Treatment of wound infection using omadacycline versus linezolid: Pooled results from phase 3 randomized, double-blind, multicenter studies (OASIS-1 and -2)

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Background

Skin and skin structure infections present a significant burden on healthcare systems,[3,4] with ABSSSI representing more than 800,000 hospitalizations annually in the United States and Europe.[5]

Omadacycline is a novel aminomethylcycline antibiotic approved in the United States for community-acquired bacterial pneumonia and ABSSSI in adults, and is available for intravenous and oral administration.[6]

The modifications of the chemical structure of tetracycline allow omadacycline to overcome the two main mechanisms of tetracycline resistance: efflux pumps and ribosomal protection.[7,8]

Omadacycline has reliable *in vitro* and *in vivo* activity against key pathogens, including *Staphylococcus aureus* (methicillin-resistant [MRSA] and methicillin-susceptible [MSSA]) and *Streptococcus pyogenes*.[3,8]

Methods

Methodology for OASIS-1 (NCT02378480) and OASIS-2 (NCT02877927) has been previously described.[1,2]

Briefly, patient populations included modified intent-to-treat (mITT; comprising all randomized patients without a sole Gram-negative ABSSSI pathogen, as the comparator linezolid does not provide Gram-negative pathogen coverage); and micro-mITT (all mITT patients who had ≥1 Gram-positive causative pathogen identified from the ABSSSI site or blood culture).

The primary efficacy endpoint was early clinical response (ECR) in the mITT population, defined as survival with a reduction in lesion size of ≥20% at 48–72 hours after the first dose without rescue antibacterial therapy. A key secondary efficacy endpoint was survival with resolution or improvement in signs and symptoms of infection (to the extent that further antibacterial therapy was unnecessary) at the post-treatment evaluation (PTE; 7–14 days after the last dose) in the mITT population.

Safety was assessed on the basis of adverse events, vital signs, electrocardiograms (ECGs), and laboratory results.

This study represents a *post hoc* analysis of pooled OASIS-1 and -2 data for patients with wound infection who were not PWID.

Results

Baseline demographics and medical history

In the pooled mITT population, 87 patients had wound infection, 37 of whom were treated with omadacycline and 50 with linezolid.

For omadacycline- and linezolid-treated patients with wound infection, 67.6% and 48.0% were male, mean age was 47.3 and 52.0 years, and mean body mass index was 28.9 and 29.4 kg/m^2, respectively.

Medical history regarding source of wound infection and baseline pathogen are reported in **Table 1**.

Table 1. Baseline characteristics

	Omadacycline (n=37)	Linezolid (n=50)
Source of wound infection (mITT)		
Recent trauma	29/37 (78.4)	33/50 (66.0)
Surgical procedure	7/37 (18.9)	3/50 (6.0)
Baseline pathogen (micro-mITT)	n=26	n=37
Gram-positive (aerobes)	25/26 (96.2)	37/37 (100)
Staphylococcus aureus	16/26 (61.5)	36/37 (70.3)
MRSA	6/26 (23.1)	12/37 (32.5)
MSSA	10/26 (38.5)	14/37 (37.8)
Streptococcus pyogenes	2/26 (7.7)	10/37 (27.0)
Enterococcus faecalis	5/26 (19.2)	5/37 (13.5)

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Omadacycline is an effective treatment for wound infections, including those from drug-resistant organisms

Objective

To report on the pooled *post hoc* analysis results from the OASIS-1 and -2 (Omadacycline in Acute Skin and Skin Structure Infections Study; NCT02378480; NCT02877927) phase 3 clinical program for acute bacterial skin and skin structure infections (ABSSSI) in patients who had wound infection and were not persons who inject drugs (PWID).[1,2]

Conclusions

In adults with wound infection not related to injection drug use, omadacycline was an effective treatment, with clinical efficacy for the most frequently isolated bacterial pathogens, including MRSA.

Given its reliable *in vitro* and *in vivo* activity against a number of pathogens, its ability to overcome the most common tetracycline resistance mechanisms, and its flexible administration options, omadacycline offers a treatment option to address combat wound infections, including those resulting from drug-resistant organisms.

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Results (cont.)

Omadacycline and linezolid demonstrated comparable ECR and clinical success at PTE in patients with wound infection (**Figure 1**).

- Comparable clinical success at PTE was observed for wound infections positive for monomicrobial Gram-positive, polymicrobial Gram-positive, and polymicrobial mixed (Gram-positive and Gram-negative) pathogens (**Figure 1**).
- Clinical success at PTE was comparable according to baseline pathogen (**Table 2**).

No new safety signals were identified for omadacycline and linezolid, and no patients from either arm discontinued treatment due to serious treatment-emergent adverse events (**Table 3**).

Figure 1. Clinical success in patients with wound infection. A two-sided 95% CI was calculated for the difference in the proportion of patients achieving ECR, as well as at PTE, using the unadjusted Miettinen–Nurminen method[9] without stratification. mITT, modified intent-to-treat; PTE, post-treatment evaluation

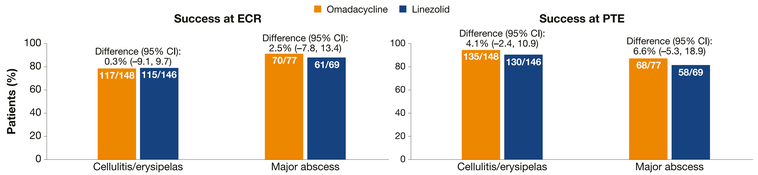

Table 2. Investigator-assessed clinical success at PTE according to baseline pathogen (micro-mITT)

	Omadacycline	Linezolid
Baseline pathogen, n/N (%)		
S. aureus	15/16 (93.8)	19/26 (73.1)
MRSA	6/6 (100)	9/12 (75.0)
MSSA	9/10 (90.0)	10/14 (71.4)
S. pyogenes	1/2 (50.0)	7/10 (70.0)
Enterococcus faecalis	5/5 (100)	3/5 (60.0)

Table 3. Adverse events (safety population)

	Omadacycline (n=40)	Linezolid (n=51)
Total number of AEs	55	34
Total number of TEAEs	53	30
Patients, n (%)		
TEAE	16 (40.0)	18 (35.3)
Serious TEAE	1 (2.5)	2 (3.9)
Serious TEAE leading to treatment discontinuation	0	0
Most common TEAEs occurring in ≥5% of patients, n (%)		
Nausea	8 (20.0)	3 (5.9)
Infusion site extravasation	3 (7.5)	1 (2.0)
ALT increase	3 (7.5)	0
Diarrhea	2 (5.0)	2 (3.9)
AST increase	2 (5.0)	0
Headache	2 (5.0)	0
Vomiting	2 (5.0)	0

ALT, alanine aminotransferase; AST, aspartate aminotransferase; TEAE, treatment-emergent adverse event.

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Acknowledgments

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