

Pirtobrutinib in Richter Transformation: Updated Efficacy and Safety Results With 18-Month Median Survival Follow-up From the Phase 1/2 BRUIN Study

WG Wierda, NN Shah, CY Cheah, D Lewis, MS Hoffman, CC Coombs, N Lamanna, S Ma, D Jagadeesh, T Munir, Y Wang, TA Eyre, J Rhodes, M McKinney, E Lech-Maranda, CS Tam, W Jurczak, K Izutsu, A Alencar, MR Patel, JF Seymour, JA Woyach, LE Roeker, PA Thompson, P Abada, C Ho, SC McNeely, N Marella, B Nguyen, C Wang, AS Ruppert, B Nair, H Liu, DE Tsai, P Ghia

Background

Richter transformation (RT) occurs in up to 10% of patients with CLL and is associated with **poor outcomes** and **limited success with cBTKi**



Pirtobrutinib is an oral, highly potent and selective, **non-covalent** (reversible) BTKi with sustained **BTK** inhibition throughout the dosing interval



An **updated analysis** of the phase 1/2 BRUIN study examined the efficacy and safety of **pirtobrutinib in patients with R/R CLL and RT**


Study design


The phase 1/2 BRUIN study examined the **efficacy** and **safety** of pirtobrutinib in 778 patients with previously treated CLL, MCL, and other B-cell NHLs

82 patients with **RT**, 74 of whom received **prior RT-directed therapy**, were evaluated for **efficacy** and **safety**

Patient characteristics in patients with RT (n=82)

- Median age was 67 years
- 67% of patients were male
- Median of 4 prior lines of therapy for CLL (2) and RT (2)

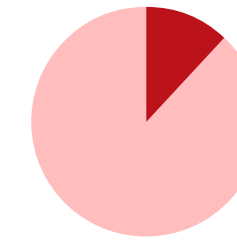
 **74%** of patients were previously treated with **cBTKi**

 **68%** of patients were previously treated with **BCL2i**

Efficacy results

Median PFS was **3.7 months** in patients with RT (n=82)

The **24-month PFS** rate was **12.6%**



Median OS was **12.5 months**

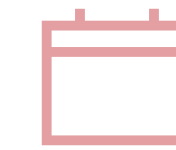
ORR was **50.0%** and **consistent across subgroups** (including high risk factors and prior CLL/RT therapy)

Median DOR was **7.4 months**



Among the 21 patients with matched samples available for clonality assessment, similar efficacy was observed in patients with clonally related (n=18) and clonally unrelated (n=3) RT

Safety results



Median time on treatment was **3.6 months** in patients with RT (n=82)

No treatment-related AEs leading to pirtobrutinib discontinuation; **3.7%** of patients had a **dose reduction** due to **treatment-related AEs**

Treatment-emergent **adverse events** (any grade; ≥15%)

Neutropenia ^a	Fatigue	Contusion	Diarrhea
29.3%	24.4%	18.3%	18.3%
Dyspnea	Platelet count decreased	Pyrexia	Cough
18.3%	18.3%	18.3%	15.9%

Adverse events of interest^b (grade ≥3; all cause)

Infections ^c	Hypertension	Atrial fibrillation/flutter ^d	Hemorrhage ^e	Rash ^f
25.6%	2.4%	1.2%	1.2%	1.2%

Summary

With a median survival follow-up of 18 months, pirtobrutinib **demonstrated promising efficacy** in patients with RT who have been heavily pretreated, a population with **historically poor overall survival**



Pirtobrutinib demonstrated **promising and consistent efficacy** across subgroups in patients with RT



Pirtobrutinib was **well tolerated** with **no discontinuations** due to drug-related toxicity

AE, adverse event; BCL2i, B-cell lymphoma 2 inhibitor; BTK, Bruton tyrosine kinase; BTKi, Bruton tyrosine kinase inhibitor; cBTKi, covalent Bruton tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; DOR, duration of response; MCL, mantle cell lymphoma; NHL, non-Hodgkin lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed/refractory.

^aAggregate of neutropenia and neutrophil count decreased. ^bAEs of interest are those that were previously associated with covalent BTKis regardless of occurrence rate. ^cAggregate of all preferred terms including infection and COVID-19. ^dAggregate of atrial fibrillation and atrial flutter. ^eAggregate of all preferred terms including hemorrhage or hematoma. ^fAggregate of all preferred terms including rash.

Infographic by Lilly using data from the presentation at the American Society of Hematology 65th Annual Meeting; San Diego, CA; December 9-12, 2023. Poster #1737.