2097: BACTERIAL INFECTIONS IN PATIENTS WITH LATE NEUTROPENIA FOLLOWING CD19 CHIMERIC ANTIGEN RECEPTOR (CAR) T-CELL THERAPY FOR NON-HODGKIN LYMPHOMA (NHL)

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INTRODUCTION

- CD19 CAR T-cell therapy has excellent clinical efficacy for treatment of relapsed and refractory hematologic malignancies but may be complicated by acute toxicities including cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) as well as delayed "on-target, off-tumor" effects such as hematologic toxicity.
- Late neutropenia, occurring more than 30 days after CAR T-cell infusion, is a frequent complication following CD19 CAR T-cell therapy, though its mechanisms are not fully elucidated.
- In other studies, acute toxicities such as CRS and prior HCT have been associated with late neutropenia.
- The impact of delayed or late neutropenia on risk for infectious complications or the need for antibacterial prophylaxis in this setting are not well understood.

METHODS

- We performed a retrospective study of 280 adults receiving CD19 CAR T-cell therapy for Non-Hodgkin lymphoma (NHL) between December 2017 and September 2021.
- Levofloxacin prophylaxis was used after CAR T-cell infusion until count recovery (absolute neutrophil count (ANC) ≥ 1000) for outpatient cell infusions.
- Patients were evaluated for late neutropenia (ANC <1000) during three time periods following cell infusion: day 30 – 100; day 100 – 365; and after day 365
- Infections were recorded if there was a microbiologic diagnosis with correlating symptoms and treatment during the period of neutropenia; infection severity was determined using Blood and Marrow Transplant Clinical Trials Network criteria.
- We compared rates of acute toxicities using the Fisher exact test or Wilcoxon test according to the nature of the covariate. Patients were censored on the first day of any additional antineoplastic therapy after relapse, death, or last follow up until 1/25/2022.

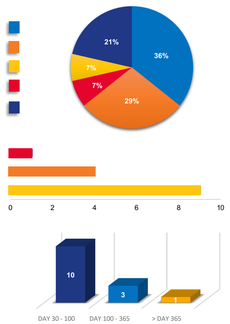
RESULTS

Baseline Characteristics	Late Neutropenia n= 116	No Late Neutropenia n=164	All Patients n=280
Demographics			
Age, median (range)	64 (19 – 79)	64 (25 – 82)	64 (19 – 82)
Male sex, no. (%)	73 (63)	112 (68)	185 (66)
Underlying Disease no. (%)			
Diffuse Large B-cell Lymphoma	55 (47)	103 (63)	158 (56)
Transformed Follicular Lymphoma	28 (24)	29 (18)	57 (20)
High-Grade B-cell Lymphoma	5 (4)	8 (5)	13 (5)
Transformed Marginal Zone Lymphoma	6 (5)	4 (2)	10 (4)
Primary Mediastinal B-cell Lymphoma	6 (5)	4 (2)	10 (4)
Follicular Lymphoma	2 (2)	7 (4)	9 (3)
Mantle Cell Lymphoma	5 (4)	3 (2)	8 (3)
Other Non-Hodgkin's Lymphoma *	3 (3)	5 (3)	8 (3)
Transformed Chronic Lymphocytic Leukemia	6 (5)	1 (0.6)	7 (2.5)
Prior HCT			
Allogeneic	8 (7)	1 (0.6)	9 (3)
Autologous	37 (32)	45 (27)	82 (29)
CAR T-cell Product, no (%)			
Axicabtagene ciloleucel	106 (91)	138 (84)	244 (87)
Tisagenlecleucel	3 (3)	19 (12)	22 (8)
Brexucabtagene autoleucel	5 (4)	3 (2)	8 (3)
Lisocabtagene maraleucel	2 (2)	4 (2)	6 (2)

* Other Non-Hodgkin's Lymphomas: T-cell Histiocytic rich diffuse B-cell lymphoma n=3; Transformed follicular lymphoma and chronic lymphocytic leukemia n=1; Gray zone lymphoma n=2; Transformed lymphoma not specified n=1; Burkitt and large B-cell lymphoma mixed phenotype n=1

Acute CAR T-cell Toxicities	Late Neutropenia n= 116	No Late Neutropenia n=164	p-value	All Patients n=280
CRS Diagnosis, no. (%)	106 (91)	134 (82)	0.025	240 (86)
CRS Grade, no. (%)			-	
Grade 1	37 (35)	65 (40)		102 (43)
Grade 2	63 (60)	62 (38)		125 (52)
Grade 3	4 (4)	4 (2)		8 (3)
Grade 4	2 (2)	3 (2)		5 (2)
ICANS Diagnosis, no. (%)	79 (68)	74 (45)	<0.001	153 (55)
ICANS Grade, no. (%)			-	
Grade 1	17 (22)	16 (10)		33 (22)
Grade 2	13 (16)	21 (13)		34 (22)
Grade 3	49 (62)	37 (23)		86 (56)
Tocilizumab Administration, no. (%)	89 (77)	91 (55)	< 0.001	180 (64)
Tocilizumab doses, median (range)	2 (1 – 4)	2 (1 – 4)	-	2 (1 – 4)
Corticosteroid Administration, no. (%)	74 (64)	81 (49)	0.020	155 (55)

Bacterial Infections During Period of Neutropenia	Patients with Late Neutropenia n=116
Infection Type	218 (7 – 1340)
Bacterial infections	11 (9)
Bloodstream Infection	5 (4)
Urinary Tract Infection	4 (4)
Enteritis	1 (1)
Otitis Externa	1 (1)
Clostridioides difficile colitis	3 (3)
Infection Severity	
Life-threatening	1 (1)
Severe	4 (3)
Moderate	9 (8)
Infection Timing	
Days to infection, median (range)	70 (30 – 584)
Infections Day 30 – 100, (n=99)	10 (9)
Infections Day 101 – 365, (n=39)	3 (3)
Infections After Day 365, (n=12)	1 (1)



Patient No.	Age	Sex	Disease	CRS or ICANS	Tocilizumab	Corticosteroids	Neutropenia Day 30 - 100	Neutropenia Day 101 - 365	Neutropenia After Day 365	Neutropenia on day of diagnosis	First Bacterial Infection	Infection type	D+ Infection	Severity of infection
1	47	Male	DLBCL	Yes	No	No	Yes	Not Checked	Not Checked	No	*C. difficile* colitis	Colitis	30	Moderate
2	51	Female	PMBCL	Yes	No	No	Yes	No	Not Checked	Yes	*E. coli* bacteremia	Bloodstream infection	32	Life-threatening
3	67	Female	DLBCL	Yes	Yes	Yes	Yes	Not Checked	Not Checked	No	*E. coli* urinary tract infection	Cystitis	37	Moderate
4	46	Male	DLBCL	Yes	Yes	Yes	Yes	Not Checked	Not Checked	Yes	*E. durans and G. adiacens* bacteremia	Bloodstream infection	37	Severe
5	56	Female	DLBCL	Yes	Yes	Yes	Yes	Not Checked	Not Checked	Yes	*S. epidermidis* CLABSI	Bloodstream infection	58	Moderate
6	71	Female	tFL	Yes	No	No	Yes	No	Not Checked	No	*E. cloacae* bacteremia and urinary tract infection	Bloodstream infection and cystitis	60	Severe
7	73	Male	tFL	Yes	Yes	Yes	Yes	Yes	Yes	No	*E. cloacae* urinary tract infection	Cystitis	62	Moderate
8	63	Male	DLBCL	Yes	Yes	Yes	Yes	Yes	No	No	*S. maltophilia* CLABSI	Bloodstream infection	77	Severe
9	58	Female	FL	Yes	Yes	Yes	Yes	Yes	Not Checked	No	*E. coli* urinary tract infection	Cystitis	92	Moderate
10	79	Male	DLBCL	Yes	No	No	Yes	No	Not Checked	No	*C. difficile* colitis	Colitis	100	Moderate
11	68	Male	DLBCL	Yes	No	No	Yes	Yes	Not Checked	Yes	*C. difficile* colitis	Colitis	109	Moderate
12	51	Male	FL	Yes	Yes	No	Yes	Yes	Not Checked	Yes	*P. aeruginosa* Otitis Externa	Otitis	220	Severe
13	58	Female	DLBCL	Yes	Yes	Yes	No	Yes	Not Checked	Yes	*E. coli* urinary tract infection	Cystitis	129	Moderate
14	58	Female	DLBCL	Yes	No	No	Yes	No	Yes	No	*C. jejuni* enteritis	Enteritis	584	Moderate

CONCLUSIONS

- Patients who developed late neutropenia after day 30 had significantly increased incidence of acute toxicities including diagnosis of CRS and ICANS and administration of tocilizumab and corticosteroids, which is consistent with prior reports that associate CRS with late hematologic toxicity.
- Despite these findings, bacterial infections were relatively uncommon in patients with late neutropenia after CD19 CAR-T therapy for NHL in the absence of antibacterial prophylaxis.
- 11 (9%) patients out of 116 with late neutropenia developed a bacterial infection and 3 patients (3%) developed C. difficile colitis after day 30.
- All but one of the severe or life-threatening bacterial infections in this population occurred between day 30 and 100.
- Further studies are needed to inform optimal prevention strategies including extended use of antibacterial prophylaxis.

KEY REFERENCES

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