



## The 65th ASH Annual Meeting Abstracts

## ORAL ABSTRACTS

## 627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

## Impact of Prior Bendamustine Exposure on Bispecific Antibody Treatment Outcomes for Patients with B-Cell Lymphoma

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**Introduction:** Bispecific antibodies (BsAbs) were recently approved for patients with relapsed/refractory (R/R) large B-cell lymphoma (LBCL) and follicular lymphoma (FL) based on phase I-II clinical trials. These T-cell engaging agents achieve 40-50% of complete responses, but information regarding prognostic factors is scarce. Given the deleterious effect of previous bendamustine (benda) reported for patients receiving chimeric antigen receptor (CAR) T-cell therapy, we aimed to assess if prior benda exposure had an impact on BsAb outcomes.

**Methods:** We conducted a retrospective, multicenter study including patients with LBCL or FL treated at 5 centers with BsAbs from November 2017 to March 2023. We analyzed baseline characteristics, response rates and survival outcomes according to prior benda exposure. Then, we carried out subgroup analyses according to histology (LBCL and FL) and treatment partner (monotherapy and combination regimens), assessing the impact of benda in each of these cohorts. Finally, we examined the impact of benda dose and washout before BsAb start on efficacy outcomes.

**Results:** We included 143 patients (104 LBCL, 39 FL) who received BsAb therapy, 43 (30%) of which had been previously exposed to benda at a median of 653 days (range 31-2369 days). The BsAb targeted CD20/CD3, either in monotherapy (60%) or in combination with other agents (40%). Median follow-up for the full data set was 21.8 months (CI 95% 18.1 - 25.1 months). In terms of baseline characteristics (table) median age was 66 years and most patients had an advanced stage of disease (86%), increased LDH (65%) and at least 1 prior line of therapy (90%, median 2 [range 0-9]); CAR T-cell therapy was a prior line for 15% of patients. The benda-exposed cohort had an increased rate of transformed indolent lymphoma (47% vs 25%,  $p=0.01$ ) and more prior lines of therapy ( $>2$ , 53% vs 26%,  $p<0.01$ ) in comparison with benda-naïve patients.

First, we analyzed the impact of previous benda on several parameters. Patients with prior exposure to benda had lower median CD3+ cells (543 vs 930/mm<sup>3</sup>,  $p=0.01$ ) than benda-naïve patients. In terms of toxicity, there were no differences in the incidence or severity of cytokine release syndrome and neurotoxicity. Regarding efficacy, overall and complete response rates (ORR [CRR]) were comparable between benda-exposed and naïve patients (75% [60%] vs 72% [56%], respectively [ $p=0.73$ ]). Median PFS and OS for the full cohort were 16.0 months and 43.4 months, respectively, without significant differences for the benda-exposed and naïve cohorts (16.8 vs 15.3 months [ $p=0.88$ ] and NR vs 43.4 months [ $p=0.99$ ]). In the univariate analysis for PFS, primary refractory and bulky disease, increased LDH and  $>2$  previous lines were associated with a shorter survival. The same factors carried a negative impact for OS, with the addition of previous CAR T-cell therapy and ECOG  $>0$ .

Then, we carried out subgroup analyses according to underlying histology. In the LBCL cohort ( $n=104$ ), overall and complete response rates were similar between benda-exposed and naïve patients (74% [52%] vs 71% [55%],  $p=0.81$ ), as were PFS ( $p=0.78$ ) and OS ( $p=0.76$ ). In the FL cohort ( $n=39$ ), overall and complete response rates were also comparable (77% [71%] vs 78% [61%],  $p=0.94$ ) as were PFS ( $p=0.96$ ) and OS ( $p=0.96$ ).

We focused next on the presence of a treatment partner with the BsAb. Overall (complete) response rates were significantly increased in the combination cohort (mainly with immunotherapy [70%] or chemotherapy [30%]), compared to monotherapy

(90% [75%] vs 62% [46%],  $p < 0.01$ ), as were 12-month PFS (77% vs 36%,  $p < 0.01$ ) and 12-month OS (88% vs 55%,  $p < 0.01$ ). Inside both of these cohorts, we did not identify any differences in response rate or survival between the bnda-exposed and naïve patients.

Given the wide range in washout from last bnda dose, we analyzed the impact of this interval on efficacy outcomes. We did not identify any difference according to time between last bnda dose and BsAb start. Noteworthy, only 7 patients had a washout shorter than 6 months. In terms of the bnda dose, median number of cycles was 6 (range 1-10). We did not identify an impact of bnda cycles on response rate or survival.

**Conclusions:** Bendamustine-containing regimens do not seem to confer a negative prognostic impact before BsAb therapy, in contrast to what has been reported in the CAR T-cell setting. Longer follow-up and larger cohorts are warranted to confirm these results.

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Table.- Baseline patients characteristics according to previous bendamustine exposure.

Variables	Full population n=143	Benda-naive n=100	Benda-exposed n=43	p
<b>Patient and lymphoma characteristics</b>				
Male gender, n (%)	77 (54)	58 (58)	19 (44)	0.13
Age, median years (IQR)	66 (53 - 74)	66 (53 - 73)	68 (56 - 75)	0.47
Histology, n (%)				
- Large B-cell lymphoma	104 (73)	80 (80)	24 (56)	Ref.
- Follicular lymphoma	39 (27)	20 (20)	19 (44)	<0.01
LBCL transformed indolent, n (%)	45 (34)	25 (25)	20 (47)	0.01
> 2 prior lines, n (%)	49 (34)	26 (26)	23 (53)	<0.01
Previous SCT, n (%)	26 (18)	16 (16)	10 (23)	0.32
Previous CAR T-cell therapy, n (%)	21 (15)	14 (14)	7 (16)	0.72
Primary refractory, n (%)*	50 (39)	42 (45)	8 (24)	0.03
IPI score 3-5, n (%)**	75 (53)	51 (51)	24 (56)	0.64
LDH, n (%)**				
> ULN	93 (65)	63 (63)	30 (70)	0.48
> x2ULN	28 (20)	22 (22)	6 (14)	0.28
Stage III-IV, n (%)**	123 (86)	84 (84)	39 (91)	0.99
ECOG ≥1, n (%)**	83 (58)	57 (57)	26 (60)	0.70
Bulky disease (>7cm), n (%)	33 (23)	19 (19)	14 (33)	0.09
ALC, median (IQR)**	1060 (500-1500)	1100 (600-1600)	810 (500-1255)	0.27
CD3+ lymphocytes, median (IQR)**	800 (505-1261)	930 (570-1350)	543 (237-708)	0.01
<b>BsAb-specific variables and outcomes</b>				
Combined with other agents, n (%)	57 (40)	46 (46)	11 (26)	0.03
Chemotherapy				
- Lenalidomide	20 (14)	13 (13)	7 (16)	
- Polatuzumab	18 (13)	16 (16)	2 (5)	
- Atezolizumab	2 (1)	2 (2)	0	
CRS, n (%)				
- Grade 3	7 (5)	6 (6)	1 (2)	0.32
ICANS, n (%)				
- Grade 3-4	2 (1)	2 (2)	0	0.99
Best response, n (%)				
- CR	77 (57)	53 (56)	24 (60)	-
- PR	21 (16)	15 (16)	6 (15)	0.82
- SD	6 (4)	5 (5)	1 (3)	0.47
- PD	30 (22)	21 (22)	9 (23)	0.91

**Table\_Abbreviations:** BENDA Bendamustine, IQR interquartile range, LBCL large B-cell lymphoma, SCT stem cell transplant, IPI International Prognostic Index, LDH Lactate Dehydrogenase, ULN Upper Limit of Normal, ECOG Eastern Cooperative Oncology Group, ALC absolute lymphocyte count, CR complete response, PR partial response, SD stable disease, PD progressive disease, CRS cytokine release syndrome, ICANS immune effector cell-associated neurotoxicity syndrome

(\*) never achieving complete remission with any line of treatment

(\*\*) at time of treatment with BsAb

Figure.- Progression-free survival after bispecific antibody treatment according to previous bendamustine exposure.

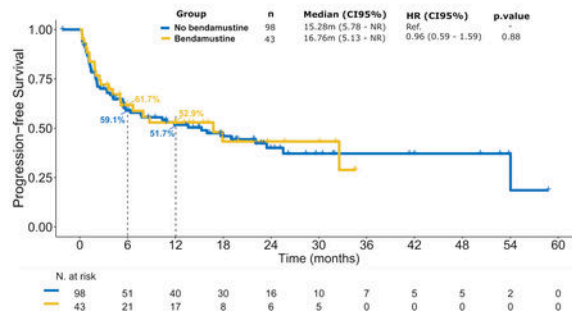


Figure 1

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