Characterizing Treatment Duration of Viridans Group Streptococci Bacteremia in Neutropenic Oncology Patients: Is 14 Days Necessary?

Yaling Vu, PharmD[1]; Jenny Wong, PharmD, BCPS[1]; Catherine Liu, MD, FIDSA[2,3]; Frank Tverdek, PharmD, BCPS AQ-ID[1,2]
[1]Department of Pharmacy, University of Washington Medical Center – Montlake Campus, Seattle, WA; [2] Fred Hutchinson Cancer Center, Seattle WA;
[3.] Division of Allergy & Infectious Diseases, University of Washington, Seattle, WA
Contact: Tverdek@uw.edu

Background

- Infection is an important cause of morbidity and mortality in patients with cancer.
- Viridans group streptococci (VGS) can cause opportunistic disease in neutropenic patients but contemporary literature on their outcome is limited.[2]
- NCCN Guidelines recommend Streptococci bacteremia treatment durations between 7 to 14 days[3], but the optimal duration of therapy is unknown.

Objective

To characterize the treatment duration and clinical course among neutropenic oncology patients with VGS bacteremia.

Methods

Design: Retrospective chart review of VGS blood cultures in neutropenic oncology patients between 6/1/2020 to 1/31/2022

Setting: Fred Hutchinson Cancer Center and University of Washington Medical Center – Montlake, a 570-bed tertiary care referral center

Primary Outcome: Total duration of antibiotic therapy

Secondary Outcomes: Total duration of fever, mortality, recurrence of VGS bacteremia, *Clostridium difficile* infection

Figure 1. Study Flowchart

Oncology patients treated for VGS blood culture (N=86)
- ≥18 years old
- ≥ 1 positive blood culture for VGS
- Antibiotic treatment ≥ 48 hours
- ANC < 1000 cells/mm^3

Excluded Patients (N=29)
- 15 polymicrobial infection
- 8 complicated infection
- 5 non-neutropenic
- 1 treatment discontinued for goals of care

Patients included in final analysis (N=57)

Results

Table 1. Baseline Demographics

Demographics *n (%)*	**N=57**
Age, years, *median (IQR)*	52.2 (40-67)
Male	34 (59.6%)
Baseline ANC, cell/mm^3, *median (IQR)*	15 (0-560)
Antimicrobial Prophylaxis	56 (98.2%)
Levofloxacin	56 (98.2%)
Isolated Species	
Streptococcus mitis	49 (86%)
Streptococcus salivarius	8 (14%)
Primary Oncologic Disease	
AML	26 (45.6%)
Lymphoma	9 (15.8%)
ALL	8 (14%)
Most Recent Oncologic Treatment	
Allo-HSCT	15 (29.8%)
GCLAM†-based	14 (24.6%)
Auto-HSCT	8 (14.0%)
Other Cytarabine-based	6 (10.5%)
HyperCVAD-based	4 (7.0%)
CAR-T	2 (3.5%)
Other‡	6 (10.5%)

†G-CSF, cladribine, cytarabine, and mitoxantrone
‡Other regimens included ALL R3, azacitidine, C10403, DA-EPOCH + inotumumab, and decitabine + venetoclax

Figure 2. Treatment Duration Distribution

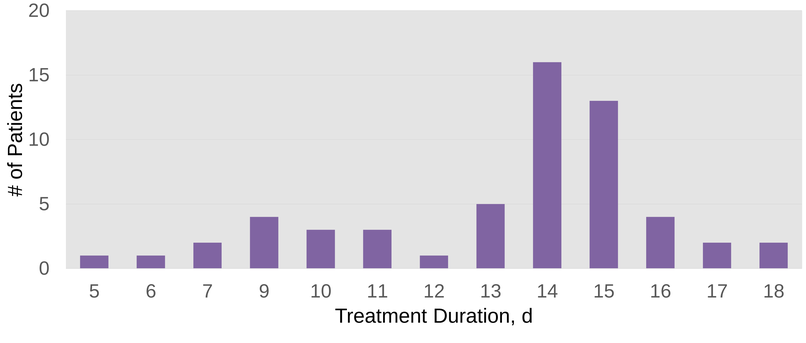

Table 2. Susceptibilities

Antibiotic	Ceftriaxone	Clindamycin	Erythromycin	Levofloxacin	Moxifloxacin	Penicillin	Vancomycin
Sensitive	95%	84%	27%	16%	21%	54%	100%
Intermediate	4%	4%	32%	2%	-	42%	-
Resistant	2%	13%	41%	82%	79%	4%	-
Total Tested	56	56	56	57	56	57	55

- Most common empiric treatment regimen was cefepime with vancomycin (64.9%)
- All VGS isolates were susceptible to at least one drug used in the empiric regimens

Table 3. Outcomes – Overall and Stratified by Treatment Duration *median (IQR) or n (%)*

Treatment Duration	**Overall**	***< 10 d***	***10 ≤ t < 14 d***	***≥ 14 d****
N (%)	57	55*		
		7 (12.7%)	11 (20%)	37 (67.3%)
Duration of treatment, days	14 (12, 15)	9 (6, 9)	11 (10, 13)	15 (14, 15)
Duration of fever, days	3 (2, 5)	2 (1, 3)	2 (1, 4)	3 (2, 5.5)
Time until culture clearance, days	1 (1, 2)	1 (0.8, 2)	1 (1, 2)	1 (1, 1.8)
Clinical Outcomes				
Hospitalized	56 (98.2%)	7 (100%)	10 (91%)	37 (100%)
Admitted for neutropenic fever	31 (54.4%)	4 (57%)	5 (45%)	21 (57%)
Length of hospitalization, days	12 (4, 23)	5 (5, 21)	12 (4, 22)	12 (4, 28)
ICU admission	6 (10.5%)	0%	0%	5 (14%)
Length of ICU admission, days	4 (2, 7)	-	-	4 (2, 9)
Mortality within 30 days	3 (5%)	1 (14%)	0	0
Recurrence within 30 days	1 (1.8%)	-	-	1 (3%)
Clostridium difficile infection	3 (5.3%)	-	1 (9.1%)	2 (5.4%)

*2 patients excluded from stratified data who died while being actively treated
** Patients were treated for greater than 14 days in 21 (38%) of cases and for 14 or less days in 34 (62%) of cases

Conclusion

- Treatment exceeded 14 days of therapy in 38% (n=21) of VGS bacteremia treatment cases
- Fever persisted for several days despite active antimicrobials and culture clearance, consistent with prior reports
- Low rates of recurrence and death at any treatment duration suggests treatment durations of less than 14 days for VGS bacteremia may be feasible

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