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642. CHRONIC LYMPHOCYTIC LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

Patient-Reported Outcomes (PROs) Among Patients with Previously Treated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) Receiving Pirtobrutinib: Analysis from the BRUIN Phase 1/2 Study

Catherine C. Coombs, MD¹, Jennifer A. Woyach, MD², Jennifer R. Brown, MD PhD³, Paolo Ghia, MD PhD⁴, Lindsey E. Roeker, MD⁵, Krish Patel, MD⁶, Toby A. Eyre, MBChB, DipMedEd, MRCP, FRCPath, MD⁷, Constantine S. Tam, MD MBBS⁸, John F. Seymour, MBBS, PhD FRACP⁹, Nirav N. Shah, MD¹⁰, Ian W. Flinn, MD PhD¹¹, Chan Y. Cheah, MBBS, FRACP, FRCPA, DMSc¹², Shuo Ma, MD PhD¹³, Joanna M. Rhodes, MD¹⁴, Koji Izutsu, MD PhD¹⁵, Wojciech Jurczak, MD PhD¹⁶, William G. Wierda, MD PhD¹⁷, Angely Loubert, MSc, PharmD¹⁸, Nalin Payakachat, PhD¹⁹, Lisa M. Hess, PhD¹⁹, Paolo Abada, MD²⁰, Nicole Lamanna, MD²¹

¹ University of California, Irvine, Irvine, CA

² The Ohio State University Comprehensive Cancer Center, Columbus, OH

³ Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA

⁴ Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milano, Italy

⁵ Memorial Sloan Kettering Cancer Center, New York, NY

⁶ Swedish Cancer Institute, Seattle, WA

⁷ Oxford University Hospitals NHS Foundation Trust, Churchill Cancer Center, Oxford, United Kingdom

⁸ The Alfred Hospital and Monash University, Melbourne, Australia

⁹ Peter MacCallum Cancer Center, Royal Melbourne Hospital and University of Melbourne, Melbourne, Australia

¹⁰ Medical College of Wisconsin, Milwaukee, WI

¹¹ Sarah Cannon Research Institute, Tennessee Oncology, Nashville, TN

¹² Linear Clinical Research and Sir Charles Gairdner Hospital, Perth, Australia

¹³ Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, IL

¹⁴ Rutgers Cancer Institute of New Jersey, New Brunswick, NJ

¹⁵ National Cancer Center Hospital, Tokyo, Japan

¹⁶ Maria Skłodowska-Curie National Research Institute of Oncology, Krakow, Poland

¹⁷ MD Anderson Cancer Center, Houston, TX

¹⁸ Modus Outcomes, Lyon, France

¹⁹ Eli Lilly and Company, Indianapolis, IN

²⁰ Loxo@Lilly, Indianapolis, IN

²¹ Herbert Irving Comprehensive Cancer Center, Columbia University, New York

Background

PROs including health-related quality of life (HRQoL) and symptom burden can provide helpful information to support benefit-risk assessment of a new treatment. Pirtobrutinib, a highly selective, non-covalent (reversible) Bruton tyrosine kinase inhibitor (BTKi), inhibits both wildtype and C481-mutant BTK with equal low nM potency, and has favorable oral pharmacology that enables continuous BTK inhibition throughout the dosing interval regardless of intrinsic rate of BTK turnover. Pirtobrutinib recently received regulatory approval in the US for the treatment of patients with relapsed or refractory mantle cell lymphoma after two or more lines of systemic therapy, including a covalent BTKi (cBTKi). BRUIN (NCT03740529) is an ongoing, open-label, multi-center phase 1/2 study investigating the safety and efficacy of pirtobrutinib for the treatment of B-cell malignancies, including CLL/SLL. This current analysis reports PROs among patients enrolled in the BRUIN study with relapsed or refractory (R/R) CLL/SLL treated with prior cBTKi-containing regimens.

Methods

Pretreated patients with R/R CLL/SLL in the BRUIN study completed PRO assessments at each clinic visit. The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core-30 (QLQ-C30) was used to measure physical function (PF) and HRQoL via PF and Global Health Status/QoL subscales. Patient-reported CLL/SLL symptoms and fatigue were assessed using 13 and 6 EORTC Item Library (IL) items, respectively. All subscales are scored

0-100. Higher scores represent better PF and HRQoL; and higher scores represent worse CLL/SLL symptoms and fatigue. Pre-specified clinically meaningful within patient change (MWPC) thresholds of at least 10-point changes in each PRO score were used to categorize patients based on their individual change from Cycle 1 Day 1 (i.e., baseline). Mean changes from baseline and proportions of patients with improved, stable, and worsened PROs from baseline were summarized by treatment cycle. PRO data were presented from Cycle 1 to 24 (a 28-day cycle) since the study median progression-free survival by investigator assessment was 19.6 months. The data cutoff date was 22 July 2022.

Results

There were 263 patients with CLL/SLL at the time of analysis; median (Quartile 1 and 3) age was 69 (62, 74) years and the majority were male (68%). All patients had received prior cBTKi; 21% received 2 or more prior cBTKi lines and 20% discontinued from their most recent cBTKi treatment due to toxicity. The mean overall completion rate of PRO instruments was 83% at baseline. 76% of all patients in the analysis completed at least one subsequent PRO assessment. Baseline mean (\pm SD [standard deviation]) score was 80.8 (\pm 19.5) for PF, 61.6 (\pm 23.2) for QoL, 24.8 (\pm 18.4) for CLL/SLL symptoms, and 33.5 (\pm 24.7) for fatigue. The majority of patients reported stable or clinically improved outcomes from baseline at each of the post-baseline visits (through Cycle 24) for PF (proportion of stable/improved ranged from 72.5% to 95.5%), QoL (range 80.4% to 95.0%), CLL/SLL symptoms (range 77.8% to 96.3%), and fatigue (range 77.3% to 89.9%).

Conclusion

Overall, consistent with the favorable safety profile of pirtobrutinib, HRQoL and symptoms were stable or improved for over 70% of patients with pretreated R/R CLL/SLL throughout the first 24 cycles of pirtobrutinib treatment. These PRO data should be interpreted with caution due to single arm trial design and small numbers of patients available for assessment in later cycles.

Disclosures Coombs: Mingsight: Honoraria; MEI Pharma: Honoraria; TG Therapeutics: Honoraria; Bluebird Bio: Current equity holder in publicly-traded company; Loxo Oncology/Eli Lilly and Company: Consultancy, Honoraria, Research Funding; AstraZeneca: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; BeiGene: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; Genentech: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; AbbVie: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; Janssen: Honoraria; Octapharma: Consultancy. **Woyach:** AbbVie Inc, Karyopharm Therapeutics, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MingSight Pharmaceuticals, MorphoSys, Schrödinger, Verastem Inc.: Other: Contracted Research; AbbVie Inc, ArQule Inc, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Genentech, a member of the Roche Group, Janssen Biotech Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Newave Pharmaceutical Inc, Pharmacyclics LLC, an AbbVie: Other: Advisory Committee and Consulting Agreements. **Brown:** Acerta/AstraZeneca: Consultancy; Pharmacyclics: Consultancy; Loxo/Lilly: Consultancy, Research Funding; TG Therapeutics: Research Funding; Numab Therapeutics: Consultancy; Kite: Consultancy; SecuraBio: Research Funding; Pfizer: Consultancy; Merck: Consultancy; MEI Pharma: Research Funding; iOnctura: Consultancy, Research Funding; Gilead: Research Funding; BeiGene: Consultancy, Research Funding; Alloplex Biotherapeutics: Consultancy; Genentech/Roche: Consultancy; Grifols Worldwide Operations: Consultancy; Hutchmed: Consultancy; Abbvie: Consultancy. **Ghia:** MSD: Consultancy, Honoraria, Research Funding; BeiGene: Consultancy, Honoraria, Research Funding; Janssen: Consultancy, Honoraria, Research Funding; BMS: Consultancy, Honoraria, Research Funding; AbbVie: Consultancy, Honoraria, Research Funding; Lilly/Loxo Oncology: Consultancy, Honoraria, Research Funding; AstraZeneca: Consultancy, Honoraria, Research Funding; Roche: Consultancy, Honoraria, Research Funding. **Roeker:** Aptose Biosciences: Research Funding; Adaptive Biotechnologies: Research Funding; Abbott Laboratories: Current equity holder in publicly-traded company; Dren Bio: Research Funding; Pharmacyclics: Consultancy; AbbVie: Consultancy, Research Funding; Ascentage: Consultancy; TG Therapeutics: Consultancy; Genentech: Research Funding; Beigene: Consultancy; Qilu Puget Sound Biotherapeutics: Research Funding; Loxo Oncology: Consultancy, Other: travel support, Research Funding; AstraZeneca: Consultancy, Research Funding; Janssen: Consultancy; Pfizer: Consultancy, Research Funding; PeerView: Other: CME speaker; Medscape: Other: CME speaker; Curio: Other: CME speaker; DAVA: Other: CME speaker. **Patel:** ADC Therapeutics: Consultancy; Abbvie: Consultancy; Nurix: Research Funding; TG Therapeutics: Consultancy, Speakers Bureau; Adaptive Biotechnologies: Research Funding; Genentech/Roche: Consultancy, Research Funding; Fate Therapeutics: Research Funding; Epizyme: Consultancy, Research Funding; Curis, Inc: Research Funding; CRISPR Therapeutics: Research Funding; Caribou Biosciences: Consultancy; Bristol Myers Squibb: Consultancy, Research Funding, Speakers Bureau; BeiGene: Consultancy; AstraZeneca: Consultancy, Research Funding, Speakers Bureau; Morphosys: Consultancy; Pharmacyclics/Janssen: Consultancy, Research Funding; Kite: Consultancy, Research Funding, Speakers Bureau; Loxo Oncology: Consultancy, Research Funding; MEI Pharma: Consultancy, Research Funding; Merck: Consultancy, Research Funding; Sunesis Pharmaceuticals: Research Funding; Trilium Therapeutics/Pfizer: Consultancy, Research Funding; Xencor: Consultancy, Research Funding. **Eyre:** Roche: Consultancy, Honoraria, Speakers Bureau; KITE Gilead: Consultancy, Honoraria, Speakers Bureau; Beigene: Consultancy, Honoraria, Research Funding, Speakers Bureau; Incyte: Consultancy; AstraZeneca: Consultancy, Honoraria, Research Funding, Speakers Bureau; Autolus: Consultancy; AbbVie: Consultancy, Honoraria, Speakers Bureau; Janssen: Consultancy, Honoraria, Speakers Bureau; Loxo@Lilly: Consultancy, Honoraria, Speakers Bureau. **Tam:** Roche: Honoraria; Novartis: Honoraria; LOXO: Honoraria; BeiGene: Honoraria, Research Funding; AbbVie: Honoraria, Research Funding; Janssen: Honoraria, Research Funding. **Seymour:** Hoffmann-La Roche: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; BMS: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; TG

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OffLabel Disclosure: Pirtobrutinib is approved in the USA for the treatment of relapsed or refractory MCL after at least 2 lines of systemic therapy, including prior BTKi.

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