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BRUIN CLL-314: A Phase 3, Open-Label, Randomized Study of Pirtobrutinib versus Ibrutinib in Patients with Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (Trial in Progress)

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Background

- Covalent (c) Bruton tyrosine kinase inhibitors (BTKi) have transformed the management of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), but these agents are not curative
- cBTKi have low oral bioavailability and a short half-life, which may lead to suboptimal BTK target coverage, especially in rapidly proliferating tumors with high BTK protein turnover
- Pirtobrutinib, a highly selective, non-covalent (reversible) Bruton tyrosine kinase inhibitor (BTKi), inhibits both wildtype and C481-mutant BTK with equal low nM potency, and has favorable oral pharmacology that enables continuous BTK inhibition throughout the dosing interval regardless of intrinsic rate of BTK turnover
- In the phase 1/2 BRUIN study, pirtobrutinib demonstrated promising overall response rates and progression-free survival, and was well tolerated in patients with pre-treated chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) regardless of prior therapy (including cBTKi), number of prior lines of therapy, BTK C481 mutation status, or reason for prior cBTKi discontinuation[1]
- The objective of this study is to compare efficacy and tolerability of pirtobrutinib versus ibrutinib in patients with CLL/SLL

Study Design

BRUIN CLL-314 is a Randomized, Open-Label, Global, Phase 3 Study (NCT05254743)

N~650

Key Inclusion Criteria

- Confirmed diagnosis of CLL/SLL with requirements for therapy (as defined by iwCLL 2018[2] criteria)
- Treatment naïve (up to 30%) or pretreated with non-BTKi therapy
- ≥18 years of age and ECOG 0–2

1:1 Randomization

Arm A
Pirtobrutinib 200 mg orally once daily

Arm B
Ibrutinib 420 mg orally once daily

Stratification factors

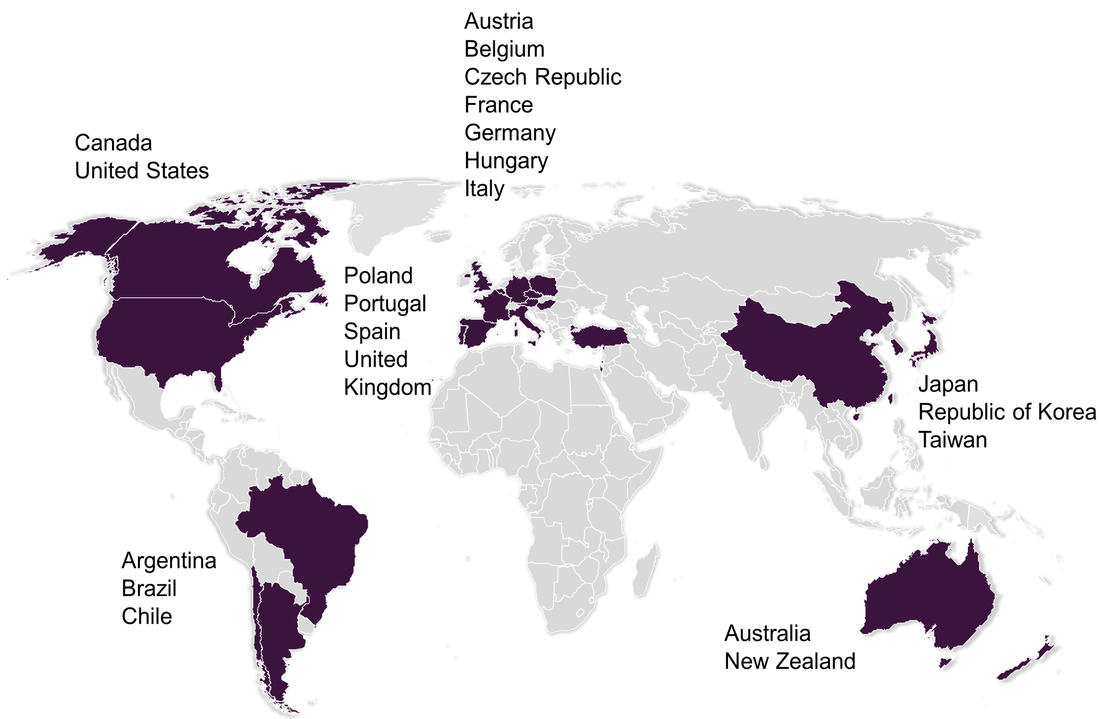
- 17p deletion (present vs not present)
- Number of prior lines of therapy (0 vs 1 vs ≥2)

28-day continuous cycles, until progressive disease or unacceptable toxicity

Study Endpoints

- **Primary**
  - To establish non-inferiority of pirtobrutinib versus ibrutinib by comparing the overall response rate per iwCLL 2018[2] criteria as assessed by IRC
- **Key Secondary**
  - To determine the superiority of pirtobrutinib versus ibrutinib with respect to IRC-assessed event-free survival and progression-free survival
- **Other Secondary**
  - To assess the overall survival at the time of the final analysis
  - To determine duration of response and time to next treatment, as assessed by investigator
  - To evaluate serious adverse events, adverse events, and patient-reported outcomes

Study Sites



Key Exclusion Criteria

- Prior exposure to any BTKi
- Use of warfarin or other vitamin K antagonists
- Recent myocardial infarction or Grade ≥3 heart failure
- Active infection

Abbreviations: 17p deletion, deletion of the short arm of chromosome 17; ECOG, Eastern Cooperative Oncology Group; IRC, Independent Review Committee; iwCLL, International Workshop on Chronic Lymphocytic Leukemia.

Trial Progress Update

- Enrollment is ongoing for previously treated patients
- Enrollment is complete for treatment-naïve patients

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References

1. Mato A, et al. *Lancet.* 2021;397:892–901.
2. Hallek M, et al. *Blood.* 2018;131(25): 2745-2760.

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