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ORAL ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Chimeric Antigen Receptor T-Cell Therapy in Elderly Patients with Relapsed or Refractory Large B-Cell Lymphoma: A Multicenter Study

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Background: Anti-CD19 chimeric antigen receptor T-cell (CART) therapy is a standard of care in patients (pts) with relapsed or refractory (RR) large B-cell lymphoma (LBCL). However, it remains underutilized in elderly pts due to limited efficacy and safety data. We therefore evaluated real world outcomes of CART in such pts.
Methods: Seven academic centers participated in this retrospective study. Pts aged ≥65 years with RR LBCL who received a commercial CART product were included. Baseline characteristics, treatment data, CART toxicity, and clinical outcomes were collected. Progression-free survival (PFS; time from infusion to disease progression or death) and overall survival (OS; time from infusion to death from any cause) were analyzed using Kaplan-Meier method. Cumulative incidences of non-relapse mortality (NRM) and disease relapse/progression were estimated accounting for competing risks. Statistical analyses were performed in JMP v15 and XLSTAT v2022.1.2.
Results: 209 pts were identified. Baseline characteristics and treatment pattern are shown in Table. Median age at infusion was 71 years (range 65-89), and 25 (12%) were ≥80 years. 131 (63%) were male, 188 (90%) were white, and 27 (13%) had ECOG PS of ≥2. The median HCT-CI was 1 (range 0-6), and 39 (22%) pts had a score of ≥3. 165 (84%) had stage III-IV disease, 131 (70%) had extranodal involvement, 24 (18%) had bulky disease, and 24 (11%) had high grade B-cell lymphoma (HGBL; double- or triple-hit lymphoma, n=15; HGBL, NOS, n=9). The median number of prior lines of therapy was 2 (range 1-8), and 99 (48%) pts had ≥3 prior lines of therapy, 45 (22%) had prior bendamustine, and 44 (21%) had prior stem cell transplant (SCT; auto-SCT, n=41; allo-SCT, n=2; both auto- and allo-SCT, n=1).
Bridging therapy was given to 100 (52%) pts; among those, 57 had chemotherapy, 20 had radiotherapy, 6 had both chemotherapy and radiotherapy, 10 had lenalidomide-based regimen, and 7 had CD20 antibody and/or corticosteroids. Axicabtagene ciloleucel (axi-cel) was most frequently used (63%, n=131), followed by lisocabtagene maraleucel (liso-cel) (24%, n=49) and tisagenlecleucel (tisa-cel) (13%, n=27).
Cytokine release syndrome (CRS) occurred in 75% of pts, and a minority (6%) had grade ≥3. Immune effector cell associated neurotoxicity syndrome (ICANS) occurred in 55%, and 29% had grade ≥3. The management of CRS and ICANS included corticosteroids in 101 (49%) pts, tocilizumab in 116 (56%) pts, and other biologic agents (anakinra, siltuximab, basiliximab) in 8 (4%) pts.
Day 30 response was evaluable in 195 pts with an objective response rate (ORR) of 84%, and a complete response rate (CR) of 52%. 82% of the responders continued to have a response at 3 month follow up. The ORR/CR rates were 86%/53% for axi-cel, 64%/44% for tisa-cel, and 89%/52% for liso-cel, respectively.
At a median follow up of 19.1 months (95% CI 16.1-23.6) after infusion, the median PFS was 6.7 months (95% CI 5.1-11.5), with 6- and 12-month PFS rates of 54% (95% CI 47-61) and 43% (95% CI 35-50), respectively. The median OS was 16.5 months

(95% CI 13.2-26.7), and the 6-and 12-month OS rates were 70% (95% CI 64-77) and 61% (95% CI 54-68), respectively. The NRM rate was 17% (95% CI 11-24) at 1 year, primarily due to infections including 5 COVID-19 related deaths. In univariate analysis, ECOG PS ≥2, bulky disease, elevated LDH, and the need for bridging therapy were associated with inferior PFS and OS. No significant difference in PFS and OS was seen based on age at infusion with a median PFS of 6.4 vs 9.6 vs 6.4 vs 6.0 months (*P*=0.93) (Figure) and OS of 16.4 vs 19.2 vs 28.5 vs 12.7 months (*P*=0.85) in age groups ≥65-69 vs ≥70-74 vs ≥75-79 vs ≥80-89. In addition, there was no statistically significant difference in PFS and OS based on type of CART with a median PFS of 6.4 vs 5.6 vs 12.7 months (*P*=0.16) and OS of 15.1 vs vs 16.1 vs NR months (*P*=0.24) in pts treated with axi-cel vs tisa-cel vs liso-cel. **Conclusions:** In this large multicenter study of elderly pts with RR LBCL, CART therapy demonstrated favorable efficacy and safety profile comparable to that in pivotal registration trials. Survival outcomes appeared similar regardless of patient age, including those aged ≥80 years, and type of CART product used. Similar to younger pts, high tumor burden and poor performance status at CART infusion were associated with inferior survival. This analysis confirms that older pts should not be excluded from receiving CART therapy solely due to chronological age.

Disclosures Pophali: *SeaGen:* Honoraria. **Fenske:** *Beigene:* Consultancy, Speakers Bureau; *Kite (Gilead):* Consultancy, Speakers Bureau; *Servier Pharmaceuticals:* Consultancy, Speakers Bureau; *MorphoSys:* Consultancy, Speakers Bureau; *TG Therapeutics:* Consultancy, Speakers Bureau; *SeaGen:* Consultancy, Speakers Bureau; *Adaptive Biotechnologies:* Consultancy, Speakers Bureau; *Astrazeneca:* Consultancy, Speakers Bureau; *Pharmacyclics (AbbVie):* Consultancy, Speakers Bureau; *Sanofi:* Consultancy, Speakers Bureau. **Karmali:** *Genentech/Roche:* Consultancy, Honoraria; *BeiGene:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *Calithera:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *BMS:* Consultancy, Honoraria, Research Funding; *Takeda:* Research Funding; *AstraZeneca:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *Miltenyi:* Consultancy, Honoraria, Research Funding; *Kite/Gilead:* Consultancy, Honoraria, Research Funding; *Lilly:* Consultancy, Honoraria; *Morphosys:* Consultancy, Speakers Bureau; *Janssen:* Consultancy.

Table: Baseline variables and treatment pattern of elderly patients with RR LBCL undergoing CAR-T (n=209)

Summary	Number
Age, median (range)	71 (65–89)
≥65–69	84 (40%)
≥70–74	55 (26%)
≥75–79	45 (22%)
≥80–89	25 (12%)
Sex, male	131 (63%)
Race, White	188 (90%)
ECOG PS ≥ 2	27 (13%)
HCT-CI, median (range)	1 (0–6)
0	66 (36%)
1–2	76 (42%)
≥3	39 (22%)
Histology	
DLBCL, NOS	154 (74%)
Transformed indolent lymphoma	31 (15%)
HGBL†	24 (11%)
Bulky disease, ≥ 7 cm	24 (18%)
Stage, III-IV	165 (84%)
Extranodal involvement	131 (70%)
LDH, elevated	99 (51%)
Prior therapies	
Prior lines, median (range)‡	2 (1–8)
Prior lines, ≥3	99 (48%)
Prior bendamustine	45 (22%)
Prior SCT§	44 (21%)
Refractory to last therapy	88 (60%)
Bridging therapy	100 (52%)
Lymphodepleting chemotherapy, dose reduction	69 (48%)
Type of CAR-T	
Axicabtagene ciloleucel	131 (63%)
Tisagenlecleucel	27 (13%)
Lisocabtagene maraleucel	49 (24%)

†15 patients had double- or triple - hit lymphoma and 9 had HGBL, NOS
‡16 patients had 1 prior line of therapy
§41 patients had prior auto-SCT; 2 had prior allo-SCT; and 1 had both prior auto- and allo-SCT
Abbreviations: RR, relapsed or refractory; LBCL, large B-cell lymphoma; CAR-T, chimeric receptor T-cell; ECOG PS, Eastern Cooperative Oncology Group performance status; HCT-CI, hematopoietic cell transplantation-specific comorbidity index; DLBCL, diffuse large B-cell lymphoma; HGBL, high grade B-cell lymphoma; LDH, lactate dehydrogenase; auto-SCT, autologous stem cell transplant; allo-SCT, allogeneic stem cell transplant

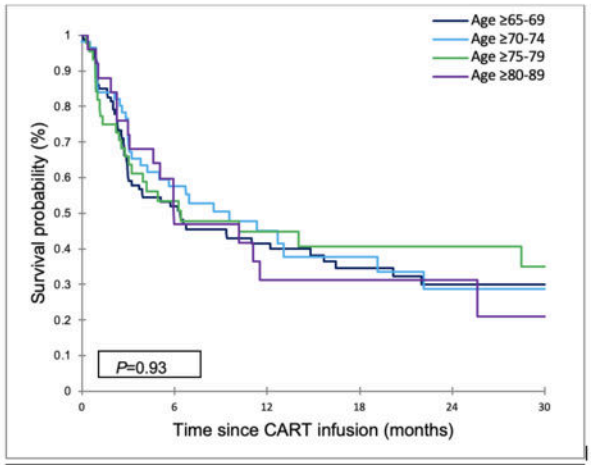

Figure: PFS of the study patients based on age groups
Abbreviations: CART, chimeric antigen receptor T-cell; PFS, progression-free survival

Figure 1

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