CLL-495

Treatment Characteristics and Outcomes of Patients with Chronic/Small Lymphocytic Leukemia (CLL) Treated with Venetoclax and Bruton Tyrosine Kinase Inhibitor (BTKI) Combination Therapies

Hande H. Tuncer, MD[1], Nilanjan Ghosh, MD[2], Isabelle Fleury, MD[3], Lori A. Leslie, MD[4], Beenish S. Manzoor, PhD[5], Nicole Lamanna, MD[6], Toby A. Eyre, MD[7], Brian T. Hill, MD[8], Jennifer R. Brown, MD[1], Wendy Sinai, PharmD[5], Catherine C. Coombs, MD[9], Chaitra Ujjani, MD[10], Lindsey E. Roeker, MD[11], Nnadozie Emechebe, PhD[5], Paul M. Barr, MD[12], Matthew S. Davids, MD[1], Nicolas Martinez-Calle, MD[13], Joanna M. Rhodes, MD[14], Frederick Lansigan, MD[15], Laurie Pearson, MD[16], Yun Choi, MD[17], Stephen J. Schuster, MD[18], Alan P. Skarbnik, MD[19], Bita Fakhri, MD[20], Michael Coyle, MD[21], Deborah M. Stephens, DO[22], Meghan C. Thompson, MD[11], Christopher E. Jensen, MD[22], Steven E. Marx, PharmD[5], Dureshahwar Jawaid, MPH[5], Irina Pivneva, PhD[23], Talissa Watson, MSc[23], Annie Guerin, MSc[23], Mazyar Shadman, MD[9]

Affiliations: [1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Levine Cancer Institute/Atrium Health, Charlotte, NC, USA; [3]Hôpital Maisonneuve-Rosemont, University of Montreal, Canada; [4]John Theurer Cancer Center, Hackensack Meridian Health, Hackensack, NJ, USA; [5]AbbVie, Inc., North Chicago, IL, USA; [6]Columbia University, New York, NY, USA; [7]Churchill Hospital, Oxford University, Oxford, UK; [8]Cleveland Clinic, Cleveland, OH, USA; [9]University of California Irvine, Irvine, CA, USA; [10]Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [11]CLL Program, Leukemia Service, Division of Hematologic Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [12]Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY, USA; [13]Nottingham University Hospitals, NHS Trust, Nottingham, UK; [14]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA; [15]Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA; [16]University of Massachusetts, Worcester, MA, USA; [17]Tufts Medical Center, Boston, MA, USA; [18]University of Pennsylvania, Philadelphia, PA, USA; [19]Lymphoma and CLL Program, Novant Health Cancer Institute, Charlotte, NC, USA; [20]Stanford Cancer Institute, Stanford University, Stanford, CA, USA; [21]Lowell General Hospital, Worchester, MA, USA; [22]Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; [23]Analysis Group, Inc., Montreal, Canada

OBJECTIVE

To evaluate clinical and treatment characteristics and outcomes among patients with chronic lymphocytic leukemia /small lymphocytic lymphoma (CLL/SLL) treated with venetoclax+BTKi combination therapies

CONCLUSIONS

This study is the first real-world study to demonstrate the treatment effectiveness of venetoclax+BTKi based therapy, across lines of therapy

Venetoclax+BTKi regimens were well-tolerated across 1L/2L+, with less than half of patients experiencing treatment interruptions/reductions and few experiencing progression or intolerance

For additional information or to obtain a PDF of this poster

Scan QR code or utilize the following link to download an electronic version of this presentation and other AbbVie SOHO Semi-hybrid Congress 2024 scientific presentations: https://abbvie1.outsystemsenterprise.com/CongressPublications/CongressHome?CongressId=837
QR code expiration: Aug 4, 2025
To submit a medical question, please visit www.abbviemedinfo.com

This study was funded by AbbVie. AbbVie contributed to its design, and the collection, analysis, and interpretation of the data. AbbVie participated in the writing, review and approval of the poster content in collaboration with the other authors. All authors contributed to the development of the publication and maintained control over the final content.

CORE

SOHO Semi-hybrid Event 2024; September 4-7, 2024; Houston, Texas

INTRODUCTION

- Venetoclax, a B-cell lymphoma 2 (BCL2i) agent, has shown to be effective across lines of therapy, in clinical trial settings[1,2,3]
- However, there is a lack of data on real-world effectiveness among patients receiving venetoclax and cBTKi-based (venetoclax+BTKi) combination therapies

METHODS

- The global, retrospective CLL Collaborative Study of Real-World Evidence (CORE) data from 24 medical centers collected from June 1, 2018 until March 15, 2024 on adult patients diagnosed with CLL/SLL were included if the patient initiated venetoclax+BTKi combination therapies
- All data assessed from the CORE study were collected retrospectively based on patient medical records
- Clinical outcomes assessed were:
  - Overall response rate (ORR): the proportion of patients who achieved a complete or partial response to therapy as indicated in the patient medical chart
  - Progression-free survival (PFS): time between venetoclax+BTKi initiation to disease progression, death or end of follow-up
  - Time to next treatment/death (TTNT-D): time between venetoclax+BTKi initiation to next line of therapy, death or end of follow-up
- Results were reported overall and stratified by:
  - Line of therapy
    - First line [1L]
    - Second line and later [2L+]
  - Therapy (not mutually exclusive)
    - Venetoclax+ibrutinib-based [VI-based]
    - Venetoclax+acalabrutinib-based [VA-based]
    - Venetoclax+other BTKi-based [VOther-based]

RESULTS

Patient and clinical characteristics

- Of 2,296 total patients, venetoclax+BTKi-based therapies were initiated by 65 patients (*by line of therapy*: 1L: 37 [56.9%], 2L: 13 [20.0%] , 3L: 7 [10.8%] , 4L+: 8 [12.3%]; *by therapy*: VI-based 45 [69.2%], VA-based 17 [26.2%], and VOther-based 4 [6.2%]) who had a median follow-up of 16.7 months
- Among the 65 patients, the median age was 64.1 years (unmutated IGHV: 59.0%; del[17]p/TP53 mutation: 17.5%; cardiovascular comorbidities: 44.6%) and 73.8% received therapy as part of a clinical trial

Table 1. Patient & clinical characteristics at time of initiation of therapy[1,2]

Patient & clinical characteristics	Overall (N=65)	VI-based (N=45)	VA-based (N=17)	VOther-based[3] (N=4)
Age at initiation of line of therapy (years), median (IQR) [mean ± SD]	64.1 (56.0, 68.7) 62.7 ± 10.8	62.7 (55.3, 68.3) 61.9 ± 10.8	65.4 (57.4, 68.2) 63.5 ± 11.8	67.2 (64.1, 70.8) 67.6 ± 4.2
Male sex, N (%)	43 (66.2)	30 (66.7)	10 (58.8)	3 (75.0%)
ECOG assessed, N (%)[4,5]				
Grade 0	27 (41.5)	18 (40.0)	8 (47.1)	1 (25.0)
Grade 1 – 3	36 (55.4)	25 (55.6)	9 (52.9)	3 (75.0)
Tumor burden assessed, N (%)[4]				
Low	21 (32.3)	16 (35.6)	4 (23.5)	2 (50.0)
Medium	23 (35.4)	15 (33.3)	7 (41.5)	1 (25.0)
High	6 (9.2)	2 (4.4)	3 (17.6)	1 (25.0)
Unmutated IGHV	**23 (59.0)**	**14 (58.3)**	**6 (46.2)**	**3 (100.0)**
17p deletion or TP53 mutation	**10 (17.5)**	**7 (17.5)**	**3 (21.4)**	**0 (0.0)**
Therapy received outside of clinical trial	**17 (26.2)**	**12 (26.7)**	**4 (23.5)**	**1 (25.0)**
Comorbidities at initiation of line of therapy[6], N (%)				
Cardiovascular	29 (44.6)	16 (35.6)	10 (58.8)	3 (75.0)
Endocrine/ metabolic	12 (18.5)	9 (20.0)	3 (17.6)	0 (0.0)
Musculoskeletal	9 (13.8)	5 (11.1)	3 (17.6)	1 (25.0)

Table 1 & 2 abbreviations: ECOG: Eastern Cooperative Oncology Group; IGVH: immunoglobulin heavy-chain variable region gene; IQR: interquartile range; SD: standard deviation; TLS: tumor lysis syndrome. **Table 1 & 2 notes:** 1. Patient and clinical characteristics, and treatment characteristics were summarized descriptively. 2. Categories are not mutually exclusive. One patient was in both the VI-based and VA-based categories and their treatment combination was venetoclax+ibrutinib+acalabrutinib+obinutuzumab. 3. VOther-based treatments include venetoclax in combination with pirtobrutinib+rituximab (2 [50.0%]), pirtobrutinib+obinutuzumab (1 [25.0%]), and zanubrutinib+obinutuzumab (1 [25.0%]). 4. Reported for patients with available response data. 5. 0 patients had ECOG Grade 4, 6. Categories are not mutually exclusive. 7. Disease relapse or treatment failure includes stable disease, non-response, or progression. 8. Duration of line based on the study design was calculated as the time from initiation of the line of therapy until the earliest date of (1) next line of therapy, or (2) end of follow-up or death.

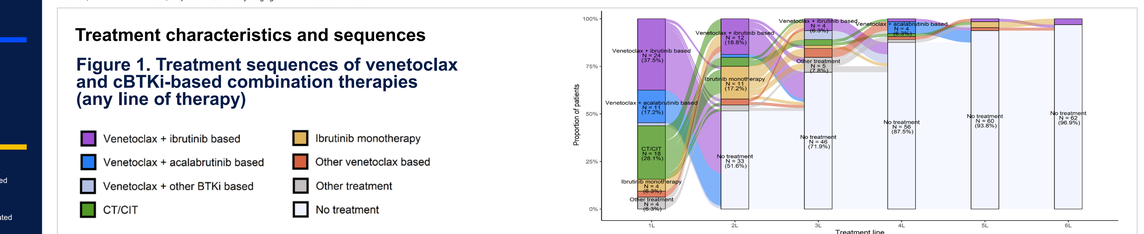
Table 2. Treatment characteristics of therapy[1,2]

Treatment characteristics	Overall (N=65)	VI-based (N=45)	VA-based (N=17)	VOther-based[3] (N=4)
Reason for choosing venetoclax-based therapy[6], N (%)				
Disease relapse or treatment failure[7]	24 (36.9)	17 (37.8%)	4 (23.5)	3 (75.0)
Expected efficacy of treatment	22 (33.8%)	12 (26.7)	11 (64.7)	0 (0.0)
Tolerability of selected treatment	6 (9.2)	6 (13.3)	0 (0.0)	0 (0.0)
Reasons for ending current line[6], N (%)				
Still on this line of therapy	39 (60.0)	25 (55.6)	11 (64.7)	3 (75.0)
Completed scheduled duration of therapy	16 (24.6)	13 (28.9)	3 (17.6)	1 (25.0)
Disease progression	4 (6.2)	4 (8.9)	0 (0.0)	0 (0.0)
Intolerance	3 (4.6)	2 (4.4)	1 (5.9)	0 (0.0)
Dosage reduced, N (%)	**15 (23.1)**	**9 (20.0)**	**6 (35.3)**	**1 (25.0)**
Treatment interruption, N (%)	**24 (36.9)**	**19 (42.2)**	**5 (29.4)**	**1 (25.0)**
Time from diagnosis to initiation of line of therapy, median (IQR) [mean ± SD]	**52.7 (17.0, 100.1) 66.5± 64.0**	**54.1 (17.0, 96.8) 63.7± 56.7**	**29.4 (13.5, 112.8) 62.0± 80.3**	**102.8 (50.3,153.5) 101.1± 73.5**
Treatment duration (months), median (IQR) [mean ± SD][8]	**14.0 (8.4, 38.4) 22.7± 19.5**	**18.3 (10.7,47.6) 27.5± 20.8**	**9.5 (6.5, 15.3) 13.8± 12.9**	**8.0 (5.9, 16.5) 14.4± 17.2**
1L, median (IQR) [mean ± SD][8]	13.0 (8.9, 23.3) 20.1± 17.0	16.6 (11.9, 40.6) 23.9± 18.6	9.4 (7.4, 12.4) 13.2± 13.2	39.8 (39.8 39.8) 39.8± NA
2L+, median (IQR) [mean ± SD][8]	17.2 (8.1, 47.0) 26.2± 22.2	25.6 (10.5, 53.9) 31.9± 23.1	15.3 (4.2, 22.1) 15.3± 13.3	7.2 (4.5, 8.0) 6.0± 3.6
Outside of clinical trial, median (IQR) [mean ± SD][8]	17.1 (7.2, 29.8) 20.0± 14.8	17.2 (8.4,34.1) 21.4± 16.2	18.7 (9.7, 27.9) 18.8± 12.3	7.2 (7.2, 7.2) 7.2± NA
Time from treatment initiation to end of follow-up (months), median (IQR) [mean ± SD][8]	**16.7(8.9, 40.7) 24.6 ± 20.0**	**22.3 (12.0, 51.2) 30.2± 20.8**	**10.0 (6.5, 15.8) 13.9 ± 12.9**	**8.0 (5.9, 16.6) 14.4 ± 17.2**

Figure 1 abbreviations: 1L: first-line; 2L: second-line; 2L+: second-line or later; 3L: third-line; 4L: fourth-line; 5L: fifth-line; 6L: sixth-line. **Figure 1 notes:** 1. Categories are mutually exclusive; 1 of the 65 patients in the study who received venetoclax + ibrutinib + acalabrutinib + obinutuzumab was excluded. 2. Among the 33 patients without a treatment received in 2L+, 32 (97.0%) patients were still alive, 1 (3.03%) died, and 0 (0.0%) patients were lost to follow-up. 3. For patients who initiated their venetoclax+BTKi combination in 2L+, 13 (46.4%) patients initiated in 2L, 7 (25.0%) initiated in 3L, and 8 (28.6%) initiated in 4L or later. 4. Labels have been excluded from nodes with less than 5% of the sample. 5. Other treatment category included: acalabrutinib, alemtuzumab, epcoritamab, ibrutinib + BR, idelalisib, lenalidomide, monoclonal antibodies + other agents, rituximab, umbralisib + ublituximab, unspecified BCL2i + alkylating agents + monoclonal antibodies.

Treatment characteristics and sequences

Figure 1. Treatment sequences of venetoclax and cBTKi-based combination therapies (any line of therapy)



LIMITATIONS

- Given the data is medical record data, there may have been incomplete recording of data, errors during data entry, or inconsistencies in data interpretation; however, these inconsistencies are mitigated through center-based training, interim quality checks, and regular communication with the participating centers by the CORE research team
- As the sample size was small, most of the observed combinations were covalent BTKis
- Further research with longer follow-up times will need to be conducted to assess non-covalent BTKi combinations as its use in treatment of CLL continues to increase

Clinical outcomes

Figure 2: ORR for the overall study sample stratified by therapy and line of therapy

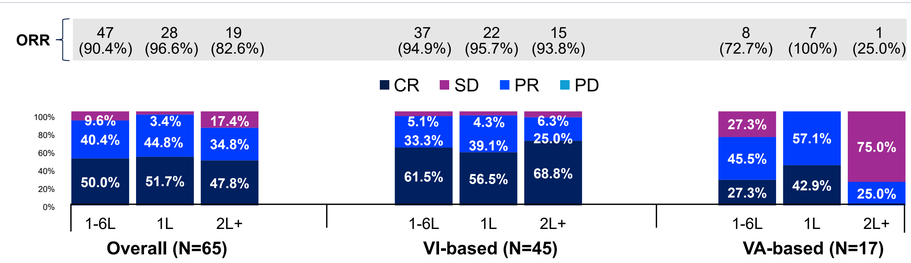


Figure 3: PFS[1,2]

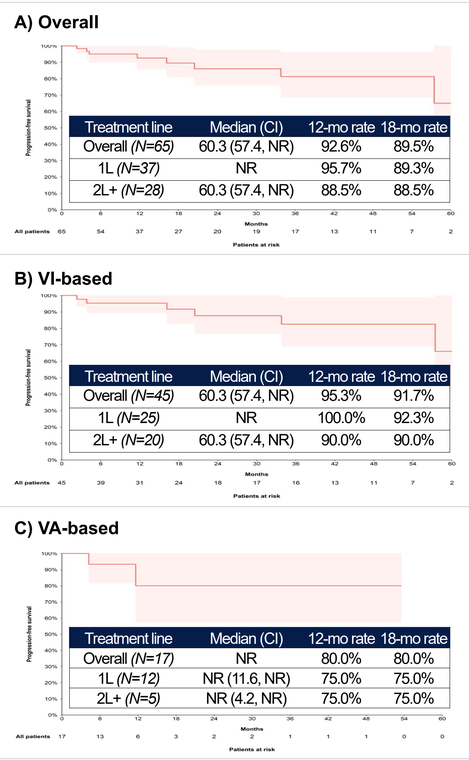


Figure 4: TTNTD[2,3]

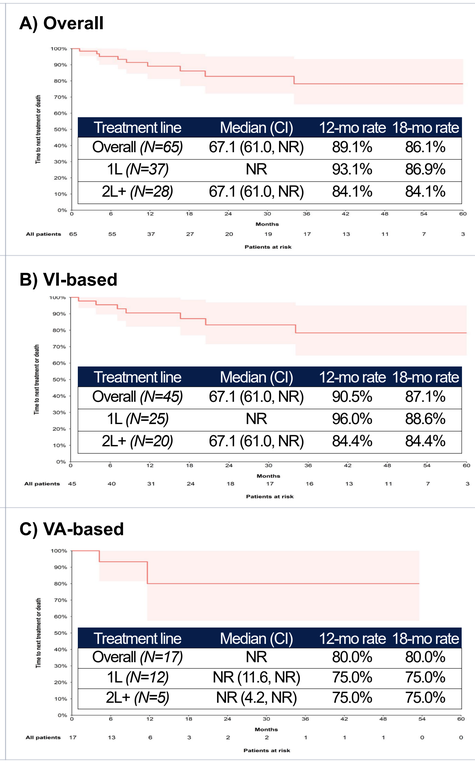


Figure 2 &3 abbreviations: 1L: first-line; 2L+: second line or later; CI: confidence interval; CR: complete response; Mo: months; NR: not reached; ORR: overall response rate; PD: progressive disease; PFS: progression-free survival; PR: partial response; SD: stable disease; TTNT-D: time to next treatment or death. **Figure 2 notes:** 1. ORR, i.e., the proportion of patients with physician-defined CR/PR, among those with available response data. CR/PR is not defined as in clinical trials (i.e., did not require a bone marrow biopsy), but based on the data available in the patient charts. 2. Among the 4 patients with VOther-based therapy, 3 had available response data reported all of which had PR. **Figure 3 notes**: 1. PFS, i.e., time from venetoclax+BTKi initiation to disease progression/death or end of follow-up. 2. Due to limited data, 0 events were reported for the VOther-based therapy group. 3. TTNT-D, i.e., time from venetoclax+BTKi initiation to subsequent treatment/death or end of follow-up.