EFFICACY WAS IMPROVED WITH LENALIDOMIDE/RITUXIMAB (R2) VS RITUXIMAB/PLACEBO IN PATIENTS WITH FOLLICULAR LYMPHOMA IRRESPECTIVE OF POD24 STATUS IN THE PHASE III AUGMENT STUDY

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Background
Less favorable prognosis and survival have been reported for follicular lymphoma (FL) patients who relapse within 2 years of initial chemoimmunotherapy (ie, POD24; Casulo et al. *Blood.* 2019).

Aims
The objective of this analysis was to evaluate the potential impact of POD24 on efficacy in the randomized phase III AUGMENT study of lenalidomide/rituximab (R^2) vs rituximab/placebo (R/placebo).

Methods
Patients had relapsed/refractory (R/R) FL grade 1-3a after ≥ 1 prior systemic therapy, but were not refractory to rituximab. R^2 treatment was lenalidomide PO 20 mg/day (d), d1-21/28 X12 cycles plus rituximab IV 375 mg/m^2 given cycle 1, d1, 8, 15, 22 and d1, cycles 2-5. Rituximab and placebo control were given on the same schedule. The primary endpoint was progression-free survival (PFS) per 2007 IWG (without PET) by independent central review. POD24 was defined post-hoc as progression or relapse within 2 years of initial antilymphoma treatment, which included immuno- and/or chemotherapy.

Results
As of 22June2018, 147 FL grade 1-3a patients were randomized to R^2 and 148 to R/placebo. FL patients had a median age of 62 years (range, 26-88), 74% with Ann Arbor stage III/IV disease, 34% high FLIPI score, 84% received prior rituximab, and 53% prior antilymphoma treatment within 2 years of enrollment. 56 (38%) R^2 and 57 (39%) R/placebo patients were identified as relapsing/progressing within 2 years of initial treatment (POD24). Median PFS was improved in patients receiving R^2 vs R/placebo, irrespective of POD24 status (R^2 vs R/placebo: HR = 0.41 [95% CI, 0.24-0.68] with POD24 and HR = 0.43 [95% CI, 0.28-0.65] with no POD24; Table). Best responses (ORR and CR) were similar within each arm in patients with or without POD24. Treatment with R^2 (vs R/placebo) reduced the risk of relapse/progression by 59% in patients with POD24, and improved both ORR and CR. Similar outcomes were shown for patients who relapsed within 2 years from diagnosis (data not shown).

Table. Efficacy of R^2 vs R/placebo by POD24 Status in Patients With R/R Follicular Lymphoma

	R^2			R/Placebo		
	All FL Patients (n = 147)	POD24 (n = 56)	No POD24 (n = 89)	All FL Patients (n = 148)	POD24 (n = 57)	No POD24 (n = 89)
Median PFS, mo (95% CI)	39.4 (23.1-NR)	30.4 (16.8-NR)	39.4 (22.9-NR)	13.9 (11.2-16.0)	13.8 (6.7-16.9)	13.9 (11.2-16.6)
ORR, %	80	80	80	55	51	58
CR, %	35	30	37	20	18	21

Conclusion
The efficacy of R^2 was superior over R/placebo in patients with FL grade 1-3a. Improvements with R^2 were evident in the subgroup of patients with POD24, patients who have historically been associated with less favorable outcomes.