Abstract S223

Real-World Early Outcomes of Axicabtagene Ciloleucel for Relapsed or Refractory Follicular Lymphoma

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Disclosures

Abintus Bio (Consulting/advisory role); AbbVie (Consulting/advisory role); ADC Therapeutics (Consulting/advisory role); Bristol Myers Squibb/Celgene (Consulting/advisory role); Caribou Bio (Consulting/advisory role); Daiichi Sankyo (Consulting/advisory role); ImmPACT Bio (Consulting/advisory role); Instil Bio (Consulting/advisory role); Ipsen (Consulting/advisory role); Kite, a Gilead company (Consulting/advisory role and research funding); Miltenyi Biotec (Consulting/advisory role); MorphoSys (Consulting/advisory role); Novartis (Consulting/advisory role); Synthekine (Consulting/advisory role); Pfizer (Research funding)

Background

- Axi-cel is an autologous anti-CD19 CAR T-cell therapy, which includes a CD28 costimulatory domain to elicit rapid and robust expansion, that results in target-specific cytotoxicity and helps to overcome the limitations of the immune system[1,2]
- In the US, axi-cel is approved for the treatment of adult patients with R/R FL after ≥2 lines of systemic therapy based on the outcomes from the pivotal ZUMA-5 study[1]
- ZUMA-5 is a multicenter, single-arm, Phase 2 trial of axi-cel in patients with R/R iNHL, including FL and MZL[3]
  - In the primary analysis of ZUMA-5, 94% of patients who received axi-cel to treat R/R FL achieved an overall response with a 79% CR rate[3]
  - Grade ≥3 CRS occurred in 6% of patients[3]
  - Grade ≥3 neurologic events occurred in 15% of patients[3]
- In the real world, patients receiving axi-cel for R/R FL may have broader demographics, disease characteristics, and comorbidities that would otherwise have made them ineligible for ZUMA-5
- The PASS of axi-cel aims to enroll 300 patients with R/R FL for long-term follow-up of 15 years

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1. YESCARTA® (axicabtagene ciloleucel) Prescribing information. Kite Pharma, Inc; 2022. 2. Savoldo B, et al. *J Clin Invest.* 2011;121:1822-1826.
3. Jacobson CA, et al. *Lancet Oncol.* 2022;23:91-103.

Axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; FL, follicular lymphoma; iNHL, indolent non-Hodgkin lymphoma; MZL, marginal zone lymphoma; PASS, post-authorization safety study; R/R, relapsed or refractory; US, United States.

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Objective

- To describe the early effectiveness and safety outcomes of axi-cel for the treatment of patients with R/R FL in the real-world setting, including outcomes in those who would have been ineligible for ZUMA-5, older adults (aged ≥65 years), and those with other relevant variables

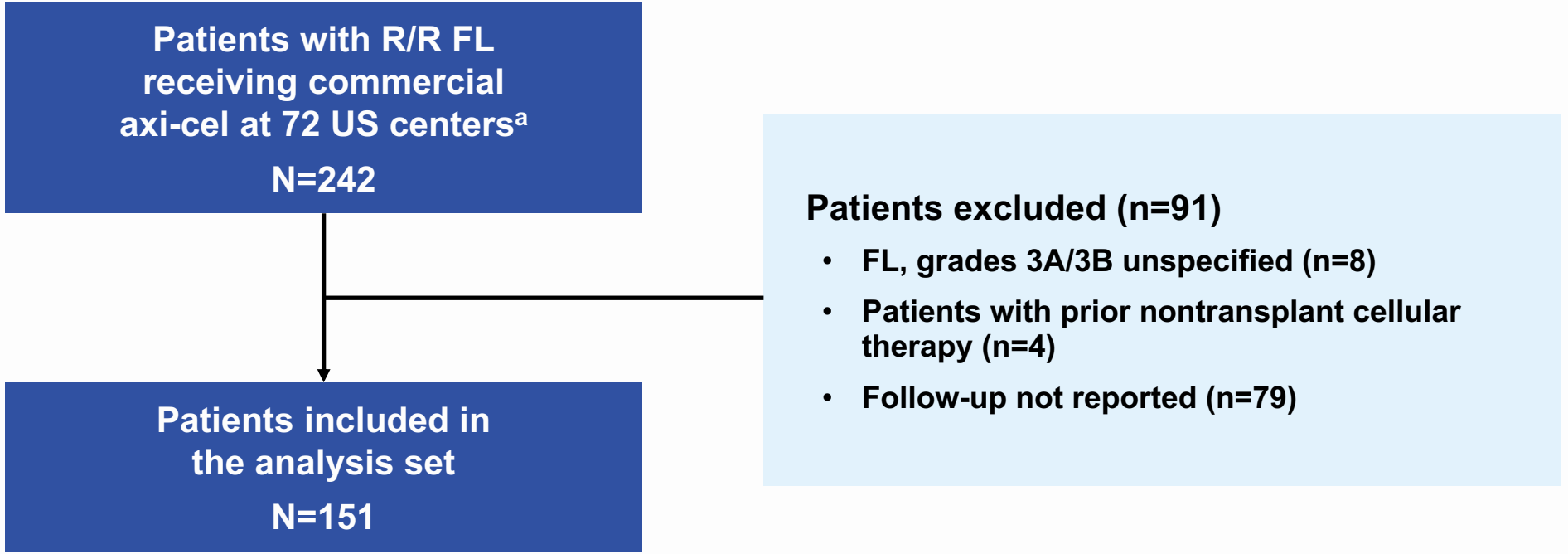
Axi-cel, axicabtagene ciloleucel; FL, follicular lymphoma; R/R, relapsed or refractory.

Methods

- Eligibility
  - Patients treated with commercial axi-cel for R/R FL between March 2021 and September 2022, with informed consent and enrolled in the PASS, were eligible
- Key exclusion criteria for the analysis set
  - Receiving axi-cel in a clinical trial or other noncommercial setting
  - FL grade 3B or 3A/3B unspecified or other B-cell malignancies
  - Received prior nontransplant cellular therapy (including prior CAR T-cell therapy)
  - Follow-up not due or not reported
- Endpoints of interest
  - **Effectiveness**: ORR per investigator (defined as CR or PR), CR, DOR, PFS, and OS
  - **Safety**: CRS,[a] ICANS,[a] and prolonged cytopenias (including neutropenia and thrombocytopenia)
- Statistical methods
  - Percentages and 95% Clopper-Pearson exact CIs were calculated for dichotomous outcomes
  - DOR, PFS, and OS were described using the Kaplan-Meier estimator
  - Time to resolutions of CRS and ICANS were estimated by cumulative incidence functions

[a] CRS and ICANS were graded per ASTCT consensus grading (Lee DW, et al. *Biol Blood Marrow Transplant.* 2019;25:625-638).
ASTCT, American Society for Transplantation and Cellular Therapy; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; FL, follicular lymphoma; ICANS, immune effector cell-associated neurotoxicity syndrome; ORR, overall response rate; OS, overall survival; PASS, post-authorization safety study; PFS, progression-free survival; PR, partial response; R/R, relapsed/refractory.

Analysis Population



- Data cutoff date: September 23, 2022
- Median follow-up: 6.2 months (95% CI, 6.0-6.3)
- Median time from leukapheresis to infusion was 28 days (IQR, 26-33)

[a] Identified from the CIBMTR registry.
Axi-cel, axicabtagene ciloleucel; CIBMTR, Center for International Blood and Marrow Transplant Research; FL, follicular lymphoma; IQR, interquartile range; R/R, relapsed/refractory; US, United States.

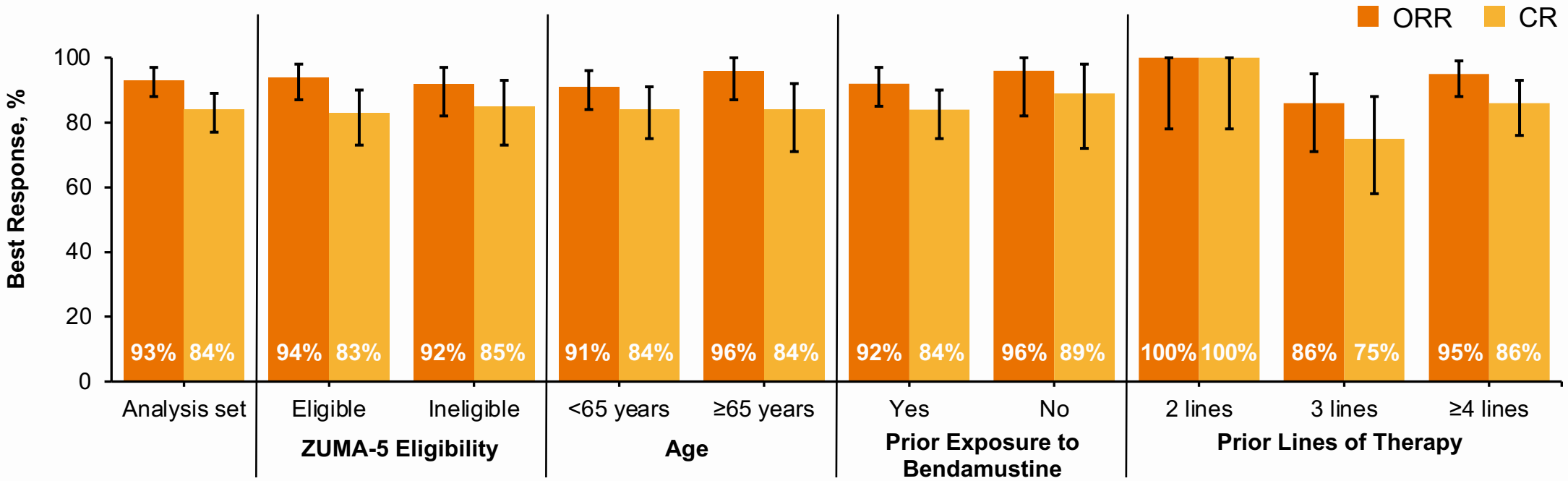
Baseline Characteristics for Analysis Set, by ZUMA-5 Eligibility, and by Age

Key Variable of Interest	Enrolled Patients in Analysis Set N=151	ZUMA-5 Eligibility[a]		Age	
		Eligible n=90	Ineligible n=61	<65 years n=95	≥65 years n=56
Median age (IQR), years	61 (55-68)	60 (54-68)	62 (55-69)	57 (51-61)*	70 (68-74)*
Male sex, n (%)	94 (62)	50 (56)*	44 (72)*	66 (69)*	28 (50)*
White race, n (%)	132 (87)	80 (89)	52 (85)	82 (86)	50 (89)
Hispanic ethnicity, n (%)	12 (8)	8 (9)	4 (7)	8 (9)	4 (7)
ECOG PS 0-1 at infusion,[b] n (%)	143 (98)	87 (100)	56 (95)	88 (97)	55 (100)
Clinically significant comorbidities,[c] n (%)	113 (75)	56 (62)*	57 (93)*	69 (73)	44 (79)
Disease stage at diagnosis[d]: III-IV, n (%)	79 (76)	46 (78)	33 (73)	57 (78)	22 (71)
Median no. of lines of prior therapies (IQR)	4 (3-5)	4 (3-5)	4 (3-5)	4 (3-5)	4 (3-5)
Prior bendamustine,[e] n (%)	107 (79)	62 (78)	45 (80)	69 (79)	38 (79)
Prior ASCT, n (%)	20 (13)	12 (13)	8 (13)	16 (17)	4 (7)
Elevated LDH prior to infusion,[f,g] n (%)	26 (28)	15 (26)	11 (32)	15 (26)	11 (32)
Chemoresistant prior to infusion,[h] n (%)	101 (80)	61 (82)	40 (77)	65 (78)	36 (84)
Median time from last line of therapy to infusion (IQR), months	7.1 (3.0-19.3)	7.9 (3.1-20.0)	5.8 (3.0-18.8)	5.6 (2.7-11.1)*	13.7 (4.6-25.7)*
Bridging therapy[i]: any type / systemic / radiation, n (%)	12 (9) / 10 (8) / 2 (2)	6 (8) / 5 (6) / 1 (1)	6 (11) / 5 (9) / 1 (2)	7 (8) / 7 (8) / 0	5 (10) / 3 (6) / 2 (4)
Outpatient,[j] n (%)	22 (15)	16 (18)	6 (10)	13 (14)	9 (16)

- Of 151 patients enrolled in the analysis set, 61 (40%) would have been considered ineligible for ZUMA-5
  - Reasons for ineligibility included comorbidities (70%), history of prior malignancy (18%), platelet count <75,000/μL (15%), pleura extranodal involvement (15%), cerebrovascular disease (11%), and ECOG PS ≥2 (5%)

[a] Reasons for ZUMA-5 ineligibility are not mutually exclusive. [b] The remaining 2% pertain to patients with an ECOG PS >1 or missing information.
[c] Comorbidities were defined per the HCT-CI and included a body mass index <20.5 (Sorror ML, et al. *Blood.* 2005;106:2912-2919). [d] Forty-seven patients did not report disease stage at initial diagnosis. [e] Sixteen patients did not report prior bendamustine exposure. [f] Elevated LDH is defined as above the upper limit of normal. [g] Fifty-nine patients did not report LDH prior to infusion. [h] Chemoresistance is defined as patients who had SD or PD prior to infusion. Twenty-five patients did not report chemoresistant status prior to infusion. [i] Nineteen patients did not report the presence or absence of bridging therapy.
[j] Planned number of outpatients.
*P<0.05 per Fisher's exact test.
ASCT, autologous stem cell transplantation; ECOG PS, Eastern Cooperative Oncology Group performance status; HCT-CI, hematopoietic cell transplantation-specified comorbidity index; IQR, interquartile range; LDH, lactate dehydrogenase; PD, progressive disease; PR, partial response; SD, stable disease.

Overall Response in Analysis Set, by ZUMA-5 Eligibility, Age, Prior Bendamustine Exposure, and Prior Lines of Therapy

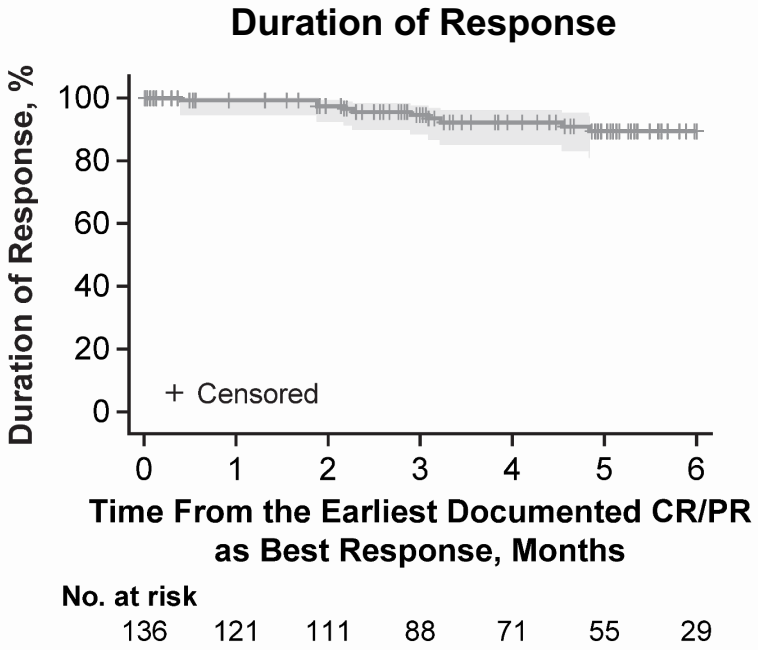


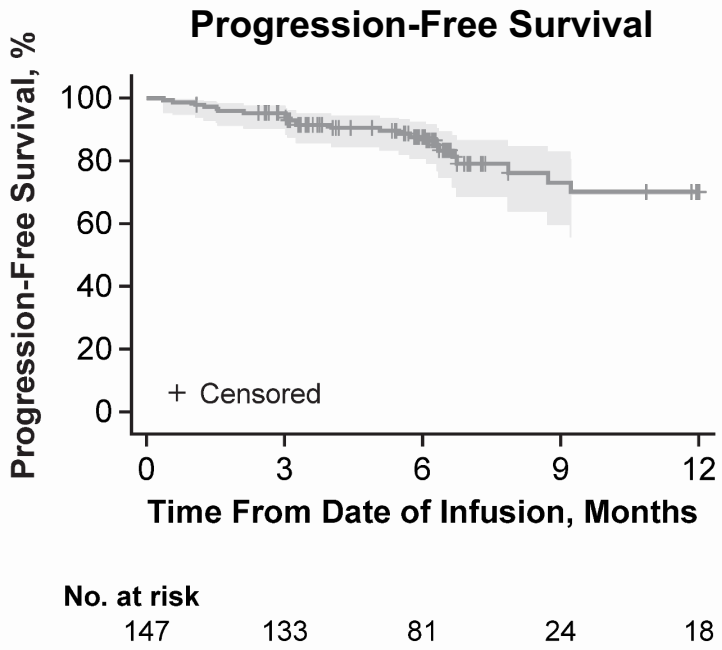
No. of patients	138	124	83	73	55	51	85	78	53	46	96	87	27	25	15	15	31	27	75	68
N	148	148	88	88	60	60	93	93	55	55	104	104	28	28	15	15	36	36	79	79

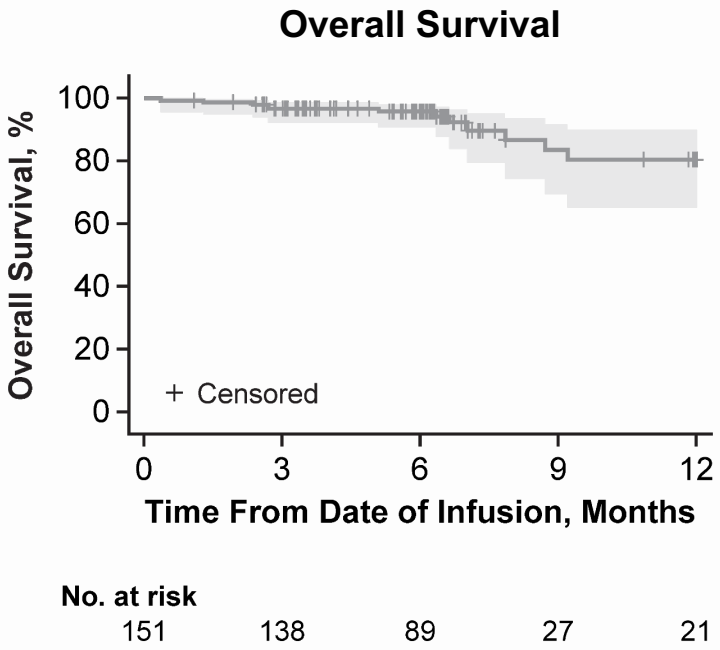
- Among 148 patients evaluable for response, for whom the median follow-up was 6.2 months, **138 patients (93%; 95% CI, 88-97) had an overall response, with 124 patients (84%; 95% CI, 77-89) achieving a CR**
- Overall response was comparable regardless of ZUMA-5 eligibility, age, prior exposure to bendamustine, and prior lines of therapy

Error bars denote 95% CIs.
CR, complete response; ORR, overall response rate.

Duration of Response, Progression-Free Survival, and Overall Survival in the Analysis Set



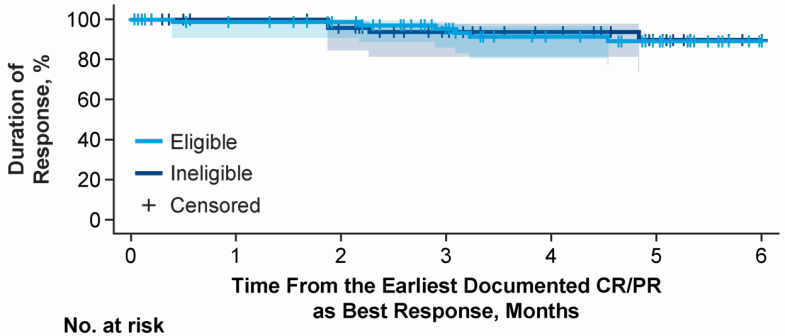




Shaded bands denote 95% CIs.
CR, complete response; PR, partial response.

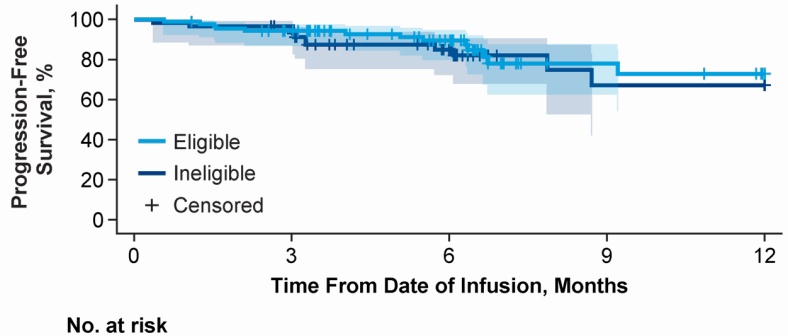
Duration of Response, Progression-Free Survival, and Overall Survival by ZUMA-5 Eligibility and by Age

Duration of Response



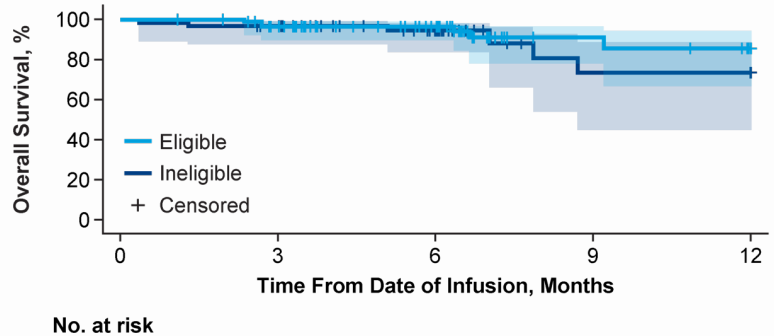
No. at risk							
Eligible	82	71	65	52	42	35	18
Ineligible	54	50	46	36	29	20	11

Progression-Free Survival



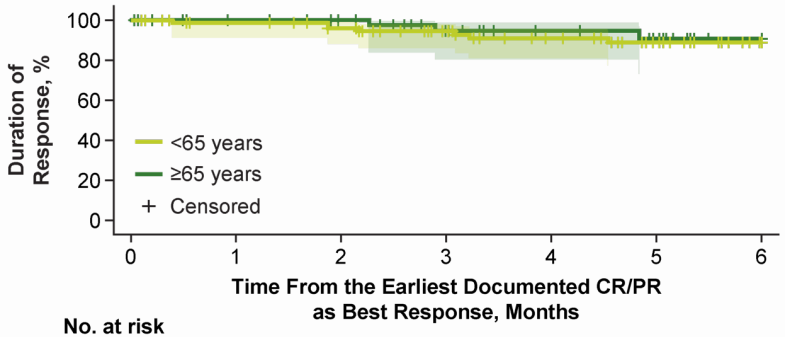
No. at risk						
Eligible	88	78	49	15	10	
Ineligible	59	55	32	9	8	

Overall Survival



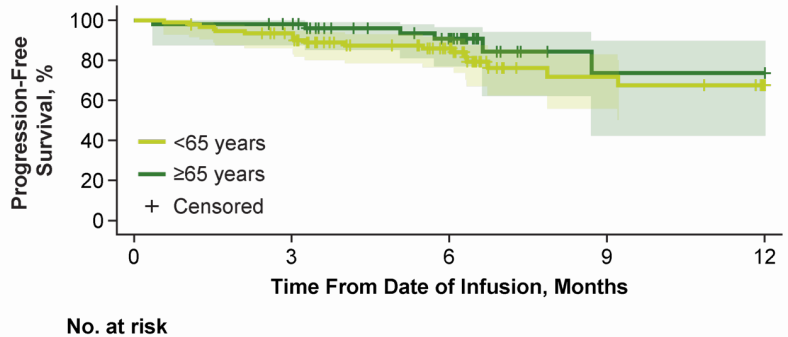
No. at risk						
Eligible	90	81	53	17	12	
Ineligible	61	57	36	10	9	

Duration of Response



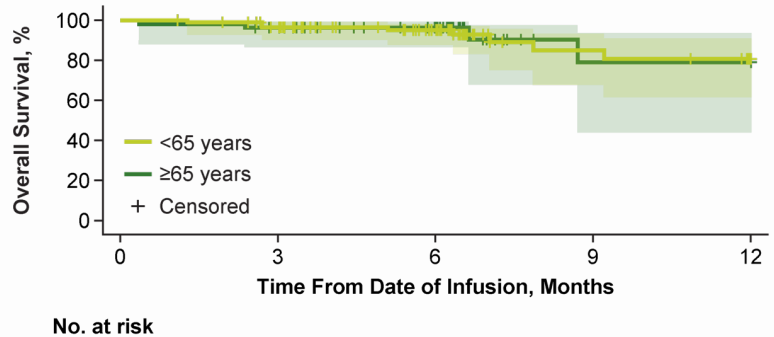
No. at risk							
<65 years	84	75	69	56	46	34	20
≥65 years	52	46	42	32	25	21	9

Progression-Free Survival



No. at risk						
<65 years	93	82	49	17	11	
≥65 years	54	51	32	7	7	

Overall Survival



No. at risk						
<65 years	95	86	55	20	14	
≥65 years	56	52	34	7	7	

Shaded bands denote 95% CIs.
CR, complete response; PR, partial response.

Any-Grade CRS and ICANS by ZUMA-5 Eligibility and Age

Parameter	Enrolled Patients in Analysis Set (N=151)	ZUMA-5 Eligibility		Age	
		Eligible n=90	Ineligible n=61	<65 years n=95	≥65 years n=56
Any-grade CRS,[a,b] n (%)	109 (73)	70 (79)	39 (64)	70 (74)	39 (70)
Grade ≥3 CRS,[a,b] n (%)	3 (2)	1 (1)	2 (3)	2 (2)	1 (2)
Median time from infusion to CRS, any-grade, days (range)	5 (1-15)	6 (2-12)	5 (1-15)	5 (1-12)	6 (2-15)
Corticosteroids to treat CRS,[c] n(%)	43 (39)	26 (37)	17 (44)	23 (33)	20 (51)
Tocilizumab to treat CRS,[c] n(%)	84 (77)	53 (76)	31 (79)	52 (74)	32 (82)
Any-grade ICANS,[a,d] n (%)	58 (39)	38 (43)	20 (33)	33 (35)	25 (45)
Grade ≥3 ICANS,[a,d] n (%)	18 (12)	8 (9)	10 (16)	12 (13)	6 (11)
Median time from infusion to ICANS, any-grade, days (range)	8 (2-19)	8 (2-16)	8 (6-19)	8 (3-16)	8 (2-19)
Corticosteroids to treat ICANS,[c] n(%)	48 (83)	33 (87)	15 (75)	26 (79)	22 (88)
Tocilizumab to treat ICANS,[c] n(%)	7 (12)	2 (5)	5 (25)	5 (15)	2 (8)

[a] CRS and ICANS were graded per ASTCT consensus criteria (Lee DW, et al. *Biol Blood Marrow Transplant.* 2019;25:625-638). [b] One patient did not report CRS data. [c] Among patients who developed any-grade CRS/ICANS by Day 100. [d] Two patients did not report ICANS data.

ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

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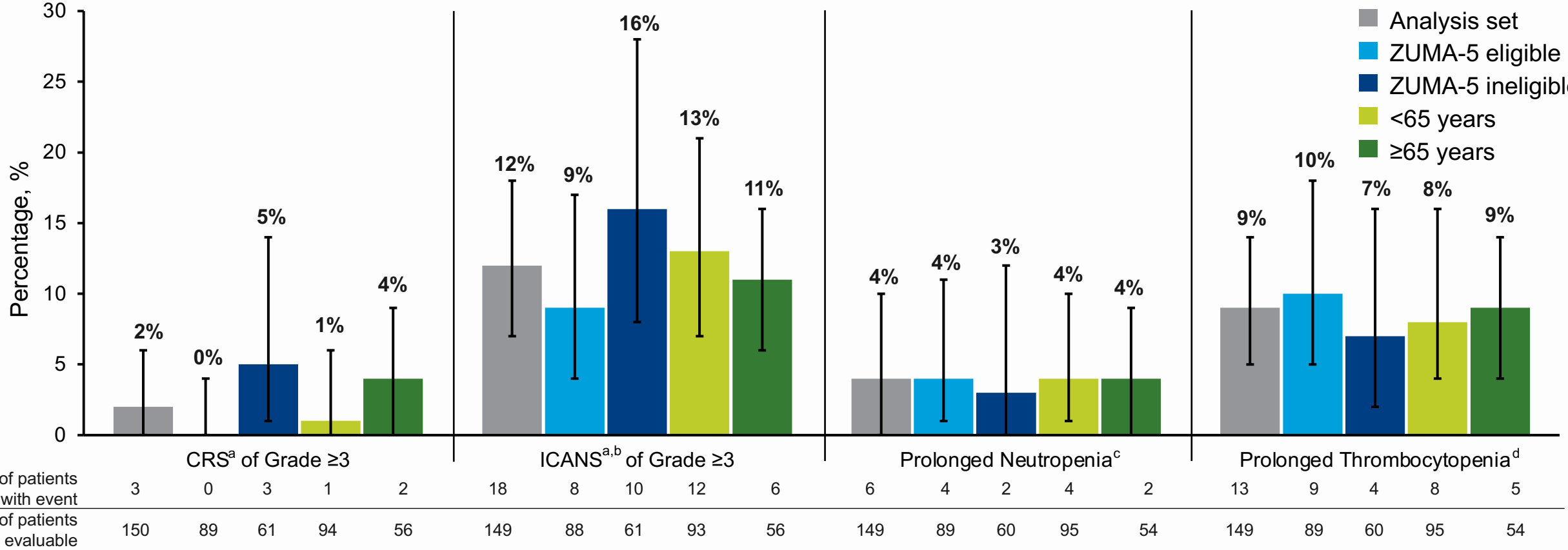
Grade ≥3 CRS, Grade ≥3 ICANS, and Prolonged Cytopenias in the Analysis Set, by ZUMA-5 Eligibility and Age



[a] CRS and ICANS were graded per ASTCT consensus criteria (Lee DW, et al. *Biol Blood Marrow Transplant.* 2019;25:625-638.). [b] Among patients who developed any-grade ICANS by Day 100. [c] Prolonged neutropenia is defined as failure to recover ANC ≥500/mm^3 and/or sustain 3 lab values within the first 30 days after infusion. [d] Prolonged thrombocytopenia is defined as failure to recover platelet count ≥20×10^9/L within the first 30 days after infusion.
ANC, absolute neutrophil count; ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

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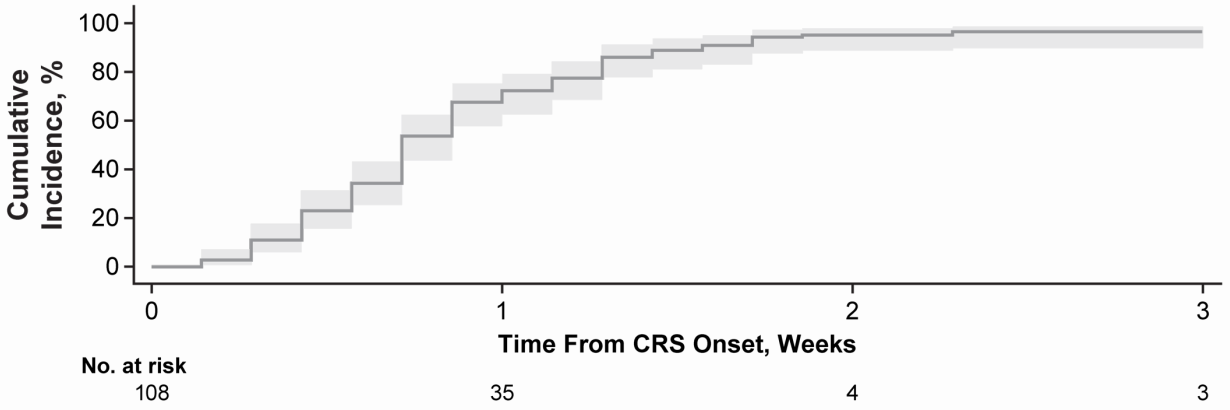
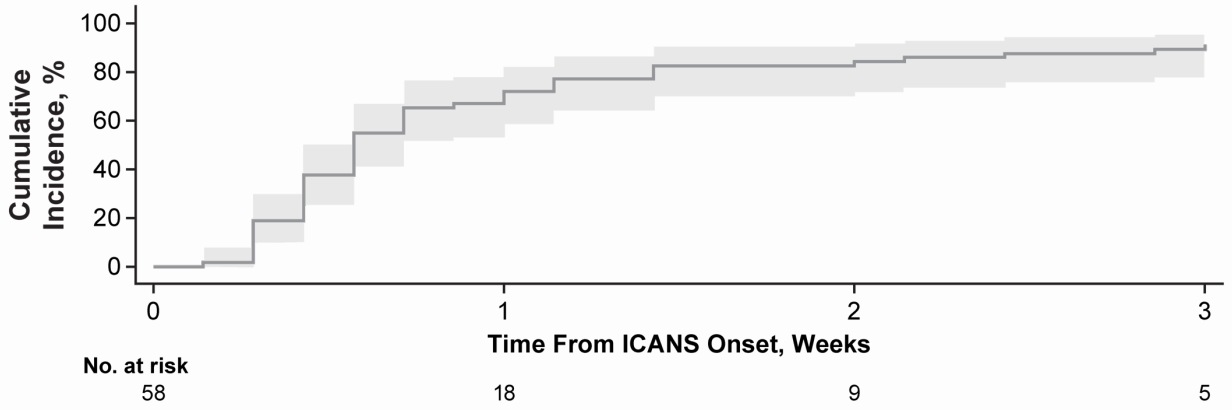
Cumulative Incidence Rate of Any-Grade CRS Resolution and Any-Grade ICANS Resolution in the Analysis Set

Cumulative Incidence of Any-Grade CRS[a] Resolution



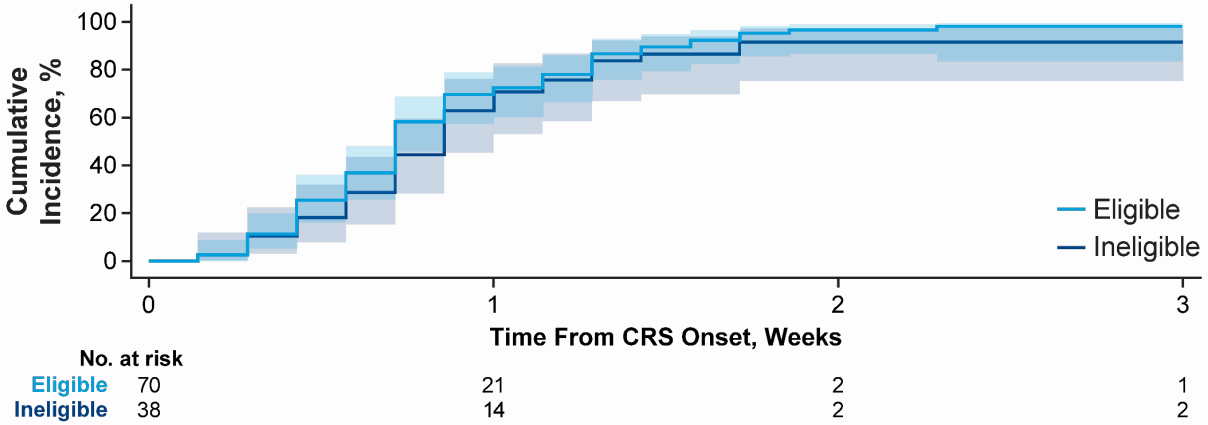
Cumulative Incidence of Any-Grade ICANS[b] Resolution



[a] Among patients experiencing CRS onset within 30 days post-infusion. The date of CRS resolution was not reported for 1 patient.
[b] Among patients experiencing ICANS onset within 100 days post-infusion.
CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

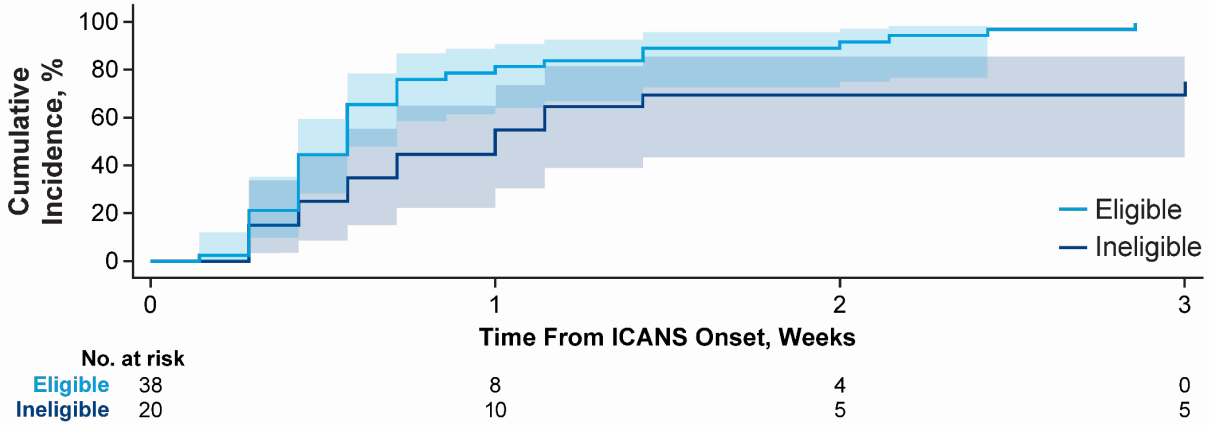
Cumulative Incidence Rate of Any-Grade CRS Resolution and Any-Grade ICANS Resolution by ZUMA-5 Eligibility and Age

Cumulative Incidence of Any-Grade CRS[a] Resolution by ZUMA-5 Eligibility



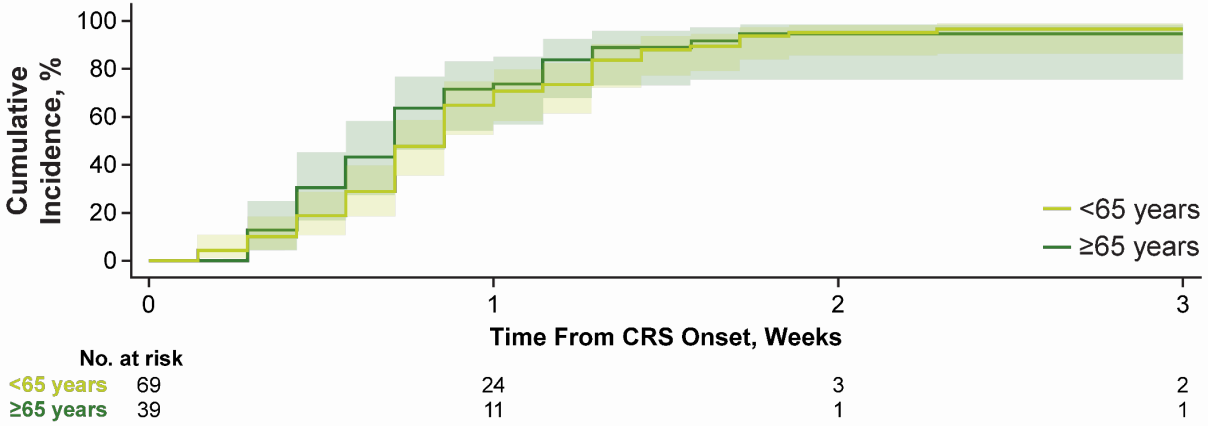
No. at risk				
Eligible	70	21	2	1
Ineligible	38	14	2	2

Cumulative Incidence of Any-Grade ICANS[b] Resolution by ZUMA-5 Eligibility



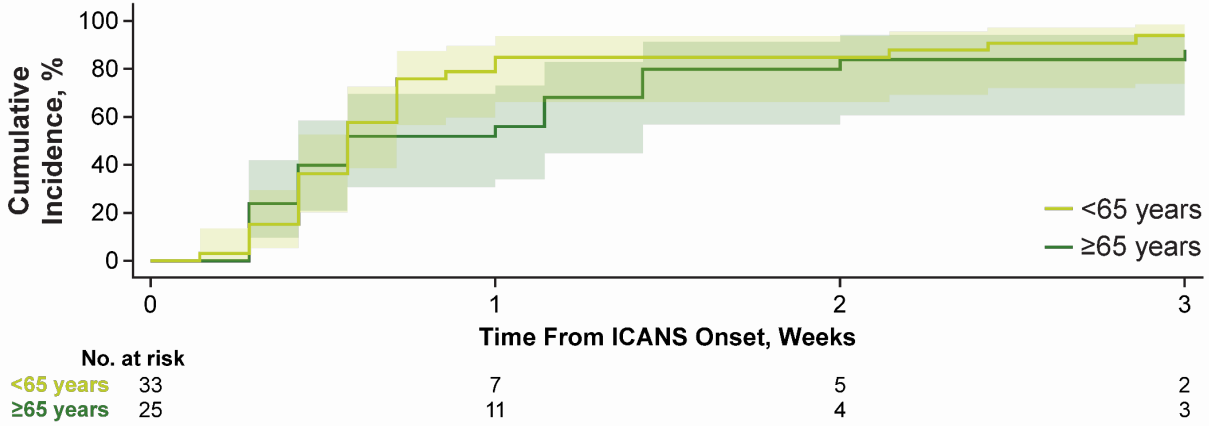
No. at risk				
Eligible	38	8	4	0
Ineligible	20	10	5	5

Cumulative Incidence of Any-Grade CRS[a] Resolution by Age



No. at risk				
<65 years	69	24	3	2
≥65 years	39	11	1	1

Cumulative Incidence of Any-Grade ICANS[b] Resolution by Age



No. at risk				
<65 years	33	7	5	2
≥65 years	25	11	4	3

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[a] Among patients experiencing CRS onset within 30 days post-infusion. The date of CRS resolution was not reported for 1 patient.
[b] Among patients experiencing ICANS onset within 100 days post-infusion.
CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

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Other Treatment-Emergent Adverse Events of Interest by ZUMA-5 Eligibility and Age

Parameter	Enrolled Patients in Analysis Set (N=151)	ZUMA-5 Eligibility		Age	
		Eligible n=90	Ineligible n=61	<65 years n=95	≥65 years n=56
Clinically significant infection,[a] n (%)	51 (34)	29 (32)	22 (36)	35 (37)	16 (29)
Bacterial	19 (13)	13 (14)	6 (10)	11 (12)	8 (14)
Fungal	2 (1)	0	2 (3)	1 (1)	1 (2)
Viral	38 (25)	17 (19)	21 (34)	28 (29)	10 (18)
Subsequent neoplasms,[b] n (%)	3 (2)	1 (1)	2 (3)	3 (3)	0
Deaths, n (%)	12 (8)	6 (7)	6 (10)	8 (8)	4 (7)
Primary disease	3 (2)	2 (2)	1 (2)	3 (3)	0
CRS	2 (1)	0	2 (3)	1 (1)	1 (2)
COVID-19	4 (3)	3 (3)	1 (2)	3 (3)	1 (2)
Organ failure[c]	2 (1)	1 (1)	1 (2)	0	2 (4)
Prior malignancy	1 (1)	0	1 (2)	1 (1)	0

[a] Clinically significant infection is defined as any infection diagnosed after the date of infusion that requires treatment. However, the following were not considered as events: culture-negative neutropenic fever without clear source; upper respiratory infections that are presumed viral, but no virus has been identified; candida detected in oral or stool samples (including oral thrush); toenail fungus; yeast infection in the groin, vagina, or under the breasts; surveillance cultures in which normal flora is present and the recipient is asymptomatic; infections persisting from a prior reporting period (including infections that have progressed to new sites since the last report); or certain bacterial, viral, and/or fungal infections recurring within prespecified time frames. [b] Subsequent neoplasms were basal cell skin malignancy (n=1), basal cell skin malignancy + melanoma + squamous cell skin malignancy (n=1), and myelodysplasia (n=1).
[c] One patient died due to renal failure and the other patient died due to multiple organ failure.
CRS, cytokine release syndrome.

Conclusions

- Among the 151 patients with R/R FL treated with axi-cel in the real-world setting, 61 (40%) had a broad range of demographics, disease characteristics, and treatment history that could have made them ineligible for enrollment in ZUMA-5[1]
  - The most common reasons for ZUMA-5 ineligibility were comorbidities
- Despite the broader patient population in the real-world setting, axi-cel demonstrated high effectiveness and a manageable safety profile that was comparable with outcomes from ZUMA-5[1]
  - Outcomes were comparable regardless of ZUMA-5 eligibility, age, prior exposure to bendamustine, and prior lines of therapy
- Future work will assess real-world outcomes with a longer follow-up and in a larger patient population
- Overall, findings from the real-world setting support broader use of axi-cel to treat R/R FL

1. Jacobson CA, et al. *Lancet Oncol.* 2022;23:91-103.
Axi-cel, axicabtagene ciloleucel; FL, follicular lymphoma; R/R, relapsed/refractory.

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On behalf of the CIBMTR® Cellular Immunotherapy for Cancer Working Committee; CIBMTR® is a research collaboration between National Marrow Donor Program®/Be The Match® and the Medical College of Wisconsin, and operates the Cellular Immunotherapy Data Resource (CIDR)

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