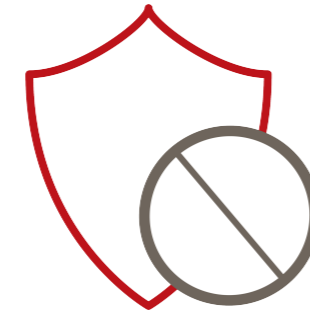


Pirtobrutinib in Post-cBTKi CLL/SLL: ~30 Months Follow-Up and Subgroup Analysis With/Without Prior BCL2i From the Phase 1/2 BRUIN Study

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Background

There are limited prospective data and treatment options in the post-cBTKi setting



Pirtobrutinib is an oral, highly potent and selective, non-covalent (reversible) BTK inhibitor 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 post-cBTKi CLL with a median 30-month follow-up

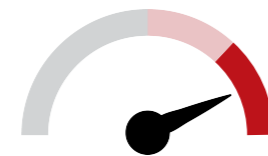
Study design

The BRUIN phase 1/2 study examined the **efficacy** and **safety** of pirtobrutinib in 778 patients with previously treated CLL or other B-cell non-Hodgkin lymphoma

282 patients with **cBTKi pretreated CLL** were evaluated for **efficacy** and **safety**

Patient characteristics

Patients were generally considered **high risk** and were **heavily pretreated** (median of 4 prior lines of therapy)



BTK C481 mutations in 96/245 (39%)



17p deletion and/or TP53 mutation in 104/217 (48%)



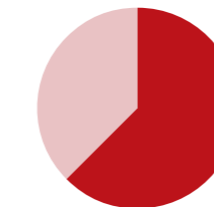
IGHV unmutated in 193/225 (86%)



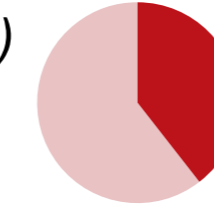
Efficacy results

Patients with prior cBTKi (n=282) had a median **PFS** of **19.4 months** and an **18-month PFS rate** of **52.8%**

Patients naïve to BCL2i (n=154)
Median PFS: 23.0 months
18-month PFS rate: 62.5%



Patients exposed to BCL2i (n=128)
Median PFS: 15.9 months
18-month PFS rate: 39.6%



Median OS was not reached. 18-month OS rates showed similar trends as PFS for BCL2i-naïve and exposed patients. In contrast, overall response rate was consistent, regardless of prior BCL2i exposure

Safety results



Median time on treatment for the CLL population with prior cBTKi was **18.7 months**

7 patients (2.5%) **permanently discontinued** due to treatment-related adverse events

Treatment-emergent adverse events (any grade; ≥20%)

Fatigue	Neutropenia ^a	Diarrhea	Cough	Contusion
36.9%	34.4%	28.4%	27.3%	26.2%
COVID-19	Dyspnea	Nausea	Abdominal pain	
25.9%	22.3%	22.0%	21.3%	

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

Infections ^b	Hemorrhage ^c	Hypertension
30.9%	2.1%	4.3%
Atrial fibrillation/flutter ^d	Arthralgia	Rash ^e
1.8%	1.4%	1.1%

Summary

With a median follow-up of 30 months, pirtobrutinib continues to show **clinically meaningful and durable efficacy** in heavily pretreated patients with CLL/SLL post-covalent BTKi



Longer PFS was observed in **patients naïve to a BCL2i** than in **patients exposed to a BCL2i**



Low rates of discontinuation due to drug-related toxicity