POLATUZUMAB VEDOTIN (POLA) + OBINUTUZUMAB (G) AND LENALIDOMIDE (LEN) IN PATIENTS (PTS) WITH RELAPSED/REFRACTORY (R/R) FOLLICULAR LYMPHOMA (FL): INTERIM ANALYSIS OF A PHASE IB/II TRIAL

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Background
Pola-G-Len has the potential to enhance anti-tumor immune response in R/R FL. Here, we report a pre-planned interim analysis of a phase Ib/II study (NCT02600897) of Pola-G-Len in pts with R/R FL.

Aims
To assess the safety and efficacy of induction and maintenance with Pola-G-Len in pts with R/R FL.

Methods
This is an ongoing, open-label, multicenter study of pts with R/R FL (excluding grade [Gr] 3b) who have received ≥1 prior anti-CD20 antibody-containing chemo-immunotherapy regimen**.** The study comprises an initial 3+3 dose-escalation (DE) phase (to determine the recommended phase II dose [RP2D] of both Pola and Len for the Pola-G-Len regimen) followed by an expansion phase to assess the RP2D of Pola and Len. Pts received induction treatment with 6x 28-day (D) cycles (C) of: G 1000mg IV (C1: D1, D8, D15; C2–6: D1); Pola 1.4mg/kg or 1.8mg/kg (DE) or RP2D (expansion) IV (D1); and Len 10–20mg (DE) or RP2D (expansion) PO (D1–21). Pts with complete response (CR)/partial response (PR)/stable disease (SD) at the end of induction (EOI) received G 1000mg (D1 every 2mo, for 24mo), and Len (10mg, D1–21 monthly, 12mo). Primary endpoints were C1 dose-limiting toxicities (DLTs), safety/tolerability, CR rate at EOI (modified Lugano criteria).

Results
At the interim data cut-off (6 July 2018), 52 pts were enrolled: 9 discontinued the study (adverse events [AE], n=3; death due to PD, n=4; pt withdrawal, n=1; other, n=1). At baseline, the median pt age was 62 (range 32–87) years; 60% were male; 58% had FLIPI Gr 3–5; 79% had received ≥2 prior therapy lines; 50% were refractory to their last treatment; 17% had bulky disease (≥7cm). Two DLTs were reported in the cohort receiving Pola 1.8mg/kg + Len 10mg during the DE period (Gr 4 lipase/amylase elevation; asymptomatic, resolved with supportive care; Gr 3 thrombocytopenia leading to a delay in the initiation of cycle 2). Therefore, Pola 1.4mg/kg + Len 20mg was selected as the RP2D for expansion. Gr ≥3 AEs were experienced by 75% of pts: neutropenia (46%), thrombocytopenia (17%), anemia (12%) and infections (12%) were the most common AEs. AEs leading to Len dose reduction or interruption occurred in 31% and 52% of pts, respectively. One Gr 5 AE was reported (septic shock after PD in pt receiving subsequent therapy). The RP2D was determined as Pola 1.4mg/kg + Len 20mg. Preliminary efficacy data suggest high activity, with an independent review committee-assessed Modified Lugano response rate of 89% and a CR rate of 67% (**Table**). Median progression-free survival was not reached (median follow-up duration 8.95 mo in the efficacy-evaluable population).

Table Responses at end of induction (efficacy-evaluable population; recommended phase II dose; N=18)				
Best overall response, n (%)	Modified Lugano 2014		Lugano 2014	
	INV	IRC	INV	IRC
Objective response rate	16 (89)	16 (89)	16 (89)	16 (89)
CR	11 (61)[1]	12 (67)[2]	14 (78)	14 (78)
PR	5 (28)	4 (22)	2 (11)	2 (11)
SD	1 (6)	1 (6)	1 (6)	1 (6)
PD	0	0	0	0
Missing/unevaluable	1 (6)[3]	1 (6)[3]	1 (6)[3]	1 (6)[3]
[1]3 pts and [2]2 pts downgraded from CR to PR with Modified Lugano due to missing bone marrow biopsy; [3]1 pt had PR by CT (interim scan) but no PET at EOI performed before SCT				
CR, complete response; EOI, end of induction; INV, investigator assessment; IRC, independent review committee assessment; PD, progressive disease; PR, partial response; SD, stable disease.				

Conclusion

The safety profile of Pola-G-Len is consistent with known profiles of the individual drugs. Response rates at EOI with Pola-G-Len are promising, with high CR compared with available R/R FL treatments.