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Poster Number

Treatment of Acute Bacterial Skin and Skin Structure Infection (ABSSSI) with Single Dose Dalbavancin in an Outpatient Setting

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INTRODUCTION

- Dalbavancin is a long acting lipoglycopeptide approved by FDA and EMA for treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults
- Potent activity against gram-positive pathogens responsible for ABSSSI: *Staphylococcus aureus*, including methicillin-resistant *S. aureus* (MRSA), and streptococci
- ABSSSI remains a significant cause of morbidity in the outpatient as well as the inpatient settings
- Due to its unique pharmacokinetic-pharmacodynamic properties, we sought to characterize the efficacy of dalbavancin in the subset of patients treated in the outpatient setting

PURPOSE

- The objective of this analysis is to describe the demographics and outcomes for patients with ABSSSI treated in the outpatient setting in a phase 3 clinical trial evaluating the efficacy of a single 1500 mg dose of dalbavancin relative to the approved two-dose regimen

METHODS

- Randomized, double-blind trial in 698 adult patients with ABSSSI, conducted between April 2014 and March 2015 at 60 centers in US, Eastern Europe, Russia and South Africa
- Patients were randomized to receive dalbavancin 1500 mg as a single IV infusion over 30 minutes *or* 1000 mg IV on Day 1 followed one week later by 500 mg IV[1]
- In this subgroup analysis, we compared outcomes for patients treated entirely in the outpatient setting with those for patients admitted to a hospital for the treatment of ABSSSI
- **Primary Outcome Measure**

  ≥ 20% reduction in erythema associated with the infection at 48-72 hours after start of treatment (ITT)
- **Secondary Outcome Measures**
  - Clinical status at Day 14 and Day 28 (ITT, CE)
  - Investigator assessment at Day 14 and 28
- **Statistics**
  - Non-inferiority design with the lower limit of the 95% CI at -10%
  - Sample size adjustment if point estimate < 80%
- **Key Inclusion Criteria**
  - Patients having an ABSSSI involving deeper soft tissue or requiring significant surgical intervention

    - Major cutaneous abscess *or*, Surgical site or traumatic wound infection, *or* Cellulitis
  - Patients must present with at least ONE of the following systemic signs of infection

    - An elevated body temperature ≥ 38°C/100.4°F *or*, White blood cell count > 12,000 cells/mm^3 *or*, White blood differential count with ≥ 10% band forms
  - In addition to erythema, at least 2 of the following signs of ABSSSI:

    - Purulent drainage/discharge, Fluctuance, Heat/localized warmth, Tenderness to palpation, Swelling/induration
- **Key Exclusion Criteria**
  - Gram-negative bacteremia, burns, diabetic foot infection, decubitus ulcer, infected device, venous catheter entry site infection

RESULTS

- Of the **698 patients** randomized, **386 outpatients** and **312 inpatients** were analyzed (Table 1)
- Patients treated in the **outpatient** setting were more likely to be **younger**, be enrolled in **North America**, have a history of **intravenous drug use,** and have **MRSA** versus those admitted to the hospital for the treatment of the ABSSSI
- More **outpatients** had **major abscess** and **traumatic wound infection** as the type of infection relative to **inpatients** who were more likely to have **cellulitis** as the type of ABSSSI
- More **inpatients** met **SIRS** criteria and had a plasma **lactate > 4 mmol/L**
- **Outcome rates** at 48-72 hours, Day 14 and Day 28 were **similar** between patients treated in the **outpatient or inpatient** setting with either a **single dose** of dalbavancin or the **two-dose** dalbavancin regimen (Table 2)
- **Safety profile** was similar between patients treated in the outpatient or inpatient setting with either regimen (Table 3)

Table 1. Demographics and Baseline Patient and Disease Characteristics (ITT Population)

Characteristic	Outpatients (N=386)		Inpatients (N=312)	
	Dalbavancin Single Dose (N=190)	Dalbavancin Two Dose (N=196)	Dalbavancin Single Dose (N=159)	Dalbavancin Two Dose (N=153)
Age (mean), years (SD)	45.4 (13.36)	45.2 (13.06)	51.1 (15.92)	52.4 (15.79)
Female	78 (41.1%)	74 (37.8%)	67 (42.1%)	72 (47.1%)
Race				
White	157 (82.6%)	163 (83.2%)	155 (97.5%)	148 (96.7%)
Black or African American	26 (13.7%)	26 (13.3%)	2 (1.3%)	5 (3.3%)
Other	7 (3.7%)	7 (3.6%)	2 (1.3%)	0
Intravenous Drug Use	104 (54.7%)	105 (53.6%)	1 (0.6%)	2 (1.3%)
Diabetes Mellitus	18 (9.5%)	17 (8.7%)	17 (10.7%)	24 (15.7%)
Creatinine Clearance, n/N (%)				
≥ 30 mL/min	190/190 (100.0%)	194/194 (100.0%)	157/159 (98.7%)	146/153 (95.4%)
Body Mass Index (kg/m²)				
Mean (SD)	28.3 (6.7)	28.6 (7.8)	29.2 (8.2)	29.5 (6.6)
Median (Min, Max)	27.1 (18.9, 53.2)	27.1 (17.9, 65.5)	26.8 (15.9, 70.6)	28.3 (18.2, 53.3)
BMI Distribution				
< 25 kg/m²	69 (36.3%)	74 (37.8%)	46 (28.9%)	48 (31.4%)
25-30 kg/m²	62 (32.6%)	60 (30.6%)	61 (38.4%)	39 (25.5%)
> 30 kg/m²	59 (31.1%)	62 (31.6%)	52 (32.7%)	66 (43.1%)
Location of trial center				
North America	155 (81.6%)	157 (80.1%)	3 (1.9%)	3 (2.0%)
Rest of World	35 (18.4%)	39 (19.9%)	156 (98.1%)	150 (98.0%)
Cellulitis	66 (34.7%)	67 (34.2%)	99 (62.3%)	99 (64.7%)
Major cutaneous abscess	63 (33.2%)	66 (33.7%)	25 (15.7%)	25 (16.3%)
Traumatic wound/surgical site infection	61 (32.1%)	63 (32.1%)	35 (22.0%)	29 (19.0%)
Temperature ≥ 38°C	140 / 190 (73.7%)	139 / 193 (72.0%)	150 / 159 (94.3%)	144 / 153 (94.1%)
WBC > 12,000 cells/mm^3	73 / 189 (38.6%)	76 / 191 (39.8%)	59 / 159 (37.1%)	50 / 151 (33.1%)
Bands ≥ 10%	13 / 144 (9.0%)	19 / 154 (12.3%)	43 / 119 (36.1%)	27 / 114 (23.7%)
Median infection area, cm² (range)	301.4 (77, 3120)	278.7 (77, 2070)	289.0 (56, 4235)	314.5 (80, 2668)
Systemic Inflammatory Response Syndrome (SIRS)†	66 / 190 (34.7%)	68 / 196 (34.7%)	83 / 159 (52.2%)	86 / 153 (56.2%)
Median CRP, mg/L (range)§	51.3 (1, 300)	43.0 (1, 300)	72.8 (1, 300)	58.3 (0, 300)
Plasma lactate (mean), mmol/L (SD)	1.5 (0.84)	1.6 (0.66)	1.9 (1.03)	2.0 (1.09)
> 4 mmol/L, n/N (%)	1/173 (0.6%)	0/172 (0%)	6/138 (4.3%)	6/139 (4.3%)
Pathogen at Baseline	116 (61.1%)	126 (64.3%)	94 (59.1%)	94 (61.4%)
MRSA, n/N (%)	34/116 (29.3%)	56/126 (44.4%)	2/94 (2.1%)	5/94 (5.3%)
MSSA, n/N (%)	39/116 (33.6%)	40/126 (31.7%)	64/94 (68.1%)	56/94 (59.6%)
Gram-negative aerobic organism, n/N (%)	13/116 (11.2%)	15/126 (11.9%)	6/94 (6.4%)	13/94 (13.8%)

Data are presented as No. (%) unless otherwise specified. *Differences between treatment groups done using Fisher's exact test for categorical variables and Wilcoxon Rank Sum test for continuous variables. †Systemic inflammatory response syndrome (SIRS) is defined as having 2 or more of the following: temperature <36°C or >38°C; heart rate >90 beats per minute; respiratory rate >20 breaths per minute; WBC count <4000 cells/mm^3 or >12,000 cells/mm^3 or >10% bands
§In outpatient subgroup, CRP values were available for 189 patients (single dose arm) and 194 patients (two-dose arm)

Table 2. Efficacy at Various Time-points for Outpatients and Inpatients

Timing	Outcome Measure	Outpatients (N=386)		Inpatients (N=312)	
		Dalbavancin Single Dose n/N (%)	Dalbavancin Two Dose n/N (%)	Dalbavancin Single Dose n/N (%)	Dalbavancin Two Dose n/N (%)
48-72 hours	Treatment response (ITT)	156 /190 (82.1)	162 /196 (82.7)	128 /159 (80.5)	132 /153 (86.3)
	95% CI	-0.5 (-8.3, 7.1)		-5.8 (-14.1, 2.6)	
Day 14	Clinical success (CE)	142 /162 (87.7)	151 /169 (89.3)	125 /140 (89.3)	119 /133 (89.5)
	95% CI	-1.7 (-8.8, 5.3)		-0.2 (-7.7, 7.5)	
Day 28	Clinical success (CE)	136 /150 (90.7)	139 /150 (92.7)	114/121 (94.2)	108/117 (92.3)
	95% CI	-2.0 (-8.6, 4.5)		1.9 (-4.8, 9.0)	
	Investigator Assessment of Cure, Day 14 (CE)	154/162 (95.1%)	164/169 (97.0%)	138/140 (98.6%)	128/132 (97.0%)
	95% CI	-2.0 (-6.9, 2.5)		1.6 (-2.4, 6.3)	
	Investigator Assessment of Cure, Day 28 (CE)	142/150 (94.7%)	146/150 (97.3%)	121/121 (100.0%)	112/116 (96.6%)
	95% CI	-2.7 (-7.9, 2.0)		3.4 (0.3, 8.5)	

ITT: Intention-to-treat. CE: Clinically Evaluable

Table 3. Safety Profile for Outpatients and Inpatients

Characteristic	Outpatients (N=386)		Inpatients (N=312)	
	Dalbavancin Single Dose n/N (%)	Dalbavancin Two Dose n/N (%)	Dalbavancin Single Dose n/N (%)	Dalbavancin Two Dose n/N (%)
Patients experiencing ≥ 1 of:				
TEAE	45/190 (23.7%)	41/193 (21.2%)	25/159 (15.7%)	28/153 (18.3%)
Drug-related TEAE	18/190 (9.5%)	15/193 (7.8%)	7/159 (4.4%)	11/153 (7.2%)
Serious TEAE	5/190 (2.6%)	0/193 (0%)	2/159 (1.3%)	5/153 (3.3%)
TEAE leading to premature discontinuation of study drug	5/190 (2.6%)	1/193 (0.5%)	1/159 (0.6%)	4/153 (2.6%)

TEAE: treatment-emergent adverse event.

CONCLUSIONS

- Outpatient treatment in this study was almost exclusively practiced in North American centers and the majority of patients were intravenous drug users
- Outcome rates at 48-72 hours, Day 14 and Day 28 treated with either a single dose or a two-dose dalbavancin regimen were similar whether patients were treated in the outpatient or inpatient setting. Amongst inpatients, response rates at Day 28 tended to be higher in the single dose treatment group.
- The safety profile of dalbavancin overall was similar in either setting, though the adverse event rate was slightly higher for the outpatients
- Based on this experience, patients with ABSSSI can be successfully treated with dalbavancin in an ambulatory setting

REFERENCES

1. Dunne MW, Puttagunta S, Giordano P, et al. A Randomized Clinical Trial of Single-Dose Versus Weekly Dalbavancin for Treatment of Acute Bacterial Skin and Skin Structure Infection. Clin Infect Dis. 2016 Mar 1;62(5):545-51.
2. Data on file (CSR Tables 1-4, 11-12, 15-16) Allergan plc.
3. Boucher HW, Wilcox M, Talbot GH et al. Once-weekly dalbavancin versus daily conventional therapy for skin infection. N Engl J Med 2014; 370:2169-2179.

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DISCLOSURES

This study was sponsored by Durata Therapeutics and Allergan plc. UR, PLG, JSM are current employees of Allergan, plc. UR holds stock in Allergan, plc and held stock in Durata Therapeutics. SP, MD were former employees of Allergan, plc and held stock in Durata Therapeutics. All authors met the ICMJE authorship criteria. Neither honoraria nor payments were made for authorship.

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