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POSTER ABSTRACTS

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

Real-Life Experience with Lenalidomide Plus Anti-CD20 Antibodies for the Treatment of Patients (pts) with Relapsed/Refractory (R/R) Indolent Non-Hodgkin Lymphoma (iNHL)

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Introduction: The combination of lenalidomide and anti-CD20 antibodies (Ab) is an accepted treatment for R/R iNHL and often used as comparator in registration-directed clinical trials. In pts with R/R marginal zone lymphoma (MZL) or follicular lymphoma (FL) lenalidomide plus rituximab (R2) produced a median PFS of 27.6 months and 5-year OS 83.2% (Leonard, ASH 2022). Similarly, lenalidomide and obinutuzumab (RO) led to high PFS and OS rates in pts with R/R FL (2-year PFS 65% and OS 87%, Morschhauser, Lancet Haematol. 2019). Whether these results are reproducible in clinical practice is unknown.
Methods: We retrospectively analyzed our institutional experience in patients with R/R FL or MZL treated at MSK with R2 or RO identified on our electronic lymphoma database. Patients with previous history of histological transformation (HT) or who received R2/RO in combination with other agents were excluded. Planned lenalidomide starting dose was 20 mg orally daily for 21/28 days for twelve 28-day cycles; dose adjustments were considered in case of impaired renal function per standard practice. Rituximab was administered at 375 mg/m2 weekly for 4 weeks, then every 28 days for five 28-day cycles; and obinutuzumab at 1000 mg on D1, 8, and 15 of C1, then on D1 of each 28-day cycle for 6 cycles. Response was assessed according to the 2014 Lugano criteria; for splenic MZL and extranodal MZL patients, the ESMO guidelines were adopted to assess disease response (Zucca, Annals of Onc. 2020). PFS was defined as the time from treatment initiation to disease progression or death, and OS as the time from treatment initiation to death from any cause. Patients undergoing autologous (auto) or allogeneic (allo) stem cell transplantation (SCT) were censored at that time.
Results: 85 pts were treated between June 2013 and December 2022. Median age was 65 years (range 39-94); 71 patients (83.5%) had FL and 14 (16.5%) had MZL, and 18 patients (21%) had bulky disease (>7cm). The median number of prior therapies was 2 (range 1-8), 39 pts (46%) had ≥3 prior treatments, and 44 (53%) were refractory to their last regimen; 86% received R2 and 14% RO (Table).
At the time of this analysis, pts had received a median of 9 cycles and 8 (10%) received more than 12 cycles. Eight (9%) pts are on therapy, 35 (41%) completed the planned treatment, 17 (20%) discontinued due to progression, 4 (5%) due to adverse events (AEs), 5 (6%) because they underwent auto- or allo-SCT, and 7 (8%) by medical decision, while in 9 cases (11%), treatment

was prematurely discontinued in pts who achieved complete response (CR) after 6 cycles. Lenalidomide dose reduction was required in 47 pts (53%) due to non-hematologic AE (20 pts), cytopenia (12), impaired renal function (6), or other reasons (9). AEs of any grade occurred in all but one pt. The most frequent were neutropenia (45%), fatigue (47%), thrombocytopenia (33%), constipation (32%), rash (25%), and anemia (22%). Five patients (6%) developed a second cancer, including myelodysplastic syndrome (1), mucoepidermoid carcinoma (1), and non-melanoma skin cancers (3).

The median duration of follow-up is 30.8 months. End of treatment disease response was evaluable in 76 patients; the remaining 8 were still receiving treatment at time of data cutoff and 1 discontinued R2 due to grade 3 colitis before the first disease assessment. The overall response rate (ORR) was 66%, with 55% achieving CR. There were no differences in response rates between pts receiving R2/RO in 2nd line or ≥3rd line, or between pts treated with R2 and RO. The median PFS was 21 months, and the 2-year PFS rate was 44.3% (95% CI: 32.7-60.0%). Seventeen pts died, 10 due to lymphoma and 7 due to other causes. HT occurred in 6 pts. The median OS was not reached, and the 2-year OS rate was 84.4% (95% CI: 75.9-92.6%) (Figure).

Conclusion: This is the first real-life study of combined lenalidomide and anti-CD20 Ab for pts with R/R iNHL. Efficacy results were comparable to those reported in clinical trials and we observed no new safety signals. Our findings reaffirm the role of lenalidomide plus anti-CD20 Ab in the management of R/R iNHL and help define the benchmark for registration-directed clinical trials that utilize R2/RO as the control arm.

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Table. Baseline Demographics and Disease Characteristic of the Cohort (N = 85)

Characteristic	N (%)
Median age (range)	67 (42-81)
Age ≥ 65 years	45 (53)
Male sex	48 (57)
Ann Arbor stage	
I-II	14 (16.5)
III-IV	71 (83.5)
Bulky disease (>7 cm)	18 (21)
Histology	
FL	71 (83.5)
Grade 1-2	57 (67.1)
Grade 3A	13 (15.2)
Not available	1 (1.2)
MZL	14(16.5)
Extranodal MZL	3 (3.5)
Nodal	7(8.3)
Splenic	4 (4.7)
Prior number of lines	
1	29 (34)
2	17 (20)
3	16 (19)
4	22 (27)
Refractory to last regimen (N=83)	44 (53)

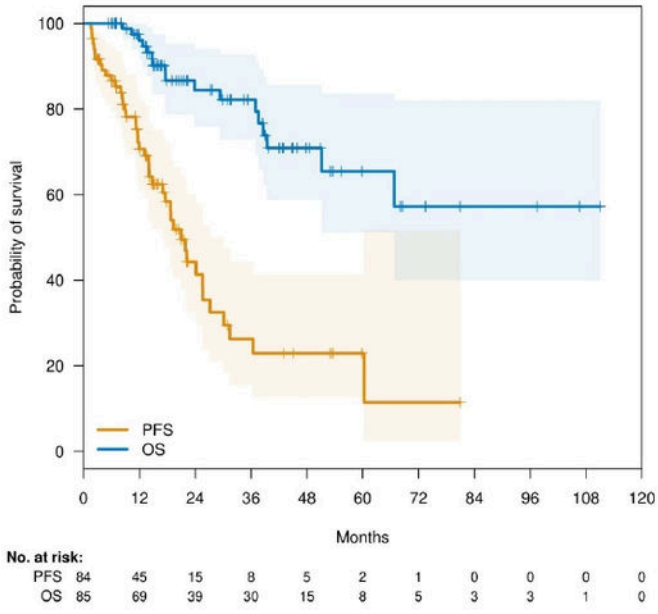

Figure 1

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