Poster
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Outcomes of Subsequent Anti-Lymphoma Therapies in Patients With Relapsed/Refractory Large B-Cell Lymphoma Treated With Axicabtagene Ciloleucel or Standard of Care (ZUMA-7)

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BACKGROUND

- Axicabtagene ciloleucel (axi-cel) is a CD19-directed genetically modified autologous T-cell immunotherapy with a CD28 co-stimulatory domain that provides rapid and strong expansion and reprograms T cells to trigger target-specific cytotoxicity of cancer cells[1,2]
- Axi-cel has demonstrated strong and durable efficacy in adult patients with relapsed/refractory (R/R) large B-cell lymphoma (LBCL) after ≥2 lines of systemic therapy[3,4]
  - In pivotal Cohorts 1+2 of ZUMA-1, the objective response rate (ORR) was 83% (complete response [CR] rate: 58%)[3] and 5-year overall survival (OS) rate was 43%[4]
  - In the ZUMA-7 axi-cel arm, the ORR was 83% (CR rate: 65%) and estimated 2-year OS rate, evaluated as an interim analysis, was 61%[5]
- Axi-cel significantly improved outcomes versus second-line (2L) standard of care (SOC; event-free survival hazard ratio, 0.398, *P*<.0001) in ZUMA-7 (NCT03391466)[5]
- Thus, chimeric antigen receptor (CAR) T-cell therapy has been proposed as the new SOC for 2L treatment for eligible patients[6]
- Nonetheless, patients may require additional therapy and the question of optimal management after 2L therapy remains

OBJECTIVE

- To present outcomes for patients who received subsequent anti-lymphoma treatment in ZUMA-7

METHODS

- Full ZUMA-7 study details, including primary results, were previously reported[5]
- Subsequent third-line (3L) therapy classifications for this analysis are shown in **Figure 1**
- For this intent-to-treat analysis, subsequent therapy was defined as any new, off-protocol lymphoma therapy, regardless of whether randomized protocol therapy was given
- Patients who did not meet the criteria for a progression-free survival (PFS) event were censored at fourth-line treatment initiation, if any, or last known alive date
- Patients who received subsequent stem cell transplantation (SCT) while in a response from 3L axi-cel retreatment were censored at the time of SCT
- Kaplan-Meier estimates for PFS and OS were calculated from 3L treatment initiation

Figure 1. Subsequent 3L Therapy Classifications

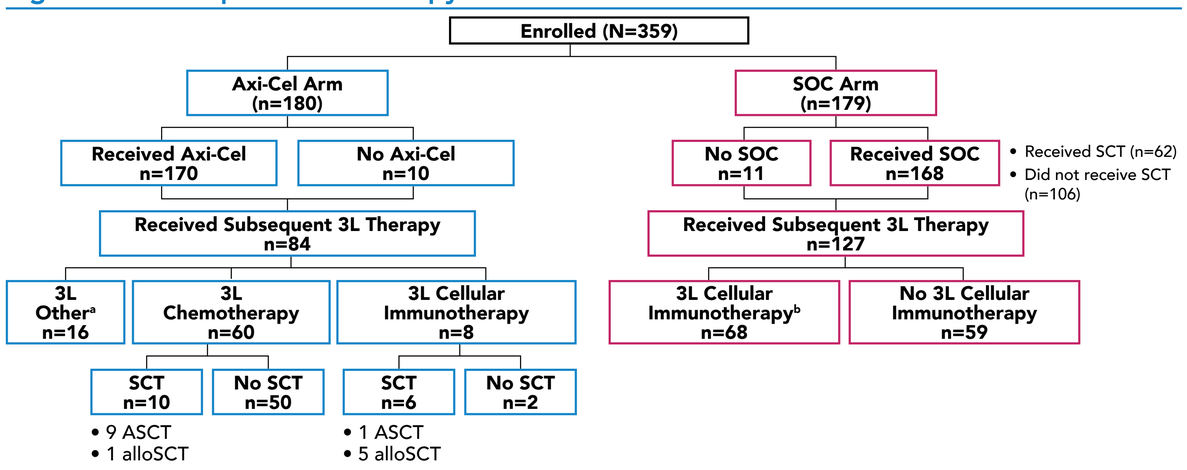
Axi-Cel Arm	Chemotherapy
	Cellular immunotherapy (axi-cel retreatment on protocol for patients who initially responded to axi-cel)
	Other
SOC Arm	Cellular immunotherapy
	Non-cellular immunotherapy

3L, third-line; axi-cel, axicabtagene ciloleucel; SOC, standard of care.

RESULTS

Overview of Subsequent 3L+ Therapy

Figure 2. Subsequent 3L+ Therapy



[a] Other 3L regimens included nivolumab, radiation, pembrolizumab, R-lenalidomide, varlilumab, alloSCT (n=1), oral dihydroorotate (clinical trial), CPI-613, dexamethasone, HDT-ASCT (n=1), and ipilimumab. [b] Patients received axi-cel (n=51); other autologous anti-CD19 CAR T-cell therapy (n=10); unspecific CAR T-cell therapy (n=4); anti-CD19/CD22 CAR T-cell therapy, allogeneic CRISPR-Cas9 engineered T cells, and NK cell infusion (n=1 each).
3L, third-line; alloSCT, allogeneic stem cell transplantation; ASCT, autologous stem cell transplantation; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; HDT, high-dose therapy; NK, natural killer; SCT, stem cell transplantation; SOC, standard of care.

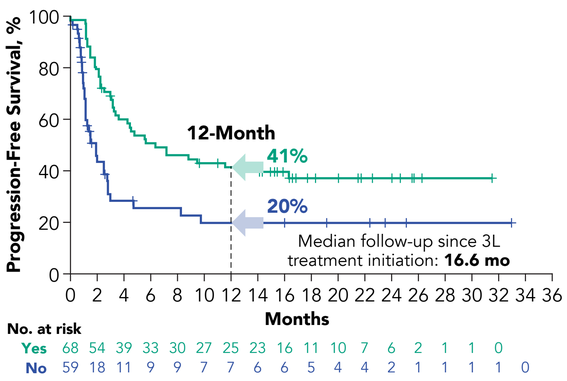
- Among randomized patients, 84/180 (47%) and 127/179 (71%) patients in the axi-cel and SOC arms, respectively, required 3L+ subsequent therapy (**Figure 2**)
- Median time to 3L therapy was 4.4 months in the axi-cel arm and 2.8 months in the SOC arm
- Six (3%) patients in the axi-cel arm and 8 (4%) patients in the SOC arm did not receive 3L therapy after disease progression

3L Treatment in the SOC Arm

Figure 3. PFS and OS by 3L Cellular Immunotherapy in the SOC Arm Since 3L Treatment Initiation

PFS

3L Cellular Immunotherapy	Median PFS (95% CI), mo
Yes (n=68)	6.3 (3.4-16.3)
No (n=59)	1.9 (1.1-2.7)

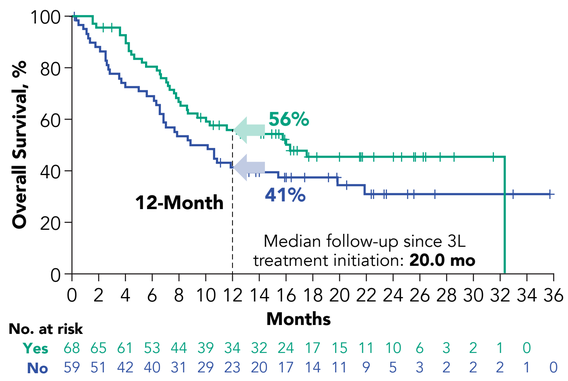


No. at risk

Yes	68	54	39	33	30	27	25	23	16	11	10	7	6	2	1	1	0
No	59	18	11	9	9	7	7	6	6	5	4	4	2	1	1	1	1	0

OS

3L Cellular Immunotherapy	Median OS (95% CI), mo
Yes (n=68)	16.3 (8.7-NE)
No (n=59)	9.5 (6.6-15.4)



No. at risk

Yes	68	65	61	53	44	39	34	32	24	17	15	11	10	6	3	2	1	0
No	59	51	42	40	31	29	23	20	17	14	11	9	5	3	2	2	2	1	0

3L, third-line; mo, month; NE, not evaluable; OS, overall survival; PFS, progression-free survival; SOC, standard of care.

- Of 127 patients in the SOC arm who required 3L subsequent therapy, 68 received 3L cellular immunotherapy (**Figure 2**)
- For patients who received 3L cellular immunotherapy (n=68), median PFS was 6.3 months and median OS was 16.3 months (**Figure 3**), with a 57% ORR (34% CR rate)
- Patients who did not receive cellular immunotherapy (n=59) had a median PFS and median OS of 1.9 months and 9.5 months, respectively

RESULTS *(Continued)*

Figure 4. Outcomes for Patients Who Received 3L Cellular Immunotherapy in the SOC Arm Versus 2L Axi-Cel

2L Axi-Cel[5]

- **Median PFS, months:** 14.7 (5.4-NE)
- **Median OS, months:** NR (28.3-NE)
- **ORR, %:** 83 (77-88)
  - **CR, %:** 65 (58-72)

3L Cellular Immunotherapy in the SOC Arm[a]

- **Median PFS, months:** 6.3 (3.4-16.3)
- **Median OS, months:** 16.3 (8.7-NE)
- **ORR, %:** 57 (45-69)
  - **CR, %:** 34 (23-46)

Data in parentheses show 95% CI.
[a] Data are since 3L treatment initiation.
2L, second-line; 3L, third-line; axi-cel, axicabtagene ciloleucel; CR, complete response; NE, not evaluable; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; SOC, standard of care.

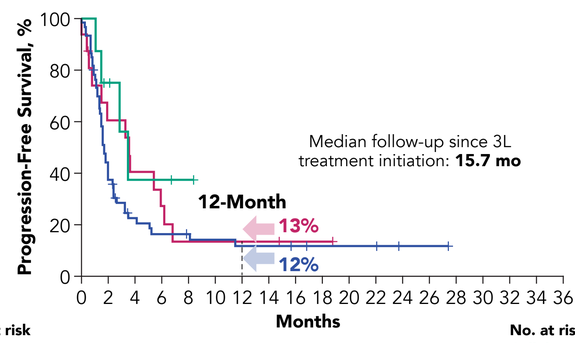
- While no formal comparative statistical analyses were conducted, outcomes for patients who received 2L axi-cel treatment appeared better compared with outcomes for patients who received 3L cellular immunotherapy in the SOC arm (**Figure 4**)

3L Treatment in the Axi-Cel Arm

Figure 5. PFS and OS by 3L Treatment in the Axi-Cel Arm Since 3L Treatment Initiation

PFS

	Median PFS (95% CI), mo
Cellular Immunotherapy (n=8)	3.5 (1.1-NE)
Chemotherapy (n=60)	1.7 (1.4-2.0)
Other (n=16)	3.5 (0.8-5.9)

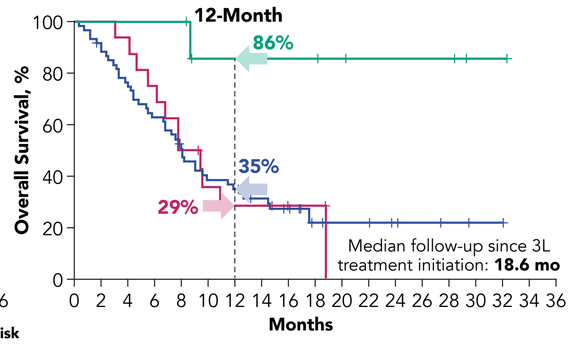


No. at risk

Cellular Immunotherapy	8	5	2	2	1	0																						
Chemotherapy	60	25	11	8	7	6	5	5	4	3	3	3	1	1	0													
Other	16	9	6	4	2	2	2	2	1	1	0																	

OS

	Median OS (95% CI), mo
Cellular Immunotherapy (n=8)	NR (8.7-NE)
Chemotherapy (n=60)	8.1 (5.8-11.5)
Other (n=16)	8.6 (5.5-NE)



No. at risk

Cellular Immunotherapy	8	8	8	8	8	5	5	5	5	5	4	3	3	3	3	1	1	0										
Chemotherapy	60	54	45	37	29	22	20	16	13	7	6	6	4	3	2	1	1	0										
Other	16	16	15	12	8	5	4	4	2	2	0																	

3L, third-line; axi-cel, axicabtagene ciloleucel; mo, month; NE, not evaluable; NR, not reached; OS, overall survival; PFS, progression-free survival.

- In the axi-cel arm, 84 patients required 3L subsequent therapy (chemotherapy, n=60; cellular immunotherapy, n=8; other, n=16; **Figure 2**)
- Patients who received 3L chemotherapy (n=60) had a 25% ORR (13% CR rate)
- For 34 patients who received 3L chemotherapy after initial response to 2L axi-cel, overall median PFS was 1.7 months and median OS was 8.1 months (**Figure 5**), with a 32% ORR (18% CR rate)
- For 8 patients who received 3L cellular immunotherapy, median PFS was 3.5 months and median OS was not reached (**Figure 5**)
- Of patients who received 3L chemotherapy, only 17% (n=10/60) received SCT (**Figure 2**)
- While results are descriptive due to low patient numbers, outcomes for patients who received SCT following 3L chemotherapy in the axi-cel arm appear improved compared with patients who did not receive SCT
  - With SCT following 3L chemotherapy (n=10): median PFS and OS were 11.5 (95% CI, 2.4-not estimable) and 17.5 (95% CI, 2.4-not estimable) months, respectively
  - Without SCT following 3L chemotherapy (n=50): median PFS and OS were 1.6 (95% CI, 1.2-1.8) and 7.2 (95% CI, 4.8-9.1) months, respectively
  - It is unknown how many patients who received 3L therapy were intended for SCT
- Eight patients in the axi-cel arm received 3L cellular immunotherapy; 6 received subsequent SCT (1 autologous SCT, 5 allogeneic SCT), 3 (allogeneic SCT) of which immediately followed 3L axi-cel (**Figure 2**)
- Of the 6 patients who received SCT, 5 remained in CR
  - 1 patient who had a partial response after axi-cel retreatment proceeded to allogeneic SCT with best response of CR, but relapsed 7.3 months after SCT
- All 6 patients were alive at data cutoff date (median follow-up since 3L treatment initiation, 24.4 months)

CONCLUSIONS

- While results are descriptive and definitive conclusions cannot be made due to the small number of patients, these data suggest that
  - Outcomes for patients who received subsequent cellular therapy appeared better when cellular therapy is given earlier (2L versus 3L)
  - 3L CAR T-cell therapy after initial response to axi-cel in 2L appears to be a viable option as patients were able to achieve clinically meaningful responses
  - Though a minority of patients who received 3L chemotherapy reached SCT, SCT can be considered for patients who are chemosensitive post 2L CAR T-cell therapy
- These findings may help inform subsequent treatment choices that provide meaningful clinical benefit for patients after failure of 2L therapy for R/R LBCL

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- These data were previously presented at the 2022 Annual Meeting of the American Society of Hematology[7]

DISCLOSURES

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