Poster # CLL-116

BRUIN CLL-322: A Phase 3 Open-Label, Randomized Study of Fixed Duration Pirtobrutinib Plus Venetoclax and Rituximab Versus Venetoclax and Rituximab in Previously Treated 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, these treatments are not curative, and many patients will require additional treatment
- The MURANO trial established the time-limited combination of 2 years venetoclax plus rituximab as a clinically important regimen for patients with R/R CLL/SLL.[1] However, the trial almost exclusively enrolled patients who were BTKi naive, a population less relevant in the context of today's standard of care
- 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[2]
- Adding pirtobrutinib to the time-limited MURANO regimen may allow for deeper and more prolonged disease control in BTK-pretreated CLL/SLL patients

Study Design

BRUIN CLL-322 is a randomized, open-label, global phase 3 study (NCT04965493)

Key Inclusion Criteria

- Confirmed CLL/SLL per iwCLL 2018[3]
- Previously treated CLL/SLL (including a covalent BTKi or covalent BTKi naïve [limited to 20% of total enrollment])
- Known 17p status
  - If 17p status is unknown, local or central FISH test results during screening can be used
- No prior venetoclax
- ≥18 years of age and ECOG 0-2

N=600

1:1 Randomization

Arm A (PVR)
Pirtobrutinib + Venetoclax + Rituximab
- Pirtobrutinib, 200 mg oral, once daily from C1D1 - C28
- Rituximab, IV, 375 mg/m² on C1D1
  500 mg/m² on D1 of C2-C6
- Venetoclax, oral, daily from C5 - C28: 400 mg
  • Dose Ramp (5 weeks) from C4D1: 20-400 mg

Arm B (VR)
Venetoclax + Rituximab
- Rituximab, IV, 375 mg/m² on C2D1
  500 mg/m² on D1 of C3-C7
- Venetoclax, oral, daily from C2 - C25: 400 mg
  • Dose Ramp (5 weeks) from C1D1: 20-400 mg

Each cycle is 28 days; C1 of Arm B is 35 days

Stratification factors
- 17p status (deleted/wildtype)
- Prior experience of BTKi (discontinuation due to PD or other vs no prior BTKi)

Key Exclusion Criteria

- Richter 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
- Active second malignancy
- CNS involvement by CLL/SLL

Study Endpoints

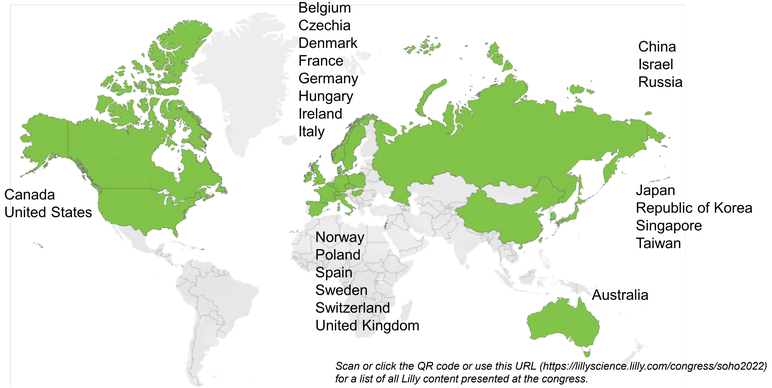
Primary Endpoint

- PFS per iwCLL 2018[3], as assessed by Independent Review Committee (IRC)

Secondary Endpoints

- PFS, as assessed by investigator
- ORR, 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. Seymour, et al. *N Engl J Med* 2018;378:1107-1120
2. Mato, et al. *Lancet* 2021;397 (10277):892-901
3. Hallek, et al. *Blood* 2018;131(25): 2745-2760

Abbreviations: AEs, adverse events; EFS, event-free survival; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; SAE, serious adverse events; TTNT, time to next treatment

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