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P1145 OUTCOMES AND TREATMENT PATTERNS AFTER FIRST RELAPSE IN PATIENTS WITH WALDENSTRÖM MACROGLOBULINEMIA

Topic: 18. Indolent and mantle-cell non-Hodgkin lymphoma - Clinical

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Background: Waldenström macroglobulinemia (WM) is a rare, B cell lymphoma, with a relapsing-remitting course. Despite expansion of therapeutic options, WM remains incurable. Data on outcomes of patients (pts) after first relapse or primary refractory disease are sparse. Frequently used salvage therapies include chemoimmunotherapy (CIT), proteasome inhibitor (PI) based regimens and Bruton tyrosine kinase inhibitors (BTKi).

Aims: Analyze the outcomes of pts with WM after initial relapse and/or refractory (RR) disease and the impact of the type of therapy used in the second line setting.

Methods:

ecords of pts with WM seen at Mayo Clinic between 2000 and 2021 were reviewed. Pts with RRWM requiring second line therapy were included in the primary analysis. Response rates were assessed per the modified IWWM-6 criteria. All time to event analyses, barring progression free survival 2 (PFS2), were calculated from the start of the second line treatment, using the Kaplan Meier method. Pts were grouped based on sequence of therapy and response to frontline treatment for additional subgroup analysis.

Results:

Records of 220 pts with WM were reviewed; 92 had RRWM and were treated with a second line therapy. For the entire cohort, frontline regimens included dexamethasone, rituximab, cyclophosphamide (DRC) (n=93, 42%), bendamustine rituximab (BR) (n=71, 32%), bortezomib, dexamethasone, rituximab (BDR) (n=33, 15%), BTKi (n=20, 9%), and other (n=3, 1%). Median follow-up of RRWM cohort from second line therapy was 5.1 years (95% CI: 4.5-6.3). Pts with RRWM received the following therapies at first relapse: BR (n=24, 26%), BTKi (n=24, 26%), PI (n=17, 19%), DRC (n=6, 7%), autologous transplant (n=4, 4%), and other (n=17, 18%). Following second-line treatment, the overall response rate and major response rate (MRR) were 72% and 67% (CR=5%, VGPR=15%, and PR=47%), respectively. The median PFS was 2.7 years (CI: 1.7-4). 2-year overall survival (OS) rate was 87%. The median PFS2 from frontline therapy was 7.03 years (CI: 5.5-9.8).

Baseline characteristics were similar for subgroups in all the following subgroup analyses. With first-line therapy, 54% of pts (n=50) achieved MRR vs. 46% (n=42) who did not. The former group had similar progression-free survival (PFS) rates as well as overall survival (OS) rates and response rates (MRR and ORR) to the second-line treatment compared to their counterparts who did not achieve MRR with the frontline regimen (**Table**).

Thiry one pts received BTKi as either first or second line and 61 pts received no BTKi in either line. As expected, the BTKi group was enriched for pts with *MYD88*^{L265P} mutation (n=29, 94%) vs 49% (n=30) in the no BTKi group, p<0.001. The outcomes between the 2 groups were comparable (**Table**). The group that received frontline BTKi followed by CIT/PI based Rx as second line (n=7) was compared to that receiving frontline CIT/PI based Rx followed by BTKi (n=21). The outcomes were similar (**Table**).

Image:

Table 1. Outcomes and Treatment Responses from Second-line therapy for RRWM; subgroup analysis based on response to primary therapy and subsequent treatment strategies

	MRR (n=50)	No MRR (n=42)	p-value	BTKi (n=31)	No BTKi (n=61)	p-value	BTKi → CIT/PI (n=7)	CIT/PI → BTKi (n=21)	p-value
Age, median, range, y	65 (60-72)	66 (58-73)	0.5	68 (62-74)	63 (57-72)	0.05	73 (66-77)	65 (62-74)	0.3
Follow-up, median, 95% CI, y	4.5 (2.7-6.2)	6.1 (4.7-8.4)	**0.04**	2.4 (1.9-4.4)	6.5 (5.6-7.1)	**<0.001**	2 (1-NR)	2.9 (2.4-NR)	0.06
2-y PFS (%), 95% CI	58 (45-75)	57 (43-74)	0.9	55 (38-78)	60 (48-73)	0.5	57 (24-100)	50 (32-80)	0.2
2-y OS (%), 95% CI	90 (82-99)	83 (73-95)	0.09	88 (76-100)	86 (77-95)	0.4	100 (NR)	83 (67-100)	0.2
MRR (%)	70	64	0.6	67	67	0.9	57	66	0.6
ORR (%)	76	81	0.6	74	80	0.5	71	71	0.99

CIT/PI: Chemoimmunotherapy plus proteasome inhibitor based therapy, BTKi: Bruton Tyrosine Kinase inhibitor, ORR: Overall response rate, MRR: Major response rate, PFS: Progression (or death) free survival, TTNT: Time to next treatment, VGPR: Very Good Partial Response, CR: Complete Response, OS: Overall survival, NR: Not reached, f/b: followed by

Summary/Conclusion: Currently available second line therapies are effective in RRWM. Achieving MRR with frontline regimen does not significantly affect overall outcomes with the second-line therapy. Although follow up is short, using a BTKi as the first- or second-line therapy appears to show comparable outcomes after second line treatment as compared to not treating with a BTKi in the upfront setting or in second-line setting. Similarly, using frontline BTKi followed by CIT as second line shares similar outcomes to treating with CIT initially followed by a BTKi. These findings require confirmation in prospective studies.