ADDING POLATUZUMAB VEDOTIN (POLA) TO BENDAMUSTINE AND RITUXIMAB (BR) TREATMENT IMPROVES SURVIVAL IN PATIENTS WITH RELAPSED/REFRACTORY DLBCL: RESULTS OF A PHASE 2 CLINICAL TRIAL

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All contributions

Abstract: S802

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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).

Aims

The primary objective is complete response rate by PET scan (PET-CR) 6-8 weeks after end of treatment by independent review committee (IRC) using modified Lugano criteria (PET-CR required PET score 1-3 and negative bone marrow if positive at screening).

Methods

After informed consent was obtained, 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). Pts were stratified by duration of response to last treatment ≤12 mo or >12 mo. FL pts were also stratified by high vs low disease burden.

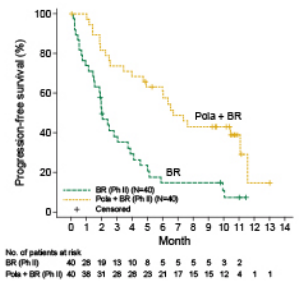
Results

For FL pts (pola+BR *vs* BR), median age was 65 *vs* 63 years, both arms had median 2 prior therapies, 41% *vs* 42% were refractory to last therapy, and 64% *vs* 37% had FLIPI 3–5. As of 24 Oct 17, median follow up was 15 months. DLBCL characteristics and follow up were previously described (Sehn, ASH 2017). **Safety:** The most common grade 3–5 adverse events (AEs) that were higher in pola+BR *vs* BR in both FL and DLBCL were cytopenias, febrile neutropenia, and infections. Serious AEs higher in pola+BR *vs* BR were febrile neutropenia (FL, DLBCL) and infection (FL). Grade 5 AE rates were similar between treatment arms per histology: 5% (FL) and 18% (DLBCL). **Efficacy:** PET-CR by IRC and progression-free survival (PFS) by investigator (INV) were similar between FL arms (Figure A). In DLBCL, pola+BR showed significantly higher IRC-PET-CR rates (p=0.012) and longer median (m) INV-PFS (p<0.0001) and overall survival (mOS; p=0.0008) (Figure A,B,C). Also 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 *vs* BR in months): 2L (11.1 *vs* 3.7), 3L+ (6.0 *vs* 2.0), relapsed (11.1 *vs* 5.1), refractory (6.0 *vs* 1.9). mOS: 2L (not reached [NR] *vs* 5.9), 3L+ (11.5 *vs* 3.8), relapsed (NR, NR), refractory (11.5 *vs* 3.8).

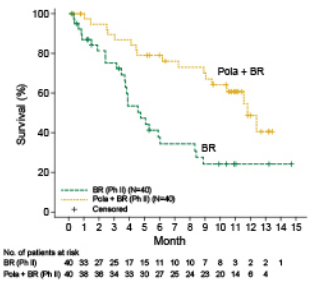
A. Efficacy (ITT)

	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)

B. Kaplan-Meier Curve for PFS, DLBCL



C. Kaplan-Meier Curve for OS, DLBCL



Conclusion

The toxicity of pola+BR was manageable and as expected. In FL, pola+BR showed similar PET-CR rate compared to BR. Time-to-event endpoints are immature at this time due to low event rate. In contrast, in DLBCL, pola+BR led to significantly higher PET-CR rate and notably longer PFS and OS compared to BR regardless of prior treatment status.

Session topic: 21. Aggressive Non-Hodgkin lymphoma - Clinical

Keyword(s): Diffuse large B cell lymphoma, Follicular lymphoma, Immunoconjugate, Phase II

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