

P-1512

The Efficacy and Safety of Pirtobrutinib in Patients with CLL/SLL: A Phase 2 Dose Optimization Trial in Progress



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OBJECTIVES

PART 1- Dose Optimization

- To evaluate the efficacy and safety of 3 different dosages of pirtobrutinib in a 1-3 prior line and post-cBTKi CLL/SLL population that better reflects current treatment patterns

PART 2- Treatment-naïve Cohort

- To evaluate the efficacy and safety of pirtobrutinib in patients with CLL/SLL who are treatment-naïve with del(17p)

BACKGROUND

- Covalent Bruton tyrosine kinase inhibitors (cBTKi) have significantly improved the outcomes for patients with chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL)
- However, resistance and intolerance to these agents are common, limiting the duration of treatment, and resulting in poorer outcomes after cBTKi failure
- Pirtobrutinib, a highly selective, non-covalent BTKi, demonstrated clinically meaningful efficacy and a favorable safety profile amongst patients who had received a prior cBTKi in the pivotal 1/2 BRUIN study (LOXO-BTK-18001, NCT03740529), leading to FDA accelerated approval for adults with CLL/SLL after at least two prior lines of therapy including a BTK inhibitor and a BCL-2 inhibitor
- Pirtobrutinib exhibited efficacy across a wide range of doses (25-300 mg daily), with no dose-limiting toxicities. The efficacy and safety were confirmed in a randomized phase 3 study (BRUIN CLL-321, NCT04666038) in patients with relapsed/refractory CLL/SLL
- However, most data reflect later-line use, and relatively few patients received doses below the recommended dose of 200 mg. This has prompted further evaluation of lower doses in earlier lines of treatment to determine if there is an improved safety profile without compromising efficacy
- Additionally, enrollment of patients with treatment-naïve CLL with del(17p) will further our clinical understanding of pirtobrutinib activity in this patient population and fill an important clinical gap

STUDY DESIGN

This is an ongoing, randomized, open-label, phase 2 study (NCT06588478)

PART 1

PART 1- Key Inclusion Criteria

- 1-3 lines of prior treatment including cBTKi
- Known 17p deletion status

PARTS 1+2- Common Eligibility Criteria

- Confirmed diagnosis of CLL/SLL per iwCLL 2018¹
- Require treatment per iwCLL 2018¹
- ECOG PS of 0-2
- No CNS involvement by CLL/SLL
- No Prior Richter's transformation
- No history of allogeneic transplant
- No history of autologous stem cell transplant or chimeric antigen receptor T-cell therapy within 90 days

PART 2

PART 2- Key Inclusion Criteria

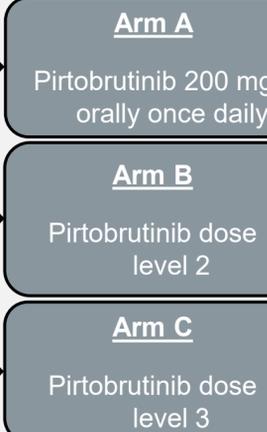
- No prior treatment for CLL/SLL
- 17p deletion positive status

Stratification Factors:

- del(17p) status (present/absent)
- 1 vs 2-3 lines of prior treatment

Randomization 1:1:1

N= ~249



N ≤ 100

Pirtobrutinib 200 mg orally once daily

For Part 1 and 2, 28-day cycles until discontinuation criteria are met, including disease progression, withdrawal of consent, receipt of subsequent anticancer therapy, the investigator deems it necessary for safety reasons, or criteria are met for the end of the study

STUDY ENDPOINTS

PART 1

Primary

Investigator-assessed ORR per iwCLL 2018¹

Secondary

Investigator-assessed DOR
Incidence of ≥ Grade 3 adverse events of special interest
Additional safety outcomes, including:

- ≥ Grade 3 treatment-emergent adverse events
- Serious adverse events
- Treatment discontinuations and dose modifications due to adverse events

Exploratory

Progression-free survival
Overall survival
Biomarker assessment
Pharmacokinetics of pirtobrutinib

PART 2

Primary

ORR as assessed by IRC per iwCLL 2018¹

Secondary

ORR as assessed by Investigator per iwCLL 2018¹
DOR as assessed by IRC and Investigator
Safety and tolerability, Including, but not limited to:

- Grade ≥3 TEAEs
- SAEs
- Deaths, and
- Laboratory abnormalities per NCI CTCAE v5.

Exploratory

ORR and DOR including partial remission with lymphocytosis by IRC and Investigator
Progression-free survival
Overall survival

STUDY SITES

136 sites in 18 countries



References:

1. Hallek M, Cheson BD, Catovsky D, et al. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. Blood. 2018;131(25):2745-2760. doi:10.1182/blood-2017-09-806398

Abbreviations:

DOR= Duration of response is defined as the time from the date of the first documented complete remission (CR), complete remission with incomplete hematologic recovery (CRI), nodular partial remission (nPR), or partial remission (PR) to disease progression (per iwCLL 2018) or death from any cause; ECOG PS= Eastern Cooperative Oncology Group Performance Status; IRC= Independent Review Committee; ORR= Overall response rate, defined as the proportion of participants who achieve a best overall response of CR, CRI, nPR, or PR at or before the initiation of subsequent anticancer therapy

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