Provider perceptions impacting treatment choice in mantle cell lymphoma: An analysis of the SHINE trial evaluating ibrutinib + bendamustine and rituximab versus bendamustine and rituximab in first-line

Poster #HSD56

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Background

- Chemo-immunotherapy regimens are the standard first-line treatment for older patients with mantle cell lymphoma (MCL) who are ineligible for transplantation.
  - Bendamustine-rituximab (BR) is the most used chemo-immunotherapy regimen for this patient population.
  - BR is often followed by rituximab (R) maintenance therapy with the goal of increasing progression-free survival (PFS).
- BR has demonstrated PFS improvements and favorable safety profiles in older patients; however, since these patients are typically not suitable candidates for aggressive treatment or autologous stem cell transplantation, current clinical outcomes are unsatisfactory.
- Ibrutinib is an oral Bruton tyrosine kinase (BTK) inhibitor that demonstrated durable activity in relapsed/refractory MCL and demonstrated anti-tumor activity in early phase trials incorporating ibrutinib with BR in the first-line (1L) setting.
- The SHINE trial is a phase III clinical trial (NCT01776840) evaluating the combination of ibrutinib plus BR and R maintenance therapy compared with BR and R maintenance therapy for transplant-ineligible patients aged ≥65 years with stage II-IV MCL.
  - The primary endpoint of PFS was met with >27 months improvement in median PFS with addition of ibrutinib (median PFS: 80.6 months vs. 52.9 months in the placebo group).
  - Overall survival, one of several secondary endpoints, was similar in the two groups (median follow-up of 84.7 months).
  - The discontinuation rates in the ibrutinib plus BR and BR arms were similar (84% and 77%, respectively) with greater intolerance in the ibrutinib plus BR arm and greater progression in the BR arm.
- Statistically significant clinical trial outcomes are not always clinically meaningful to prescribers, especially in chronic and life-threatening disease states where improved overall survival is not a demonstrated outcome.
- The present study surveyed oncologists and hematologists to evaluate their perceptions of the SHINE trial and impact on future treatment decisions for their older patients with MCL.

Methods

- In June 2022, U.S.-based oncologists were invited to attend one of two live meetings to discuss abstracts presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting.
- A premeeting survey was used to collect demographic information (**Table 1**).
- The perceptions and reactions of providers to abstract data, including an abstract detailing the findings from the SHINE trial, were captured via audience response system (ARS) technology during the live meetings.
- Eligibility criteria for this analysis included that the participant both managed patients with MCL and answered every question related to the SHINE trial.
- Responses were aggregated and analyzed using descriptive statistics; values may not sum to 100% due to rounding or multiple answers selected.

Results

- A total of 84, primarily community-based physicians (86%), participated.
- Of the 84 participants, average clinical experience was 21 years, with 70% identifying hematology/oncology as their primary specialty, and 30% identifying medical oncology as their primary specialty.
- Together, these physicians spend 89% of their working time in direct patient care and see approximately 18 patients/day.

Results

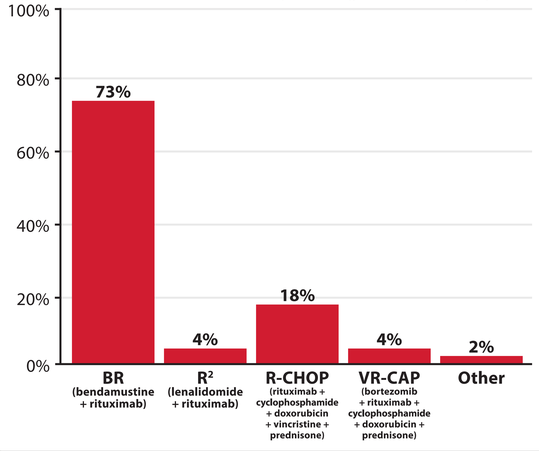
Table 1. Demographics and characteristics

N=84	n
U.S. region of practice	
Northeast	21 (25.0%)
Midwest	21 (25.0%)
South	34 (40.5%)
West	8 (9.5%)
Practice setting	
Community, privately owned	41 (48.8%)
Community, non-privately owned	31 (36.9%)
Non-community	12 (14.2%)
Years in practice	
1-10	17 (20.2%)
11-20	24 (28.6%)
>20	43 (51.2%)
Patient volume per day	
1-10	14 (16.7%)
11-20	46 (54.8%)
>20	24 (28.6%)

Key Factors in Treatment Decision Making for Transplant-Ineligible Mantle Cell Lymphoma Patients

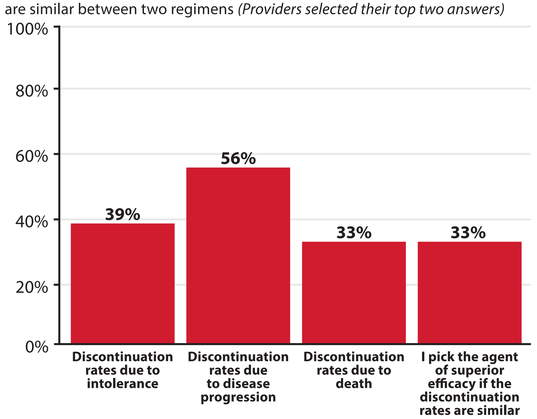
- Prior to viewing the SHINE trial data, participants indicated that BR is the preferred 1L treatment regimen for their patients with transplant-ineligible MCL (**Figure 1**).
- The majority of participants indicated that disease progression as the reason for treatment discontinuation had the greatest influence on treatment decisions (**Figure 2**).

Figure 1. Preferred 1L treatment for transplant-ineligible mantle cell lymphoma



Results

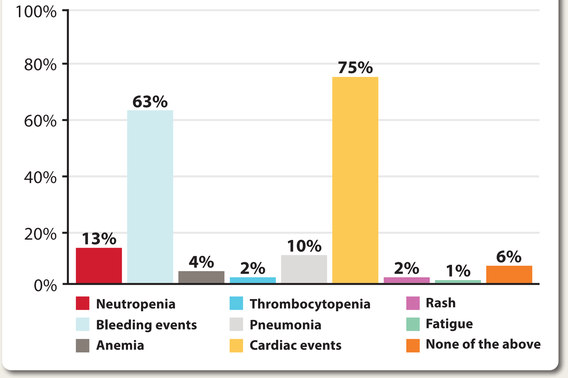
Figure 2. Discontinuation reasons most impactful when discontinuation rates are similar between two regimens *(Providers selected their top two answers)*



Perceptions of Incorporating Ibrutinib With Chemo-Immunotherapy Regimens for Transplant-Ineligible Mantle Cell Lymphoma Patients Following SHINE Trial

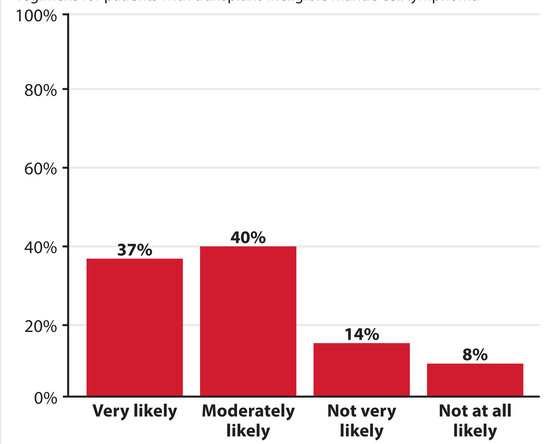
- Following the presentation of the SHINE trial, atrial fibrillation (75%) and bleeding (63%) were the most concerning adverse events (**Figure 3**).
- Approximately three-fourths of respondents indicated that they were very likely or moderately likely to incorporate ibrutinib with BR therapy (**Figure 4**).

Figure 3. Most concerning adverse events reported from the SHINE trial when incorporating ibrutinib into 1L BR treatment for patients with transplant-ineligible mantle cell lymphoma *(Providers selected their top two answers)*



Results

Figure 4. Likelihood of incorporating ibrutinib into chemo-immunotherapy regimens for patients with transplant-ineligible mantle cell lymphoma



Conclusions

- Overall, the perceptions of the SHINE trial were positive.
- Despite similar discontinuation rates in the ibrutinib plus BR and BR arms, physicians favored the ibrutinib plus BR regimen, 77% vs 22%.
- Participants indicated that disease progression had more influence when considering treatment discontinuation when compared with treatment intolerance, 56% vs 39%.
- Development of second generation BTK inhibitors have demonstrably improved safety and efficacy profiles, and many physicians expressed a desire to see additional studies with second-generation BTK inhibitors added to the BR therapy backbone as a potential future regimen.
- Future research by Cardinal Health Specialty Solutions will aim to interpret the role of emerging therapeutic strategies and their impact on treatment considerations for patients with transplant-ineligible MCL.
- As of April 6, 2023, the sponsors of the SHINE trial have withdrawn ibrutinib from accelerated FDA approval for patients with MCL who have received at least one prior therapy.

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Abbreviations: 1L, first-line; ARS, audience response system; BR, bendamustine-rituximab; BTK, Bruton tyrosine kinase; MCL, mantle cell lymphoma; OS, overall survival; PFS, progression-free survival; R, rituximab.