MAGNIFY: PHASE IIIB INTERIM ANALYSIS OF INDUCTION R2 FOLLOWED BY MAINTENANCE IN PATIENTS WITH RELAPSED/REFRACTORY INDOLENT NON-HODGKIN LYMPHOMA

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Background
There is a lack of standard treatment approaches for patients with relapsed indolent non-Hodgkin lymphoma (iNHL). Current study results with PI3K inhibitors have reported a median PFS of < 1 y in the relapsed/refractory setting (R/R) for patients with iNHL. Lenalidomide, an immunomodulatory agent, enhances the activity of rituximab when combined into a regimen known as R^2, which has recently reported a median PFS of 39.4 mo in patients with R/R iNHL patients from the phase III AUGMENT study (Leonard. ASH 2018:445).

Aims
These analyses examine the 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
The multicenter, non-registrational phase IIIb MAGNIFY trial in patients with R/R follicular lymphoma (FL) grade 1-3a and marginal zone lymphoma (MZL) was designed to determine the optimal duration of lenalidomide (NCT01996865). R^2 treatment includes lenalidomide 20 mg/d, d1-21/28 plus rituximab 375 mg/m^2/wk cycle 1 and q8wk cycles 3+ given for 12 cycles, and is followed by 1:1 randomization in patients with stable disease or better to continued R^2 vs rituximab maintenance.

Results
370 enrolled patients (80% FL grade 1-3a; 20% MZL) had a median age of 66 y, 83% stage III/IV disease, and a median of 2 prior therapies (95% prior rituximab-containing). At a median 16.7 mo follow-up, efficacy-evaluable patients demonstrated a 73% ORR and 45% complete response (CR; Table). Similar efficacy results were shown for patients by histology. Overall, the median time to response (TTR) was 2.7 mo, median duration was response (DOR) was 36.8 mo, and median progression-free survival (PFS) was 36.0 mo. According to their refractory status to rituximab at baseline, patients who were rituximab-refractory and non-refractory, respectively, had an ORR (CR) of 63% (40%) and 78% (47%), and median PFS of 18.1 mo and not reached. Of 370 patients who were randomized, 142 (38%) have entered the maintenance phase. The most common all-grade adverse events were 48% fatigue, 40% neutropenia, 35% diarrhea, 30% nausea, and 29% constipation. Although the grade 3/4 adverse event neutropenia was 34%, all others were < 6%.

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

	ORR, %	CR, %	Median TTR, mo (range)	Median DOR, mo (95% CI)*	Median PFS, mo (95% CI)*
Overall	73	45	2.7 (1.6-12.0)	36.8 (35.8-NR)	36.0 (26.5-NR)
By histology					
FL gr 1-3a	74	46	2.8 (1.6-12.0)	NR (27.7-NR)	30.2 (23.0-NR)
MZL	65	38	2.7 (1.9-11.1)	35.8 (NR-NR)	38.4 (26.5-38.4)
Rituximab-refractory status					
Yes	63	40	2.8 (1.6-12.0)	35.8 (19.2-NR)	18.1 (15.5-26.5)
No	78	47	2.7 (1.6-11.6)	NR (36.8-NR)	NR (36.0-NR)

*If patients were already in maintenance at data cutoff, then response assessments also contributed to DOR and PFS.

Conclusion

R^2 therapy is an active treatment regimen in patients with R/R FL grade 1-3a and MZL, including patients refractory to rituximab, and with a tolerable safety profile.