CLL-414

Phase 3 BELLWAVE-011 Study: Nemtabrutinib Versus Ibrutinib or Acalabrutinib in Previously Untreated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

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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 that has shown promising antitumor activity in patients with CLL/SLL[1]
- In the ongoing BELLWAVE-011 trial (NCT06136559), we evaluate the efficacy and safety of nemtabrutinib compared to investigator's choice of ibrutinib or acalabrutinib in patients with untreated CLL/SLL

Objectives

Primary

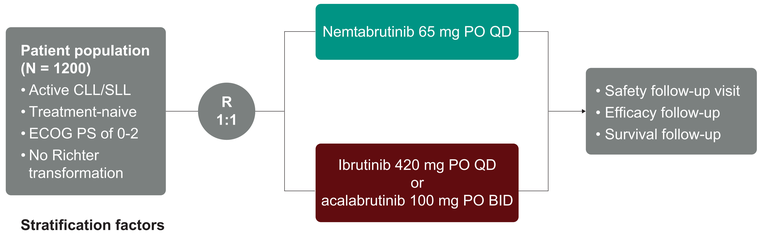
- To evaluate objective response rate (ORR) per the International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria 2018 by blinded independent central review (BICR)
- To evaluate PFS per iwCLL criteria 2018 by BICR

Secondary

- To evaluate duration of response (DOR) per iwCLL criteria 2018 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.

Patient eligibility criteria

Key inclusion criteria	Key exclusion criteria
• Confirmed diagnosis of CLL/SLL with at least 1 of the following – 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 of 0-2 • Adequate organ function	• Diagnosis of Richter transformation or active CNS involvement by CLL/SLL • Clinically significant cardiovascular disease, including – 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 AV block • History of severe bleeding disorder • Active second malignancy

AV, atrioventricular; CNS, central nervous system; QTcF, QT corrected for heart rate by Fridericia's cube root formula.

Assessments and follow-up

Assessment	Detail
AEs	• AEs will be monitored and assessed by investigators throughout the trial and for 30 days (90 days for serious adverse events) after the last dose of trial treatment • Severity will be graded per iwCLL criteria 2018 and NCI CTCAE v5.0
Tumor response	• Assessed by imaging, symptom assessment, physical examination, hematological evaluation, and bone marrow exam (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.

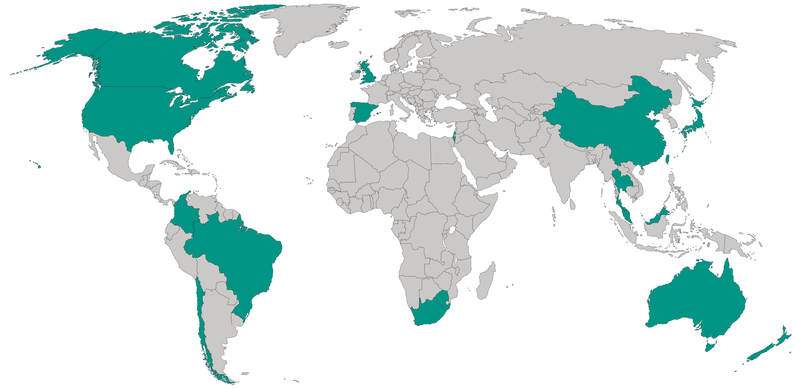
Analyses

Analysis	Detail
Efficacy	• Safety analyses will be conducted in the APaT population, consisting of all randomly assigned patients who received ≥1 dose of trial treatment
Safety	• Efficacy analyses will be conducted in the ITT population of all randomly assigned patients • 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

APaT, all-patients-as-treated; ITT, intent-to-treat.

Status

- BELLWAVE-011 will be enrolling at sites in Australia, Brazil, Canada, Chile, China, Columbia, the European Union, Israel, Japan, Malaysia, New Zealand, South Africa, Taiwan, Thailand, the United Kingdom, and the United States



References

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

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