Poster ABCL-314

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Durable efficacy and manageable safety in patients aged ≥75 years with relapsed/refractory large B-cell lymphoma treated with tisagenlecleucel in the real-world setting

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KEY FINDINGS & CONCLUSIONS

- In the first analysis of patients aged ≥75 years, tisagenlecleucel demonstrated similar efficacy and rates of CRS and neurotoxicity in patients with R/R LBCL aged ≥75 years compared with aged <75 years
- Real-world evidence for patients aged ≥75 years supports consideration of tisagenlecleucel as a treatment option for this population
  - Tisagenlecleucel resulted in similar efficacy and similar low rates of severe toxicity compared with patients aged <75 years

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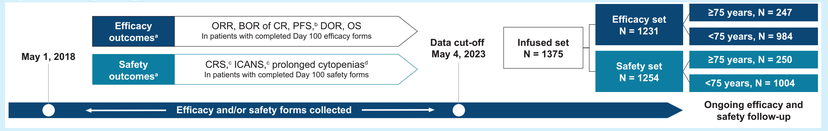
INTRODUCTION

- Large B-cell lymphoma (LBCL) is the most common form of non-Hodgkin's lymphoma (NHL) accounting for up to 40% of NHL cases worldwide[1-3]
  - Characterized by its aggressive behavior, LBCL is usually in advanced stage upon diagnosis[2,3]
  - Approximately 25% to 40% of patients experience relapsed or refractory (R/R) disease; prognosis is poor for patients not cured by first-line therapy[1,3]
- Previously, salvage chemotherapy followed by high-dose therapy and autologous stem cell transplantation (ASCT) was the standard of care for patients with R/R LBCL; however, eligibility for this approach depends largely on several factors including age and comorbidities[1,3]
  - Transplant-ineligible patients usually receive less-intensive treatments and have a poor prognosis[3]
  - Previous reports have shown that there was improved event-free survival with chimeric antigen receptor (CAR)-T cell therapy compared with salvage chemotherapy and ASCT[4,5]
- Tisagenlecleucel is an autologous CD19-directed CAR-T cell therapy approved for the treatment of patients with R/R LBCL who have received ≥2 lines of prior therapy[6]
- The Center for International Blood & Marrow Transplant Research (CIBMTR) registry is the largest dataset of patients treated with commercial tisagenlecleucel[7-11]
- Previous analysis of the CIBMTR registry showed high rates of durable response with progression-free survival (PFS), duration of response, and overall survival (OS) rates at 24 months of 28%, 53%, and 44%, respectively[12]
  - Similar durable efficacy outcomes were reported among patients ≥65 years of age and <65 years of age[12]
- Although patients treated with CAR-T cell therapy in the real world are generally older than those included in pivotal trials, limited data on outcomes among patients aged ≥75 years are available
- Here we present data on the efficacy and safety of tisagenlecleucel in patients aged ≥75 years with R/R LBCL who received tisagenlecleucel in the real-world setting

METHODS

- Data were collected as a part of a noninterventional, prospective, longitudinal study using the CIBMTR cellular therapy registry (**Figure 1**)
- All patients were treated in the United States, Canada, or Israel
- Efficacy outcomes analyzed included overall response rate (ORR), complete response rate (CRR), PFS, and OS
- Key safety outcomes included the incidence and severity of adverse events (AEs), cytokine release syndrome (CRS), and neurotoxicity
- Nominal *P* values are reported without adjusting for multiplicity

Figure 1. Study Design



ASTCT, American Society for Transplantation and Cellular Therapy; BOR, best overall response; CIBMTR, Center for International Blood and Marrow Transplant Research; CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; ICANS, immune effector cell-associated neurotoxicity syndrome; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.
[a]Center-reported. [b]Defined as time from first tisagenlecleucel infusion to first documented disease progression or death due to any cause. [c]ASTCT grading criteria. [d]Patients with longer than 30 days of follow-up and who failed to recover neutrophil/platelet levels at Day 30 (never recovered or recovered after Day 30).

RESULTS

- At data cut-off of May 4, 2023, 1375 patients had received tisagenlecleucel (infused set); 278 were aged ≥75 years
- Patients aged ≥75 years had similar baseline characteristics as the rest of the patient population (**Table 1**)
  - Same proportion of patients with Eastern Cooperative Oncology Group performance status 0-1 and those with elevated lactate dehydrogenase (LDH) in both populations
  - Received similar lymphodepleting regimens; bendamustine was used in ~15% of patients and fludarabine-based therapy was used in ~85% of patients
  - Received tisagenlecleucel in a similar number of days post relapse
  - Patients aged ≥75 years had a low frequency of prior autologous hematopoietic cell transplantation
  - Comorbidities observed in patients aged ≥75 years were similar to the rest of the patient population (**Table 1**)

Table 1. Baseline Characteristics by Age Group

	<75 years (N = 1097)	≥75 years (N = 278)
Median age at infusion, years	64.6	77.9
ECOG PS, n (%)		
0-1	930 (84.8)	237 (85.3)
≥2	61 (5.6)	12 (4.3)
Not reported	106 (9.7)	29 (10.4)
Disease status at infusion, n (%)		
Active disease	1012 (92.2)	260 (93.5)
Morphological CR	81 (7.4)	14 (5.0)
Unknown	4 (0.4)	4 (1.4)
Median number of prior lines of therapy	3.0	3.0
Any comorbidity, n (%)[a]	466 (42.5)	121 (44.0)
Pulmonary disease	288 (26.3)	65 (23.0)
Cardiac disease	154 (14.0)	60 (22.0)
Hepatic disease	114 (10.4)	21 (8.0)
Elevated LDH prior to infusion, n (%)	517 (47.1)	131 (47.1)
Lymphodepleting chemotherapy, n (%)		
Bendamustine	169 (15.4)	36 (12.9)
Fludarabine-based	909 (82.9)	239 (86.0)
Median time from relapse to infusion, days	85.0	81.0
Prior auto-HCT, n (%)	285 (26.0)	33 (11.9)

CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; auto-HCT, autologous hematopoietic cell transplantation; LDH, lactate dehydrogenase.
[a]Pulmonary disease was reported as moderate or severe; cardiac disease was reported if the patient had any history of disease; hepatic disease was reported as mild or moderate/severe.

Efficacy

- Among efficacy-evaluable patients, the ORR (complete response [CR] + partial response [PR]) was similar between patients aged ≥75 years and those <75 years (**Table 2**)
  - CRR was also similar between age groups

Table 2. Best Overall Response and Survival by Age Group

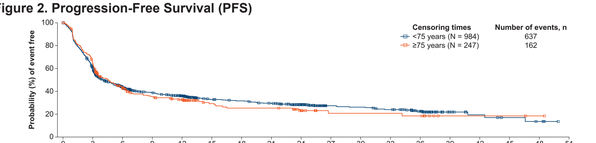
	<75 years (N = 984)	≥75 years (N = 247)
ORR, % (95% CI)[a]	60.1 (56.9-63.1)	64.4 (58.1-70.3)
BOR of CR, % (95% CI)	46.3 (43.2-49.5)	47.4 (41.0-53.8)
Month 24 PFS, % (95% CI)	28.3 (25.1-31.7)	23.1 (16.7-30.1)
Month 24 OS, % (95% CI)	44.0 (40.1-47.8)	39.3 (31.2-47.2)

BOR, best overall response; CR, complete response; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response.
[a]ORR = CR + PR.

Efficacy (cont)

- Median follow-up (infusion to data cutoff) among all patients was 30 months
- Median PFS for patients aged ≥75 years who had achieved CR was 23.8 months (95% CI, 13.68-not evaluable [NE]) versus 11.0 months (95% CI, 6.35-16.51) for patients who either had CR or PR as best overall response (BOR)
- 24-month PFS (with censoring) in patients aged ≥75 years was 23.1% (95% CI, 16.7-30.1) and was 28.3% (95% CI, 25.1-31.7) in patients aged <75 years (**Figure 2**)
  - When analyzed according to BOR, 24-month PFS in patients aged ≥75 years who had achieved CR was 47.6% (95% CI, 35.3-58.9; **Figure 3**)

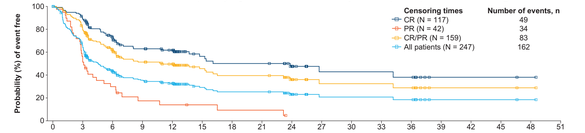
Figure 2. Progression-Free Survival (PFS)



	<75 years (N = 984)	≥75 years (N = 247)
Progression-free survival, median (95% CI), months	**4.0 (3.52-4.97)**	**4.6 (3.39-5.99)**
6-month PFS	43.8 (40.5-47.0)	43.4 (36.9-49.8)
12-month PFS	35.9 (32.7-39.1)	32.7 (26.4-39.1)
24-month PFS	28.3 (25.1-31.7)	23.1 (16.7-30.1)

PFS was defined as the time from the date of first tisagenlecleucel infusion to the date of event defined as the first documented progression or death due to any cause.

Figure 3. Progression-Free Survival (PFS) by Best Overall Response (BOR) in Patients Aged ≥75 Years

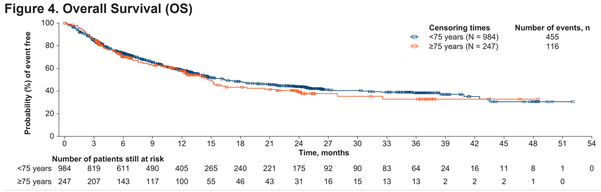


	CR (n = 117)	PR (n = 42)	CR/PR (n = 159)	All patients (N = 247)
Progression-free survival, median (95% CI), months	**23.8 (13.68-NE)**	**3.1 (2.76-5.13)**	**11.0 (6.35-16.51)**	**4.6 (3.39-5.99)**
6-month PFS	72.7 (63.3-80.1)	29.9 (16.4-44.6)	61.8 (53.5-69.1)	43.4 (36.9-49.8)
12-month PFS	61.8 (51.6-70.4)	14.0 (4.8-27.9)	49.6 (40.9-57.6)	32.7 (26.4-39.1)
24-month PFS	47.6 (35.3-58.9)	NE	36.1 (26.4-45.8)	23.1 (16.7-30.1)

CR, complete response; NE, not estimable; PR, partial response.
PFS was defined as the time from the date of first tisagenlecleucel infusion to the date of event defined as the first documented progression or death due to any cause.

- Median OS in patients aged ≥75 years was 14.7 months (95% CI, 12.27-20.49) and was 16.4 months (95% CI, 14.41-20.39) in patients aged <75 years (**Figure 4**)
- 24-month OS in patients aged ≥75 years was 39.3% (95% CI, 31.2-47.2) and was 44.0% (95% CI, 40.1-47.8) in patients aged <75 years (**Figure 4**)

Figure 4. Overall Survival (OS)



	<75 years (N = 984)	≥75 years (N = 247)
Overall survival, median (95% CI), months	**16.4 (14.41-20.39)**	**14.7 (12.27-20.49)**
6-month OS	73.3 (70.4-76.1)	70.3 (63.9-75.8)
12-month OS	58.3 (54.9-61.6)	57.8 (50.7-64.2)
24-month OS	44.0 (40.1-47.8)	39.3 (31.2-47.2)

Safety

- AE frequency in patients aged ≥75 years (N = 250) was comparable with patients aged <75 years (N = 1004) (**Table 3**)
- CRS
  - Incidences of all-grade CRS (57% vs 60%, respectively; *P*=0.31) and grade ≥3 CRS (7.2% vs 6.8%) were comparable between age groups
  - Grade 5 CRS occurred in 2 (0.8%) patients aged ≥75 years vs 6 (0.6%) patients aged <75 years
  - Tocilizumab was used to manage CRS in 65.5% of patients aged ≥75 years vs 55.6% of patients aged <75 years
  - Median time to onset of CRS was 3.0 days (interquartile range, 2.0-4.0) for both age groups

Table 3. Reported Adverse Events Within 100 Days

	<75 years (N = 1004)	≥75 years (N = 250)
CRS		
CRS any grade, n (%)[a]	606 (60.4)	142 (56.8)
Grade ≥3	68 (6.8)	18 (7.2)
Patients given tocilizumab for CRS[b]	335 (55.3)	93 (65.5)
CRS grade on receipt of tocilizumab[c]		
Grade 1	138 (41.2)	36 (38.7)
Grade 2	132 (39.4)	40 (43.0)
Grade ≥3	65 (19.4)	17 (18.3)
ICANS		
ICANS any grade, n (%)[a]	218 (21.7)	68 (27.2)
Grade ≥3	74 (7.4)	22 (8.8)
Patients given corticosteroids for ICANS	142 (65.1)	46 (67.6)

ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.
[a]CRS was graded using the ASTCT grading criteria and neurotoxicity was graded using ICANs grading (onset within 100 days of first infusion). [b]Percentages calculated from total number of patients who were reported to have CRS. [c]At 100-day reporting. Percentages calculated from total number of patients who received tocilizumab for CRS

- Immune effector cell-associated neurotoxicity syndrome (ICANS)
  - All-grade ICANS frequency in patients aged ≥75 years was comparable with patients aged <75 years (27.2% vs 21.7%, respectively; *P*=0.06)
  - Grade ≥3 ICANS was experienced by 8.8% of patients aged ≥75 years and 7.4% of patients aged <75 years
  - 4 patients aged ≥75 years experienced grade 5 ICANS vs 1 patient aged <75 years
  - Median time to onset of ICANS was similar in patients aged ≥75 years (4.5 days, interquartile range 2.0-6.5) and patients aged <75 years (5 days, interquartile range 3.0-8.0)
  - Corticosteroids were used with similar frequency to manage ICANS in patients aged ≥75 years (67.6%) and in patients aged <75 years (65.1%)
  - The most common symptom of ICANS was depressed level of consciousness in 32.4% and 28.9% in patients aged ≥75 years and <75 years, respectively

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