AFFIRM-AL STUDY

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A Confirmatory Phase 3, Multicenter, Global, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Birtamimab Plus SoC Compared With Placebo Plus SoC in Patients With Mayo Stage IV AL Amyloidosis[1]

STUDY OVERVIEW

Objective: Evaluate the efficacy and safety of the investigational drug birtamimab with SoC by assessing time to all-cause mortality

Special Protocol Assessment Agreement With FDA: Based on the potential survival benefit from the VITAL study post hoc analysis of Mayo Stage IV patients, the primary endpoint of AFFIRM-AL must achieve a significance level of 0.10

Study Start Date: August 2021

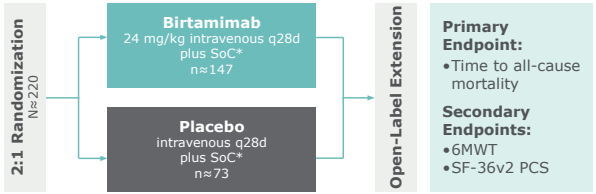
Estimated Enrollment: ≈220 newly diagnosed Mayo Stage IV patients aged ≥18 years with AL amyloidosis

Primary Outcome Measure: Time from the first dose of study drug until the pre-defined number of events (all-cause mortality) have been reached

Key Secondary Outcome Measures:

- Change from baseline to month 9 in 6MWT distance
  - 6MWT assesses cardiopulmonary functioning during exercise by measuring the distance an individual is able to walk over 6 minutes on a hard, flat surface
- Change from baseline to month 9 in SF-36v2 PCS score
  - SF-36v2 is a 36-item self-administered QoL questionnaire that measures health on functional status, wellbeing, and overall evaluation of health. The PCS score of SF-36 is derived primarily from questions regarding physical functioning, physical problems, bodily pain, and general health questions

STUDY DESIGN



*SoC consists of a bortezomib-containing chemotherapy regimen. SoC may also include daratumumab, but daratumumab must be initiated at randomization and not later in the study.[2]

PATIENT ELIGIBILITY

Key Inclusion Criteria:

- Newly diagnosed treatment-naïve AL amyloidosis with cardiac involvement
- Confirmed diagnosis of AL amyloidosis
- Confirmed Mayo Stage IV AL amyloidosis as defined by NT-proBNP ≥1800 pg/mL, troponin T ≥0.025 ng/mL or high sensitivity cardiac troponin T ≥40 ng/L, and dFLC ≥18 mg/dL
- Planned first-line chemotherapy contains bortezomib administered subcutaneously weekly

Key Exclusion Criteria:

- Non-AL amyloidosis
- NT-proBNP >8500 pg/mL
- Meets IMWG definition of MM except for malignancy biomarker of involved/uninvolved serum FLC ratio ≥100
- Patient is eligible for and plans to undergo ASCT or organ transplant during the study

6MWT, 6-minute walk test; AL, light chain; ASCT, autologous stem cell transplant; dFLC, difference in involved and uninvolved serum free light chains; FLC, free light chain; FDA, Food and Drug Administration; IMWG, International Myeloma Working Group; MM, multiple myeloma; NT-proBNP, N-terminal pro-brain natriuretic peptide; PCS, physical component summary; q28d, once every 28 days; QoL, quality of life; SF-36v2, Short Form-36 questionnaire, version 2; SoC, standard of care.

For more information, contact Prothena at 650-837-8550 or medicalinfo@prothena.com.
Birtamimab is an investigational drug and not approved by any regulatory authority.

1. AFFIRM-AL Amyloidosis Study; NCT04973137. Accessed April 2024. https://www.clinicaltrials.gov/study/NCT04973137;
2. Wechalekar AD, et al. *Amyloid.* 2023;30:3-17.

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For more information on the AFFIRM-AL clinical trial, please scan here

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