Oritavancin Compared to the Standard-of-Care for the Treatment of Gram-positive Blood Stream Infections

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Background

Little data is available comparing oritavancin (ORT) to the standard-of-care (SOC) for the treatment of gram-positive blood stream infections (BSI).

Methods

This was a retrospective study of all patients in the Veterans Affairs Health Care System who had received at least 1 dose of oritavancin or at least 5 days of vancomycin, daptomycin, ceftaroline, ampicillin, ampicillin-sulbactam, nafcillin, oxacillin, or cefazolin for a documented gram-positive BSI from 1 January 2015 to 30 June 2021. Patients with polymicrobial blood cultures or positive cultures from other sites were included if the organisms were susceptible to the incident antimicrobial; no concomitant antimicrobials could be used once the incident agent was started. Individuals were also excluded if they were diagnosed with endocarditis, had a neutrophil count <500 cells/mm^3, or had a diagnosis of Human Immunodeficiency Virus (HIV) on their problem list.

The primary composite outcome was clinical failure, defined as all-cause mortality within 30-days from the end of therapy, or any additional blood cultures positive for the incident organisms ≥72 hours after administration of the first dose and ≤30 days from the administration of the final dose of the study antimicrobial, or any drug or line-related readmissions within 30-days of hospital discharge. Secondary outcomes included all-cause 30-day readmission and rates or acute kidney injury (AKI).

Figure 1: Antimicrobials Used in the SOC Group (N=69)

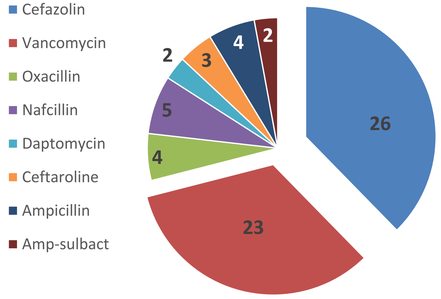

Table 1: Baseline Characteristics

Baseline Characteristics	Oritavancin (n=27)	Standard-of-care (n=69)	P-value
Age (years), median	62	69	0.05
Male, n (%)	26 (96.3)	69 (100)	0.281
Race, n (%)	White 18 (69.2) Black 6 (23.1) Other 2 (7.7)	White 53 (81.5) Black 9 (13.8) Other 3 (4.7)	0.491
Creatinine clearance (mL/min), median (IQR)	103.5 (60.5)	88.5 (51.6)	0.079
History of IVDU, n (%)	5 (18.2)	4 (5.8)	0.111
History of OPAT use within previous 2 years, n (%)	1 (3.7)	3 (4.3)	1.0
History of medication non-compliance, n (%)	9 (33.3)	10 (14.5)	0.037
History of MRSA in the previous 2 years, n (%)	4 (14.8)	8 (11.6)	0.735
History of VRE in the previous 2years, n (%)	0	0	---
Greater than 96 hours of antimicrobials BEFORE incident antimicrobial initiation, n (%)	19 (70.4)	9 (13.4)	<0.001
Organisms cultured, n (%): MSSA MRSA *S.epidermidis* *E.faecalis* *E.faecium*	 9 (33.3) 6 (22.2) 5 (18.5) 0 1 (3.7)	 32 (46.4) 17 (24.6) 7 (10.4) 6 (8.7) 0	
Likely source of infection, n (%): SSTI Central line Urinary Other	 17 (62.9) 2 (7.4) 1 (3.7) 6 (22.2)	 28 (40.6) 4 (5.8) 5 (7.3) 13 (18.8)	
Length of stay (days), median (IQR)	12 (9)	5 (3)	<0.001
Length of treatment (days), median (IQR) ***each dose of ORT was considered to be14-days of therapy*	14 (14)	14.5 (17)	0.986
Time between initial culture obtained and start of incident antimicrobial (days), median (IQR)	6 (3)	2 (2)	<0.001
Doses of oritavancin, n (%): 1 dose 2 doses 3 doses 4 doses	 19 (70.4) 4 (14.8) 3 (11.1) 1 (3.7)		

Results

Figure 2: Clinical Failure and Components – Whole Cohort

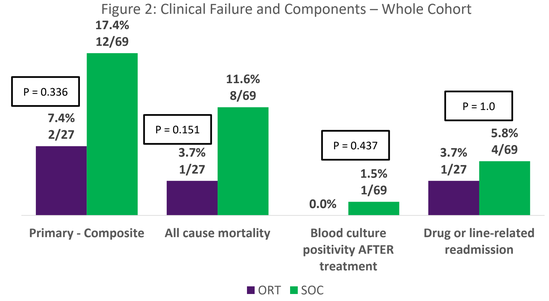

Figure 3: Secondary Outcomes – Whole Cohort

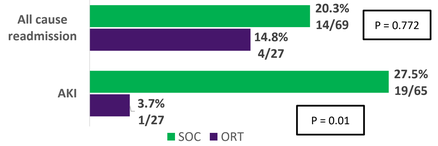

Figure 4: Clinical Failure and Components – *Staphylococcus aureus* Cohort

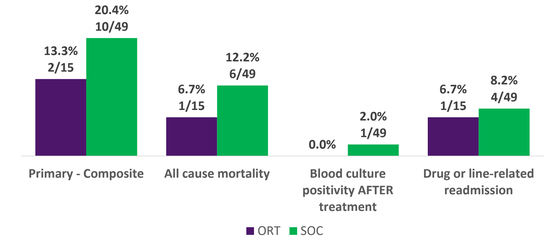

Figure 5: Secondary Outcomes – *Staphylococcus aureus* Cohort

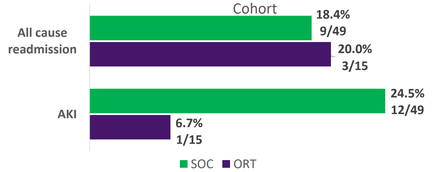

Table 2: Univariate Analysis – Whole Cohort

Covariate	Clinical Failure	No Clinical Failure	P-value
Received oritavancin therapy	2	25	0.227
Received more than 1 dose of oritavancin	2	6	0.392
MRSA isolated from the blood	**7**	**16**	**0.019**
Enterococcus isolated from the blood	0	7	0.976
Received daptomycin	2	0	0.976
Received vancomycin	5	18	0.271
BMI ≥ 30	**4**	**39**	**0.195**
Received >96 hours of prior antibiotics	**2**	**26**	**0.200**
Other cultures positive	3	28	0.353

**Variables with a p-value of ≤0.2 were include in the multivariate regression

Table 3: MVR Analysis – Whole Cohort

Covariate	OR (95% CI)	P-value
MRSA isolated from blood	**3.52 (1.06-11.76)**	**0.04**
BMI ≥ 30	0.44 (0.12-1.61)	0.217
Received >96 hours of prior antibiotics	0.38 (0.07-1.92)	0.241

Table 4: Univariate Analysis – *Staphylococcus aureus* Cohort

Covariate	Clinical Failure	No Clinical Failure	P-value
Received oritavancin therapy	2	13	0.542
Received more than 1 dose of oritavancin	2	6	0.348
MRSA isolated from the blood	**7**	**16**	**0.081**
Enterococcus isolated from the blood	---	---	---
Received daptomycin	2	0	0.974
Received vancomycin	4	10	0.293
BMI ≥ 30	4	26	0.303
Received >96 hours of prior antibiotics	2	16	0.337
Other cultures positive	2	20	0.167

**Variables with a p-value of ≤0.2 were include in the multivariate regression

Table 5: MVR Analysis – *Staphylococcus aureus* Cohort

Covariate	OR (95% CI)	P-value
MRSA isolated from blood	2.74 (0.73-10.2)	0.134

Conclusions

ORT appears to be a safe and effective option when directly compared to the SOC for non-endocarditis BSIs. Similar outcomes were observed in a cohort of patients with *S.aureus* BSIs. Only MRSA isolated from the blood was identified as an independent risk factor for clinical failure.

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Disclaimer

- This material is the result of work supported with resources and the use of facilities at the VA St. Louis Health Care System
- The contents do not represent the views of the U.S. Department of Veterans Affairs or the United States Government
- This study was approved by the Institutional Review Board at the VA St. Louis Health Care System

This study was supported by an Investigator Initiated Trial Grant from Melinta Therapeutics, Inc.