Real-world treatment patterns and patient characteristics of venetoclax combination time-limited therapy for chronic lymphocytic leukemia

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Background:
The use of targeted therapies, such as combinations of anti-CD20 monoclonal antibodies and BCL2 inhibitors, is rapidly evolving in the treatment of chronic lymphocytic leukemia (CLL). Venetoclax plus obinutuzumab (VO) is approved as a first-line (1L) therapy with a fixed 12-month duration, while venetoclax plus rituximab (VR) is approved for second-line and later (2L+) treatment over a 24-month period. This study aims to evaluate real-world utilization and treatment patterns of venetoclax-based combination regimens across distinct lines of therapy in patients with CLL.

Methods:
The IntegraConnect PrecisionQ Database, containing electronic health records from 3 million deidentified community oncology patients in the United States, was used to create a retrospective cohort of CLL patients who initiated venetoclax, stratified by 1L and 2L+ based on the FDA approval date of each combination regimen and duration of the time-limited therapy. Patients receiving 1L V-based therapies were identified from 15 May 2019 to 28 Feb 2024, and patients receiving 2L+ V-based therapies were identified from 08 Jun 2018 to 28 Feb 2023. All patients were followed through 28 Feb 2025. Descriptive analyses were used to identify treatment patterns (e.g. duration of therapy and frequency of use) and baseline characteristics were examined including age, gender, race, Eastern Cooperative Oncology Group performances status (ECOG PS), and comorbidities.

Results:
A total of 1590 and 1456 pts were identified at 1L and 2L+, respectively. The most common venetoclax-based regimens were VO in 1L (61.4%); VR and VO in 2L+ (24.9% and 21.1%). Median age of patients who received venetoclax in 1L and 2L+ was 70 yrs (IQR: 63-77) and 73 yrs (IQR: 66-79), respectively. In 1L however, VO was used by more patients who were younger (age <70 vs 70+: 64.3% vs 58.7%) and male (male vs female: 63.0% vs 58.4%). Use of VO and VR also differed between White and African American patients in 1L (72.4% vs 66.8%) and 2L+ (5.4% vs 7.2%), respectively. ECOG PS was better in 1L than 2L+ (PS 0, 1, ≥2: 49.9%, 42.2%, 7.9% vs 41.0%, 46.5%, 12.4%), and baseline comorbidity differences were observed between 1L and 2L+: anemia (73.0% vs 79.6%), thrombocytopenia (69.9% vs 76.0%), leukopenia (40.8% vs 35.9%), transaminitis (18.7% vs 26.6%), and atrial fibrillation (5.0% vs 9.3%). Median treatment duration for 1L VO was 15.2 months; 2L+ VR was 22.8 months; 2L+ VO was 17.0 months. However, among patients who had 1L VO treatment, 70.6% received therapy for longer than the recommended 12 months; many patients remained on therapy for an additional year, as only 57.4% discontinued treatment by 24 months. For those who had 2L+ VR, 48.0% received therapy longer than the recommended 24 months, and 52.3% discontinued treatment by 36 months.

Conclusions:

In the US community oncology setting, there are baseline demographic and clinical differences in CLL venetoclax use between 1L and 2L+. VO is commonly utilized in both 1L and 2L+, and many patients remain on 1L VO and 2L+ VR for an extended period beyond the recommended, fixed treatment duration. Real-world venetoclax-based time-limited treatment utilization in CLL appears longer than observed in clinical trials or indicated per label. Future research may explore reasons for these differences.