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An Analysis of Infectious Complications Post-Treatment With Actalycabtagene Autoleucel

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INTRODUCTION

- Grade 3 or 4 infectious complications occur in up to 31% of patients post-CAR T cell therapy, constituting the leading non-relapse cause of mortality [1]
- Patients receiving CAR T cell therapy have risk factors for infection including -
  - The underlying malignancy
  - Multiple prior lines of chemotherapy
  - Lymphodepleting conditioning therapy[2]
  - Hypogammaglobulinemia
  - ICU admission and immunosuppression for complications such as cytokine release syndrome (CRS) [3]
- Actalycabtagene Autoleucel(Actaly-cel) is an indigenously developed, humanized, CD19 directed CAR-T cell therapy, approved for marketing in India. [4]
- Understanding the pattern of infections in patients receiving this therapy, will help to improve prophylaxis and management of infections in future patients.

AIM

To determine the incidence, pattern, and outcomes of infections in patients receiving Actaly-cel.

METHODS

Design: Single-centre retrospective study.

Data was extracted from the electronic medical records of the Tata Memorial Hospital.

Participants: Patients aged 15 years and above who underwent infusions of Actaly-cel from June 2021 to December 2023.

Main Outcome Measures:

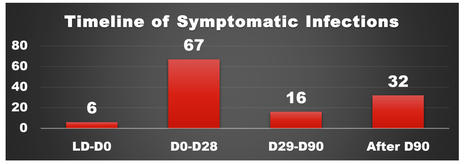
1. Median number of infections per patient
2. Timeline of infections after infusion
3. Correlation between infection rates and
   a. Absolute Lymphocyte count (ALC) and IgG levels at baseline
   b. Duration of neutropenia
4. Mortality rate due to infection

RESULTS

Baseline Characteristics	n=48
Gender	
Male	40(83.3%)
Female	8(16.6%)
Diagnosis	
B-ALL	12(25%)
DLBCL	30(62.5%)
PMBCL	3(6.3%)
LGL	3(6.3%)
ECOG PS	
1	46(95.8%)
2	2(4.2%)
Number of previous lines of therapy	
1-2 lines	33(68.75%)
3-4 lines	11(22.9%)
5-6 lines	4(8.3%)
Previous Stem Cell Transplant	2(4.1%)
Laboratory Parameters	
Median ANC(IQR)	1.71(.67-3.82)x10^9/L
Median ALC(IQR)	.08(.02-.55) x10^9/L
Median IgG Level(IQR)	820(568-983) mg/dl

CAR-T Infusion Data	n=48
Number of infusions	
1	46
2	2
Median Dose of CAR-T cells(IQR)	9.09(6.05-14.32)x10^6 cells/kg
Neutropenia	
Median Day of Onset(IQR)	2(0-4)
Median Day of Nadir(IQR)	6(3-8)
Median duration of Neutropenia(IQR)	9(5-13)
Complications	
CRS	31(64.6%)
ICANS	0
HLH	6(12.5%)
Usage of immunosuppressive medication	
Tocilizumab	23(47.9%)
Corticosteroid	10(20.8%)
Anakinra	3(6.3%)

Infection data	
Total Number of infections recorded	121
Median number of infections per patient	2(1-3)



Microbiological Profile of Recorded Infections	
Number of infections with microbiological confirmation	35(28.9%)
Number of infections with multiple organisms identified	13(10.7%)

Organism	Total	LD-D0	D0-D28	D29-D90	After D90
Viruses identified					
CMV - Blood PCR	14	0	8	2	4
COVID 19 - Nasopharyngeal Swab	6	0	2	0	4
Dengue - NS1 Antigen	1	0	0	1	0
Influenza A - Nasopharyngeal Swab	2	1	0	1	0
RSV - Nasopharyngeal Swab	1	0	1	0	0
Bacteria isolated in culture					
Gram Negative Bacilli	21	0	12	0	9
Gram Positive Cocci	6	0	5	1	0
MDR organisms	20	1	13	0	6
Fungal infections					
Proven fungal pneumonia	0	0	0	0	0
Probable fungal infection	7	1	2	0	4
Possible fungal pneumonia	5	1	3	0	1
Fungal Sinusitis	1	0	0	0	1

Presenting Clinical Syndrome	n=121
Febrile Neutropenia	33(27.2%)
Non-neutropenic Undifferentiated Febrile Illness	18(14.8%)
Fever with Rash	2(1.6%)
Septic Shock	1(0.8%)
Central Line Associated Blood Stream Infection	1(0.8%)
Respiratory Tract Infection	
Lower Respiratory Tract Infection	15(12.3%)
Upper Respiratory Tract Infection	24(19.8%)
Gastrointestinal Infection	
Gastroenteritis	12(9.9%)
Perianal Infection	2(1.6%)
GI Sepsis	2(1.6%)
Central Nervous System Infection	
Encephalitis	1(0.8%)
Dental Infection	4(3.3%)
Skin and Soft tissue infection	4(3.3%)
Taenia Corporis	1(0.8%)
Scabies	1(0.8%)

Correlation of number of infections with risk factors		
Risk factors	Correlation Coefficient	p value
ALC at Baseline	0.06	0.68
IgG Level at baseline	-0.23	0.11
Duration of Neutropenia	0.13	0.375

Infections were a contributory cause of death in 8.3%(n=4/48) patients

- Bacterial pneumonia(n=1)
- GI sepsis(n=1)
- COVID pneumonia(n=1)
- Neutropenic sepsis(n=1)

Median time to death - 46 days(IQR:32-101) after infusion

CONCLUSIONS

Patients receiving Actaly-cel primarily developed infections between days 0-28, post-infusion. The most common clinical syndrome was febrile neutropenia. The number of infections per patient did not correlate with ALC, IgG level at baseline or the duration of neutropenia.

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