Characterization of Infectious Complications Following CAR T Cell Therapy and the Need for Antibiotic Treatment During the Expected Period of Cytokine Release Syndrome

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Introduction

Cytokine release syndrome (CRS) is a well-known treatment-related toxicity of CAR T cell therapy and typically occurs with fever within the first 14 days of treatment.

CRS may be difficult to distinguish from an infection, which poses a particular risk within the first thirty days. Thus, early infectious work up is initiated in patients who become febrile post-CAR T cell therapy, with a low threshold to initiate broad spectrum antibiotics. However, a fever within the expected CRS period may be related to CRS over infection.

Aim

This retrospective single-center study aims to characterize the nature of infectious complications during the expected CRS period.

Methods

We completed a retrospective review of 329 patients at Mount Sinai Hospital who received CAR T cell products from April 2017 until August 2024.

Patients with relapsed/refractory multiple myeloma (MM), B cell lymphoma, and acute lymphoblastic leukemia (ALL) were included in the analysis. Treatment involved either of the six approved commercial CAR T cell therapy products or clinical trial protocol.

CRS onset was defined as first fever post infusion without another clear explanation within the expected CRS period for each respective cell product.

Results

A total of 329 patients received CAR T cell therapy
- 71% MM (233/329)
- 24% B-cell lymphoma (80/329)
- 5% ALL (16/329)

Of the total patients
- 86% developed CRS (283/329)
- Median onset occurred within the expected CRS period for each respective CAR T product.

During this CRS period
- 80% received broad spectrum antibiotics
- 29% were neutropenic
- 24% were on antibiotic prophylaxis

Of the total 329 patients
- 295 had blood cultures collected
  - 3.3% (10/295) of patients had positive results
- 25% had documentation of any infection (including respiratory and gastrointestinal) within the first thirty days post CAR T cell infusion
  - 6.4% were grade 3 or above

	Total	MM	Lymphoma	ALL
Number of patients, n (%)	329 (100)	233 (71)	80 (24)	16 (5)
Age at time of CAR-T in years, median (IQR)	61 (15)	62 (13)	61 (22)	33 (22)
Male, n (%)	198 (60)	136 (59)	52 (65)	10 (63)
Previous Lines of Therapies, median (IQR)	4 (3)	5 (3)	3 (1)	3.5 (1)
Previous Autologous Stem Cell Transplant, n (%)	206 (63)	193 (83)	12 (15)	1 (6)
Previous Allogeneic Stem Cell Transplant, n (%)	7 (2)	2 (1)	0 (0)	5 (31)
Bridging Therapy, n (%)	217 (66)	165 (71)	42 (53)	10 (63)

Table 1: Patient Characteristics for Entire Patient Population

A) CRS by CAR T therapy	Total (n=329)	Ide-cel (n=72)	Liso-cel (n=10)	Cilta-cel (n=126)	Tisa-cel (n=3)	Brexu-cel (n=16)	Axi-cel (n=67)	Other* (n=35)
CRS, n (%)	283 (86)	61 (85)	6 (60)	109 (87)	3 (100)	16 (100)	61 (91)	26 (74)
CRS onset day, median (IQR)	3 (5)	1 (1)	3 (5)	6 (2)	4 (4)	5 (3)	3 (3)	2 (3)
CRS duration in days, median (IQR)	4 (5)	3 (5)	1 (1.5)	3 (4)	5 (1)	4.5 (2.5)	5 (6)	4 (7)
B) Neutropenia and ATB management	**Total (n=283)**	**Ide-cel (n=61)**	**Liso-cel (n=6)**	**Cilta-cel (n=109)**	**Tisa-cel (n=3)**	**Brexu-cel (n=16)**	**Axi-cel (n=61)**	**Other* (n=26)**
ANC <0.5 at time of first fever, n (%)	83 (29)	16 (26)	2 (33)	31 (28)	2 (67)	4 (25)	23 (38)	5(19)
ATB prophylaxis at onset of CRS, n (%)	76 (24)	10 (16)	1 (16)	32 (29)	3 (100)	5 (31)	20 (33)	5 (19)
Broad-spectrum ATB during CRS, n (%)	225 (80)	48 (79)	5 (83)	91 (83)	2 (67)	15 (94)	46 (75)	18 (82)
C) Infectious outcomes	**Total (n=329)**	**Ide-cel (n=72)**	**Liso-cel (n=10)**	**Cilta-cel (n=126)**	**Tisa-cel (n=3)**	**Brexu-cel (n=16)**	**Axi-cel (n=67)**	**Other* (n=35)**
Infection from D0-D30, n (%)	82 (25)	13 (18)	2 (20)	41 (33)	0 (0)	6 (38)	16 (24)	4 (11)
Infection grade >3, n (%) DO	21 (6.4)	5 (8)	0 (0)	9 (11)	0 (0)	2 (15)	5 (9)	0 (0)
Infectious workup, n (%)- Blood cultures	295 (90)	62 (86)	7 (70)	115 (91)	3 (100)	16 (100)	64 (96)	28 (80)
Infectious workup, n (%)- Positive blood Cultures	10/295 (3.3)	1/62 (2)	0/7 (0)	5/115 (4)	0/3 (0)	1/16 (6)	3/64 (5)	0/28 (0)

Table 2: CRS and Infectious Outcomes by CAR-T Type
*other refers to experimental CAR-T products

Conclusions

These results suggest that the vast majority of febrile patients during the expected CRS period do not have an infection, and thus, more judicious antimicrobial stewardship should be considered, particularly in non-neutropenic patients.

References

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