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BRUIN CLL-321: A Phase 3 Open-Label, Randomized Study of Pirtobrutinib Versus Investigator's Choice of Idelalisib Plus Rituximab or Bendamustine Plus Rituximab in BTK Inhibitor Pretreated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (Trial in Progress)

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BRUIN CLL-321 CLINICAL TRIAL

Background

- Covalent Bruton's Tyrosine Kinase inhibitors (BTKi) have transformed the management of patients with CLL/SLL. However, these treatments are not curative and many patients will require additional treatment
- Covalent BTKi share pharmacologic liabilities (e.g. low oral bioavailability and short half-life) that collectively may lead to suboptimal BTK target coverage, especially in rapidly proliferating tumors with high BTK protein turnover such as CLL/SLL
- 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]

Study Design

BRUIN CLL-321 is a randomized, open-label, global phase 3 study (NCT04666038)

N=250

Key Inclusion Criteria

- Confirmed CLL/SLL per iwCLL 2018[2]
- Prior therapy with covalent BTKi
- Known 17p status
  - If 17p status is unknown, local or central FISH test results during screening can be used
- ≥18 years of age and ECOG 0-2

1:1 Randomization

Arm A
Pirtobrutinib
200 mg oral, once daily

Arm B
Investigator's Choice of Idelalisib / Rituximab, or Bendamustine / Rituximab per labeled doses

Stratification factors

- 17p deletion (yes/no)
- Prior venetoclax treatment (yes/no)

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

Key Exclusion Criteria

- Richter's Transformation to DLBCL, prolymphocytic leukemia or Hodgkin lymphoma any time pre-enrollment
- Major bleeding event on prior covalent BTKi
- History of allogeneic stem cell transplant or autologous stem cell transplant or CAR T-cell therapy within 60 days of randomization
- CNS involvement by CLL/SLL
- Significant cardiovascular disease

Study Endpoints

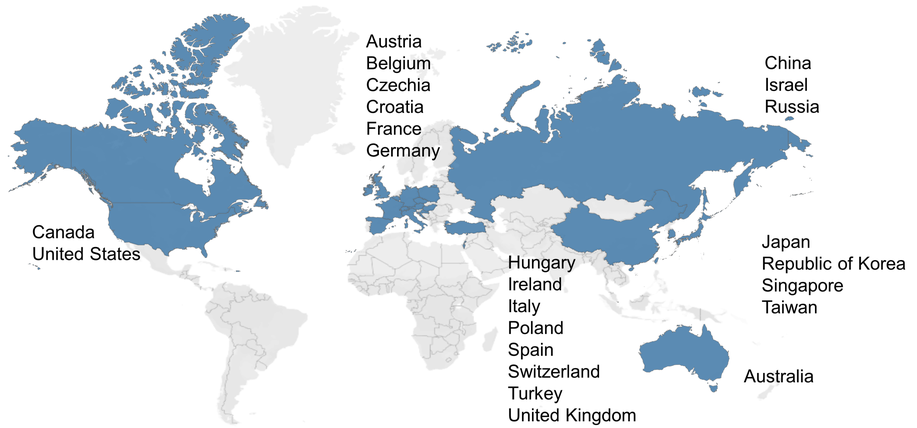
Primary Endpoint

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

Secondary Endpoints

- PFS, as assessed by investigator
- ORR, DoR, as assessed by investigator and IRC
- OS, TTNT, EFS, 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: DoR, duration of response; EFS, event-free survival; IC, inhibitory concentration; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; QD, once daily; TTNT, time to next treatment

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