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BRUIN CLL-313: A Phase 3 Open-Label, Randomized Study of Pirtobrutinib Versus Bendamustine Plus Rituximab in Untreated Patients With Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (Trial in Progress)

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Background

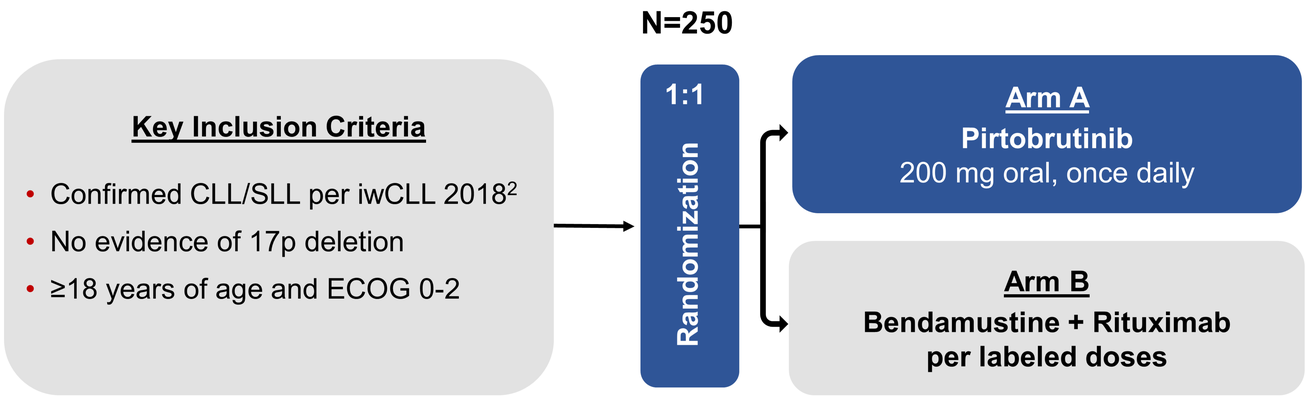
- Covalent Bruton's Tyrosine Kinase inhibitors (BTKi) have transformed the management of patients with CLL/SLL. However, many patients still receive bendamustine + rituximab as first-line therapy
- Covalent BTKi share pharmacologic liabilities, such as low oral bioavailability and short half-life. Collectively, this may lead to suboptimal BTK target coverage, especially in rapidly proliferating tumors with high BTK protein turnover such as accelerating CLL/SLL and acquired resistance in some patients
- Pirtobrutinib is a highly potent and selective, non-covalent (reversible) BTKi that inhibits both wild type and C481-mutated BTK with equal low nM potency
- In the phase 1/2 BRUIN study, pirtobrutinib achieved pharmacokinetic exposures that exceeded its BTK IC_{96} at trough, was well tolerated and demonstrated promising efficacy in CLL/SLL patients regardless of prior therapy, number of prior lines of therapy, or BTK C481 mutation status[1]

Key Exclusion Criteria

- Prior systemic therapy for CLL/SLL
- Richter's Transformation to DLBCL, prolymphocytic leukemia or Hodgkin lymphoma any time pre-enrollment
- Active second malignancy
- CNS involvement by CLL/SLL
- Significant cardiovascular disease

Study Design

BRUIN CLL-313 is a randomized, open-label, global phase 3 study (NCT05023980)



Stratification factors
- Status of IGHV mutation (mutated vs unmutated)
- Rai stage (low / intermediate vs high)

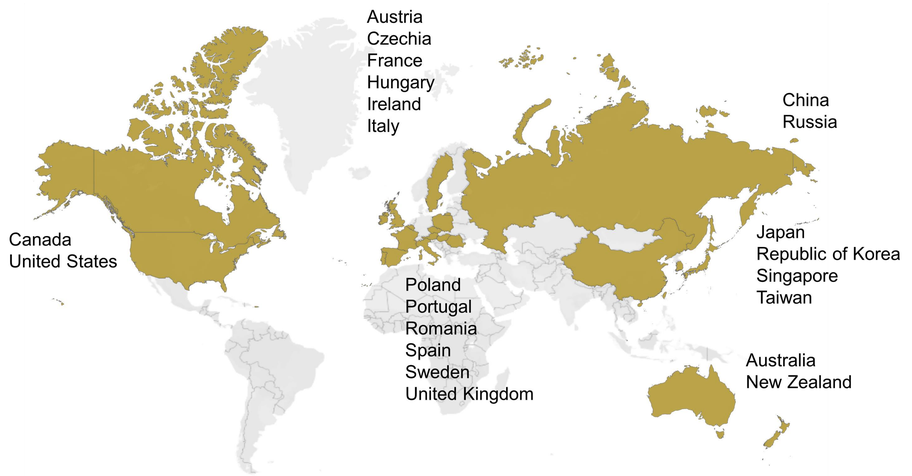
- Patients in Arm B who have PD, as assessed by IRC, are allowed to crossover to Arm A

Study Endpoints

Primary Endpoint
- PFS per iwCLL 2018[2], as assessed by Independent Review Committee (IRC)

Secondary Endpoints
- PFS, as assessed by investigator
- ORR, DoR, as assessed by investigator and IRC
- OS, TTNT, as assessed by investigator
- SAEs, AEs per CTCAE v5.0
- Patient reported outcomes

Study Sites



References

1. Mato et al. *Lancet* 2021;397 (10277):892-901.
2. Hallek, M, et al. *Blood* 2018;131(25): 2745-2760.

Abbreviations: DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; IGHV, immunoglobulin heavy chain variable region; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; TTNT, time to next treatment

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