Prior SARS-CoV-2 in patients with CAR-T negatively impacts overall survival, highlighting the need for targeted prophylaxis strategies

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Why did we perform this research?

- Patients with hematologic malignancies who are candidates for chimeric antigen receptor T (CAR-T) cell therapy are at increased risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection[1,2]
- CAR-T cell therapy guidelines recommend that treatment is deferred when a patient develops SARS-CoV-2 infection prior to CAR-T infusion.[3–5] Such delays may put patients at risk of underlying disease progression.[6] The total impact of SARS-CoV-2 infection on CAR-T patients' treatment and disease journey is unknown

Objective

We characterized real-world outcomes among patients who underwent CAR-T cell therapy, to describe the impact of SARS-CoV-2 infection prior to CAR-T on patients' disease progression and treatment journey

How did we perform this research?

A descriptive, retrospective, observational cohort study

Patients in the USA who were prepared for CAR-T cell therapy for hematologic conditions were identified using the Loopback Analytics electronic health records system

Index period:
January 1, 2020 to December 31, 2022

Patients were classified based on whether they had a SARS-CoV-2 infection prior to CAR-T cell therapy

SARS-CoV-2 confirmed by polymerase chain reaction or antigen coronavirus disease 2019 (COVID-19) test within 1 week prior to leukapheresis through to CAR-T infusion

Patients were assessed for real-world overall survival (rwOS)*, real-world time to next treatment (rwTTNT)†, hospitalizations, and adverse events of special interest (AESI)

Patients were followed for a minimum of 6 months until June 30, 2023, or death

*rwOS, length of time from the date of CAR-T cell therapy to the date of death; †rwTTNT, time from the date of CAR-T therapy to the date of subsequent treatment (including subsequent CAR-T episode) or death.

- This study used data from Risk Evaluation and Mitigation Strategies sites within the Loopback Analytics electronic health records system. This system is ideal for robust assessments as it represents over 500 academic and community hospitals in the USA across 30 integrated health systems, encompassing more than 30 million patient lives

How do these real-world data inform clinical practice?

- This study underscores that patients with SARS-CoV-2 prior to receipt of CAR-T cell therapy experience delays in treatment, and an increased percentage may die during the follow-up period vs patients without SARS-CoV-2
- The impact of SARS-CoV-2 on the timely delivery of care and clinical outcomes suggests a need for targeted prevention of infection in patients waiting to receive CAR-T cell therapy

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What did we find?

Study population and characteristics

- We identified 440 patients who received CAR-T cell therapy for hematologic malignancies between January 1, 2020 and December 31, 2022
- Of these, 26 (6%) had SARS-CoV-2 confirmed within 1 week prior to leukapheresis through to CAR-T infusion, and 414 (94%) had no SARS-CoV-2 infection during this period (**Table 1**)
- Median time from first preparatory procedure (i.e., leukapheresis or lymphodepletion) to CAR-T cell therapy was numerically longer in patients who had SARS-CoV-2 (38 [interquartile range (IQR): 27–48] days) than those without (28 [IQR: 25–38] days)
- In a separate analysis of patients with evidence of leukapheresis as a preparatory procedure (N=384), 18% of patients who had no SARS-CoV-2 prior to leukapheresis did not proceed to CAR-T cell therapy due to death, other infections (possibly unidentified SARS-CoV-2), or other unknown reasons

Table 1. Patient and treatment characteristics

Characteristic		SARS-CoV-2 prior to CAR-T (N=26)	No SARS-CoV-2 prior to CAR-T (N=414)
Age at CAR-T infusion, years			
	Mean (SD)	60.97 (13.92)*	61.26 (13.34)†
	Median (min, max)	62.85 (28.59, 83.53)*	64.30 (9.02, 84.27)†
Race, n (%)			
	White	19 (73)	320 (77)
	Asian	2 (8)	27 (7)
	Black or African American	0	16 (4)
	Unknown	5 (19)	51 (12)
Hematologic malignancy, n (%)			
	Diffuse large B-cell lymphoma	12 (46)	228 (55)
	Follicular lymphoma	1 (4)	30 (7)
	Mantle cell lymphoma	1 (4)	34 (8)
	Other B-cell lymphoma	1 (4)	39 (9)
	Multiple myeloma	10 (38)	59 (14)
	Acute lymphoblastic leukemia	1 (4)	24 (6)
Selected prior therapies, n (%)‡			
	HSCT	16 (62)	292 (71)
	CD-20	11 (42)	159 (38)
	Bone marrow transplant	10 (38)	108 (26)
Administration setting, n (%)			
	Inpatient	20 (77)	321 (78)†
	Outpatient	6 (23)	88 (21)†
Duration of follow-up from CAR-T, months			
	Mean (SD)	9.70 (5.20)	12.88 (8.49)
	Median (IQR)	10.28 (5.79–12.18)	10.81 (6.87–18.05)
	Min, max	1.12, 21.75	0.13, 41.76

*N=25: one patient had missing data; †N=409: five patients had missing data; ‡Patients may have received multiple therapies, including therapies not listed.
CAR-T, chimeric antigen receptor T; CD-20, B-lymphocyte antigen CD-20; HSCT, hematopoietic stem cell transplantation; IQR, interquartile range; max, maximum; min, minimum; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

Outcomes

Real-world overall survival (rwOS)

- Of patients who received CAR-T cell therapy, 8 (31%) and 118 (29%) patients in the prior SARS-CoV-2 and no prior SARS-CoV-2 groups died during the study, respectively (**Figure 1**). Total person-time at risk was 252 and 5334 months, respectively
- rwOS probabilities at 6–24 months post-CAR-T cell therapy are shown in **Figure 2**

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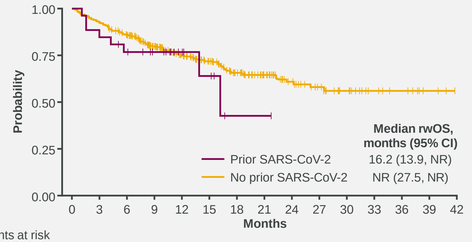
Figure 1. Kaplan–Meier estimates of rwOS

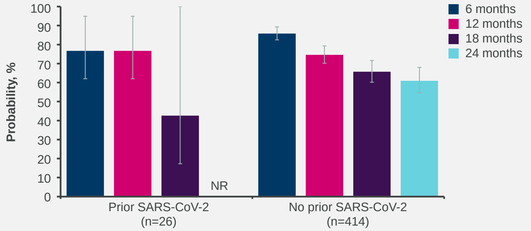


No. of patients at risk

Prior SARS-CoV-2	26	23	19	15	8	5	1	1	0	0	0	0	0	0	0
No prior SARS-CoV-2	414	383	337	245	181	143	104	73	45	32	20	12	8	3	0

rwOS was defined as the length of time from the date of CAR-T cell therapy to the date of death. Individuals who initiated a subsequent CAR-T episode, were lost to follow-up, or remained alive at the end of the study were censored (denoted by a cross). CI, confidence interval; no., number; NR, not reached; rwOS, real-world overall survival; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Figure 2. rwOS probability



rwOS was defined as the length of time from the date of CAR-T cell therapy to the date of death. Error bars depict 95% confidence intervals. NR, not reached; rwOS, real-world overall survival; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Relapse and real-world time to next treatment (rwTTNT)

- Median time to disease relapse (i.e., requiring subsequent treatment for disease) was 2.1 and 5.0 months in the prior and no prior SARS-CoV-2 groups, respectively
- Overall, median (95% CI) rwTTNT was numerically shorter for patients with prior SARS-CoV-2 infection compared with those with no prior SARS-CoV-2 (**Figure 3**)

Hospitalizations and length of stay post CAR-T cell therapy

- Across the prior SARS-CoV-2 and no prior SARS-CoV-2 groups, most patients had an inpatient stay following CAR-T (96% vs 94%), with patients in the prior SARS-CoV-2 group having a numerically longer median (IQR) length of stay (12 [7–35] vs 9 [3–31] days)
- All but one patient (who had no prior SARS-CoV-2) had an outpatient visit following CAR-T. Patients in the prior SARS-CoV-2 group had numerically more visits (median [IQR] was 63 [37–98] vs 51 [28–89])

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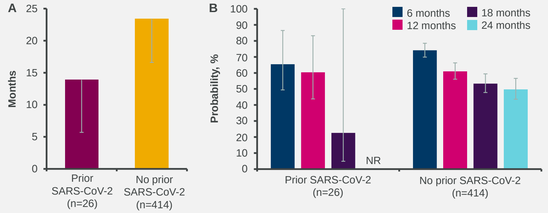
Figure 3. rwTTNT (A) median; (B) probability

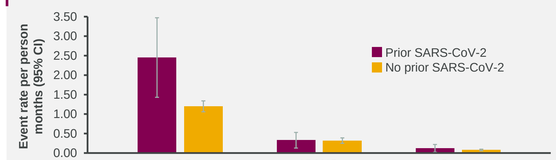


rwTTNT was defined as time from the date of CAR-T cell therapy to the date of subsequent treatment (including subsequent CAR-T episode) or death. Error bars depict 95% confidence intervals. rwTTNT, real-world time to next treatment; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Adverse events of special interest (AESIs)

- Incidence rates of cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and sepsis were examined (**Figure 4**)
  - The proportion of patients with AESIs of any grade was similar between groups with prior and no prior SARS-CoV-2: 85 vs 73% for CRS, 40 vs 40% for ICANS, and 19 vs 14% for sepsis
- Notably, patients with prior SARS-CoV-2 (vs no prior) appeared to have greater incidence of CRS

Figure 4. Incidence rates of AESIs



The highest grade of CRS or ICANS that occurred during follow-up was reported.
AESI, adverse event of special interest; CI, confidence interval; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Conclusions

This study underscores that patients with SARS-CoV-2 prior to receipt of CAR-T cell therapy may experience delay in therapy, and an increased percentage may relapse and/or die during the follow-up period (vs patients without SARS-CoV-2). The impact on timely delivery of care and clinical outcomes suggests a need to prevent SARS-CoV-2 in these patients

Our data suggest that individuals with SARS-CoV-2 prior to CAR-T cell therapy may be at greater risk of CRS

Limitations

- Lower-grade adverse events may have been under-reported in clinical capture, resulting in underestimation of event rates. Sensitivity analyses (not presented) that supplemented CRS rates with drug and blood culture data and ICANS with drug data found higher rates of both events
- There was potential for under-capture of SARS-CoV-2 events based on in-hospital testing and reporting of diagnosis codes
- Small sample sizes may limit ability to draw firm conclusions; cautious interpretation is warranted