-specific sample size requirements. Patients who are randomized in China on or after the date 28 October 2020 will be considered to be in the China ME2 cohort.

The analyses for the Study AMAN protocol will be conducted on the global cohort. The details of the analyses are described in the global AMAN SAP. This China ME2 SAP addendum describes the efficacy and safety analyses based on the Chinese patients, defined as all randomized patients from sites in China for both the primary study cohort and the ME2 cohort. The analysis of this Chinese population will be based upon statistical considerations provided in the global AMAN 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 AMAN 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 AMAN SAP. The efficacy analysis will be as described in the global AMAN 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 AMAN SAP. The subgroup analysis will be as describe in global AMAN 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 AMAN SAP. No interim analyses are planned for the patients enrolled in ME2 cohort.

6. Unblinding Plan

Patients and site personnel will remain blinded until the ME2 final analysis is conducted, at the addendum completion, prespecified study team members will remain blinded to patient's treatment assignment in the ME2 cohort until the ME2 cohort final database lock. Details will be provided in a separate unblinding plan for Study AMAN, including the global main cohort and ME2 cohort.

Leo Document ID = 6902da51-e4ec-4b54-a0ae-96145c4b2818

Approver: PPD

Approval Date & Time: 02-Mar-2021 00:52:44 GMT

Signature meaning: Approved