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ORAL ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Efficacy of Chimeric Antigen Receptor T-Cell Therapy Is Not Impaired By Previous Bispecific Antibody Treatment in Patients with Large B-Cell Lymphoma

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Introduction: Potential T-cell exhaustion after bispecific antibody (BsAb) treatment remains an open question, raising the theoretical concern that prior BsAb exposure could affect subsequent chimeric antigen receptor (CAR) T-cell efficacy. Clinical data on CAR T-cell outcomes after prior BsAb treatment in the setting of large B-cell lymphoma (LBCL) are scarce and highly awaited to better define treatment sequencing in relapsed/refractory (R/R) patients.
Methods: We conducted a retrospective, international study including R/R LBCL patients treated with CD19-targeted CAR T-cells at 15 centers between July 2018 and January 2023 who had been exposed to BsAbs prior to apheresis. Then, we identified a control cohort from patients included in the DESCAR-T Registry (n=764). We carried out a 1:1 propensity score matching (PSM) to achieve balance between cohorts; 13 baseline covariates were included in the PSM. We compared response rates, survival outcomes and toxicity after CAR T-cell therapy, according to previous BsAb exposure.
Results: We identified 47 LBCL patients who received BsAb therapy prior to CAR T-cell apheresis. Median age was 65 years (range 31-82), with a male predominance (66%), and median prior lines of therapy before BsAb were 2 (IQR 2-3) (Table). The BsAbs targeted CD20/CD3 (91%) or CD22/CD3 (9%), either in monotherapy (n=41, 87%) or in combination with other agents (n=6, 13%) (lenalidomide [n=2], polatuzumab [n=1], chemotherapy [n=2], missing [n=1]). The median time on BsAb treatment was 98 days (IQR 56-160) with a best overall (complete) response rate (ORR [CRR]) of 47% (19%). Median progression-free survival (PFS) and duration of response (DOR) were 3.1 months (95% CI 2.7-4.4 months) and 8.8 months (95% CI 2.2-NR), respectively. Cytokine release syndrome (CRS) occurred in 59% of patients (grade 3 in 4%). No neurologic toxicity (NT) was reported. In 26 (55%) patients, bispecific antibody was the last line before CAR T-cell therapy. Median washout between the last BsAb dose and lymphocyte apheresis for CAR T-cell manufacturing was 43 days (range 34-103 days).

In terms of the subsequent CAR T-cell therapy, patients received axi-cel (n=22, 47%), tisa-cel (n=20, 43%) or liso-cel (n=5, 11%). Most patients developed CRS after infusion (79%, 6% grade >2), with a low rate of NT (23%, 2% grade >2). Neutropenia and thrombocytopenia grade >2 were reported in 66% and 45% of patients, respectively. Regarding efficacy, ORR after infusion was 83% (CR 43%). Median PFS and overall survival (OS) were 6.6 months (95% CI 2.6-not reached [NR]) and NR (95% CI 9.0-NR), respectively. The rate of overall (complete) response was similar between patients who had previously responded (CR or PR) or not (SD or PD) to BsAb therapy (82% [41%] vs 84% [44%], respectively, p=0.64). However, all 9 patients achieving CR after BsAb achieved subsequent response to CAR T-cells. Given the wide variability in the washout between last BsAb dose and lymphocyte apheresis, we evaluated the impact of this interval on CAR T-cell efficacy. The 6-month PFS and OS of patients previously exposed to BsAb within 45 days of lymphocyte apheresis was similar to patients who had a longer washout (59% vs 47% [p=0.25] and 83% vs 67% [p=0.21], respectively).

In the second part of the analysis, we matched our cohort with a control group of CAR T-cell recipients not previously exposed to BsAbs. The final analysis included 2 sets of 42 patients with comparable characteristics. Median follow-up from CAR T-cell infusion was 11.5 months for the BsAb cohort (CI 95% 6.4-19.0 months) and 18.8 months for the control cohort (CI 95% 10.9-23.0 months). Patients with previous BsAb exposure showed a similar PFS (p=0.10, Figure) and OS (p=0.08) after CAR T-cell infusion in comparison to the control group. In terms of toxicity, there were no differences in the incidence of CRS (p=0.41) or NT (p=1.0) after infusion.

Conclusions: Previous exposure to bispecific antibody treatment targeting different antigens does not have a negative impact on survival outcomes after CAR T-cell therapy. Lack of response to a previous BsAb does not predict for lower response rates after CAR T-cell infusion.

Disclosures Iacoboni: *MSD:* Honoraria; *Novartis:* Consultancy, Honoraria; *Gilead Sciences:* Consultancy, Honoraria; *Janssen:* Honoraria; *Celgene/Bristol-Myers Squibb:* Consultancy, Honoraria; *Miltenyi:* Consultancy, Honoraria; *Autolus:* Consultancy; *Abbvie:* Honoraria; *AstraZeneca:* Honoraria. **Bachy:** *Hospices Civils de Lyon Claude Bernard Lyon 1 University:* Current Employment; *Takeda:* Honoraria; *Pfizer:* Honoraria, Other: Personal Fees; *Incyte:* Honoraria; *Novartis:* Honoraria, Other: Personal Fees; *Bristol Myers Squibb:* Honoraria, Other: Personal Fees, Research Funding; *Amgen:* Research Funding; *Roche:* Consultancy, Honoraria; *Kite, a Gilead Company:* Honoraria, Other: Personal Fees. **Herbaux:** *AbbVie, F. Hoffmann-La Roche Ltd, AstraZeneca, Janssen:* Honoraria; *AbbVie, Takeda:* Research Funding; *AbbVie, F. Hoffmann-La Roche Ltd, AstraZeneca, Janssen:* Consultancy; *Physician and professor of Hematology at academic center (CHU Montpellier France):* Current Employment. **Kwon:** *Pfizer:* Speakers Bureau; *Kite-Gilead:* Consultancy, Speakers Bureau; *Jazz:* Speakers Bureau. **Martinez-Cibrian:** *Kite:* Honoraria, Other: Travel support. **Castilla-Llorente:** *Gilead/Kite:* Consultancy, Other: Travel support; *Nektar Therapeutics:* Consultancy. **Guerreiro:** *MSD:* Honoraria, Other: TRAVEL; *Novartis:* Honoraria, Other: travel; *BMS:* Honoraria, Other: travel support; *Kite-Gilead:* Honoraria, Other: travel; *Pierre Fabre:* Honoraria, Other: travel. **Sarkozy:** *Prelude Therapeutics:* Consultancy; *Beigene:* Consultancy; *BMS:* Consultancy; *Incyte Bioscience:* Consultancy, Other: Travel, Accommodations, Expenses; *GSK:* Consultancy; *Gilead:* Other: Congress fees; *Gilead:* Other: Travel, Accommodations, Expenses; *Roche:* Other: Travel, Accommodations, Expenses, Research Funding; *Janssen:* Consultancy; *Lilly:* Honoraria; *AbbVie:* Honoraria; *Takeda:* Other: Travel, Accommodations, Expenses. **Camus:** *Kite-Gilead:* Honoraria. **Guidez:** *Gilead/Kite:* Honoraria; *Astra-Zeneca:* Honoraria; *Incyte:* Honoraria; *Takeda:* Honoraria. **Deconinck:** *GILEAD KITE:* Other: Hospitality, Research Funding; *NOVARTIS:* Research Funding; *STEMLINE MENARINI:* Consultancy; *Immunogen Inc.:* Honoraria. **Barba:** *BMS:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Nektar:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Miltenyi Biotech:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Amgen:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Kite/Gilead:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Pierre-Fabre:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Allogene:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Jazz Pharmaceutical:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Incyte:* Consultancy, Membership on an entity's Board of Directors or advisory committees. **Houot:** *Kite/Gilead, Novartis, Incyte, Janssen, MSD, Takeda, F. Hoffmann-La Roche Ltd:* Honoraria; *Kite/Gilead, Novartis, Bristol-Myers Squibb/Celgene, ADC Therapeutics, Incyte, Miltenyi:* Consultancy. **Morschhauser:** *Novartis:* Consultancy; *Roche:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Gilead:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *BMS:* Consultancy; *Genmab:* Consultancy.

Table.- Baseline characteristics of CAR T-cell recipients according to their previous exposure to bispecific antibody therapy.

Variables	BsAb cohort n=42	Control cohort n=42	SMD
Patient and lymphoma characteristics			
Male gender, n (%)	29 (69)	31 (74)	-0.085
Age, median years (range)	63 (31-82)	67 (21-78)	0.061
Histology, n (%)			
- DLBCL/HGBL	35 (83)	31 (74)	0.196
- PMBL/Transformed	7 (17)	11 (26)	
> 2 prior lines, n (%)	36 (86)	36 (86)	0
Previous SCT, n (%)	8 (19)	7 (17)	-0.05
Bulky disease, n (%)	15 (36)	19 (45)	0.16
CRP > 3mg/dL, n (%)	16 (38)	12 (29)	-0.164
LDH > 2xULN, n (%)***	12 (29)	16 (38)	0.168
ECOG >1, n (%)***	4 (10)	3 (7)	-0.069
CAR-T related characteristics			
Axi-cel, n (%)	22 (52)	20 (48)	-0.078
Months between last prior treatment and CAR-T infusion, median (IQR)	2.7 (2.3-3.8)	2.5 (2.0-3.5)	0.201
Response to bridging, n (%)			
- Responder	8 (19)	5 (12)	-0.159
- Non responder	26 (62)	22 (52)	
- No bridge	5 (12)	11 (26)	
- Not evaluated	3 (7)	4 (10)	
Year of CAR-T infusion ≥2020, n (%)	29 (69)	29 (69)	0

Table_Abbreviations: IQR interquartile range, DLBCL diffuse large B-cell lymphoma, HGBL high grade B-cell lymphoma, PMBL primary mediastinal B-cell lymphoma, SCT stem cell transplant, CRP C-Reactive Protein, LDH Lactate Dehydrogenase, ULN Upper Limit of Normal, ECOG Eastern Cooperative Oncology Group, CAR chimeric antigen receptor.

Figure.- Progression-free survival (PFS) after CAR T-cell therapy, according to previous exposure to bispecific antibodies (BsAbs).

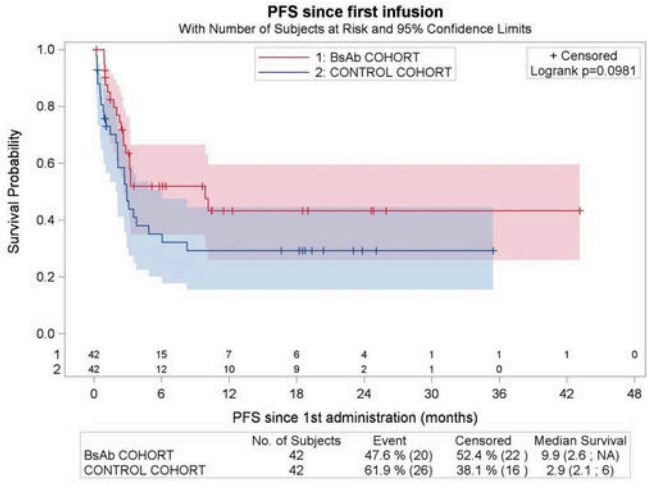

Figure 1

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