

Nemtabrutinib in Untreated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: Phase 3 BELLWAVE-011 Study

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Background

- Bruton tyrosine kinase (BTK) inhibitors have significantly improved progression-free survival (PFS) and overall survival (OS) in patients with chronic lymphocytic leukemia (CLL) and small lymphocytic leukemia (SLL). However, resistance can develop, which has been attributed to BTK-C481S and other mutations
- Nemtabrutinib is a reversible noncovalent inhibitor of wild-type and C481S-mutated BTK and has shown promising antitumor activity in patients with CLL/SLL¹
- In the ongoing BELLWAVE-011 trial (NCT06136559), we are evaluating the efficacy and safety of nemtabrutinib compared with investigator's choice of ibrutinib or acalabrutinib in participants with untreated CLL/SLL

Objectives

Primary

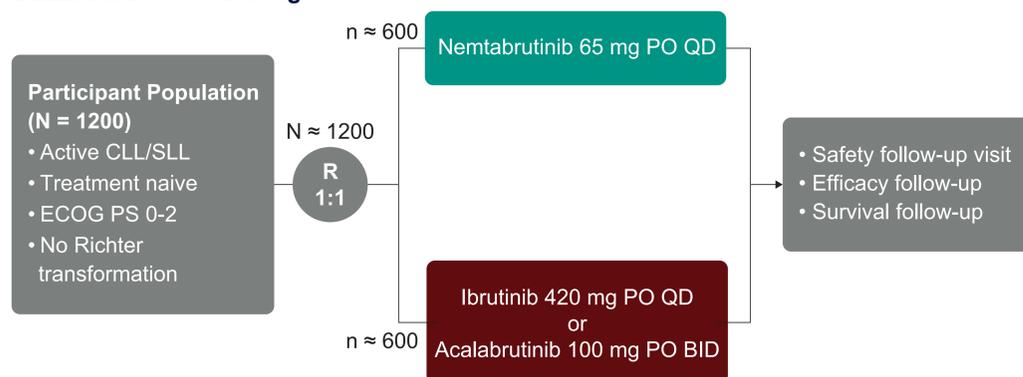
- To evaluate objective response rate (ORR) per the International Workshop on Chronic Lymphocytic Leukemia (iwCLL) 2018 criteria by blinded independent central review (BICR)
- To evaluate PFS per iwCLL 2018 criteria by BICR

Secondary

- To evaluate duration of response (DOR) per iwCLL 2018 criteria by BICR and OS
- To evaluate safety and tolerability

Methods

BELLWAVE-011 trial design



Stratification factors

- TP53 aberration
- Clinical stage
- Investigator's choice of comparator
- Region

BID, twice daily; ECOG PS, Eastern Cooperative Oncology Group performance status; PO, by mouth; QD, once daily; R, randomization.

Participant eligibility criteria

Key inclusion criteria	Key exclusion criteria
<ul style="list-style-type: none"> • Confirmed diagnosis of CLL/SLL with ≥ 1 of the following: <ul style="list-style-type: none"> – Progressive marrow failure or lymphocytosis – Massive, progressive, or symptomatic splenomegaly or lymphadenopathy – Autoimmune complications – Extranodal involvement – Disease-related symptoms • Treatment naive • Provision of blood, bone marrow, and/or a lymph node sample • ECOG PS 0-2 • Adequate organ function 	<ul style="list-style-type: none"> • Diagnosis of Richter transformation or active CNS involvement by CLL/SLL • Clinically significant cardiovascular disease, including the following: <ul style="list-style-type: none"> – Myocardial infarction or unstable angina – New York Heart Association class III or IV congestive heart failure – Clinically significant arrhythmias – QTcF prolongation >450 ms – Second-degree type II or third-degree atrioventricular block • History of severe bleeding disorder • Active second malignant neoplasm

CNS, central nervous system; QTcF, QT corrected for heart rate by the Fridericia cube root formula.

Assessments and follow-up

Assessment	Detail
AEs	<ul style="list-style-type: none"> • AEs will be monitored and assessed by investigators throughout the trial and for 30 days (90 days for serious AEs) after the last dose of trial treatment • Severity will be graded per iwCLL 2018 criteria and NCI CTCAE v5.0
Tumor response	<ul style="list-style-type: none"> • Assessed by imaging, symptom assessment, physical examination, hematologic evaluation, and bone marrow examination (as needed) every 12-24 weeks until disease progression or trial discontinuation

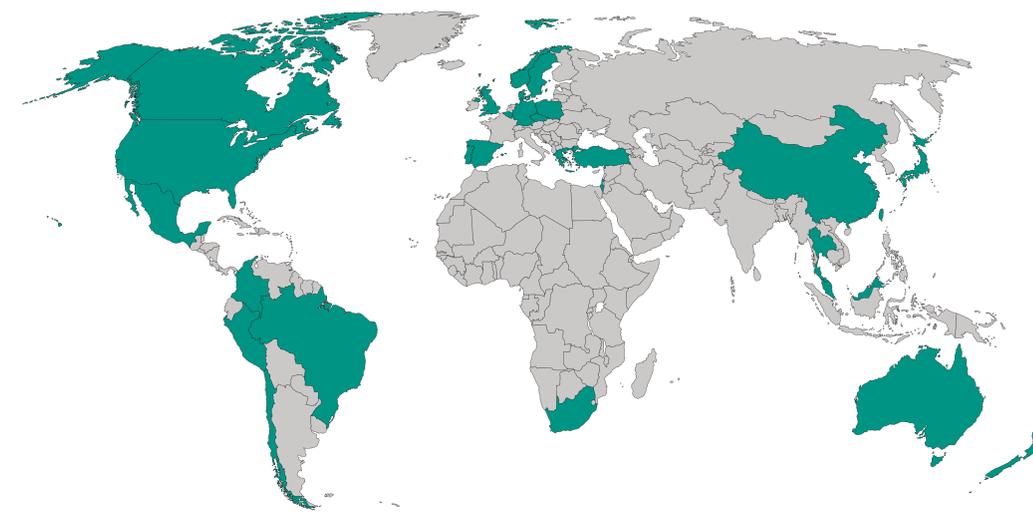
AE, adverse event; NCI CTCAE v5.0, National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0.

Analyses

Analysis	Detail
Efficacy	<ul style="list-style-type: none"> • Safety analyses will be conducted in the all-participants-as-treated population, consisting of all randomly assigned participants who received ≥ 1 dose of trial treatment
Safety	<ul style="list-style-type: none"> • Efficacy analyses will be conducted in the intention-to-treat population of all randomly assigned participants • ORR will be estimated and its 95% CI calculated using the Clopper-Pearson method • OS, PFS, and DOR will be analyzed using the Kaplan-Meier method

Status

Sites of participant enrollment for BELLWAVE-011 (green)



Reference

1. Woyach JA et al. *Cancer Discov.* 2024;14(1):66-75.

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