Pirtobrutinib in Relapsed/Refractory Mantle Cell Lymphoma Patients With Prior cBTKi: Updated Safety and Efficacy, Including High-Risk Subgroup Analyses From the Phase 1/2 BRUIN Study

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Background

Although **cBTKi**'s are effective against **MCL**, resistance (which is poorly understood) often develops, resulting in an **unmet need post cBTKi**

Pirtobrutinib is a highly selective, **noncovalent (reversible) BTKi** with accelerated approval in the United States to treat R/R MCL following at least 2 lines of prior therapy, including **prior cBTKi**

An **updated analysis** of the phase 1/2 BRUIN study examined the efficacy and safety of pirtobrutinib in patients with R/R MCL with a median survival follow-up time of 2 years

Study design

The phase 1/2 BRUIN study examined the **efficacy** and **safety** of pirtobrutinib in patients with MCL, **with or without previous cBTKi treatment**

- Efficacy-evaluable patients
  - **Prior cBTKi** (n=152)
  - **cBTKi naïve** (n=14)
- Safety was assessed in patients with MCL (n=166)

Prior cBTKi patient characteristics (n=152)

- Median age 70 years
- 53% with bone marrow involvement
- Majority classified as intermediate or high-risk sMIPI
- Heavily pretreated (median # prior systemic lines=3)
- 84% discontinued any prior BTKi due to progressive disease

Efficacy results: prior cBTKi (n=152)

Prior cBTKi *(n=152)*

Median PFS: 5.6 months
18-month PFS rate: 31.8%

ORR was 49.3%
Median DOR was 21.6 months
Median OS was 23.5 months

Clinically meaningful ORRs were observed in high-risk subgroups, including Ki-67 ≥30% and *TP53*-mutated

Efficacy results: cBTKi-naïve (n=14)

cBTKi-naïve *(n=14)*

ORR was 85.7%
18-month PFS rate: 83.9% (median NE)

Safety results in patients with MCL (n=166)

Median time on treatment for the MCL population was **5.5 months**

Discontinuations due to TRAEs occurred in **3%** (n=5) of MCL patients

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

Fatigue 31.9%	**Diarrhea** 22.3%	**Dyspnea** 17.5%
Anemia 16.9%	**Platelet count decreased** 15.1%	

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

Infections[a] 19.9%	**Hemorrhage**[b] 2.4%	**Hypertension** 0.6%
Atrial fibrillation/flutter[c] 1.8%	**Arthralgia** 1.2%	**Rash**[d] 0.6%

Summary

With a median survival follow-up of 2 years, **pirtobrutinib** continues to show **promising efficacy** in heavily pretreated patients with **R/R MCL** after a prior cBTKi

Consistent response rates were seen in patients with **high-risk disease features**, including elevated Ki-67 index and *TP53* mutations

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

BTK, Bruton tyrosine kinase; cBTKi, covalent Bruton tyrosine kinase inhibitor; DOR, duration of response; Ki-67, antigen Ki-67 proliferation marker; MCL, mantle cell lymphoma; NE, not evaluable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; R/R relapsed/refractory; TP53: tumor protein p53; TRAE, treatment-related adverse event. [a]Aggregate of all preferred terms including infection and COVID-19. [b]Aggregate of all preferred terms including hemorrhage or hematoma. [c]Aggregate of atrial fibrillation and atrial flutter. [d]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 #981.