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ORAL ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Multicenter Study of Mantle Cell Lymphoma Outcomes Following First-Line Bendamustine-Rituximab and Second-Line Bruton's Tyrosine Kinase Inhibitor Therapy

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Background: Bendamustine and rituximab (BR) is a standard-of-care first-line (1L) therapy for older or unfit patients with mantle cell lymphoma (MCL). The SHINE trial compared BR with rituximab maintenance plus ibrutinib vs placebo in patients ≥65 years old and showed that the ibrutinib arm had significantly improved progression-free survival (PFS; median 80.6 vs 52.9 months) but similar overall survival (OS; 57% vs 55% at 7 years) compared to the placebo arm. Whether sequential treatment with BR in 1L and a Bruton's tyrosine kinase inhibitor (BTKi) in second-line (2L) can result in a similar cumulative PFS compared to 1L BR plus BTKi combination therapy is unknown. To provide insight to this question, we modeled observational data to evaluate MCL outcomes after 1L BR and 2L BTKi therapy in the BTKi era.
Methods: Patients with MCL who received 1L BR with or without rituximab maintenance in 2014-2020 at one of the 27 participating centers were included. Exclusion criteria included participation in the SHINE or ECHO trials, any additional 1L therapy other than BR (with or without rituximab maintenance), and stem cell transplant consolidation after 1L BR. Baseline characteristics, treatment, and follow-up data were abstracted by chart review. Event-free survival (EFS) was defined as time from index line treatment start to the first event (progression, relapse, retreatment, or death). OS was defined as time from index line treatment start to death. Using an intention-to-treat (ITT) framework, EFS2 was defined as time from 1L BR start to progression, relapse, or retreatment following 2L BTKi treatment or death. Patients who received a non-BTKi treatment at 2L were censored for EFS2 at 2L treatment start; living patients without an event following 1L BR or 2L BTKi were censored for EFS2 at last follow-up.
Results: A total of 618 patients with MCL who received 1L BR in 2014-2020 were included. The median age was 71 (IQR 65-76) years, and 447 (72%) were male. 59 (11%) patients had an ECOG PS ≥2, 566 (93%) had stage III-IV disease, and simplified MIPI was low in 105 (21%), intermediate in 200 (39%), and high in 202 (40%) patients.
The median follow-up following 1L BR start was 57.4 (95% CI 53.8-63.2) months. Response data were available in 580 patients, and the best ORR was 92% (79% complete response [CR] and 13% partial response [PR]). 258 (42%) patients received rituximab maintenance. As of last follow-up, 255 patients were alive and in remission after 1L BR, 92 patients died without 2L therapy, and 271 patients received a 2L therapy. The median EFS was 34.1 (95% CI 31.0-40.0) months. The median OS was 97.8 (95% CI 81.2-NA) months, the 5-year OS rate was 58.6% (95% CI 54.4-63.2), and the 7-year OS rate was 56.7% (95% CI 52.4-61.5) (Fig 1).
Among the 271 patients who started a 2L treatment, 203 (75%) received a BTKi at 2L - 101 (50%) ibrutinib, 76 (37%) acalabrutinib, and 26 (13%) zanubrutinib. The median follow-up following 2L BTKi start was 38.5 (95% CI 31.3-45.1) months. Response data were available in 171 patients, and the best ORR was 64% (36% CR, 28% PR). The median EFS was 10.7 (95% CI 7.7-14.0) months, and the median OS was 24.8 (95% CI 17.3-33.1) months with 2L BTKi therapy (Fig 2). By ITT analysis, the median EFS2 following 1L BR and 2L BTKi was 72.1 (95% CI 56.7-97.8) months (Fig 1).
A subset analysis of patients aged ≥65 years (n=471; 198 [42%] received rituximab maintenance) showed similar results. The median EFS with 1L BR was 32.7 (95% CI 29.1-36.3) months. The median OS was 81.5 (95% CI 65.0-NA) months, and the 7-year OS rate was 53.3% (95% CI 48.3-58.7). 208 patients received a 2L therapy, 163 (79%) with a BTKi. The median EFS was 11.5 (95% CI 7.6-15.8) months, and the median OS was 21.0 (95% CI 14.0-29.6) months with 2L BTKi therapy. By ITT analysis, the median EFS2 following 1L BR and 2L BTKi was 58.0 (95% CI 50.2-77.0) months.
Conclusion: In this multicenter retrospective study, initiation of 1L BR (with or without rituximab maintenance) resulted in a 7-year OS of 57%. Median EFS2 for sequential 1L BR and 2L BTKi was 72.1 months. In context, the SHINE study reported a median PFS of 80.6 months in the BR (with rituximab maintenance) plus ibrutinib arm and a 7-year OS of 57% in the ibrutinib arm and 55% in the placebo arm, where 39% of patients received a BTKi in 2L. Within the constraints of observational data, our results provide support for sequential use of BR in 1L and BTKi in 2L for patients with MCL.

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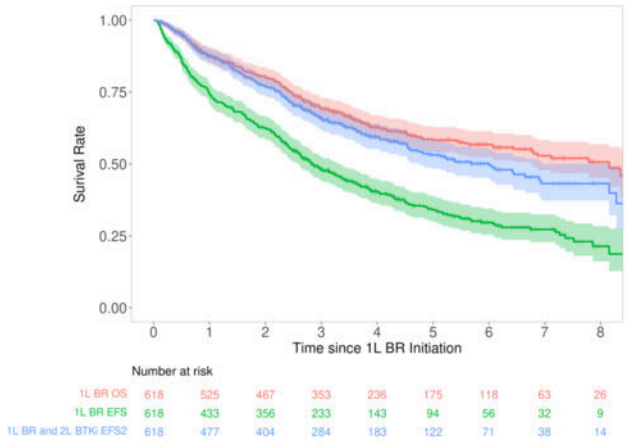

Fig 1. EFS and OS after 1L BR and EFS2 after 1L BR and 2L BTKi

Abbreviations: EFS, event-free survival; OS, overall survival; 1L, first-line; 2L, second-line; BR, bendamustine and rituximab; BTKi, Bruton's tyrosine kinase inhibitor

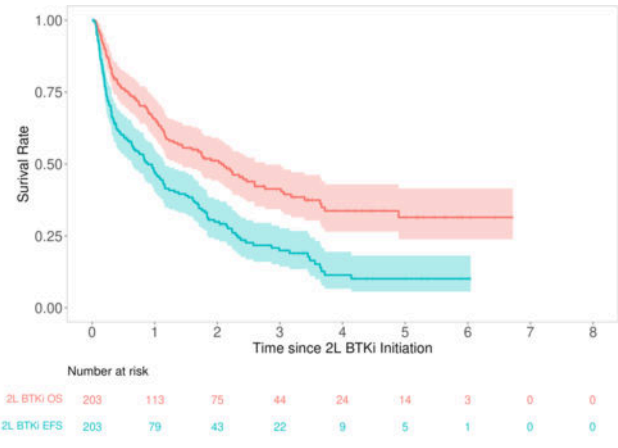

Fig 2. EFS and OS after 2L BTKi

Abbreviations: EFS, event-free survival; OS, overall survival; 2L, second-line; BTKi, Bruton's tyrosine kinase inhibitor

Figure 1

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