Efficacy of Pirtobrutinib, a Highly Selective, Non-Covalent (Reversible) BTK Inhibitor in Relapsed / Refractory Waldenström Macroglobulinemia: Results from the Phase 1/2 BRUIN Study*

Background

Many patients with **Waldenström macroglobulinemia** (WM) face limited therapeutic options and poor outcomes following cBTKi treatment due to disease progression and intolerance

Pirtobrutinib is a highly selective, **non-covalent (reversible) BTKi** with sustained inhibition throughout the dosing interval

Pirtobrutinib has demonstrated **efficacy** in various **B-cell malignancy patients who have failed prior therapies, including prior BTKi**

Study design

The BRUIN Phase 1/2 study set out to determine the **efficacy** and **safety** of pirtobrutinib in adults with B-cell malignancies, including patients with WM

Patients

- Prior therapy
  - Prior cBTKi (n=63)
  - cBTKi Naïve (n=17)
  - CIT + cBTKi (n=50)
- Safety was assessed in all BRUIN Phase 1/2 patients (n=773)

Prior cBTKi patients:

- Majority male: n=42 (67%)
- Median age: 69
- Reason for discontinuing any prior BTK inhibitor: progressive disease (n=41, 65%)
- MYD88 genotype: negative (n=7) / positive (n=52)*

Efficacy results

Major response rate

CR + VGPR rate

Median progression-free survival for prior cBTKi patients was 19.4 months

- Median follow-up was 14 months

Median overall survival was not estimable

- Median follow-up was 16 months

55.6% (35/63) of patients who received prior cBTKi **remain on pirtobrutinib**

Safety results

Median time on treatment for the overall population (n=773) was **9.6 months**

Discontinuations due to TRAEs occurred in **2.6%** (n=20) of overall patients

Dose reductions due to TRAEs occurred in **4.5%** (n=35) of overall patients

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

Fatigue	Diarrhea	Neutropenia	Bruising
28.7%	24.2%	24.2%	23.7%

Overall and **WM** safety profiles are **generally consistent**

Summary

Pirtobrutinib demonstrated **efficacy** in patients with **heavily pretreated relapsed/refractory WM**, including patients who received prior CIT and cBTKi

Patients with prior **cBTKi** showed notable **depth of response**, as indicated by **favorable VGPR rate**

Pirtobrutinib showed **low rates of discontinuation** due to drug-related toxicity

BTKi: Bruton's tyrosine kinase inhibitor; cBTKi: covalent BTKi; CIT: chemoimmunotherapy; CR: complete response; TRAE: treatment-related adverse event; VGPR: very good partial response; WM: Waldenström macroglobulinemia *Data was missing for 4 prior cBTKi patients. Data cutoff date: 29 July 2022

*Infographic by Lilly using data from the presentation at the European Hematology Association (EHA) meeting; Frankfurt, Germany & virtual; June 8-11, 2023; Abstract# P1108; M.L. Palomba, M.R. Patel, T.A. Eyre, W. Jurczak, D. Lewis, T. Gastinne, S. Ma, J.B. Cohen, K. Patel, J.R. Brown, L. Scarfò, T. Munir, E. Lech-Maranda, M.S. Hoffmann, C.S. Ujjani, B. Fakhri, M. Wang, K. Izutsu, H. Nagai, C.S. Tam, J.M. Rhodes, J. Vose, M. McKinney, J.N. Gerson, M.A. Barve, B. Kuss, Y. Koh, J.F. Seymour, W. Gao, A.S. Ruppert, R.A. Walgren, D.E. Tsai, B. Nair, K. Bao, A.R. Mato, C.Y. Cheah