Submission ID 909773



Clinical Outcomes of Ceftriaxone versus Penicillin G for Complicated Viridans Group Streptococci Bacteremia

BACKGROUND

 Viridans group streptoco 	occi (VGS) are an infrequent cause of bloodstream infections, accounting for approximately	Table 1. Baseline Characteristics		
2% of positive blood cultures in immunocompetent adults in the United States			CTX (n = 64)	PCN G/AMP (n = 30)
 In immunocompotent n 	ationts with intact host defenses. VCS is considered to have low virulance. However, VCS	Age, median years (IQR)	<u>69 (58, 81)</u>	64 (52, 80)
	atients with infact host defenses, vos is considered to have low virulence. However, vos	Male Ethnicity	42 (05.0)	22 (73)
can be a leading cause c	of bacteremia in febrile neutropenic patients, leading to shock, respiratory compromise, and	Ethnicity	EO (70 1)	21 (70)
mortality in up to 20%	of patients. Concomitant infections in VGS bacteremia such as endocarditis can occur.	African Amorican	50 (78.1) 7 (10.0)	21 (70)
requiring prolonged anti	biotic thorapy, and are accepted with mortality rates of 4 to 16%	Hispanic	7 (10.9) E (7.9)	2 (7) 2 (7)
requiring proionged and	biolic therapy, and are associated with mortality rates of 4 to 16%	Asian	5 (7.8) 2 (2.1)	2 (7) 4 (12)
 Optimal treatment stra 	tegies for VGS bacteremia have not been well-defined. Both penicillin G (PCN G) and	Asidii Other/net specified	2 (5.1)	4 (15)
ceftriaxone (CTX) are f	requently used for definitive treatment in clinical practice, and the American Health	Past Medical History	0 (0)	1 (5)
	requerte o first line treatment estimate for VCC infective and condition (IC)	Congestive heart failure	17 (26 6)	6 (20)
Association (AHA) lists b	oth agents as first line treatment options for VGS infective endocarditis (IE)	Coronary artery disease	17 (20.0)	6 (20)
 Previous observational : 	studies have described the use of different treatment options for VGS bacteremia and IE,	Dishetes mollitus	12(10.0)	0 (20) 7 (22)
hut comparative assess	ment of clinical outcomes between different agents is limited. We hypothesize that CTX is	End organ damage	2 (14.1) 2 /0 (22.2)	2/7 (20)
	There of chined butcomes between uncrent agents is innited. We hypothesize that erk is	Chronic kidnow disease (moderate or sovere)	2/9 (22.2)	2/7 (23)
associated with more ac	liverse effects than PCN G when used for complicated VGS bacteremia, and these risks may	Chronic Ridney disease (moderate of severe)	7 (10.9)	2 (7)
outweigh the benefit of	its once daily dosing	Liver disease	4 (0.3) 2 (4 7)	2(7)
5	,	Liver disease	3 (4.7)	0
			2 (3.1)	2 (7)
	OBJECTIVE		2(3.1)	0 (0)
To evaluate clinical outcom	es between CTX and PCN G for the prolonged treatment of complicated VGS bacteremia	Lympnoma Charlean comerciality index (CCI), median (IOD)		
io evaluate clinical outcom	es between CTX and PCN G for the profonged treatment of complicated vGS bacterenna	Charlson comorbidity index (CCI), median (IQR)	4 (2, 5)	3 (2, 5)
		Pitt bacteremia score (PBS), median (IQR)	0 (0, 2)	1 (0, 2)
	METHODS	Prior episode of <i>C. difficile</i> infection	0 (0)	0 (0)
Ctorde - Dis signs		Concomitant proton pump inhibitor or H2 receptor antagonist	20 (32.3)	10 (33)
Study Design		administration		
 A single-center retrospe 	ective study was performed between January 2013 and June 2019 at New York University	Table 2 VGS Bacteremia Treatment Details		
Langone Health (NVIII H) an 800-bed urban tertiary care academic medical center	VCS Pactoromia Treatment	CTV (n - 64)	DCNC/ANAD(n-2)
		Hospital length of stay, modian days (IOP)		10 (6, 12)
 Patients with 1 or more 	blood cultures positive for a VGS isolate and who received at least 1 dose of either CTX,	Admission to Intensive Care Unit (ICU)		
PCN G. or ampicillin (AN	IP) were identified and screened for inclusion.	Duration of ICU stay, modian days (IOP)	0 (12.3) 4 E (1_0)	7 (23) 6 (2, 7)
		Beta-lactam allergy	<u> </u>	0 (3, 7)
Inclusion Criteria	Exclusion Criteria	Donicillin	12/14 (02)	0
		Conhalosnarin	1/14 (33)	
≥18 years of age	Did not receive study drug therapy for at least 50% of a \geq 4 week course		16/62 (25)	12/25 (48)
Received >4 weeks of	Had polymicrobial blood culture with non-VGS isolates that were not considered	Time to source removal median days (IOP)	1 (0 0)	5(22,85)
	contaminants	Suscentibility suscentible + intermediate	I (0, 9)	5 (2.3, 6.5)
treatment for a presumed	Containinants	Denicillin	62 (96 9)	30 (100)
complicated VGS	Had a blood culture with VGS that was considered to be a contaminant	Intermediate	16/62 (25)	30 (100) 4/30 (13 3)
hacteremia enisode	Transitioned to hospice care during their treatment course	Amnicillin	10/02 (23) 61 (05 3)	30 (100)
bacterenna episode	Diad during treatment before reasining Γ_{00} of the total source	Intermediate	9/61 (1/ 1)	4/30 (13)
	Died during treatment before receiving 50% of the total course	Coffriavana	62 (06 0)	24 (20)
	Had first VGS bacteremia episode before the study period		02 (90.9) 1/62 (1.6)	24 (80) 1 /24 (4 2)
	Received therapy at an outside hospital	Empiric therapy	1/02 (1.0)	1/24 (4.2)
		Vancomycin	57 (80 1)	25 (82)
Outcomes		Coffriavono	J7 (03.1) A (6.2)	23 (83)
outcomes		Other	4 (0.3)	0 (0) E (17)
	Composite of safety endpoints, including hospital readmission due to VGS bacteremia or	Definitive therapy	5(4.7)	5 (17)
	an adverse event from antibiotic therapy <i>C</i> difficile infection (CDI) treatment	Ceftriayone	56 (87 5)	0 (0)
Primary		Penicillin G	50 (87.5) 6 (9.4)	
, i i i i i i i i i i i i i i i i i i i	modification or discontinuation due to an antibiotic-related adverse event, and		0 (5.4)	20 (87) A (12)
	development of extended spectrum beta-lactamase (ESBL) resistance	Ampicium	1 (1.0)	4 (13)
		Leiazonn Infactious Diseases consult	T (1.0)	U (U) 20 (100)
- Cocondom:	Individual safety endpoints, VGS bacteremia recurrence, hospital readmission, and all-	Combination therapy with gentamicin	(۲۵۵۲) حن ۱۲ (۱۵ ۵۱) ۲۵	(UUL) UC 12 (12)
Secondary	cause mortality	Duration median days (IOP)	12 (10.0) 2 /1 E 12 E)	נ43) 17 (ב סקב)
		Time to documented clearance of blood culture, modian days (IOP)	<u> </u>	<u>ד4 (כ.כ, ۲.כ)</u> 1 ב (ז. כ)
All outcomes were assesse	d for the 6-month period following initial positive blood culture	Duration of total therapy median days (IQR)		ـــــــــــــــــــــــــــــــــــــ
		Duration of definitive therapy, median days (IQR)	<u>41.3 (30, 44)</u> 26 5 (35 2 13)	42.3 (31.0, 47.3) 20 5 (70 11 2)
Definitions		Duration of treatment arm median days (IQR)	28 (27 12)	<u>גען גען גען גען גען גען גען גען גען גען </u>
 Complianted bacteroreit 	, requiring at least 1 weaks of therapy to treat infaction source	Outnatient line access	<u> </u>	20 (100)
 COMDIICATED DACTEREMIZ 	\mathbf{A} - TEQUITINE ATTEAN 4 WEEKS OF INELADV TO ITEAL INTECTION SOUTCE		02 (57.3)	JO (TOO)

• Viridans group streptoco	cci (VGS) are an infrequent cause of bloodstream infections, accounting for approximately	Table 1. Baseline Characteristics		
2% of positive blood cult	uros in immunocompotent adults in the United States	Variables	CTX (n = 64) P	CN G/AMP (n = 30
		Age, median years (IQR)	69 (58, 81)	64 (52, 80)
 In immunocompetent particular 	atients with intact host defenses, VGS is considered to have low virulence. However, VGS	Male	42 (65.6)	22 (73)
can be a leading cause o	f bacteremia in febrile neutropenic patients, leading to shock, respiratory compromise, and	Ethnicity		
mortality in up to 200/	of nationts. Concernitant infactions in VCS bastoremia such as endocarditis can accur	White	50 (78.1)	21 (70)
mortality in up to 20%	of patients. Concomitant infections in VGS bacteremia such as endocarditis can occur,	African American	7 (10.9)	2 (7)
requiring prolonged anti	piotic therapy, and are associated with mortality rates of 4 to 16%	Hispanic	5 (7.8)	2 (7)
Ontimal treatment strat	regies for VGS bacteremia have not been well-defined. Both penicillin G (PCN G) and	Asian	2 (3.1)	4 (13)
	tegies for ves bacterenna nave not been wen denned. Doth pentennin e (reivel) and	Other/not specified	0 (0)	1 (3)
cettriaxone (CTX) are f	requently used for definitive treatment in clinical practice, and the American Health	Past Medical History		
Association (AHA) lists be	oth agents as first line treatment options for VGS infective endocarditis (IE)	Congestive heart failure	17 (26.6)	6 (20)
 Drovious observational s 	tudios have described the use of different treatment entions for VCS besteremis and IF	Coronary artery disease	12 (18.8)	6 (20)
 Previous observational s 	tudies have described the use of different treatment options for VGS bacteremia and IE,	Diabetes mellitus	9 (14.1)	7 (23)
but comparative assessr	nent of clinical outcomes between different agents is limited. We hypothesize that CTX is	End organ damage	2/9 (22.2)	2/7 (29)
associated with more ad	verse effects than PCN G when used for complicated VGS bacteremia, and these risks may	Chronic kidney disease (moderate or severe)	7 (10.9)	2 (7)
	i i i i i i i i i i i i i i i i i i i	Chronic obstructive pulmonary disease	4 (6.3)	2 (7)
outweigh the benefit of i	ts once daily dosing	Liver disease	3 (4.7)	0
		Solid tumor	2 (3 1)	2 (7)
	ORIECTIVE		2 (3.1)	(7)
	ODJECTIVE	Lumphoma	2 (3.1)	1 (2)
To evaluate clinical outcome	es between CTX and PCN G for the prolonged treatment of complicated VGS bacteremia	Charlson comorbidity index (CCI) median (IOP)	(1.0)	2 (2 5)
	is between erv and i en e folonged treatment of complicated ves bacterenna	Ditt hastoromia score (DPS) modian (IQR)	4 (2, 3)	<u> </u>
		Price anisodo of C. difficilo infection	0 (0, 2)	1(0, 2)
	METHODS	Prior episode of <i>C. aljjiche</i> infection		0 (0)
		Concomitant proton pump inhibitor or H2 receptor antagonist	20 (32.3)	10 (33)
Study Design		administration		
• A single-center retrospe	ctive study was performed between January 2013 and June 2019 at New York University	Table 2 VCS Bactoromia Treatment Details		
Langono Hoalth (NVIII H)	an 800 had urban tartiany cara acadamic modical contar	Table 2. VGS Bacterennia Treatment Details		
	, all 800-bed, di ball, tertial y cale, academic medical center.	VGS Bacteremia Treatment	CIX (n = 64)	PCN G/AIVI
 Patients with 1 or more 	blood cultures positive for a VGS isolate and who received at least 1 dose of either CTX,	Hospital length of stay, median days (IQR)	8 (5, 11)	10 (6,
PCN G or amnicillin (AM	P) were identified and screened for inclusion	Admission to Intensive Care Unit (ICU)	8 (12.5)	/ (2
		Duration of ICU stay, median days (IQR)	4.5 (1, 9)	6 (3,
Inclusion Criteria	Exclusion Criteria	Beta-lactam allergy	14 (21.9)	0
		Penicillin	13/14 (93)	
>18 years of age	Did not receive study drug therapy for at least 50% of a \geq 4 week course	Cephalosporin	1/14 (7)	
	Had polymicrobial blood culture with pop VCS isolates that were not considered	Source removal	16/62 (25)	12/25
Received ≥4 weeks of	Had polymicrobial blood culture with non-vGS isolates that were not considered	Time to source removal, median days (IQR)	1 (0, 9)	5 (2.3,
treatment for a presumed	contaminants	Susceptibility, susceptible + intermediate		
complicated V/CS	Had a blood culture with VGS that was considered to be a contaminant	Penicillin	62 (96.9)	30 (1
complicated vGS		Intermediate	16/62 (25)	4/30 (
bacteremia episode	Transitioned to hospice care during their treatment course	Ampicillin	61 (95.3)	30 (1
	Died during treatment before receiving 50% of the total course	Intermediate	9/61 (14.1)	4/30
		Ceftriaxone	62 (96.9)	24 ({
	Had first VGS bacteremia episode before the study period	Intermediate	1/62 (1.6)	1/24
	Received therapy at an outside hospital	Empiric therapy		
		Vancomvcin	57 (89.1)	25 (;
Outcomes		Ceftriaxone	4 (6 3)	0 ((
		Other	3 (4 7)	5 (1
	Composite of safety endpoints, including hospital readmission due to VGS bacteremia or	Definitive therapy	5 (4.7)	
	an adverse event from antibiotic therapy <i>C</i> difficile infection (CDI) treatment	Ceftriavone	56 (87 5)	0.11
Primary		Bonicillin G	50 (87.5) 6 (9.4)	0 (C 26 (!
-	modification or discontinuation due to an antibiotic-related adverse event, and		0 (9.4)	20 (0
	development of extended spectrum beta-lactamase (ESBL) resistance	Ampicilin	1 (1.6)	4 (1
	dividual safety endpoints, VGS bacteremia recurrence, hospital readmission, and all-	Intectious Diseases consult		30 (1
Secondary	cause mortality	Combination therapy with gentamicin	12 (18.8)	13 (4
		Duration, median days (IQK)	3 (1.5, 13.5)	14 (5.5,
All outcomes were assessed	for the 6-month period following initial positive blood culture	Time to documented clearance of blood culture, median days (IQR)	2 (1, 3)	1.5 (1
		Duration of total therapy, median days (IQR)	41.5 (30, 44)	42.5 (31.)
Definitions		Duration of definitive therapy, median days (IQR)	36.5 (25.3, 42)	39.5 (28
		Duration of treatment arm, median days (IQR)	38 (27, 43)	39.5 (28
 Complicated bacteremia 	 requiring at least 4 weeks of therapy to treat infection source 	Outpatient line access	62 (97.9)	30 (1

- complicated bacterennia requiring at least 4 weeks of therapy to treat infection source
- VGS bacteremia recurrence development of a subsequent case of VGS bacteremia with the same species after completion of the initial treatment course

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59 (95.2)

3/62 (4.8)

All data in tables expressed as n (%) unless otherwise noted.

Midline

Peripherally inserted central catheter (PICC)

RESULTS

P value 0.422

0.455

0.393

0.714

1.000

0.080

0.319

0.490 0.886

0.265 0.603

0.714

1.000 0.549

0.590 1.000 0.539 0.386 0.764 n/a 0.918

P value

0.159 0.229 0.779 0.004

0.045

0.277

1.000

0.709

0.549

1.000 0.027

0.590

0.512 0.303 0.105

-1.000

0.012

0.034

0.079

0.334

0.354

0.961

1.000

0.548

0.548

30 (100)

0 (0)

(n = 30)





Table 3. Outcomes

	CTX (n = 64)	PCN G/AMP (n = 30)	P value
Primary Endpoint			
Composite safety endpoint	9 (14.1)	8 (26.7)	0.139
Secondary Endpoints			
Composite safety endpoint components			
At least 1 readmission due to VGS or therapy	7 (10.9)	6 (20)	0.336
Microbiological evidence of ESBL	1 (1.6)	1 (3)	0.539
C. difficile infection	1 (1.6)	1 (3)	0.539
Therapy modification or discontinuation due to adverse drug event	0 (0)	0 (0)	0.549
Infection recurrence	0 (0)	0 (0)	n/a
Hospital readmission			
At least 1 readmission in 6-months	24 (37.5)	16 (53)	0.148
Number of readmissions, median days (IQR)	0 (0,1)	1 (0,1.25)	0.341
Time to first readmission, median days (IQR)	31 (15,60)	53 (29,91)	0.135
All cause mortality	0 (0)	2 (7)	0.100

Table 4. Univariate and Multivariate Analyses

	Primary Composite	Primary Composite				
	Outcome Met (n = 17)	Outcome Not Met (n = 77)	Univariate OR (CI)	P-value	Multivariate OR (CI)	P value
СТХ	9 (52.9)	53 (71.4)	0.45 (0.154-1.316)	0.139	0.53 (0.144-1.957)	0.342
Duration of treatment arm	14 (82.4)	52 (67.5)	2.24 (0.590-8.526)	0.227	1.84 (0.433-7.776)	0.410
≥4 weeks						
Source removal	2 (11.8)	26 (33.8)	0.26 (0.056-1.231)	0.073	0.13 (0.021-0.822)	0.030
Coronary artery disease	1 (5.9)	18 (24)	0.2 (0.025-1.598)	0.181	0.10 (0.010-1.126)	0.063
Gentamicin ≥ 2 weeks	4 (23.5)	6 (7.8)	3.64 (0.901-14.713)	0.078	6.55 (0.893-48.106)	0.065
duration						
Congestive heart failure	3 (17.6)	20 (26.7)	0.59 (0.153-2.268)	0.547	-	-
Endocarditis	10 (52)	48 (62)	0.86 (0.296-2.517)	0.787	-	-
CCI	4 (3,4.5)	4 (2,5)	-	0.784	-	-
PBS	1 (0,2)	0 (0,2)	-	0.781	-	-
Age ≥65 years	8 (47.1)	46 (59.7)	0.60 (0.208-1.722)	0.338	-	-
S. mitis	6 (37.5)	23 (29.9)	1.41 (0.458-4.333)	0.563	-	-
Infection source identified	15 (88.2)	72 (93.5)	0.54 (0.095-3.028)	0.606	-	-
Moderate or severe CKD	2 (11.8)	7 (9.1)	1.33 (0.252-7.065)	0.664	-	-

CTX: ceftriaxone; CCI: Charlson comorbidity index; PBS: Pitt bacteremia score; CKD: chronic kidney disease

CONCLUSION

- Compared to PCN G and AMP, CTX was not associated with an increased risk of ESBL resistance, CDI, hospital readmission due to VGS or therapy complications, or therapy modification due to an adverse drug event
- Overall rate of patients who met the primary outcome highlights importance of identifying relevant risk factors
- Further exploration in a larger prospective trial is warranted

Disclosure: The authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities







MS: musculoskeletal; SSTI: skin and soft tissue infection; IAI: intra-abdominal infection