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P1156 MAGNIFY PHASE 3B STUDY OF LENALIDOMIDE + RITUXIMAB (R2) FOLLOWED BY MAINTENANCE IN RELAPSED/REFRACTORY INDOLENT NON-HODGKIN LYMPHOMA: COMPLETE INDUCTION PHASE ANALYSIS

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

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Background: Patients with relapsed indolent NHL (iNHL) have limited standard treatment options. Lenalidomide combined with rituximab (R^2) has shown complimentary clinical activity and is a tolerable regimen in both untreated and relapsed or refractory (R/R) patients with iNHL (RELEVANCE*: N Engl J Med* 2018;379:934 and AUGMENT: *J Clin Oncol.* 2019;37:1188).

Aims: These analyses examine the MAGNIFY interim primary endpoint of overall response rate (ORR; 1999 IWG) for induction R^2 in efficacy-evaluable patients receiving ≥ 1 treatment and who have available baseline and post-baseline assessments.

Methods: MAGNIFY is a multicenter, phase 3b trial in patients with R/R follicular lymphoma (FL) grades 1–3b, transformed FL (tFL), marginal zone lymphoma (MZL), or mantle cell lymphoma (MCL; NCT01996865) exploring optimal lenalidomide duration. In the induction phase, lenalidomide 20 mg PO on days 1–21 of a 28-day cycle + rituximab IV at 375 mg/m^2/week cycle 1 and then every 8 weeks starting with cycle 3 (R^2) are administered for 12 cycles. Patients with stable disease, partial response, or complete response/complete response unconfirmed (CR/CRu) were randomized 1:1 to R^2 vs rituximab maintenance for 18 months. Data presented here are the complete analysis from the induction phase in efficacy-evaluable patients with FL grades 1–3a or MZL (FL grade 3b, tFL, and MCL not included).

Results: As of March 5, 2021, 394 patients (318 [81%] FL gr1–3a; 76 [19%] MZL) were enrolled. The median follow-up was 40.6 mo (range, 0.6–79.6). Median age was 66 y (range, 35–91), 328 (83%) had stage III/IV disease, with a median of 2 prior therapies (94% prior rituximab-containing). ORR was 71% (n = 279) with 42% (n = 164) CR/CRu (Table). All patients have completed R^2 induction (n = 232, 59%) or discontinued study treatment (n = 162, 41%). 141 patients (36%) prematurely discontinued both lenalidomide and rituximab, primarily due to adverse events (AEs) (n = 54, 14%) or progressive disease (n = 42, 11%). The majority of patients who have completed induction have been randomized and entered maintenance (n = 217). Median duration of response in the induction period was not reached (95% CI, 43.9 mo–NR), and median progression-free survival in the induction safety population (n = 393) was 50.5 mo (95% CI, 39.5–NR). Efficacy results are reported in the table by histology subgroups (FL vs MZL), and rituximab-refractory, double-refractory, and early relapse statuses. Most common all-grade treatment emergent AEs (TEAEs) were 47% fatigue, 43% neutropenia, 37% diarrhea, 30% nausea, and 30% constipation. Grade 3/4 AEs occurring in ≥ 5% of patients included 37% neutropenia (10 patients [3%] had febrile neutropenia), 8% leukopenia, 6% thrombocytopenia, 5% anemia, and 5% fatigue. TEAEs led to discontinuation of lenalidomide in 19% of patients and rituximab in 12% of patients; reduction or interruption of lenalidomide in 64% of patients; and to interruption of rituximab in 30% of patients (dose reduction for rituximab was not allowed).

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Neutropenia was the most common TEAE leading to lenalidomide discontinuation in 6% and reduction/interruption in 32%, and rituximab discontinuation in 3%. Infusion-related reaction was the most common TEAE leading to rituximab interruption in 8%.

Image:

Table. Efficacy for induction R^2 in R/R iNHL

	ORR, n (%)	CR/CRu, n (%)	DOR, median (95% CI), mo	PFS, median (95% CI), mo*
All FL gr 1–3a + MZL, N = 394	279 (71)	164 (42)	NR (43.9–NR)	50.5 (39.4–NR)
Histology				
FL gr 1–3a, n = 318	230 (72)	134 (42)	NR (45.8–NR)	51.1 (38.7–NR)
MZL, n = 76	49 (64)	30 (39)	39.0 (29.4–NR)	41.2 (29.9–NR)
R-refractory				
Yes, n = 140	84 (60)	47 (34)	NR (34.7–NR)	27.4 (18.1–38.4)
No, n = 254	195 (77)	117 (46)	NR (43.9–NR)	NR (49.7–NR)
Double refractory				
Yes†, n = 85	43 (51)	21 (25)	27.4 (17.7–NR)	18.1 (15.5–25.9)
No, n = 309	236 (76)	143 (46)	NR (45.8–NR)	NR (41.6–NR)
Early relapse				
Yes‡, n = 133	86 (65)	43 (32)	37.0 (24.9–NR)	27.4 (20.3–41.6)
No, n = 261	193 (74)	121 (46)	NR (NR–NR)	NR (41.4–NR)

*If patients in maintenance at cutoff, response assessments also contributed to PFS.
†Refractory to both rituximab (monotherapy or combo) and alkylating agent.
‡Progressed or relapsed ≤ 2 y of initial diagnosis after 1L systemic treatment.

Summary/Conclusion: These data represent complete analysis of all patients in the induction phase of MAGNIFY which continue to support that R^2 is active with a tolerable safety profile in patients with R/R FL grade 1–3a and MZL, including rituximab-refractory, double-refractory, and early relapse patients.