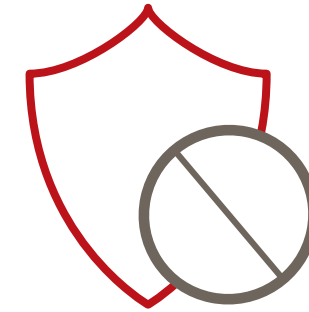


Pirtobrutinib in Relapsed/Refractory Mantle Cell Lymphoma Patients With Prior cBTKi: Updated Safety and Efficacy, Including High-Risk Subgroup Analyses From the Phase 1/2 BRUIN Study

JB Cohen; NN Shah, W Jurczak, PL Zinzani, CY Cheah, TA Eyre, CS Ujjani, Y Koh, WS Kim, SD Nasta, I Flinn, B Tessoulin, S Ma, AJ Alencar, DJ Lewis, JA Woyach, KJ Maddocks, K Patel, Y Wang, J Rhodes, CS Tam, JF Seymour, H Nagai, JM Vose, B Fakhri, MS Hoffmann, F Hernandez-Ilizaliturri, AD Zelenetz, A Kumar, T Munir, D Tsai, M Balbas, B Liu, AS Ruppert, B Nguyen, LE Roeker, ML Wang

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)

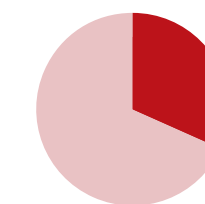
Prior cBTKi patient characteristics (n=152)

- 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)

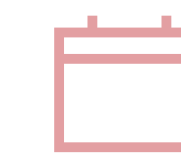
Median PFS: 5.6 months
18-month PFS rate: 31.8%



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

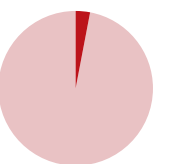
Clinically meaningful ORRs were observed in high-risk subgroups, including Ki-67 ≥30% and TP53-mutated

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