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

BCL2i, B-cell leukemia/lymphoma 2 inhibitor; BTK, Bruton tyrosine kinase; cBTKi, covalent Bruton tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; IGHV, immunoglobulin heavy chain variable region gene; OS, overall survival; PFS, progression-free survival; SLL, small lymphocytic lymphoma; TP53, tumor protein p53. [a]Aggregate of neutropenia and neutrophil count decreased. [b]Aggregate of all preferred terms including infection and COVID-19. [c]Aggregate of all preferred terms including hemorrhage or hematoma. [d]Aggregate of atrial fibrillation and atrial flutter. [e]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. Abstract 325.