ELSEVIER

Blood 142 (2023) 1908–1911

The 65th ASH Annual Meeting Abstracts

# POSTER ABSTRACTS

## 642.CHRONIC LYMPHOCYTIC LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

### Treatment Effectiveness with Venetoclax-Based Therapy after Bruton Tyrosine Kinase Inhibitors in Chronic Lymphocytic Leukemia: An International Real-World Study

*Nilanjan Ghosh, MD PhD[1], Nicole Lamanna, MD[2], Toby A. Eyre, MBChB, DipMedEd, MRCP, FRCPath, MD[3], Catherine C Coombs, MD[4], Beenish S Manzoor, PhD MPH[5], Jennifer R. Brown, MD PhD[6], Hande H. Tuncer, MD[6], Chaitra S Ujjani, MD[7], Lori A Leslie[8], Lindsey E. Roeker, MD[9], Matthew S Davids, MD MMSc[6], Joanna M. Rhodes, MD MSCE[10], Alan Skarbnik, MD[11], Nnadozie Emechebe[5], Isabelle Fleury, MD[12], Brian T. Hill, MD PhD[13], Christopher P. Fox, MD PhD[14], Paul M. Barr, MD[15], Dureshahwar Jawaid[5], Wendy J Sinai, PharmD[5], Laurie K Pearson, MD[16], Frederick Lansigan, MD[17], Yun Choi[18], Christopher E. Jensen[19], Stephen J. Schuster, MD[20], Kaitlin Kennard[20], Irina Pivneva, PhD[21], Talissa Watson[21], Annie Guerin[21], Mazyar Shadman, MD MPH[22]*

[1] Levine Cancer Institute/Atrium Health, Charlotte, NC
[2] Columbia University, New York, NY
[3] Churchill Hospital, Oxford University, Oxford, United Kingdom
[4] University of California Irvine, Irvine, CA
[5] AbbVie, Inc., North Chicago, IL
[6] Dana-Farber Cancer Institute, Boston, MA
[7] Fred Hutchinson Cancer Research Center, Seattle, WA
[8] John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ
[9] CLL Program, Leukemia Service, Division of Hematologic Oncology, Memorial Sloan Kettering Cancer Center, New York, NY
[10] Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
[11] Novant Health Cancer Institute, Lymphoma and CLL Program, Charlotte, NC
[12] Hôpital Maisonneuve-Rosemont, University of Montreal, Montreal, Canada
[13] Cleveland Clinic, Cleveland, OH
[14] School of Medicine, University of Nottingham, Nottingham, United Kingdom
[15] Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY
[16] University of Massachusetts, Worcester, MA
[17] Dartmouth-Hitchcock Medical Center, Lebanon, NH
[18] Tufts Medical Center, Boston, MA
[19] Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC
[20] University of Pennsylvania, Philadelphia, PA
[21] Analysis Group, Inc., Montreal, Canada
[22] Fred Hutchinson Cancer Center, Seattle, WA

**Introduction**: Venetoclax has demonstrated consistent efficacy and manageable toxicity in patients with previously untreated or relapsed/refractory (R/R) chronic lymphocytic leukemia/small lymphocytic leukemia (CLL/SLL). However, evidence on venetoclax use in patients previously treated with Bruton tyrosine kinase inhibitors (BTKi) is limited. This real-world evidence (RWE) study assessed clinical outcomes of patients who received venetoclax after covalent BTKi (cBTKi) therapy, i.e., response rates, time to next treatment or death (TTNT-D), and progression-free survival (PFS), overall and stratified by line of therapy.
**Methods**: The CLL Collaborative Study of Real-World Evidence (CORE), a retrospective, international, observational study (23 centers) provided data for this analysis. Adult patients diagnosed with CLL/SLL were included if they received a venetoclax-based regimen after discontinuation of a cBTKi-based regimen. Baseline characteristics at venetoclax initiation were summarized using descriptive statistics. Overall response rate (ORR) was calculated as the proportion of patients with complete response (CR) or partial response (PR) among patients with documented responses as recorded in the patients' medical charts based on physician assessment. TTNT-D was measured from date of venetoclax initiation to change of treatment/death (event) or end of follow-up, while PFS was measured from date of venetoclax initiation to disease progression/death (event) or end

of follow-up. Outcomes were reported for the overall population and stratified by line of therapy (1L→2L and 2L→3L) and also by with and without CT/CIT exposure prior to cBTKi for 2L→3L.

**Results**: Of the 2,020 patients included in CORE, 1,287 (63.7%) received a cBTKi-based regimen in ≥1 line of therapy; 184 patients (14.3%) discontinued cBTKi (intolerance: 83 [45.1%], progression: 78 [42.4%]) and initiated venetoclax-based therapy (115 venetoclax monotherapy; 69 venetoclax combined with rituximab or obinutuzumab). Mean age at venetoclax initiation was 68.6 (median: 68.2) years old, 69.0% were male, and 31.0% had Medicare. Among tested patients, 41/61 (67.2%) had unmutated IGHV, and 28/109 (25.7%) had 17p deletion or TP53 mutation at venetoclax initiation. Average follow-up time from initiation of venetoclax therapy was 19.6 months (median: 16.6).

Of the 127 patients (69.0%) with a documented response, the ORR was 78.0% (CR: 43.3%, PR: 34.6%). The median TTNT-D for these patients was 39.5 months (95% CI: 30.4, not reached [NR]) with 12- and 18-month rates of 82.3% and 72.4%, respectively. The median PFS was 43.2 months (95% CI: 31.9, NR), with 12- and 18- month PFS rates of 82.8% and 75.1%, respectively.

Among patients who started venetoclax-based therapy post-cBTKi as 1L→2L (n=65), the ORR was 84.1% (CR: 54.5%, PR: 29.5%, out of 44 documented). The median TTNT-D for these patients was NR (95% CI: 31.9, NR) but the 12- and 18-month rates were 85.0% and 73.9%, respectively. The median PFS was 43.2 months (95% CI: 39.5, NR) with 12- and 18- month rates of 86.4% and 81.8%, respectively.

Among patients who started venetoclax-based therapy post-cBTKi as 2L→3L (n=67), the ORR was 78.3% (CR: 41.3%, PR: 37.0%, out of 46 documented). The median TTNT-D for these patients was 44.2 months (95% CI: 37.0, NR) with 12- and 18-month rates were 83.1% and 76.5%, respectively. The median PFS for these patients was 44.1 months (95% CI: 31.8, NR) with 12- and 18- months rates were 85.2% and 80.4%, respectively. The results for ORR, TTNT-D, and PFS were also similar for those with and without CT/CIT exposure prior to cBTKi.

**Conclusions**: In this multicenter real-world study, results demonstrate that venetoclax is effective overall and also when used either in 2L or 3L following cBTKi therapy. Additionally, even with prior CT/CIT exposure, results support that venetoclax-based therapy remains effective as a therapeutic option. Thus, this study demonstrates that venetoclax-based therapy post-cBTKi is associated with durable remission. These results are especially timely as the CLL treatment paradigm continues to evolve with multiple treatment options available, providing clinicians with valuable evidence to inform modern clinical practice. Further analysis of this study with larger cohorts and longer follow-up time will be undertaken as part of future work to grow this body of evidence.

**Disclosures Ghosh:** *Seagen, TG Therapeutics, AstraZeneca, Phamacyclics, Janssen, Bristol Myers Squibb, Gilead Sciences, Kite Pharma, Beigene, Incyte, Lava Therapeutics, Incyte, Roche/Genentech, Novartis, Loxo Oncology, AbbVie, Genmab, Adaptive Biotech, ADC Therapeutics:* Consultancy; *TG Therapeutics, Genentech/Roche, Bristol Myers Squibb, Gilead, Morphosys, AbbVie, Pharmacyclics:* Research Funding; *AstraZeneca, Janssen, Pharmacyclics, Kite pharma, BMS, Epizyme:* Speakers Bureau; *Seagen, TG Therapeutics, AstraZeneca, Phamacyclics, Janssen, Bristol Myers Squibb, Gilead Sciences, Kite Pharma, Beigene, Incyte, Lava Therapeutics, Incyte, Roche/Genentech, Novartis, Loxo Oncology, AbbVie, Genmab, Adaptive Biotech, ADC Therapeutics, Morp:* Honoraria; *Roche NHL solutions panel:* Membership on an entity's Board of Directors or advisory committees. **Lamanna:** *AbbVie:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Celgene:* Membership on an entity's Board of Directors or advisory committees; *Roche-Genentech:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Janssen:* Membership on an entity's Board of Directors or advisory committees; *Pharmacyclics:* Membership on an entity's Board of Directors or advisory committees; *Gilead:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *AstraZeneca:* Membership on an entity's Board of Directors or advisory committees; *Verastem:* Research Funding; *Bei-Gene:* Research Funding; *TG Therapeutics:* Research Funding; *Acerta:* Research Funding. **Eyre:** *KITE:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Autolus:* Consultancy; *Loxo Oncology:* Consultancy, Honoraria, Other, Speakers Bureau; *Incyte:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Abbvie:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Beigene:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *AstraZeneca:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Eli Lilly and Company:* Consultancy, Honoraria, Speakers Bureau; *Janssen:* Consultancy, Honoraria, Speakers Bureau; *Gilead:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Loxo Lilly:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *PeerView:* Speakers Bureau; *Medscape:* Speakers Bureau; *Secura Bio:* Membership on an entity's Board of Directors or advisory committees; *Roche:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau. **Coombs:** *Genentech:* Honoraria; *MEI Pharma:* Honoraria; *Novartis:* Honoraria; *AstraZeneca:* Honoraria; *Octapharma:* Other: independent review committee; *Loxo Oncology:* Honoraria, Other: steering committee, Research Funding; *H3 Biomedicine:* Research Funding; *TG Therapeutics:* Honoraria; *Beigene:* Honoraria; *AbbVie:* Consultancy, Honoraria, Other: steering committee and independent review committee; *Incyte:* Research Funding. **Manzoor:** *AbbVie Inc.:* Current Employment, Current holder of *stock options* in a privately-held company. **Brown:** *Beigene:* Consultancy, Research Funding; *Genentech/Roche:* Consultancy; *AbbVie:* Consultancy; *Acerta/Astra-Zeneca:* Consultancy; *Merck:* Consultancy; *Alloplex Biotherapeutics:* Consultancy; *Loxo@Lilly:* Consultancy, Research Funding; *iOnctura:* Consultancy, Research Funding; *Numab Therapeutics:* Consultancy; *Hutchmed:* Consultancy; *Grifols Worldwide Operations:* Consultancy; *Kite:* Consultancy; *Pfizer:* Consultancy; *Pharmacyclics:* Consultancy; *Gilead:* Research Funding; *MEI Pharma:* Research Funding; *SecuraBio:* Research

Funding; *TG Therapeutics:* Research Funding. **Tuncer:** *AbbVie:* Consultancy; *AstraZeneca:* Consultancy. **Ujjani:** *Kite, a Gilead Company:* Consultancy, Other: Travel expenses , Research Funding; *Astrazeneca:* Consultancy, Honoraria, Research Funding; *Epizyme:* Consultancy; *Lilly:* Consultancy, Honoraria, Research Funding; *Pharmacyclics:* Consultancy, Honoraria, Research Funding; *Genentech:* Consultancy, Honoraria; *Beigene:* Consultancy, Honoraria; *Atara:* Consultancy; *PCYC:* Research Funding; *Janssen:* Consultancy, Honoraria; *Abbvie:* Consultancy, Honoraria, Research Funding. **Leslie:** *TG Therapeutics:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *ADC therapeutics:* Consultancy, Membership on an entity's Board of Directors or advisory committees; 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Research Funding; *Vincerx:* Research Funding; *Mustang Bio:* Consultancy, Research Funding; *Janssen:* Consultancy; *Genmab:* Consultancy, Research Funding; *Bristol Myers Squibb:* Consultancy, Research Funding.

https://doi.org/10.1182/blood-2023-179198