Real-World Treatment Patterns and Clinical Outcomes in Patients With Marginal Zone Lymphoma

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Ashley C. Saunders, PharmD, MPh, MSc,[1*] Ying Liu, PhD,[1] Jinender Kumar, MS,[1] Tao Gu, PhD[1]

[1]Bristol Myers Squibb, Princeton, NJ, USA

*Affiliation at the time the research was conducted

Background

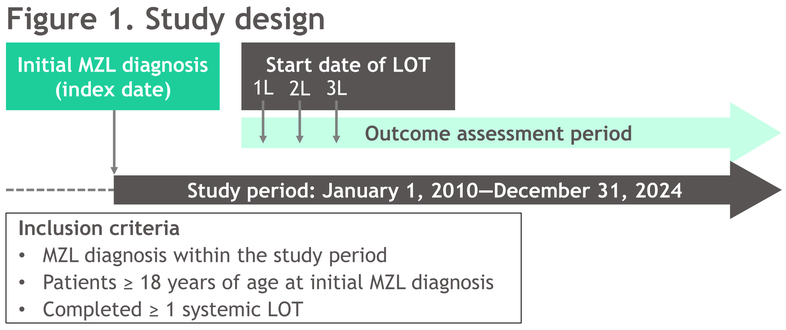
- MZL makes up ~7% of all NHL cases[1] and is the second most common indolent lymphoma in the United States[2]
- Treatment options include watchful waiting with or without radiotherapy, immunochemotherapy, Bruton tyrosine kinase inhibitors (BTKi), and more recently CAR T cell therapy[3,4]
- Patients with MZL with progression of disease ≤ 24 months (POD24) of initial treatment have worse outcomes with shorter survival and higher risk of disease transformation[5,6]
- The clinical outcomes of patients with MZL remain understudied, likely owing to its rarity and the limited number of dedicated MZL studies
- By analyzing data from a large, diverse patient population, this study seeks to provide insights into the potential unmet needs in patients with R/R MZL

Objective

- To describe real-world patient characteristics, treatment patterns, and clinical outcomes among patients with MZL who received ≥ 1 systemic line of therapy (LOT)

Methods

Figure 1. Study design



1L, first line; 2L, second line; 3L, third line.

- This was a retrospective noninterventional cohort study using electronic medical record data from the COTA real-world dataset (**Figure 1**)
- The index date was the initial date of MZL diagnosis
- ORR was defined as the proportion of patients with PR or CR
- PFS was defined as the time from the LOT start date to the first date of documented progression/relapse or death

Statistical analysis

- All results were summarized using descriptive statistics

Results

Table 1. Characteristics for patients receiving ≥ 1 LOT

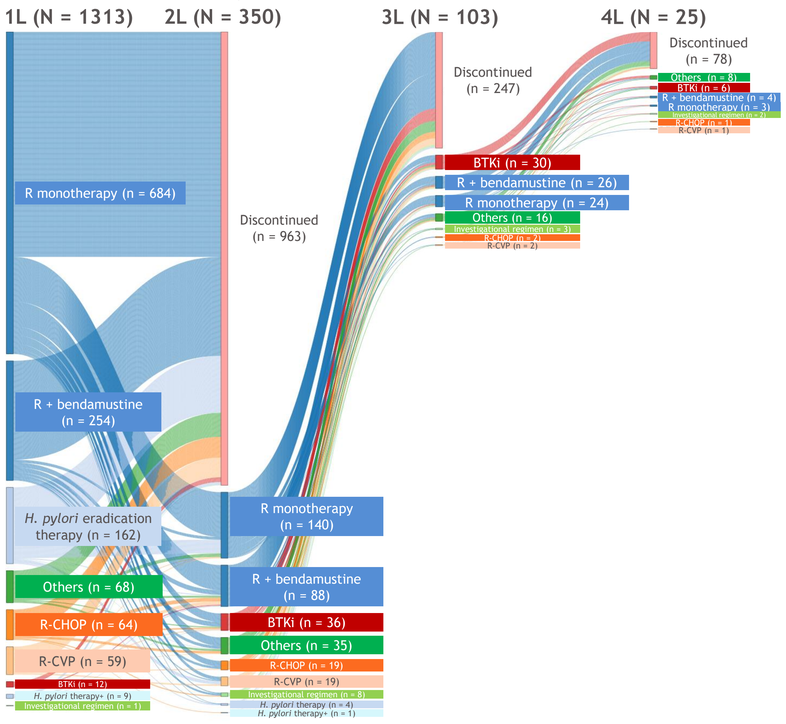
Baseline demographics and clinical characteristics[a]	Patients who received ≥ 1L (N = 1313)	POD24 yes (n = 360)	POD24 no (n = 953)
Median age on index date, y	67	68	66
< 60 y	348 (26.5)	82 (22.8)	266 (27.9)
60 to < 70 y	407 (31.0)	107 (29.7)	300 (31.5)
70 to < 80 y	360 (27.4)	90 (25.0)	270 (28.3)
≥ 80 y	198 (15.1)	81 (22.5)	117 (12.3)
Gender, n (%)			
Male	563 (42.9)	169 (46.9)	394 (41.3)
Female	750 (57.1)	191 (53.1)	559 (58.7)
White race, n (%)	956 (72.8)	258 (71.7)	698 (73.2)
Site type, n (%)			
Academic	352 (26.8)	97 (26.9)	255 (26.8)
Community	961 (73.2)	263 (73.1)	698 (73.2)
Median length of follow-up, months	56.7	42.7	62.3
Deaths, n (%)	302 (23.0)	157 (43.6)	145 (15.2)
ECOG PS, n (%)			
0	590 (44.9)	132 (36.7)	458 (48.1)
1	431 (32.8)	131 (36.4)	300 (31.5)
Ann Arbor stage, n (%)			
I	284 (21.6)	54 (15.0)	230 (24.1)
II	121 (9.2)	28 (7.8)	93 (9.8)
III	104 (7.9)	37 (10.3)	67 (7.0)
IV	471 (35.9)	140 (38.9)	331 (34.7)
Discrepant information/ND	333 (25.4)	101 (28.1)	232 (24.3)
MZL subtype, n (%)			
Gastric MALT lymphoma	277 (21.1)	72 (20.0)	205 (21.5)
Nongastric MALT lymphoma	413 (31.5)	100 (27.8)	313 (32.8)
Nodal MZL	205 (15.6)	62 (17.2)	143 (15.0)
Splenic MZL	142 (10.8)	34 (9.4)	108 (11.3)
Unspecified/ND	276 (21.0)	92 (25.6)	184 (19.3)

[a]Closest record on or after the index date to before 1L start date + 30 was reported.
MALT, mucosa-associated lymphoid tissue; ND, not documented.

Results

- Overall, 1313 patients were included; 360 (27.4%) had POD24 and 953 (72.6%) did not have POD24 (**Table 1**)
- Median age was 67 years, 57.1% were female, and 72.8% were White
- Most patients (73.2%) were treated in the community setting
- Nongastric MALT lymphoma was the most common MZL subtype (31.5%), and most patients were diagnosed at Ann Arbor stage IV (35.9%)

Figure 2. Treatment sequence for patients with MZL



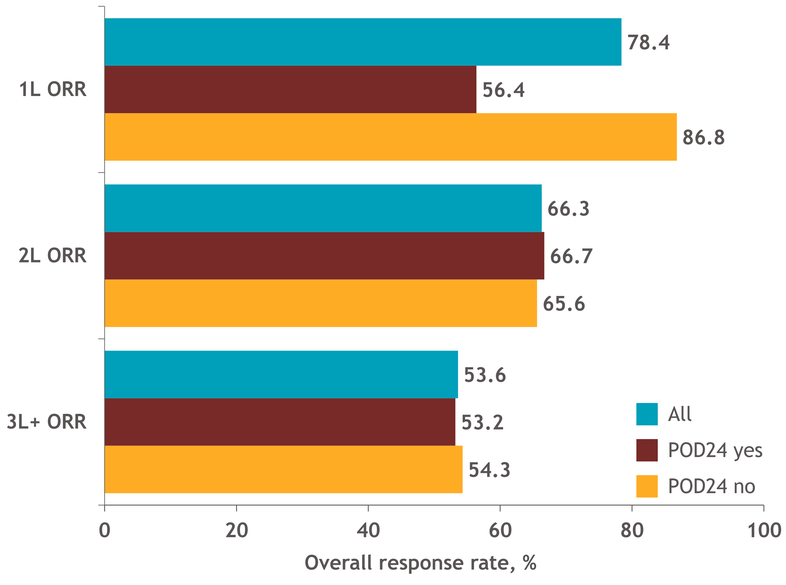
4L, fourth line; *H. pylori*, *Helicobacter pylori*; R, rituximab; R-CVP, rituximab plus cyclophosphamide, vincristine, and prednisone.

- Out of 1313 patients, 103 (7.8%) patients with MZL received 3L or later (3L+) treatments (**Figure 2**)
- The most frequently used regimens in 1L, 2L, and 3L were rituximab (52.1%, 40.0%, and 23.3%, respectively) and bendamustine plus rituximab (19.3%, 25.1%, and 25.2%, respectively)
- BTKi use increased with increasing LOT (0.9% in 1L, 10.3% in 2L, and 29.1% in 3L)

Treatment durations

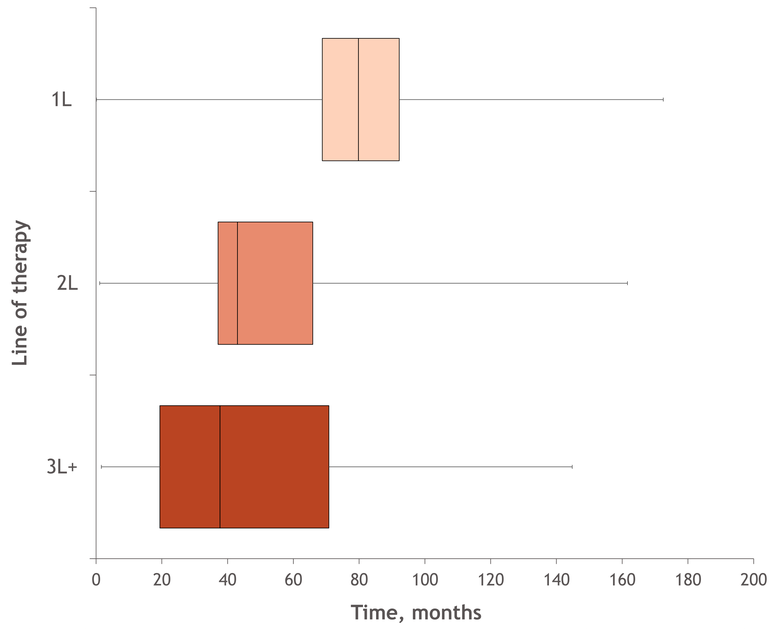
- The median (range) time from the diagnosis to the start of 1L treatment, from the end of 1L to the start of 2L treatment, and from the end of 2L to the start of 3L treatment was 1.6 months (0.0—114.6), 12.4 months (0.1—162.4), and 9.0 months (0.6—119.8), respectively
- The median (range) duration of 1L, 2L, and 3L treatments was 1.9 months (0.03—125.7), 3.0 months (0.03—120.1), and 3.9 months (0.03—44.8), respectively

Figure 3. ORR to each LOT



- ORR declined with each LOT, decreasing from 78.4% in 1L treatment to 66.3% in 2L and 53.6% in 3L+. In 1L, patients with POD24 had a lower ORR compared with those without POD24 (56.4% vs 86.8%). ORRs by POD24 status were similar in 2L and 3L+ (**Figure 3**)

Figure 4. PFS after increasing LOT



Median and 95% CI are depicted as the black line and box border, respectively. I-bars represent the min and max values.

- Overall, median (95% CI) PFS declined with increasing LOTs as follows: 79.8 months (68.8—92.2) for 1L, 43.0 months (37.1—65.9) for 2L, and 37.7 months (19.4—70.8) for 3L+ (**Figure 4**)

Discussion

- The same treatment regimens were frequently recycled from 1L to 3L+, lacking therapeutic novelty and variability
- Effectiveness of therapy decreased with each progressive LOT, resulting in worse outcomes for patients receiving 3L+ therapies
- ORR after 1L therapy was lower for patients with POD24

Conclusions

- Most patients with R/R MZL experience progressively worse outcomes in 2L and 3L+ settings
- Since the same treatment regimens are recycled from 1L to 3L+, and efficacy tends to decrease with each subsequent LOT, there is an unmet need for new 3L+ treatments that combine high efficacy with manageable safety profiles, particularly for patients with high-risk features who have poor outcomes

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