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

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## 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] **29.3%** | Fatigue **24.4%** | Contusion **18.3%** | Diarrhea **18.3%** |
| Dyspnea **18.3%** | Platelet count decreased **18.3%** | Pyrexia **18.3%** | Cough **15.9%** |

**Adverse events of interest**[b] (grade ≥3; all cause)

| | | | | |
|---|---|---|---|---|
| Infections[c] **25.6%** | Hypertension **2.4%** | Atrial fibrillation/ flutter[d] **1.2%** | Hemorrhage[e] **1.2%** | Rash[f] **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.

[a]Aggregate of neutropenia and neutrophil count decreased. [b]AEs of interest are those that were previously associated with covalent BTKis regardless of occurrence rate. [c]Aggregate of all preferred terms including infection and COVID-19. [d]Aggregate of atrial fibrillation and atrial flutter. [e]Aggregate of all preferred terms including hemorrhage or hematoma. [f]Aggregate 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.*