**Background and Importance**

In managing chronic lymphocytic leukaemia (CLL), it is recommended that patients with TP53 deletion/mutation (TP53mut), who have a poor prognosis, are treated with ibrutinib in front-line. Because of severe infectious complications, idelalisib combined with rituximab is only recommended for frontline therapy in patients not suitable for ibrutinib, if measures to prevent infection are followed. Patients unsuitable for ibrutinib/idelalisib may otherwise be treated with venetoclax.

**Aim and Objectives**

To evaluate the prescriptions and clinical outcomes of ibrutinib, idelalisib and venetoclax in a tertiary hospital.

**Material and Methods**

- An observational, retrospective study was conducted including any prescriptions of ibrutinib, idelalisib and venetoclax for CLL from November 2015 to June 2019.
- We focused on TP53 mutation status, drug exposure, survival outcomes and reasons for drug-switching or dose reduction, if applicable.
- Data were collected from electronic medical records.

**Results**

- **30 patients receiving ibrutinib (n=23), idelalisib (n=13) and/or venetoclax (n=5)**
- **17 patients (56.7%)** showed TP53mut

  - **Ibrutinib cohort:** Median drug exposure was 10.5 months and most patients (65.2%) had received it after conventional chemotherapy regimens (e.g. FCR, R-CHOP, R-bendamustine). Only 5 patients (21.7%), showing TP53mut, had taken ibrutinib as first-line therapy and 4 (17.4%) had received it after idelalisib; 2 of them because of disease progression and the other 2 because of adverse events (severe infections and colitis).
  - **Idelalisib cohort:** Median drug exposure was 4.45 months.
  - **Venetoclax** was used for a median of 0.74 months and upon ibrutinib failure in 4 patients (the one left, received prior idelalisib due to concomitant anticoagulant therapy).
  - Dose reductions were needed in 11 patients on ibrutinib (causes: bruising, respiratory tract infections and neutropenia); in 4 receiving idelalisib due to severe diarrhea (n=3) and pneumonia (n=1); and in 1 patient on venetoclax due to severe neutropenia.
  - 59.5% of patients were still alive.

**Conclusion and Relevance**

- Most patients received second-line ibrutinib and showed a long-term response duration even when TP53mut was absent.
- Adverse effects resulted in frequent dose reductions/drug-switching.
- Venetoclax represents an appropriate option for patients whose CLL has failed to respond to ibrutinib/idelalisib.