Outcomes of subsequent anti-lymphoma therapies after second-line axicabtagene ciloleucel or standard of care in ZUMA-7

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Supplementary Material

Supplementary Methods

Additional details regarding patients and study design

Adequate first-line (1L) chemoimmunotherapy included anti-CD20 monoclonal antibody and an anthracycline. Refractory disease was defined as no complete response (CR) and relapsed disease was defined as CR followed by biopsy-proven relapse ≤12 months after completion of 1L therapy.

Patients in the axicabtagene ciloleucel (axi-cel) arm received 3 days of lymphodepleting chemotherapy (cyclophosphamide 500 mg/m^2/day and fludarabine 30 mg/m^2/day) on days –5, –4, and –3 before axi-cel.

Supplementary Results

3L Treatment outcomes in the axi-cel arm

Eight patients in the axi-cel arm received third-line (3L) cellular immunotherapy (axi-cel retreatment) on protocol. Three of 6 patients had stem cell transplantation (SCT) after retreatment in the absence of progression. One patient had partial response (PR) to axi-cel retreatment on protocol and then received radiation, with best response of CR; this patient proceeded to allogeneic SCT with a best response of CR, but relapsed 7.3 months after SCT. The 2 other patients achieved CR to axi-cel retreatment on protocol and subsequently received allogeneic SCT, with best response of CR.

Of the 6 patients who received subsequent SCT after axi-cel retreatment in 3L, 3 had disease progression after 3L cellular immunotherapy and received SCT in later lines of therapy. One patient experienced disease progression at day 50 following axi-cel retreatment and received radiation and pembrolizumab; given disease progression, the patient then received chemoimmunotherapy with rituximab, gemcitabine, dexamethasone, and cisplatin (R-GDP). The patient achieved CR and went on to allogeneic SCT, with best response of CR. The second patient achieved PR to 3L axi-cel retreatment on day 50 but reported disease progression at day 100. This prompted treatment with mosunetuzumab and polatuzumab vedotin; the patient achieved CR and proceeded to allogeneic SCT, with best response of CR. The final patient achieved CR to 3L axi-cel retreatment on protocol but experienced disease progression at day 100. The patient received rituximab, dexamethasone, cytarabine, and cisplatin (R-DHAP) and achieved CR, consolidated with high-dose therapy with autologous SCT, with best response of CR.

Of the 2 patients who received 3L axi-cel but did not undergo SCT, 1 experienced disease progression after 3L axi-cel, received subsequent chemoimmunotherapy with a checkpoint inhibitor, and died 8.7 months after retreatment. The other patient remained in ongoing CR after 3L axi-cel retreatment and was alive at time of data cutoff (8.4 months after retreatment) without need for subsequent therapy.

Supplementary Tables

Supplemental Table 1. Summary of subsequent therapy in third line by therapy class

n (%)	Axi-Cel (n = 180)	SOC (n = 179)
Received any subsequent therapy	**84 (47)**	**127 (71)**
Chemoimmunotherapy*	60 (33)	44 (25)
Autologous anti-CD19 CAR T-cell therapy	8 (4)	64 (36)
Antibody-drug conjugates†	2 (1)	1 (1)
BTK inhibitor	1 (1)	3 (2)
Immunomodulatory agents	6 (3)	4 (2)
Radiation therapy alone	4 (2)	5 (3)
HDT-ASCT	10 (6)	5 (3)
Allogeneic SCT	2 (1)	0
Other cellular therapies	0	4 (2)
Allogeneic anti-CD19 CAR T-cell therapy	0	1 (1)
Autologous anti-CD19/CD22 bispecific CAR T-cell therapy	0	1 (1)
Anti-CD22 CAR T-cell therapy	0	1 (1)
Cord blood NK therapy	0	1 (1)
Other therapies (not including any anti-CD20)	12 (7)	11 (6)
4-1BB agonist	0	1 (1)
BCL2 inhibitor	0	1 (1)
BET inhibitor	0	1 (1)
Bispecific T-cell engager	0	1 (1)
Checkpoint inhibitor	8 (4)	3 (2)
CRL4-CRBN E3 ubiquitin ligase inhibitor	1 (1)	0
DHODH inhibitor	1 (1)	0
Immunotherapy not otherwise specified	0	1 (1)
Anti-CD27 monoclonal antibody	2 (1)	0
PDH-KGDH inhibitor	1 (1)	0
PI3K inhibitor	0	1 (1)
Steroids	1 (1)	3 (2)

*Including anti-CD20 therapy and POLA-BR. †Excluding POLA-BR.

Axi-cel, axicabtagene ciloleucel; BCL2, B-cell lymphoma-2; BET, bromodomain and extra-terminal domain; BTK, Bruton tyrosine kinase; CAR, chimeric antigen receptor; CRBN, cereblon; DHODH, dihydroorotate dehydrogenase; HDT-ASCT, high-dose therapy with autologous stem cell transplantation; NK, natural killer; PDH-KGHD, pyruvate dehydrogenase-ketoglutarate dehydrogenase complex; PI3K, phosphoinositide 3-kinase; POLA-BR, polatuzumab vedotin plus bendamustine and rituximab; SCT, stem cell transplantation; SOC, standard of care.

Supplemental Table 2. Summary of subsequent therapy in any line by therapy class

n (%)	Axi-Cel (n = 180)	SOC (n = 179)
Received any subsequent therapy	**84 (47)**	**127 (71)**
Chemoimmunotherapy*	70 (39)	73 (41)
Autologous anti-CD19 CAR T-cell therapy	11 (6)	97 (54)
Antibody-drug conjugates†	14 (8)	12 (7)
BTK inhibitor	11 (6)	6 (3)
Immunomodulatory agents	13 (7)	18 (10)
Radiation therapy alone	15 (8)	26 (15)
HDT-ASCT	12 (7)	7 (4)
Allogeneic SCT	13 (7)	7 (4)
Other cellular therapies	2 (1)	5 (3)
Allogeneic anti-CD19 CAR T-cell therapy	1 (1)	1 (1)
Autologous anti-CD19/CD22 bispecific CAR T-cell therapy	0	1 (1)
CAR NK anti-CD16 therapy	1 (1)	0
Anti-CD22 CAR T-cell therapy	0	2 (1)
Cord blood NK therapy	0	1 (1)
Other therapies (not including any anti-CD20)	40 (22)	39 (22)
4-1BB agonist	0	1 (1)
Anti-CCR4 and checkpoint inhibitor	1 (1)	0
BCL2 inhibitor	6 (3)	2 (1)
BET inhibitor	0	1 (1)
Bispecific T-cell engager	7 (4)	6 (3)
Checkpoint inhibitor	18 (10)	12 (7)
CRL4-CRBN E3 ubiquitin ligase inhibitor	1 (1)	0
DHODH inhibitor	1 (1)	0
EED inhibitor	1 (1)	0
Heat shock protein 90 inhibitor	0	1 (1)
Immunotherapy not otherwise specified	0	1 (1)
Investigational product on clinical study not otherwise specified	3 (2)	0
IRAK4 kinase inhibitor	0	1 (1)
Anti-CD19 monoclonal antibody	1 (1)	2 (1)
Anti-CD27 monoclonal antibody	4 (2)	2 (1)
MALT-1 inhibitor	0	1 (1)
mRNA and checkpoint inhibitor	1 (1)	0
mTOR inhibitor and asparaginase	0	1 (1)
Nuclear export inhibitor	2 (1)	0
PDH-KGDH inhibitor	1 (1)	0

PI3K and HDAC inhibitor	1 (1)	0
PI3K inhibitor	1 (1)	1 (1)
Recombinant fusion CD47 therapy	0	1 (1)
Steroids	8 (4)	16 (9)
Surgery	2 (1)	1 (1)

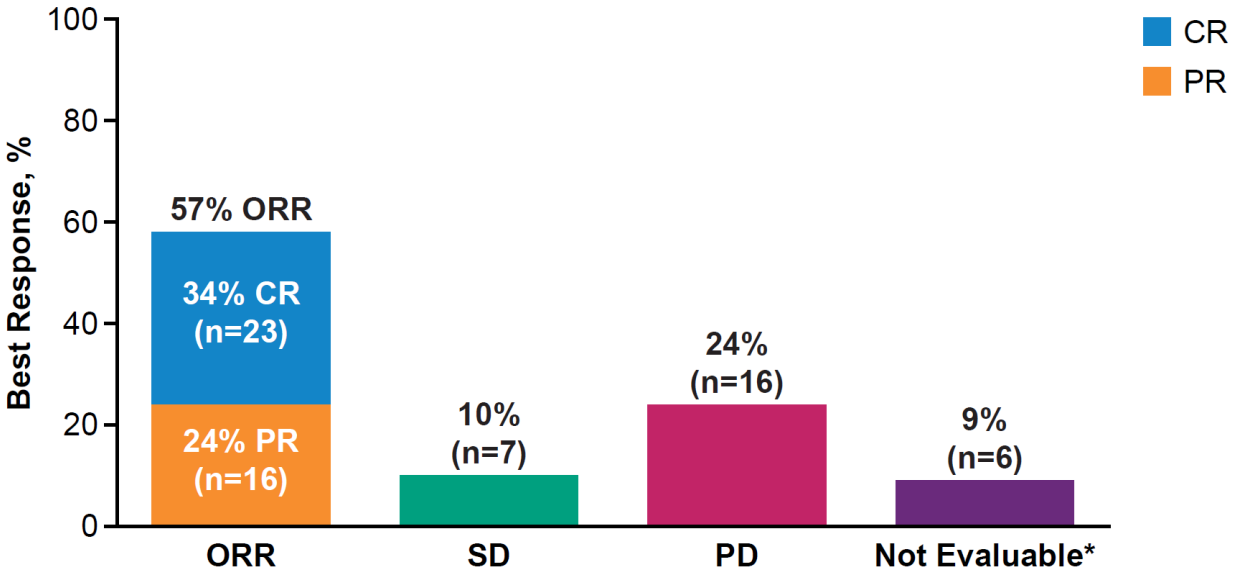
*Including anti-CD20 therapy and POLA-BR. †Excluding POLA-BR.

Axi-cel, axicabtagene ciloleucel; BCL2, B-cell lymphoma-2; BET, bromodomain and extra-terminal domain; BTK, Bruton tyrosine kinase; CAR, chimeric antigen receptor; CCR4, C-C chemokine receptor 4; CRBN, cereblon; DHODH, dihydroorotate dehydrogenase; EED, embryonic ectoderm development protein; HDAC, histone deacetylase; HDT-ASCT, high-dose therapy with autologous stem cell transplantation; IRAK4, interleukin-1 receptor-associated kinase 4; MALT-1, mucosa-associated lymphoid tissue lymphoma translocation protein 1; mRNA, messenger ribonucleic acid; mTOR, mechanistic target of rapamycin; NK, natural killer; PDH-KGHD, pyruvate dehydrogenase-ketoglutarate dehydrogenase complex; PI3K, phosphoinositide 3-kinase; POLA-BR, polatuzumab vedotin plus bendamustine and rituximab; SCT, stem cell transplantation; SOC, standard of care.

Supplementary Figures

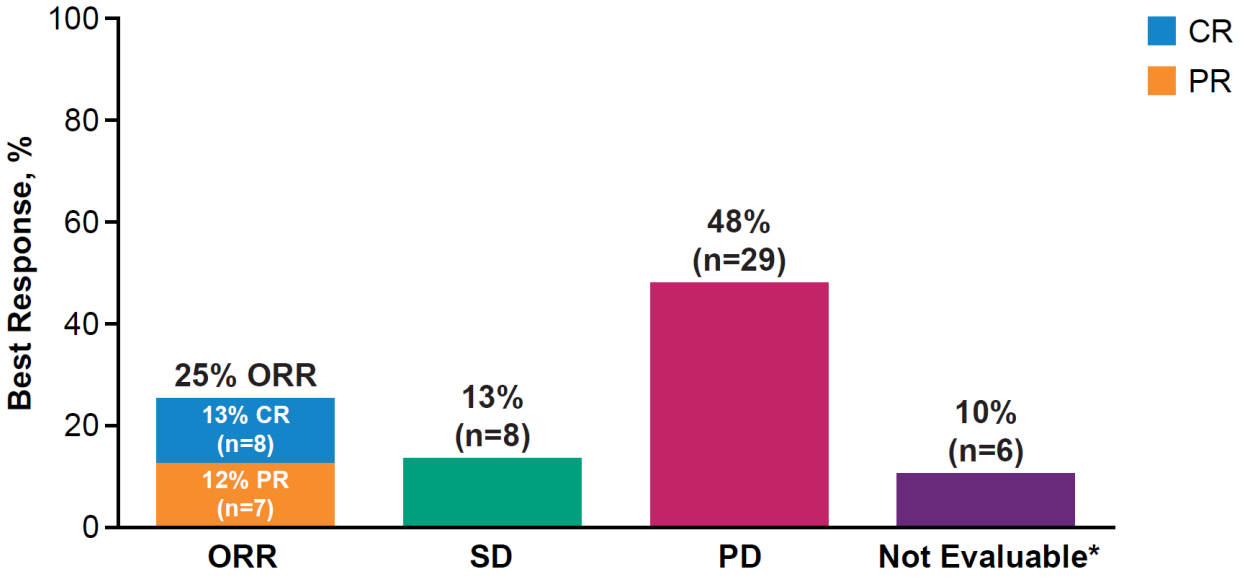
Supplemental Figure 1. Best response to 3L cellular immunotherapy in the SOC arm

Responses were per investigator assessment. *Patients in this category do not have available data (ie, either the disease assessment was not performed or it was performed but the result could not be determined per investigator). 3L, third-line; CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; SOC, standard of care.



Supplemental Figure 2. Best response to 3L chemotherapy in the axi-cel arm

Responses were per investigator assessment. Data were missing for 2 patients (3%).
*Patients in this category do not have available data (ie, either the disease assessment was not performed or it was performed but the result could not be determined per investigator). 3L, third-line; axi-cel, axicabtagene ciloleucel; CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.



Supplemental Figure 3. Best response to 3L chemotherapy prior to SCT in the axi-cel arm based on receipt of SCT after chemotherapy

Responses were per investigator assessment. (A) Responses to 3L chemotherapy for those who did not receive SCT (n = 50). Data were missing for 1 patient (2%). (B) Responses to 3L chemotherapy for those who received SCT after (n = 10). Data were missing for 1 patient (10%). *Patients in this category do not have available data (ie, either the disease assessment was not performed, or it was performed but the result could not be determined per investigator). 3L, third-line; axi-cel, axicabtagene ciloleucel; CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SCT, stem cell transplantation; SD, stable disease.