Real-World Outcomes of Axicabtagene Ciloleucel for the Treatment of Large B-cell Lymphoma by Race and Ethnicity

Frederick L. Locke, MD[1,a]; Tanya Siddiqi, MD[2]; Caron A. Jacobson, MD, MMSc[3]; Armin Ghobadi, MD[4]; Sairah Ahmed, MD[5]; David B. Miklos, MD, PhD[6]; Miguel-Angel Perales, MD[7]; Javier Munoz, MD, MBA[8]; Brent Logan, PhD[9]; Zhen-Huan Hu, MPH[10]; Harry Miao, MD, PhD[10]; Kanwarjit Singh, MD[10]; Jina Shah, MD, MPH[10]; Hairong Xu, MD, PhD[10]; Marcelo C. Pasquini, MD, MS[11,b]

[1]Moffitt Cancer Center, Tampa, FL, USA; [2]City of Hope National Medical Center, Duarte, CA, USA; [3]Dana-Farber Cancer Institute, Boston, MA, USA; [4]Washington University School of Medicine, St Louis, MO, USA; [5]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [6]Stanford University School of Medicine, Stanford, CA, USA; [7]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [8]Mayo Clinic, Phoenix, AZ, USA; [9]Division of Biostatistics, Medical College of Wisconsin, Milwaukee, WI, USA; [10]Kite, a Gilead Company, Santa Monica, CA, USA; [11]Center for International Blood and Marrow Transplant Research, Medical College of Wisconsin, Milwaukee, WI, USA

[a]Presenting author
[b]Corresponding author

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Background

- Axi-cel is an autologous anti-CD19 CAR T-cell therapy approved in the US and EU for the treatment of adult patients with R/R LBCL after ≥2 lines of prior therapy, and in the US for R/R LBCL after first-line chemoimmunotherapy[1,2]
- The incidence of DLBCL per 100,000 people in the US is 4.8 in Non-Hispanic/Black, 7.1 in Non-Hispanic/White, 6.8 in Hispanic (all races), and 5.9 in Asian/Pacific Islander populations, respectively[3]
- There is a paucity of data on outcomes by race and ethnicity in clinical trials and real-world studies of CAR T-cell therapies published to date[4-10]
- The axi-cel post-authorization safety study (PASS) of commercial axi-cel is a long-term noninterventional cohort study using the CIBMTR registry infrastructure
- **Objective:** to examine axi-cel outcomes in R/R LBCL by race and ethnicity in the real-world setting

1. YESCARTA® (axicabtagene ciloleucel) Prescribing information. Kite Pharma, Inc; 2022. 2. YESCARTA® (axicabtagene ciloleucel) [summary of product characteristics]. Amsterdam, The Netherlands: Kite Pharma EU B.V.; 2021. 3. Teras LR, et al. *CA Cancer J Clin.* 2016;66:443-459. 4. Locke FL, et al. *Lancet Oncol.* 2019;20:31-42. 5. Wang M, et al. *N Engl J Med.* 2020;382:1331-1342. 6. Abramson JS, et al. *Lancet*. 2020;396:839-852. 7. Schuster SJ, et al. *Lancet Oncol.* 2021;22:1403-1415. 8. Nastoupil LJ, et al. *J Clin Oncol*. 2020;38(27):3119-3128. 9. Jacobson CA, et al. *J Clin Oncol*. 2020;38(27):3095-3106. 10. Iacoboni G, et al. *Cancer Med.* 2021;10:3214-3223.
Axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CIBMTR, Center for International Blood and Marrow Transplant Research; DLBCL, diffuse large B-cell lymphoma; EU, European Union; LBCL, large B-cell lymphoma; R/R, relapsed/refractory; US, United States.

Study Design

- Eligibility: patients who received commercial axi-cel for R/R LBCL between October 2017 and August 2020, with informed consent and enrolled in the PASS, were eligible

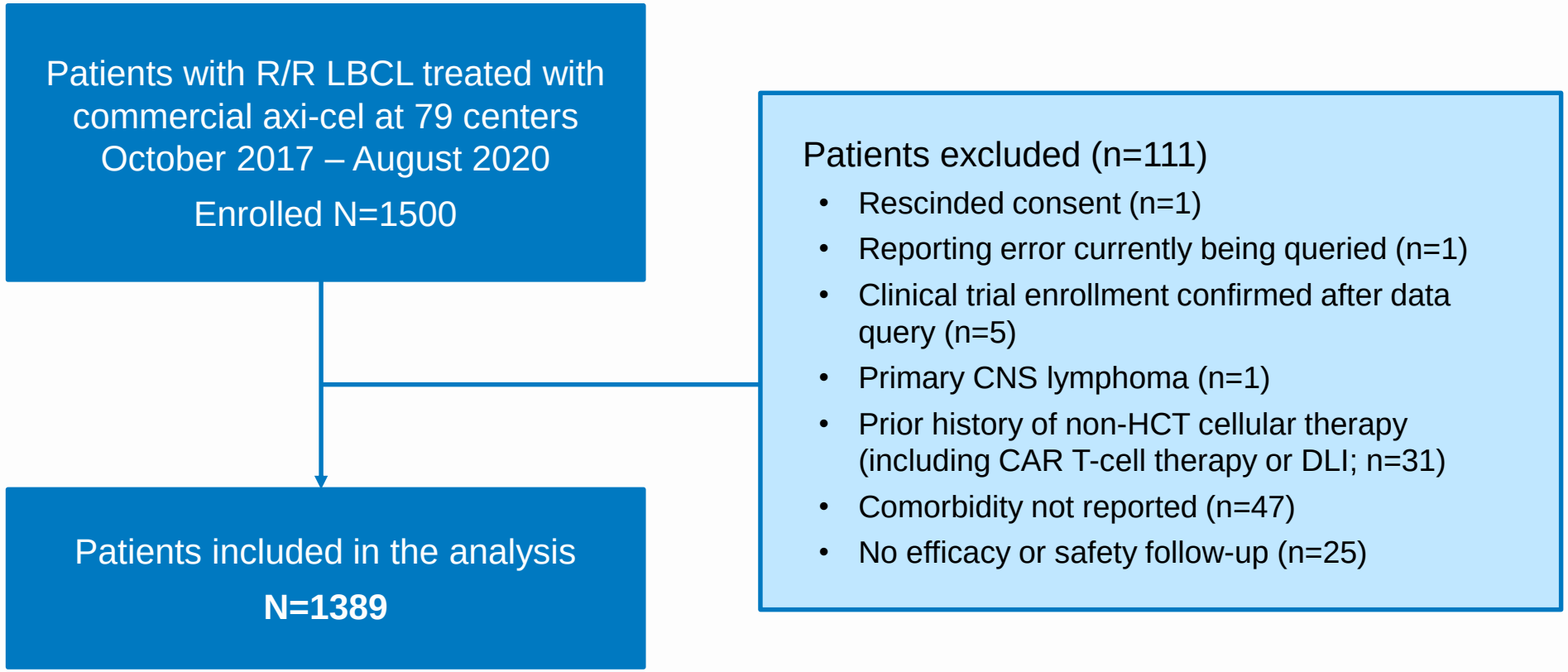
- Key exclusion criteria
  - Enrolled in clinical trial (based on data queries)
  - Received prior nontransplant cellular therapy
  - Primary CNS lymphoma
  - Comorbidities not reported
  - No efficacy or safety follow-up

- Endpoints of interest
  - **Efficacy**: ORR, CR, DOR, PFS, and OS
  - **Safety**: Grade ≥3 CRS and ICANS[a]

- Multivariate logistic and Cox regression models were used to assess the associations between race and ethnicity and efficacy and safety endpoints of interest while adjusting for other potential risk factors

[a] CRS was graded per Lee DW, et al. *Blood.* 2014;124:188-195 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; CNS, central nervous system; CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; ICANS, immune effector cell-associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; ORR, overall response rate; OS, overall survival; PASS, post-authorization safety study; PFS, progression-free survival; R/R, relapsed/refractory.

Analysis Population

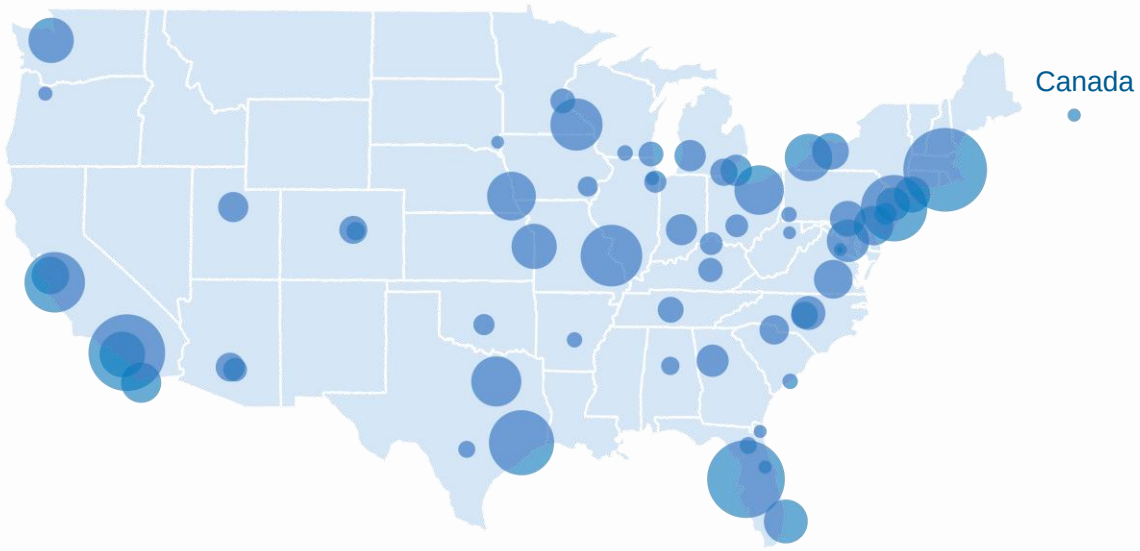


- Data cutoff date: June 22, 2021

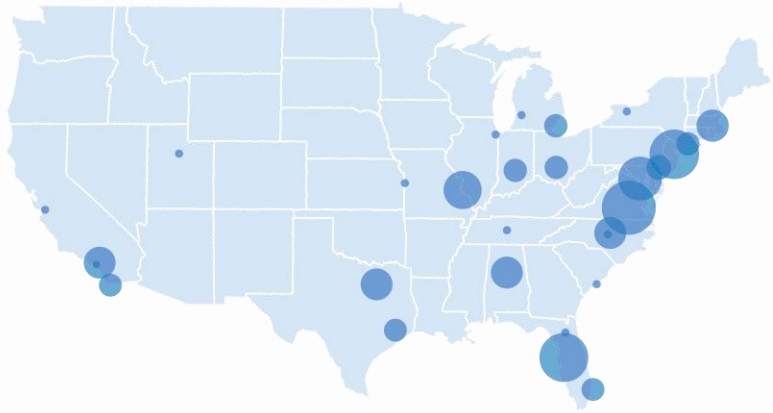
Axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CNS, central nervous system; DLI, donor leukocyte infusion; HCT, hematopoietic cell transplantation; LBCL, large B-cell lymphoma; PASS, post-authorization safety study; R/R, relapsed/refractory.

Patient Geographic Distribution

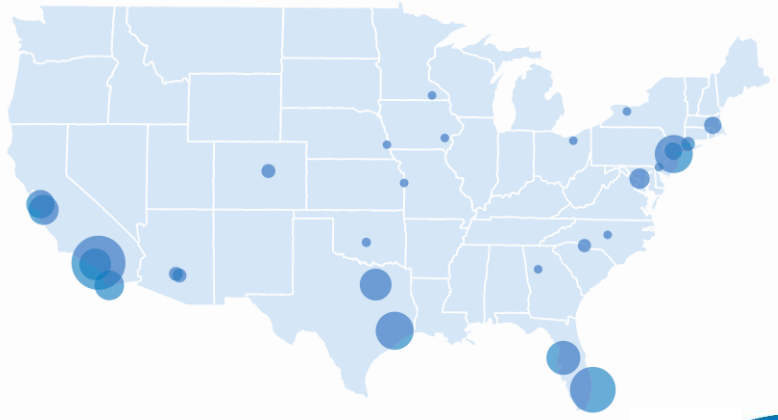
Distribution of All Patients (N=1389)



Distribution of Black or African American Patients (n=70)



Distribution of Hispanic or Latino Patients (n=152)



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Distribution of Race Versus Ethnicity

	Ethnicity			
Race, n (%)	**Hispanic or Latino**	**Not Hispanic or Latino**	**Not Reported**	**Total**
White	104 (68)	988 (85)	35 (49)	1127 (81)
Black or African American	2 (1)	67 (6)	1 (1)	70 (5)
Asian	1 (<1)	78 (7)	2 (3)	81 (6)
Other or unknown	45 (30)	32 (3)	34 (47)	111 (8)

- The “other or unknown” race group consisted of Native Hawaiian or other Pacific Islander (n=4), American Indian or Alaska Native (n=4), more than one race (n=7), and not reported (n=96)

Baseline Characteristics by Race and Ethnicity

	Race[a]			Ethnicity	
Key Variable of Interest, n (%)	White N=1127, 81%	Black or African American N=70, 5%	Asian N=81, 6%	Hispanic or Latino[b] N=152, 11%	Not Hispanic or Latino N=1165, 84%
Age ≥65 years	449 (40)	17 (24)	28 (35)	38 (25)	465 (40)
Male sex	749 (66)	42 (60)	43 (53)	99 (65)	757 (65)
ECOG PS ≥2 prior to infusion	48 (4)	1 (1)	9 (11)	4 (3)	56 (5)
Comorbidities[1]					
Pulmonary, moderate to severe	318 (28)	29 (41)	14 (17)	28 (18)	331 (28)
Prior cancer	174 (15)	3 (4)	8 (10)	9 (6)	175 (15)
Obesity (BMI >35 kg/m^2)	103 (9)	9 (13)	1 (1)	15 (10)	103 (9)
Histological transformation	328 (29)	17 (24)	18 (22)	37 (24)	333 (29)
Chemo-sensitive/resistant prior to infusion	253 (22) / 739 (66)	17 (24) / 46 (66)	20 (25) / 54 (67)	44 (29) / 92 (61)	262 (22) / 773 (66)
No. of lines of prior therapies: 1 or 2 / ≥3	310 (28) / 773 (69)	15 (21) / 50 (71)	18 (22) / 56 (69)	43 (28) / 100 (66)	321 (28) / 792 (68)
Prior HCT (any type)/prior ASCT	337 (30) / 321 (28)	18 (26) / 18 (26)	23 (28) / 22 (27)	33 (22) / 32 (21)	348 (30) / 330 (28)
Bridging therapy (any type)[c]	250 (22)	10 (14)	11 (14)	30 (20)	247 (21)
≥12 Months from diagnosis to infusion	663 (59)	50 (71)	50 (62)	89 (59)	682 (59)
≥28 Days from leukapheresis to infusion	549 (49)	42 (60)	37 (46)	73 (48)	577 (50)

[a] A total of 111 patients had other or unknown race. [b] Hispanic or Latino ethnic group included 104 White, 2 Black or African American and 1 Asian Hispanic or Latino patients. [c] The incidence of bridging therapy was derived from the number of patients who received a prior therapy after leukapheresis and before conditioning chemotherapy.

1. Sorror ML. *Blood.* 2013;121:2854-2863.

ASCT, autologous stem cell transplantation; BMI, body mass index; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; HCT, hematopoietic cell transplantation; LDH, lactate dehydrogenase.

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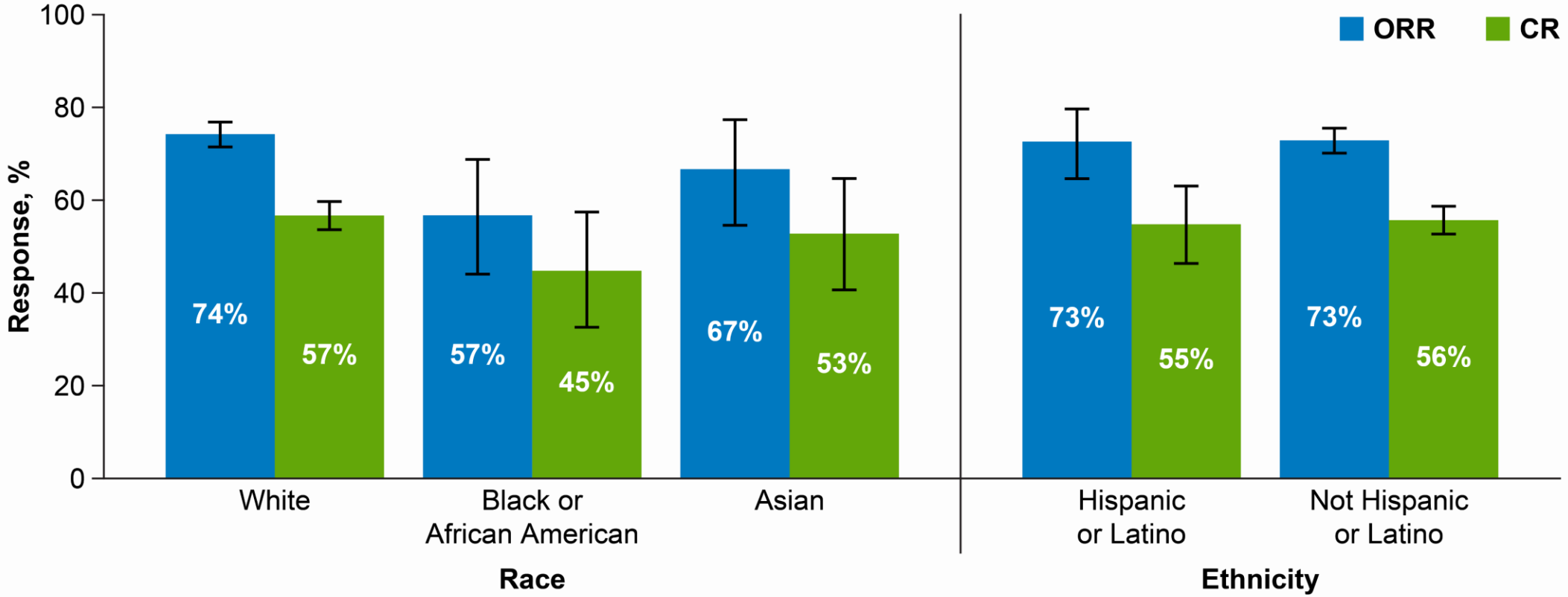
ORR and CR Rate by Race and Ethnicity

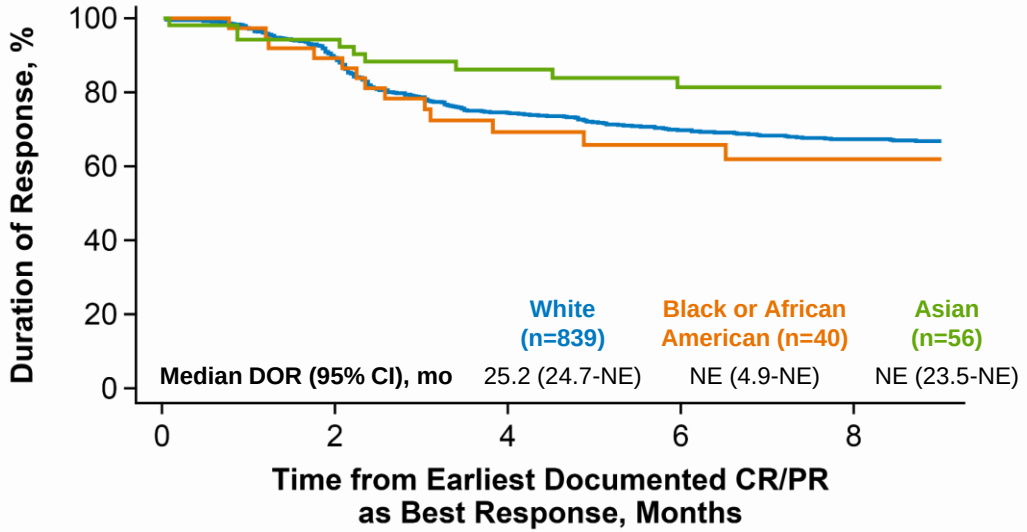


- Among patients with ≥180 days of follow-up, the ORR was 74% (CR rate, 57%) in White, 57% (CR rate, 45%) in Black or African American, 67% (CR rate, 53%) in Asian, and 73% (CR rate, 55%) in Hispanic or Latino patient groups

CR, complete response; ORR, overall response rate.

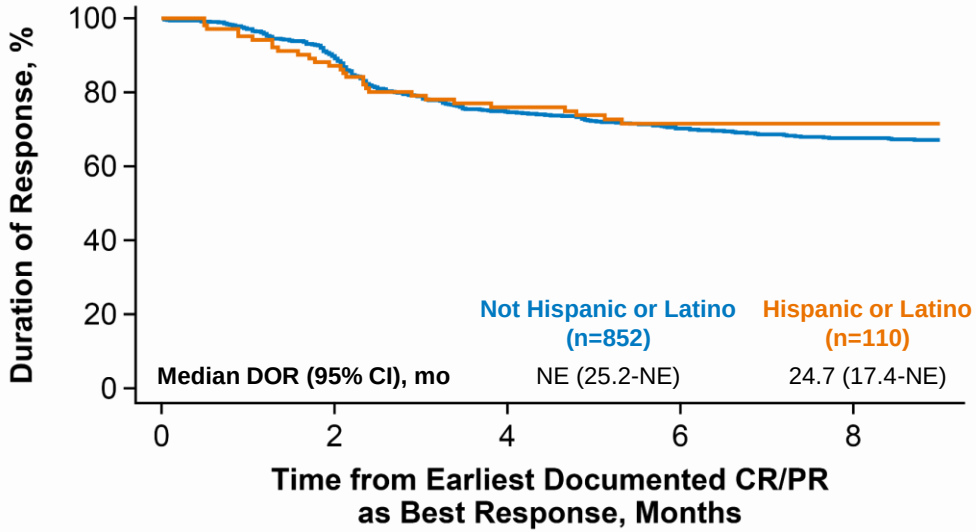
DOR by Race and Ethnicity

DOR by Race



No. at risk					
White	839	669	511	439	399
Black or African American	40	33	22	18	16
Asian	56	48	39	32	32

DOR by Ethnicity



No. at risk					
Not Hispanic or Latino	852	685	518	442	403
Hispanic or Latino	110	87	71	57	55

- The median follow-up for all patients in the analysis (N=1389) was 12.7 months
- The 6-month DOR rate was 70% in White, 66% in Black or African American, 81% in Asian, and 71% in Hispanic or Latino patients

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CR, complete response; DOR, duration of response; mo, month; NE, not evaluable; PR, partial response.

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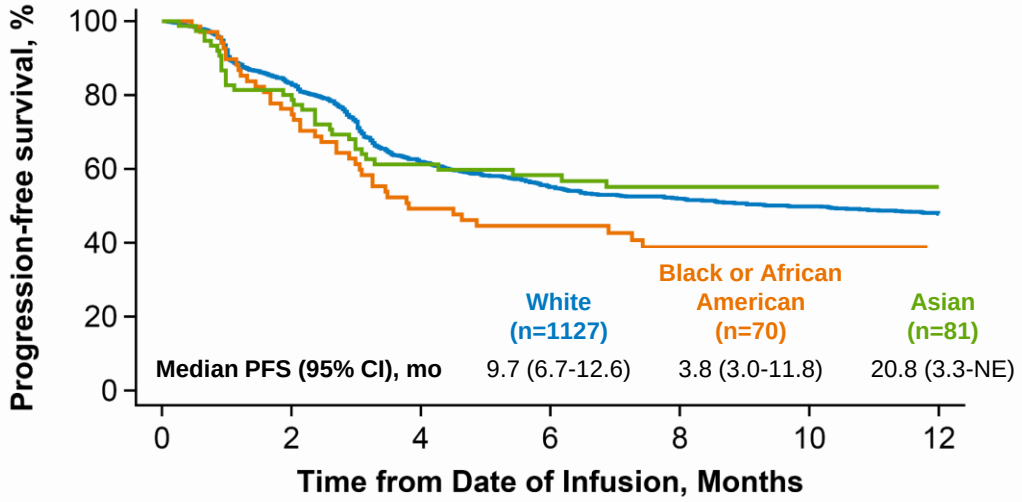
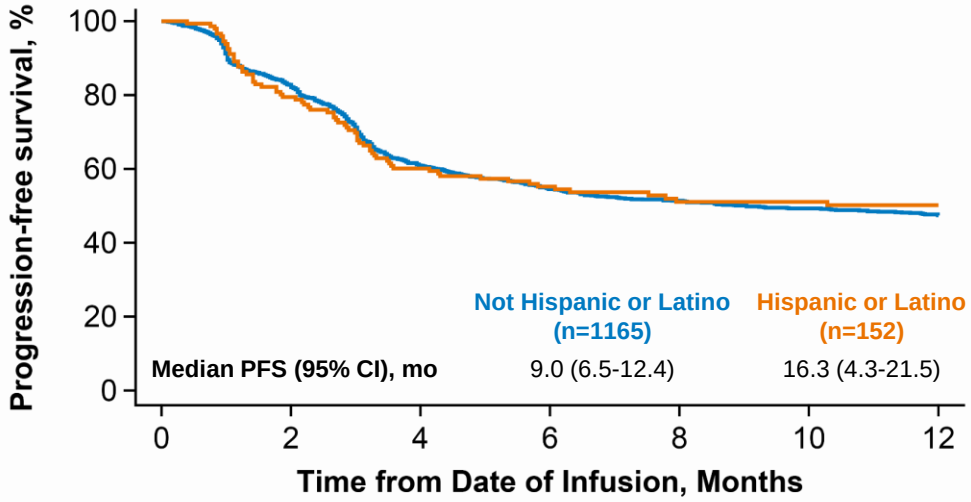
PFS by Race and Ethnicity

PFS by Race



No. at risk							
White	1127	890	644	550	466	437	367
Black or African American	70	51	32	28	18	17	14
Asian	81	60	43	38	33	33	30

PFS by Ethnicity



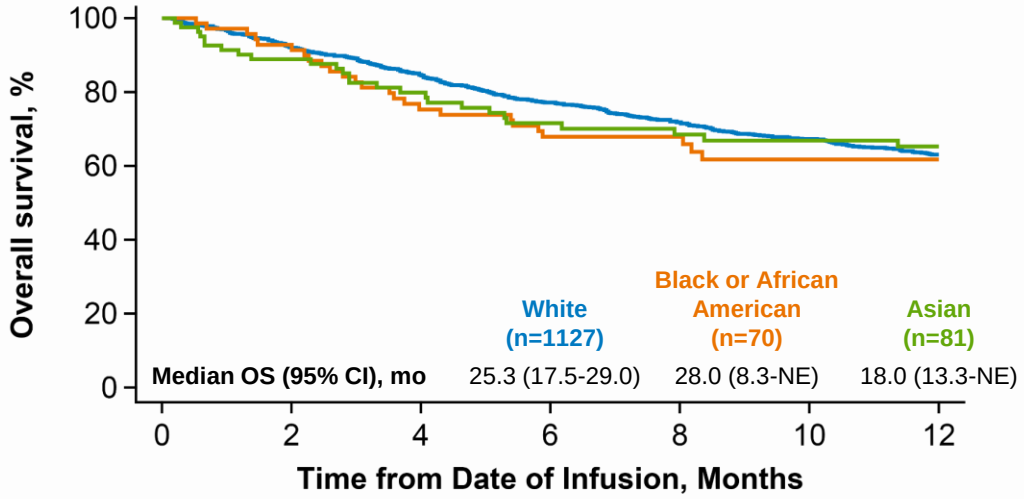
No. at risk							
Not Hispanic or Latino	1165	912	652	560	469	443	372
Hispanic or Latino	152	116	86	76	59	57	52

- The 12-month PFS rate was 48% in White, 36% in Black or African American, 55% in Asian, and 50% in Hispanic or Latino patients

PFS is censored at subsequent cell therapy/HCT.
HCT, hematopoietic cell transplantation; mo, month; NE, not evaluable; PFS, progression-free survival.

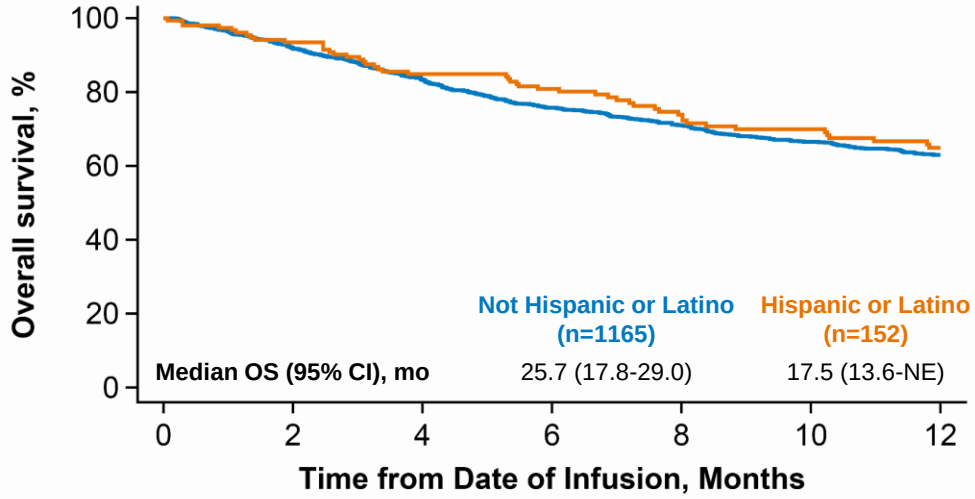
OS by Race and Ethnicity

OS by Race



No. at risk							
White	1127	1020	908	796	667	611	504
Black or African American	70	64	51	44	33	29	25
Asian	81	71	59	50	43	42	38

OS by Ethnicity

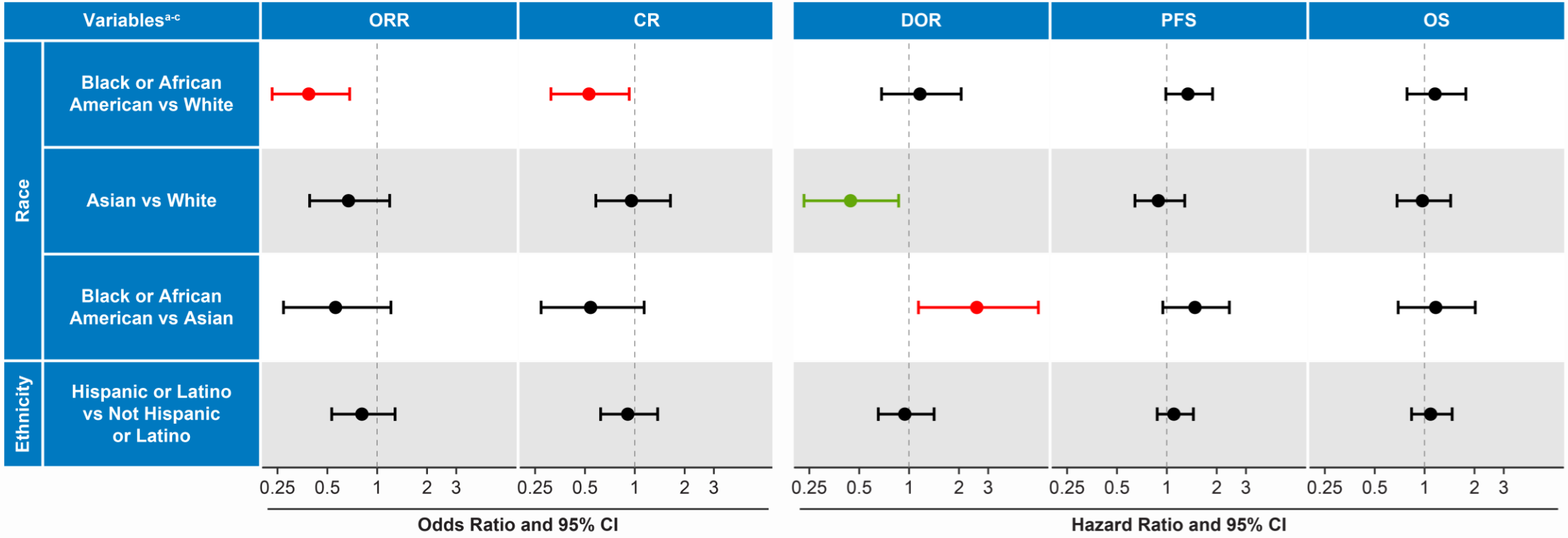


No. at risk							
Not Hispanic or Latino	1165	1053	922	806	668	615	515
Hispanic or Latino	152	142	128	115	94	87	71

- The 12-month OS rate was 63% in White, 62% in Black or African American, 65% in Asian, and 65% in Hispanic or Latino patients

Mo, month; NE, not evaluable; OS, overall survival.

Efficacy Outcomes With Multivariate Adjustment



- No statistical differences were found in OS and PFS across races, or in any efficacy outcome between Hispanic or Latino and not Hispanic or Latino patients
- Black or African American race was associated with inferior ORR (OR 0.40; 95% CI, 0.24-0.69) and CR rate (OR 0.55; 95% CI, 0.32-0.93) vs White race
- Asian patients had favorable DOR compared to both White (HR 0.46; 95% CI, 0.24-0.87) and Black or African American patients (HR 0.39; 95% CI, 0.17-0.88)

[a] Variables with multivariate *P*<.05 are highlighted in either green (favorable) or red (unfavorable). [b] OR was used for the analysis of ORR and CR which HR was used for the analysis of DOR, PFS, and OS. [c] Additional covariates associated with efficacy outcomes were adjusted (data not shown).
CR, complete response; DOR, duration of response; HR, hazard ratio; OR, odds ratio; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.

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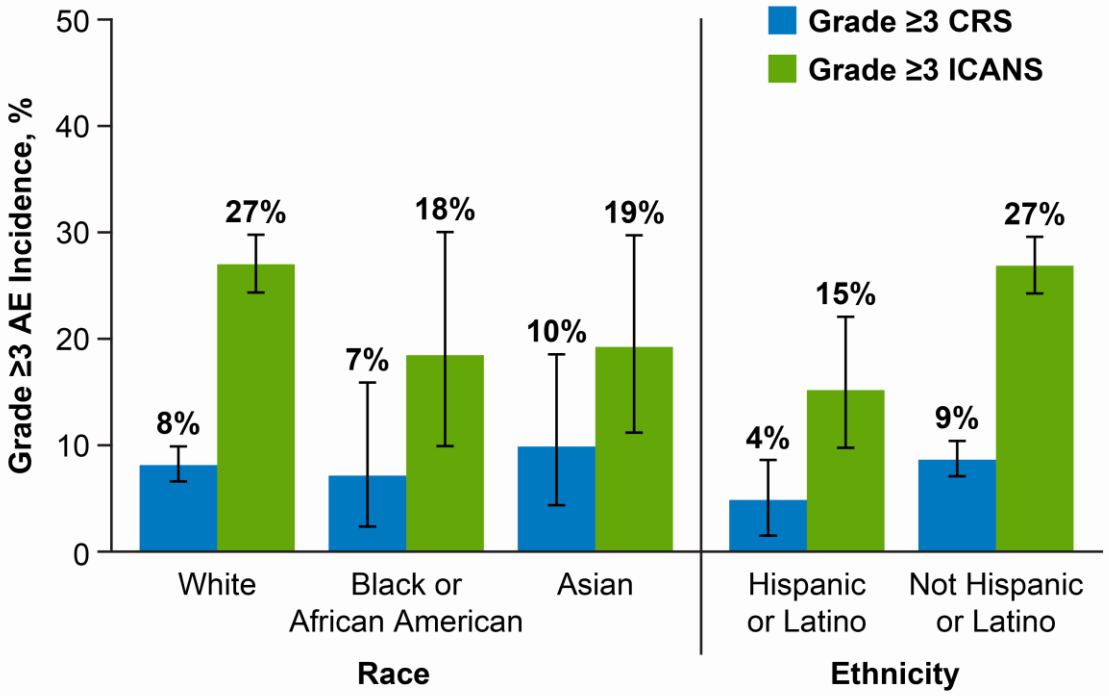
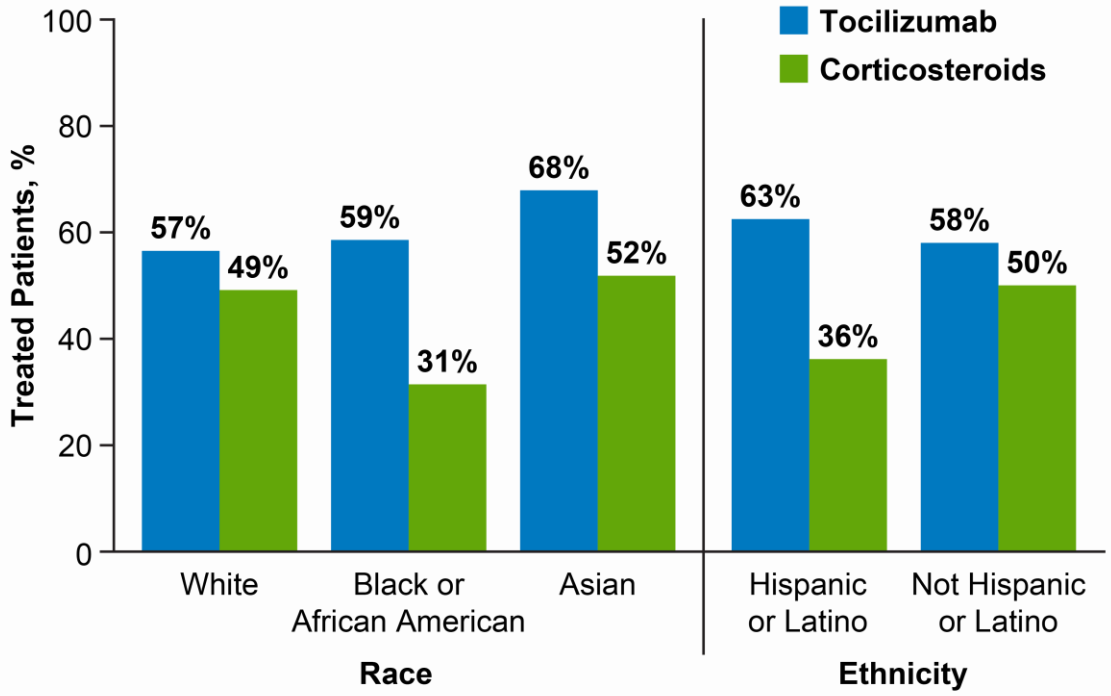
CRS and ICANS by Race and Ethnicity

Grade ≥3 CRS and ICANS by Race and Ethnicity



Treatment for CRS and ICANS by Race and Ethnicity



- Grade ≥3 CRS and ICANS occurred in 7% and 18% of Black or African American, 10% and 19% of Asian, and 8% and 27% of White patients, respectively
- Hispanic or Latino patients had lower rates of Grade ≥3 ICANS (15%) vs not Hispanic or Latino patients (27%)
- Few Black or African American patients received corticosteroids for the treatment of CRS and ICANS, compared with other races

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AE, adverse event; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

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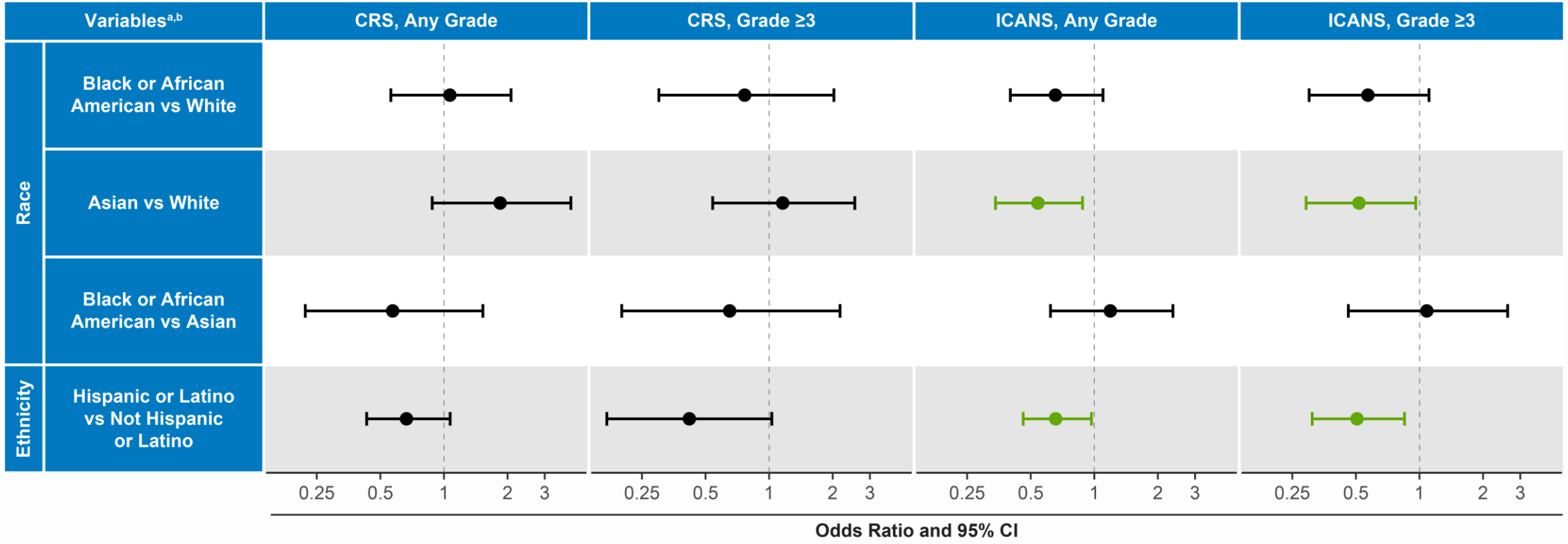
Safety Outcomes With Multivariate Adjustment



- No differences in CRS (any-grade) and Grade ≥3 CRS by race and ethnicity
- Asian patients had a lower risk vs White patients of any-grade ICANS (OR 0.55; 95% CI, 0.34-0.88) and Grade ≥3 ICANS (OR 0.52; 95% CI, 0.29-0.96)
- Hispanic or Latino patients had lower risk vs not Hispanic or Latino patients of any-grade ICANS (OR 0.67; 95% CI, 0.46-0.97) and Grade ≥3 ICANS (OR 0.51; 95% CI, 0.31-0.85)

[a] Variables with multivariate *P*<.05 are highlighted in green (favorable). [b] Additional covariates associated with safety outcomes were adjusted (data not shown).
CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; OR, odds ratio.

Conclusions

- Overall, outcomes with axi-cel CAR T-cell therapy in R/R LBCL were consistent in the real-world setting, regardless of race or ethnicity
- No differences in efficacy outcomes were observed between Hispanic or Latino and not Hispanic or Latino ethnicities
- Asian patients appeared to have favorable DOR compared with White and Black or African American patients
- Lower response rates in Black or African American patients compared to White patients warrant further investigation into factors such higher disease burden and differential access to care

Axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; DOR, duration of response; LBCL, large B-cell lymphoma; R/R, relapsed/refractory.

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