Randomized phase 2 trial of polatuzumab vedotin (pola) with bendamustine and rituximab (BR) in relapsed/refractory (r/r) FL and DLBCL.

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Abstract Disclosures

Background:
Pola is an antibody-drug conjugate targeting CD79b+ cells in B-NHL. Early results led to FDA breakthrough therapy status and EMA PRIME designation. We now report combined results for safety and efficacy from the randomized r/r FL and DLBCL cohorts of a phase 1b/2 study (ClinicalTrials.gov NCT02257567).

Methods:
80 FL and 80 DLBCL transplant-ineligible patients (pts) were randomized 1:1 to pola 1.8 mg/kg + BR (B: 90mg/m^2 x 2 days; R: 375mg/m^2) or BR for 6 cycles (q28 days FL, q21 days DLBCL). Primary endpoint: PET-CR, 6–8 weeks after treatment end, by independent review committee (IRC) using modified Lugano criteria.

Results:

For FL pts (pola+BR *v* BR), median age was 65 *v* 63 years, both arms had median 2 prior therapies, 41% *v* 42% were refractory to last therapy, and 64% *v* 37% had FLIPI 3–5. At 24 Oct 17, median follow up was 15 months. DLBCL characteristics and follow up were previously described (Sehn, ASH 2017). The most common grade 3–5 AEs higher in pola+BR *v* BR were cytopenias, febrile neutropenia, and infections. SAEs higher in pola+BR *v* BR were febrile neutropenia (FL, DLBCL) and infection (FL). Grade 5 AE rates were similar between treatment arms: 5% (FL) and 18% (DLBCL). PET-CR and PFS were similar between FL arms. In DLBCL, pola+BR showed significantly higher PET-CR rates ($p = 0.012$) and longer median (m) PFS ($p < 0.0001$) and mOS ($p = 0.0008$) (Table). In DLBCL, longer PFS and OS were seen for pola+BR in 2nd-line (2L), 3rd-line plus (3L+), relapsed, and refractory pts. mPFS (pola+BR *v* BR [months]): 2L (11.1 *v* 3.7), 3L+ (6.0 *v* 2.0), relapsed (11.1 *v* 5.1), refractory (6.0 *v* 1.9). mOS: 2L (not reached [NR] *v* 5.9), 3L+ (11.5 *v* 3.8), relapsed (NR, NR), refractory (11.5 *v* 3.8).

Conclusions:

The toxicity of pola+BR was manageable. In FL, pola+BR did not improve PET-CR rate; longer follow up is necessary to assess survival. In contrast, in DLBCL, pola+BR led to significantly higher PET-CR rates and notably longer PFS and OS *v* BR regardless of prior treatment status. Clinical trial information: NCT02257567

Efficacy (ITT).

	FL		DLBCL	
	Pola+BR (N = 39)	BR (N = 41)	Pola+BR (N = 40)	BR (N = 40)
IRC PET-CR, %	69	63	40	15
Median PFS, months (95% CI)	17 (13.4, NR)	17.3 (12.5, NR)	6.7 (4.9, 11.1)	2 (1.5, 3.7)
Median OS, months (95%CI)	NR	NR	11.8 (9.5, NR)	4.7 (3.7, 8.3)