1209. Ibrutinib plus fludarabine, cyclophosphamide and rituximab (iFCR) as initial treatment in chronic lymphocytic leukemia/ small lymphocytic leukemia with or without TP53 aberrations: A prospective real-world study in Chinese cohort

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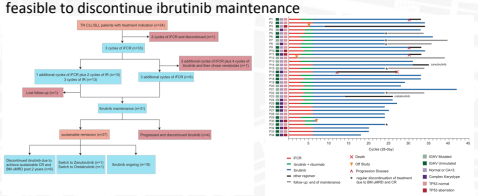
Introduction

- Bruton tyrosine kinase inhibitors (BTKi) monotherapy has introduced the concept of continuous treatment in chronic lymphocytic leukemia/small lymphocytic leukemia (CLL/SLL) until disease progression, leading to several concerns like lack of deep remission, increasing risk of toxic effects and substantial cost.
- Time-limited treatment strategies as first line treatment of CLL/SLL were comprehensively explored and BTKi combined with chemoimmunotherapy (CIT) was one of these options which could induce durable responses in young fit patients

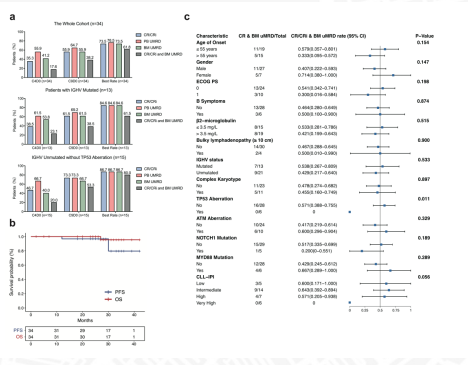
Methods

- CLL/SLL patients who were treated with iFCR as initial therapy in the First Affiliated Hospital of Nanjing Medical University (Jiangsu Province Hospital) were included without any genomic restrictions.
- Ibrutinib (420 mg daily) was given continuously for 2 years and intravenously rituximab (375 mg/m^2 in day 0 of cycle 1; 500 mg/m^2 in day 0 of cycle 2-6), fludarabine (25 mg/m^2, days 1-3) and cyclophosphamide (250 mg/m^2, days 1-3) were administered every 28-day cycle, up to maximal 6 cycles.
- Patients who achieved complete remission or complete remission with incomplete recovery (CR/CRi) and bone marrow (BM) undetectable minimal residual disease (uMRD) 2 years after iFCR initiation were feasible to discontinue ibrutinib maintenance



Results

- Thirty-four previously untreated, young fit CLL/SLL patients who received iFCR regimen between January 2019 and March 2021 were retrospectively included in our cohort. The median age was 55 years (IQR: 48-56). IGHV was unmutated in 21 of 34 (61.8%) patients; complex karyotype was present in 11 of 34 (32.4%) patients; TP53 mutation or del(17p) was detected in 6 of 34 (17.6%) patients.
- CR/CRi rate and BM uMRD rate was 35.3% (12/34) and 41.2% (14/34) after 3 cycles of iFCR and increased to 55.9% (19/34) 2 months after 6 cycles in both patients who received 3 or 4 and 6 cycles of iFCR. The best CR/CRi and BM uMRD rate were both 73.5% (25/34).
- With the median follow-up of 33 months (range 7-42 months), the 3-year PFS and OS rate was 80.0% and 95.5% respectively. CR/CRi rate and BM uMRD rate was comparable between patients with IGHV mutated and unmutated status without TP53 aberration, while all patients with TP53 aberration failed to achieve sustainable CR/CRi or BM uMRD.
- Patients who achieved MRD 10^{-6} negative post 3 cycles of iFCR sustained remission and discontinued ibrutinib maintenance.



Results

- The most common hematological adverse events were neutropenia (25/34, 73.5%) and thrombocytopenia (24/34, 70.6%), grade 3-4 neutropenia and thrombocytopenia occurred in 67.6% (23/34) and 35.3% (12/34) patients respectively. The most common non-hematological adverse events were nausea (21/34, 61.8%), fatigue (16/34, 47.1%) and vomiting (15/34, 44.1%). 35.3% (12/34) patients experienced at least one dose FC regimen reduction and 47.1% (16/34) patients experienced at least once ibrutinib dose-hold with a median duration of 7 days.

Conclusion

- The iFCR regimen could achieve high response rate and proportion of uMRD as initial treatment for young fit CLL/SLL patient without TP53 aberrations with acceptable tolerability. MRD-guided iFCR courses adjustment in patients who achieved early phase remission could achieved sustainable response and reduced toxicity

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