

CLINICAL PRESENTATION AND OUTCOMES BY SUBTYPE OF INFECTION IN PATIENTS WITH ACUTE BACTERIAL SKIN AND SKIN STRUCTURE INFECTIONS (ABSSSI) IN THE DISCOVER PROGRAM

Sailaja Puttagunta, MD¹, George H. Talbot, MD², Mark Wilcox, MD³, Helen W. Boucher, MD⁴ and Michael Dunne, MD¹

¹Durata Therapeutics, Inc., Branford, CT, USA; ²Talbot Advisors LLC, Anna Maria, FL, USA; ³Leeds Teaching Hospital, Leeds, UK; ⁴Tufts Medical Center, Boston, MA, USA

ABSTRACT

Objective: To describe the presentation and outcome of patients with subtypes of ABSSSI who were enrolled in the dalbavancin phase 3 ABSSSI clinical trials. **Methods:** DISCOVER 1 and DISCOVER 2 were double-blind, double-dummy, pharmacist-unblinded, randomized trials that enrolled patients with cellulitis, abscess or wound/surgical site infection with erythema >75cm² and either a fever, >12k white blood cells/mm³ or immature neutrophils >10%. Patients received dalbavancin 1 g IV on Day 1 and 500 mg IV on Day 8 or Vancomycin with an option to switch to oral linezolid to complete 10–14 days of therapy.

Results:

Table 1. Demographics and Baseline Characteristics by Type of ABSSSI

Characteristic	Cellulitis N=703	Major Abscess N=335	Wound Infection N=273
Mean Age, years	51.9	46.2	48.1
Male, N (%)	367 (52.2)	208 (62.1)	191 (70.0)
Race, N (%)			
White	625 (88.9)	285 (85.1)	260 (95.2)
African American	22 (3.1)	37 (11.0)	6 (2.2)
Asian	52 (7.4)	5 (1.5)	3 (1.1)
Other	4 (0.6)	8 (2.4)	4 (1.5)
Region, N (%)			
North America	179 (25.5)	214 (63.9)	80 (29.3)
Europe/Asia	524 (74.5)	121 (36.1)	193 (70.7)
Mean BMI	30.2	28.6	27.1
Lesion area (cm ²)			
Mean (SD)*	674.3 (656.4)	335.0 (232.7)	411.0 (391.9)
Median	450.0	285.0	305.0

* p value: cellulitis vs major abscess ≤0.001; cellulitis vs wound infection ≤0.001; wound infection vs abscess=0.014

Table 2. Clinical Outcomes by Type of ABSSSI

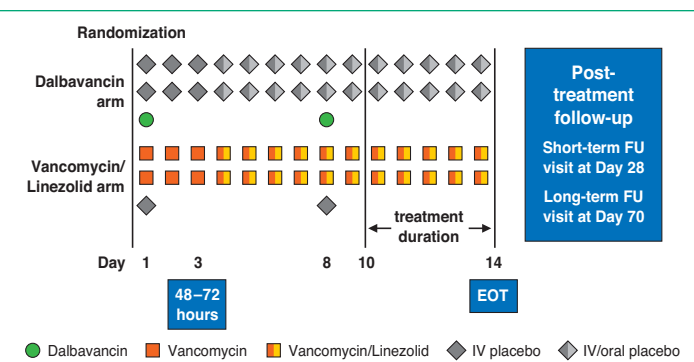
Outcomes	Dalbavancin n/N (%)	Vancomycin/ Linezolid n/N (%)	Total n/N (%)
Clinical Response at 48–72 h			
Overall	525/659 (79.7)	521/653 (79.8)	1046/1312 (79.7)
Cellulitis	281/354 (79.4)	269/349 (77.1)	550/703 (78.2)
Difference (95% CI)		2.3 (–3.8, 8.4)	
Major Abscess	133/162 (82.1)	149/173 (86.1)	282/335 (84.2)
Difference (95% CI)		–4.0 (–12.1, 3.9)	
Wound Infection	111/142 (78.2)	103/131 (78.6)	214/273 (78.4)
Difference (95% CI)		–0.5 (–10.2, 9.5)	
Clinical Success at EOT*			
Cellulitis	308/324 (95.1)	289/301 (96.0)	597/625 (95.5)
Difference (95% CI)		–1.0 (–4.4, 2.5)	
Major Abscess	129/133 (97.0)	137/139 (98.6)	266/272 (97.8)
Difference (95% CI)		–1.8 (–6.2, 2.5)	
Wound Infection	110/113 (97.4)	101/105 (96.2)	211/218 (96.8)
Difference (95% CI)		1.2 (–4.2, 7.1)	

*Investigator assessed outcomes

Conclusions: Major abscess was the predominant type of ABSSSI in North America, while cellulitis was most common in Europe/Asia. Patients with cellulitis were older and had larger lesions relative to other infections. Major abscesses appear to respond to treatment most quickly, but clinical success rates at EOT are similar.

METHODS

Figure 1. Study Design: Studies DUR001-301/302



- Patients had:
 - cellulitis, abscess or wound infection with erythema >75 cm² and
 - either a fever, an elevated white blood cell count >12k cells/mm³ 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 by subtype of infection.

RESULTS

Table 1. Demographics

Characteristic	Cellulitis (N=703)	Major Abscess (N=335)	Wound Infection (N=273)	Total (N=1311)
Mean Age, (SD)	51.9 (16.3)	46.2 (13.7)	48.1 (16.3)	49.6 (15.9)
Male Gender, n (%)	367 (52.2)	208 (62.1)	191 (70.0)	766 (58.4)
Race, n (%)				
White	625 (88.9)	285 (85.1)	260 (95.2)	1170 (89.2)
Black or African American	22 (3.1)	37 (11.0)	6 (2.2)	65 (5.0)
Asian	52 (7.4)	5 (1.5)	3 (1.1)	60 (4.6)
American Indian or Alaska Native	1 (0.1)	5 (1.5)	3 (1.1)	9 (0.7)
Other	3 (0.4)	3 (0.9)	1 (0.4)	7 (0.5)
Region, n (%)				
North America	179 (25.5)	214 (63.9)	80 (29.3)	473 (36.1)
Europe/Asia	524 (74.5)	121 (36.1)	193 (70.7)	838 (63.9)
Location, n (%)				
Inpatient	518 (82.1)	137 (49.5)	186 (74.4)	841 (72.6)
Outpatient	113 (17.9)	140 (50.5)	64 (25.6)	317 (27.4)
Elevated fasting glucose*, n (%)	303 (43.1)	83 (24.8)	126 (46.2)	512 (39.1)
Diabetes Mellitus, n (%)	108 (15.4)	41 (12.2)	21 (7.7)	170 (13.0)
CrCl <30 mL/min, n (%)	22 (3.2)	7 (2.1)	4 (1.5)	33 (2.6)
History of IVDU, n (%)	30 (4.3)	115 (34.3)	56 (20.5)	201 (15.3)
Met SIRS criteria, n (%)	388/699 (55.5)	144/333 (43.2)	136/272 (50.0)	668/1304 (51.2)
Median BMI (kg/m ²)	28.8	27.1	26.2	27.6
Mean lesion size (cm ²)	674.3	335.0	411.0	—

*Consistent with pre-diabetes/diabetes mellitus

Table 2. Baseline Pathogen

Baseline Pathogen	Cellulitis n/N (%)	Major Abscess n/N (%)	Wound Infection n/N (%)
<i>Staphylococcus aureus</i>	131/703 (18.6)	175/335 (52.2)	98/273 (35.9)
MRSA	37/131 (28.2)	84/175 (48.0)	18/98 (18.4)
MSSA	93/131 (71.0)	91/175 (52.0)	80/98 (81.6)
<i>Streptococcus pyogenes</i>	15/703 (2.1)	8/335 (2.4)	10/273 (3.7)

Table 3. Mean Duration of Antibiotic Therapy (days)

Study Drug Therapy	Cellulitis n/N (%)	Major Abscess n/N (%)	Wound Infection n/N (%)
Intravenous	4.1	3.8	5.3
Oral	6.2	6.6	5.0
Total	11.1	11.2	11.0

Figure 2. Time to ≥20% Reduction in Lesion Size

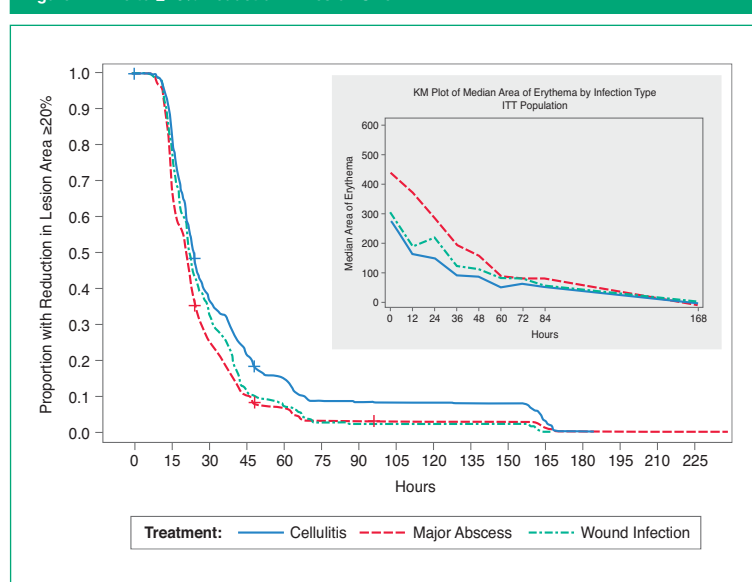


Table 4. Clinical Success by Subtype of Infection

Timepoint	Cellulitis		Major Abscess		Wound Infection	
	Dalbavancin n (%)	Comparator n (%)	Dalbavancin n (%)	Comparator n (%)	Dalbavancin n (%)	Comparator n (%)
Clinical response at 48–72 hours	281 (79.4)	269 (77.1)	133 (82.1)	149 (86.1)	111 (78.2)	103 (78.6)
Difference (95% CI)	2.3 (–3.8, 8.4)		–4.0 (–12.1, 3.9)		–0.5 (–10.2, 9.5)	
≥20% reduction in lesion size at 48–72 hrs	299 (84.5)	301 (86.2)	152 (93.8)	158 (91.3)	133 (93.7)	116 (88.5)
Difference (95% CI)	–1.8 (–7.1, 3.5)		2.5 (–3.4, 8.4)		5.1 (–1.7, 12.5)	
Investigator assessment of Success at EOT	308 (95.1)	289 (96.0)	129 (97.0)	137 (98.6)	110 (97.3)	101 (96.2)
Difference (95% CI)	–1.0 (–4.4, 2.5)		–1.6 (–6.2, 2.5)		1.2 (–4.2, 7.1)	
Investigator assessment Success at SFU	271 (93.1)	263 (94.9)	117 (96.7)	126 (98.4)	106 (98.1)	92 (95.8)
Difference (95% CI)	–1.8 (–5.9, 2.2)		–1.7 (–6.8, 2.6)		2.3 (–2.9, 8.6)	

DISCUSSION

- Major abscess
 - Was the predominant type of ABSSSI in North America
 - Patients were generally younger; IV drug abusers; treated in an outpatient setting; who were less likely to have SIRS and:
 - Had a shorter duration of intravenous therapy
 - Achieved a 20% reduction in lesion size more quickly
 - A smaller area of erythema at baseline
 - More likely to have a staphylococcal isolate at baseline
- Cellulitis
 - Predominantly seen in European patients in this program
 - Patients were generally older, more likely to be treated in an inpatient setting and:
 - Have larger lesions at baseline
 - Less likely to be associated with a pathogen at baseline
 - More likely to be diabetic
 - More likely to meet SIRS criteria
 - Resolved erythema more slowly

CONCLUSIONS

- Patients with cellulitis were older, had larger lesions and a slower reduction in lesion size relative to other infections.
- Major abscesses appear to respond to treatment most quickly.
- Dalbavancin treated patients had similar outcomes to comparator treated patients within each subtype of infection.

Presented at ECCMID 2014, May 10–13, 2014, Barcelona, Spain. Research funding provided by Durata Therapeutics, Inc.

