Evolution in the Frontline Treatment of Patients with Chronic Lymphocytic Leukemia: Experience from One European Center

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BACKGROUND

- Treatment of chronic lymphocytic leukemia (CLL) has dramatically evolved over the last decades thanks to the introduction of targeted therapies.
- Chemoimmunotherapy was a big step forward in CLL therapy, and since 2014 several small molecules inhibiting different pathways have been introduced in the CLL treatment algorithms.
- International guidelines (ESMO 2021, NCCN 2022) recommend targeted therapies including covalent BTK inhibitors (cBTKi; ibrutinib, acalabrutinib, zanubrutinib) and BCL2 inhibitors (BCL2i; venetoclax) combinations as preferred regimens for most treatment naïve CLL patients.

OBJETIVES

1. Main objective: to describe the evolution in the patterns of frontline therapies in CLL patients from a single referral institution.
2. Secondary objectives: to evaluate the impact of the targeted therapies on time to next treatment (TTNT) and overall survival (OS) in our cohort.

PATIENTS AND METHODS

This is a retrospective, single-center, and non-interventional study. We included patients treated in clinical trials and in routine clinical practice. Front-line treatment was classified into 5 groups: (1) alkylating agents, (2) purine analogs, (3) chemoimmunotherapy, (4) targeted therapies, and (5) other therapies. TTNT and OS were defined from the date of starting therapy to the event (next treatment or death, respectively), or loss to follow-up.

We included 780 patients with a diagnosis of CLL. After a median of 6.4 years (0.1-36.4) of follow-up from diagnosis, 323 of 780 CLL patients (41.4%) required frontline therapy. The median age at the time of treatment was 69.8 years (32.2-92.4). IGHV genes were unmutated in 59% (138/234), del(11q) in 17.7% (46/260), and *TP53* alterations (del(17p) and/or *TP53* mutations) in 13.7% (36/262) of patients.

RESULTS

- The frequency and evolution of treatments used as frontline therapy are presented in Figures 1 and 2, respectively.
- Survival outcomes (Figure 3): targeted therapies, chemoimmunotherapy, and mutated IGHV were related to a longer TTNT in the multivariant analysis. The median OS was not reached in patients treated with targeted therapies, and it was 5.9 years (CI 95% 4.8-7) for the rest of the patients (p=0.36). In the multivariant analysis, age younger than 65 years, female sex, and mutated IGHV were related to better OS.

Figure 1. Frequency of frontline therapy in patients with CLL from our center

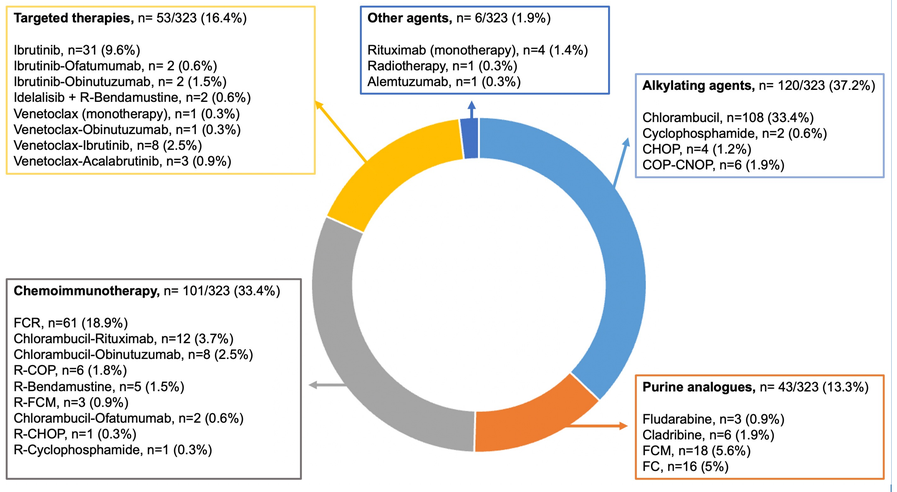


Figure 2. Evolution of frontline therapy in patients with CLL from our center

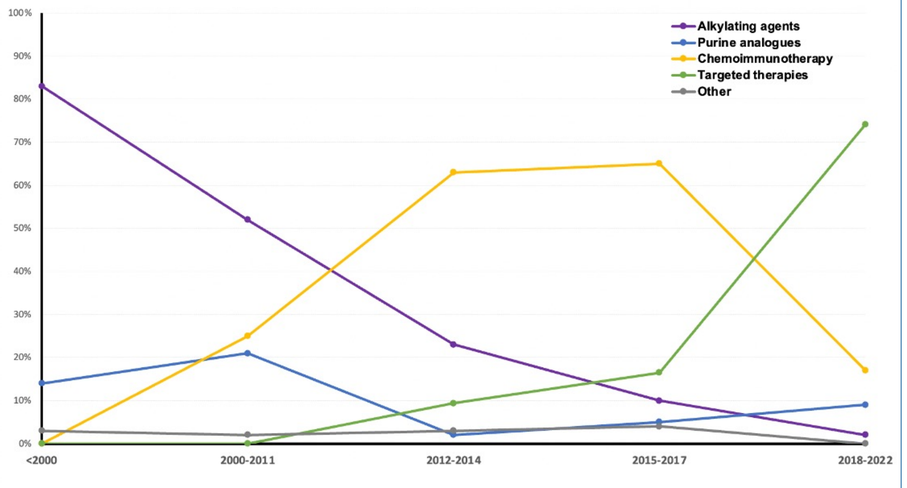
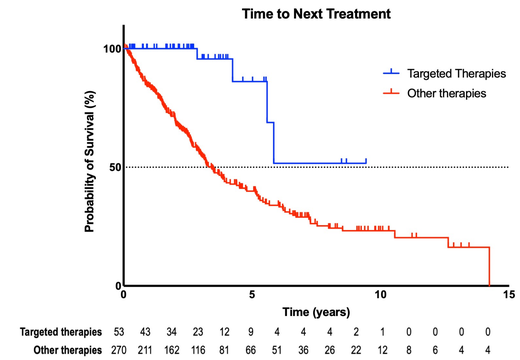
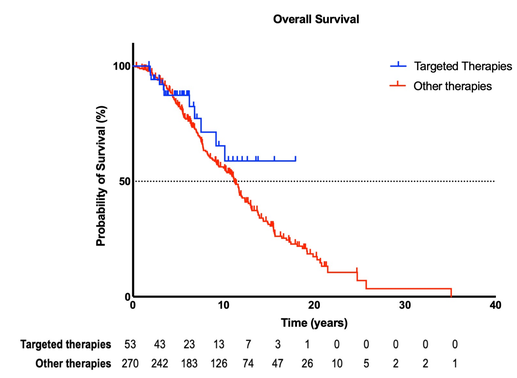


Figure 3. TTNT and OS: targeted therapies as frontline therapy vs other therapies





CONCLUSIONS

- Targeted therapies have become the most used treatment as frontline therapy in CLL in our center.
- It is necessary to include this data in the design of treatment algorithms, including best sequential treatments and optimal treatment duration.

Access to all information in the full article

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