Infections in Patients Treated with Chimeric Antigen Receptor T-cells (CAR-T) Therapy

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BACKGROUND

- CAR-T cells are genetically engineered from a patient's own T cells to better recognize and direct immune response against specific antigens on tumor cells.
- CAR-T therapy has shown promising response rates in patients with relapsed and refractory non-Hodgkin lymphoma (NHL) and acute lymphoblastic leukemia (ALL).
- Given the paucity of infection data following CAR-T therapy, which are distinct from those seen in traditional chemotherapies, our objective was to describe the epidemiology and risk factors for infections following CAR-T therapy.
- **Disclosures:** all authors – no relevant financial / non-financial relationships with any proprietary interests

METHODS

- We retrospectively reviewed electronic medical records of:
  - **39** adult and pediatric patients with relapsed and refractory ALL or NHL who received CAR-T therapy
  - **2017 to 2019** at Michigan Medicine
  - **6 months** following CAR-T therapy infusion (CTI)
  - Analyzed both infected & uninfected patients

Infection

- Defined as presence of **positive microbiologic** or histopathologic results and the **receipt of a treatment** course for the infection
- Classified as bacterial, fungal, or viral infection. Infection was then categorized into **early infection** (day 0-30) or **late infection** (day 31-180)

- **Statistical analysis**
  - Baseline and infection characteristic – Descriptive statistics (median, interquartile range, and percentage) & bivariate comparisons
  - Categorical variables – Chi-squared or Fisher's exact test
  - Continuous variables – Student's T-test

RESULTS

Table 1. Demographic, Laboratory, and Clinical Characteristics

Characteristic	All patients (n=39)	Infected-patients (n=16)	Uninfected patients (n=23)	P value
Demographics				
Age, mean ± SD, years	52.4 ± 21.8	63.3 ± 11.3	44.8 ± 24.2	0.01
Male sex, n (%)	25 (64)	10 (63)	15 (65)	>0.99
Baseline malignancy, n (%)				
Non-Hodgkin Lymphoma (NHL)	32 (82)	16 (100)	16 (70)	0.03
Acute lymphocytic leukemia (ALL)	7 (18)	0 (0)	7 (30)	0.03
Hematologic parameters prior to CTI				
ANC, median (IQR), cells/μL	1 (0.7-1.9)	1.1 (0.8-1.5)	0.8 (0.6-2.0)	0.96
ALC, median (IQR), cells/μL	0 (0-0.1)	0 (0-0.1)	0 (0-0.1)	0.41
IgG prior to CTI, median (IQR), mg/dL	430 (350-557)	393 (353-517)	432 (338-562)	0.81
Total hospital length of stay, median (IQR), days	22 (21-26)	24 (21-26)	22 (21-26)	0.22
Length of stay from CTI, median (IQR), days	16 (15-19)	16 (15-22)	16 (15-19)	0.18
ICU admission, n (%)	12 (31)	6 (38)	6 (26)	0.50
Length of ICU stay, median (IQR), days	4 (4-8)	6 (3-9)	4 (4-5)	0.42
Cytokine release syndrome (CRS), n (%)				
Grade 1-2	26 (67)	10 (63)	16 (70)	0.74
Grade 3-5	7 (18)	4 (25)	3 (13)	0.42
Tocilizumab administration due to CRS, n (%)	16 (41)	8 (50)	8 (35)	0.51
Tocilizumab doses administered, median (IQR)	0 (0-2)	1 (0-1)	0 (0-2)	0.60
Steroids administration due to CRS, n (%)	13 (33)	9 (56)	4 (17)	0.02
Duration of steroids, median (IQR), days	10 (6-13)	10 (8-12)	11 (6-17)	0.62

Table 1. SD, standard deviation; CTI, chimeric antigen receptor T-cell infusion; IQR, interquartile range; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; ICU, acute care unit; IgG, Immunoglobulin G.

Table 2. CMV, cytomegalovirus; RSV, respiratory syncytial virus; URT, upper respiratory tract
[a] Bacteremia: *P. aeruginosa,* n=1; *C. ramosum,* n=1; *S. epidermidis,* n=1; *B. fragilis,* n=1
[b] SSTI (skin and soft tissue infection): *Actinomyces* spp, n=1
[c] UTI (urinary tract infection): *P. aeruginosa,* n=1; *E. coli,* n=1
[d] Candidemia: *C. glabrata,* n=1
[e] SSTI (skin and soft tissue infection): *Aspergillus terreus* & *Rhizopus,* n=1

RESULTS

Figure 1. Comparison of early vs late infection after CTI

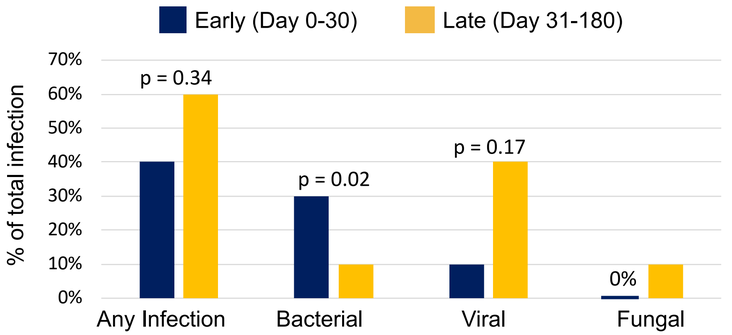

Table 2. Comparison of early vs late infection after CTI

Characteristic	All infection No. (%)	Early No. (%)	Late No. (%)
Any infection	20	8 (40)	12 (60)
Bacterial infection	8 (40)	6 (30)	2 (10)
Bacteremia[a]	4 (20)	2 (10)	2 (10)
SSTI[b]	1 (5)	1 (5)	--
UTI[c]	2 (10)	2 (10)	--
C. difficile infection	1 (5)	1 (5)	--
Viral infection	10 (50)	2 (10)	8 (40)
CMV	2 (10)	1 (5)	1 (5)
RSV	2 (10)	--	2 (10)
Other URT viruses	6 (30)	1 (5)	5 (25)
Fungal infection	2 (10)	0 (0)	2 (10)
Candidemia[d]	1 (5)	--	1 (5)
SSTI[e]	1 (5)	--	1 (5)

CONCLUSIONS

- Infectious complications are common following CAR-T therapy. We identified 20 infections in 16 of 39 patients following CTI.
- The most common infections were viral, followed by bacterial and fungal. More bacterial infections were seen in the early period post-CTI, whereas viral infections were more common during the late period. Fungal infections occurred late after CTI.
- We found the majority of infections to be caused by various bacteria or respiratory viruses in a cohort of patients with lymphoma as the most common underlying malignancy.