TREATMENT OF ACUTE BACTERIAL SKIN AND SKIN STRUCTURE INFECTION (ABSSSI) WITH DALBAVANCIN IN AN OUTPATIENT SETTING

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ABSTRACT

Objective: To describe the demographics and outcomes for patients with ABSSSI treated in the outpatient setting in the DISCOVER 1 and DISCOVER 2 trials.

Methods: These two double-blind, phase 3 trials compared dalbavancin alone with a regimen of vancomycin plus the option to switch to linezolid. Selected investigative sites could opt to provide all care in the outpatient setting to appropriate patients. Clinical outcome was measured at the end of treatment (EOT) (study day 14–15), based on resolution of signs and symptoms of infection. The pooled clinical outcome for patients in the clinical evaluable population who received all their treatment in an outpatient setting was analyzed.

Results:

Table 1. Demographics and Baseline Characteristics by Treatment Location

Characteristic	Outpatient for All Doses (N=264)
Age <65 years, N (%)	249 (94.3)
Male Gender, N (%)	170 (64.4)
Race, N (%)	
White	235 (89.0)
African American	21 (8.0)
Asian	4 (1.5)
Other	4 (1.5)
Geographic Region	
North America	263 (99.6)
Europe, South Africa and Asia	1 (0.4)
Systemic signs of infection, N (%)	
Fever	193 (73.1)
WBC count >12,000 cells/mm^3	105 (39.8)
Systemic Inflammatory Response Syndrome, N (%)	103 (39.0)
Elevated HS CRP, N (%)	236 (89.4)

Table 2. Efficacy at EOT for Patients Treated as Outpatients

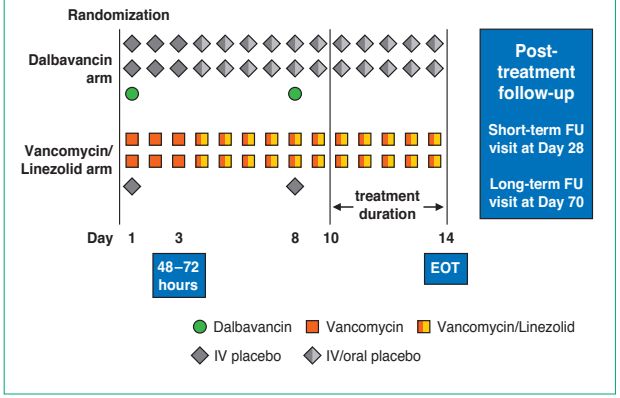
	Outpatient for All Doses	
	Dalbavancin	Vancomycin/Linezolid
N	138	126
Success	125/138 (90.6%)	114/126 (90.5%)
Failure	13/138 (9.4%)	12/126 (9.5%)
Difference in Success Rates (95% CI)	0.1 (−7.7, 8.1)	

Conclusion: Outpatient treatment was delivered significantly more often in North America than in Europe and elsewhere; those treated in the outpatient setting had substantial rates of fever, leukocytosis and SIRS criteria. Outcome rates at EOT were similar between dalbavancin and vancomycin/linezolid treated patients. Based on this predominantly North American experience, patients with ABSSSI can be successfully treated with dalbavancin in an ambulatory setting.

METHODS

Study Design

Figure 1. Studies DUR001-301/302



- Patients had:
  - cellulitis, abscess or wound infection with erythema >75cm^2 and
  - either a fever, an elevated white blood cell count >12k cells/mm^3 or immature neutrophils >10%
- Patients received:
  - Dalbavancin 1 gram IV over 30 minutes on Day 1 and 500 mg IV on Day 8, or
  - Vancomycin 1 gram (or 15 mg/kg) IV every 12 hours (q12h) for at least three days with an option to switch to oral linezolid 600 mg q12h to complete 10–14 days of therapy
- The primary endpoint was measured at 48–72 hours of therapy with success requiring both cessation of spread of the lesion and complete resolution of fever.
  - Secondary endpoints included an investigator assessment of outcome at Day 14 and Day 28
  - Efficacy results from both trials were pooled
- Data was analyzed for the subset of patients who received all of their treatment as outpatients.

RESULTS

Table 1. Demographics

Characteristic	Dalbavancin N=160	Comparator N=157
Mean Age (years)	43.6	44.9
Male Gender, n (%)	104 (65.0)	99 (63.1)
Race, n (%)		
White	137 (85.6)	138 (87.9)
American Indian or Alaska	3 (1.9)	3 (1.9)
Asian	3 (1.9)	2 (1.3)
Black or African American	16 (10.0)	13 (8.3)
Other	1 (0.6)	1 (0.6)
Region, n (%)		
North America	158 (98.8)	157 (100.0)
Europe/Asia	2 (1.3)	0
Creatinine clearance <30 mL/min, n/N (%)	2/155 (1.3)	0
Mean BMI (kg/m^2)	29.1	28.7
BMI <25 kg/m^2, n (%)	44 (27.5)	56 (35.7)
BMI ≥25 kg/m^2, n (%)	116 (72.5)	101 (64.3)
Sub-type of Infection, n (%)		
Cellulitis	57 (35.6)	56 (35.7)
Major Abscess	69 (43.1)	71 (45.2)
Wound Infection	34 (21.3)	30 (19.1)
Elevated fasting blood glucose at baseline*, n (%)	18 (11.3)	16 (10.2)
History of Diabetes Mellitus at baseline, n (%)	17 (10.6)	20 (12.7)
Met SIRS Criteria, n (%)	57 (35.6)	62 (39.5)
History of IVDA, n (%)	68 (42.5)	81 (51.6)
Baseline Pathogen, n (%)		
Staphylococcus aureus	85 (53.1)	80 (51.0)
MRSA, n/N (%)	51/85 (60.0)	36/80 (45.0)
MSSA, n/N (%)	34/85 (40.0)	43/80 (53.8)
Streptococcus pyogenes	0	3 (1.9)

*Consistent with pre-diabetes/diabetes mellitus

Table 2. Systemic Signs of Infection

Systemic Signs of Infection	Dalbavancin n/N (%)	Comparator n/N (%)
Temperature ≥38°C	120/160 (75.0)	115/157 (73.2)
WBC >12,000 cells/mm^3	60/156 (38.5)	57/150 (38.0)
Bands ≥10%	4/127 (3.1)	1/122 (0.8)

Table 3. Mean Duration of Antibiotic Therapy (days)

Study Drug Therapy	Dalbavancin	Comparator
Total Drug	10.6	10.8
Oral Drug	6.9	7.1
IV Drug	2.9	2.9

Table 4. Clinical Success for Outpatients

Endpoint	Dalbavancin n/N (%)	Vancomycin/ Linezolid n/N (%)	Difference, 95% CI
Clinical response at 48–72 hrs (ITT)	131/160 (81.9)	123/157 (78.3)	3.5 (−5.3, 12.4)
≥20% reduction in lesion size at 48–72 hrs (ITT)	146/160 (91.3)	141/157 (89.8)	1.4 (−5.2, 8.2)
Clinical Success at EOT			
CE Population	125/138 (90.6)	114/126 (90.5)	0.1 (−7.2, 7.6)
Met SIRS Criteria	43/51 (84.3)	47/52 (90.4)	−6.1 (−19.9, 7.3)
Investigator assessment of Success at EOT			
CE Population	132/138 (95.7)	119/126 (94.4)	1.2 (−4.4, 7.2)
Met SIRS Criteria	46/51 (90.2)	49/52 (94.2)	−4.0 (−16.2, 7.3)
Investigator assessment of Success at SFU			
CE Population	116/121 (95.9)	106/111 (95.5)	0.4 (−5.5, 6.5)
Met SIRS Criteria	41/45 (91.1)	41/44 (93.2)	−2.1 (−15.1, 10.7)

CONCLUSIONS

- Outpatient treatment was almost exclusively performed in North America in this program.
- Those treated in the outpatient setting had substantial rates of fever, leukocytosis and SIRS criteria.
- Outcome rates at 48–72 hours, EOT and SFU were similar between dalbavancin and vancomycin/linezolid treated patients.
- Based on this predominantly North American experience, patients with ABSSSI can be successfully treated with dalbavancin in an ambulatory setting.

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