Poster #
MCL-135

BRUIN MCL-321: A Phase 3, Open-Label, Randomized Study of Pirtobrutinib Versus Investigator Choice of BTK Inhibitor in Patients with Previously Treated, BTK Inhibitor Naïve Mantle Cell Lymphoma (Trial in Progress)

Rodrigo Ito[1], Toby A. Eyre[2], Nirav N. Shah[3], Steven LeGouill[4], Martin Dreyling[5], Elisabeth Vandenberghe[6], Wojciech Jurczak[7], Yucai Wang[8], Chan Y. Cheah[9], Mitul Gandhi[10], Christopher Chay[11], Jeff P. Sharman[12], David Andorsky[13], Ming Yin[14], Minna Balbas[14], Jennifer Kherani[14], Michael L. Wang[15]

[1]Eli Lilly and Company, Indianapolis, IN, USA; [2]Oxford University Hospitals NHS Foundation Trust, Churchill Cancer Center, Oxford, UK; [3]Medical College of Wisconsin, Milwaukee, WI, USA; [4]Service d'hématologie Clinique du CHU de Nantes, INSERM CRCINA Nantes-Angers, NeXT Université de Nantes, Nantes, France; [5]Department of Medicine III, LMU University Hospital, Munich, Germany; [6]Hope Directorate St. James Hospital, Dublin, Ireland; [7]Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland; [8]Division of Hematology, Mayo Clinic, Rochester, MN, USA; [9]Linear Clinical Research and Sir Charles Gairdner Hospital, Perth, Australia; [10]Virginia Cancer Specialists, Fairfax, VA, USA; [11]Messino Cancer Centers, Asheville, NC, USA; [12]Willamette Valley Cancer Institute and Research Center, US Oncology Research, Eugene, OR, USA; [13]Rocky Mountain Cancer Centers, US Oncology Research, Boulder, CO, USA; [14]Loxo@Lilly, Indianapolis, IN, USA; [15]University of Texas MD Anderson Cancer Center, Houston, TX, USA

Background

- Covalent Bruton's Tyrosine Kinase inhibitors (BTKi) have transformed the management of relapsed mantle cell lymphoma (MCL), but these treatments are not curative, and most patients will require additional treatment[1]
- Covalent BTKi share pharmacologic liabilities (e.g., low oral bioavailability, short half-life) that collectively may lead to suboptimal BTK target coverage especially in rapidly proliferating tumors with high BTK protein turnover such as MCL[2]
- Pirtobrutinib is a highly potent and selective non-covalent (reversible) BTKi[3]
- In the phase 1/2 BRUIN study, pirtobrutinib achieved pharmacokinetics exposures that exceeded its BTK IC_{96} at trough, was well tolerated, and demonstrated promising efficacy in heavily pretreated, poor-prognosis MCL patients, most of whom had prior treatment with a covalent BTKi[3]

Study Design

BRUIN MCL-321 is a randomized, open-label, global, phase 3 study (NCT04662255)

Key Inclusion Criteria

- Confirmed diagnosis of MCL
- ≥1 prior (non-BTKi) line of systemic therapy for MCL
- Measurable disease per Lugano criteria
- Radiographically/histologically confirmed PD on the most recent line of therapy or relapse
- ≥18 years of age and ECOG 0-2

N=500

1:1 Randomization

Arm A
Pirtobrutinib
200 mg oral, once daily

Arm B
Investigator's choice of ibrutinib, acalabrutinib, or zanubrutinib per labeled doses

Stratification Factors

- sMIPI risk group (low/intermediate vs high)
- Intended comparator BTK inhibitor (ibrutinib vs acalabrutinib/zanubrutinib)
- Number of prior lines of therapy (1 vs ≥ 2)

Key Exclusion Criteria

- Prior treatment with a BTKi
- History of allogeneic stem cell transplant or autologous stem cell transplant or CAR T-cell therapy within 60 days of randomization
- History of bleeding diathesis
- Significant cardiovascular disease, stroke, or intracranial hemorrhage within 6 months of randomization
- Major surgery within 4 weeks of randomization
- Current or prior CNS involvement
- Anticoagulation with warfarin or another vitamin K antagonist

Study Endpoints

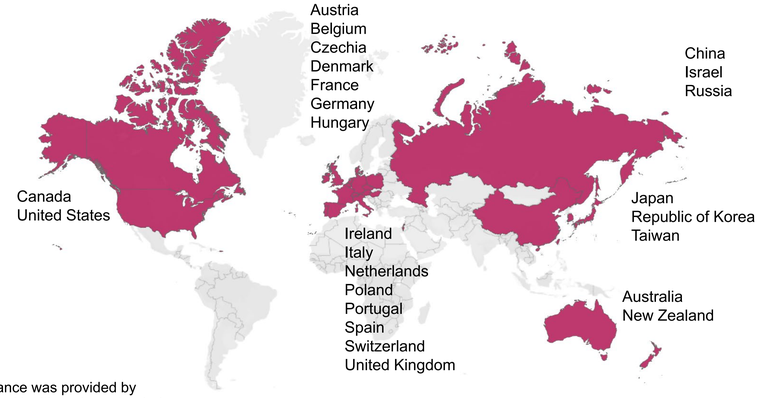
Primary Endpoint

- PFS per Lugano criteria, as assessed by blinded Independent Review Committee (IRC)

Secondary Endpoints

- PFS, as assessed by investigator
- ORR, DoR per Lugano criteria, as assessed by investigator and IRC
- OS, EFS, TTF, TTNT, PFS2, as assessed by investigator
- SAEs, AEs per CTCAE v5.0
- Patient reported outcomes

Study Sites



References

1. Dreyling et al. *Leuk Lymphoma* 2018;59(8):1814-1828
2. Cohen et al. *Clin Lymphoma Myeloma Leuk* 2021;21(1):S378-S379
3. Mato et al. *Lancet* 2021;397(10277):892-901

Abbreviations:
AE, adverse event; CAR-T, chimeric antigen receptor-modified T-cell; DoR, duration of response; EFS, event-free survival; IC, inhibitory concentration; ORR, overall response rate; PD, progressive disease; PFS2, progression-free survival 2; SAE, serious adverse event; sMIPI, Simplified MCL International Prognostic Index; TTF, time to treatment failure; TTNT, time to next treatment

Acknowledgements
Medical writing assistance was provided by Anchal Sood of Syneos Health and was funded by Loxo@Lilly

Scan or click the QR code or use this URL (https://lillyscience.lilly.com/congress/soho2022) for a list of all Lilly content presented at the congress.

Other company and product names are trademarks of their respective owners.