Clinical Response to Intravenous versus Oral Treatment in Patients with Acute Bacterial Skin and Skin Structure Infections (ABSSSI)

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Background

Current guidelines for the management of skin and soft tissue infections recommend intravenous (IV) antibiotics if there is a concern for systemic infection.[1] The preference for IV versus oral (PO) therapy should be individualized to the patient and the properties of the antibiotic.

Omadacycline, an aminomethylcycline antibiotic, has a broad spectrum of *in vitro* activity against gram-positive and -negative pathogens, including drug-resistant strains. Omadacycline can be given once daily and is available in both IV and PO formulations that are bioequivalent.

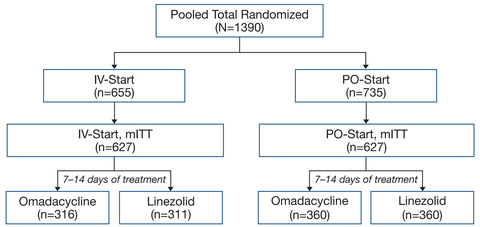
IV-to-oral omadacycline was compared with IV-to-oral linezolid in patients with acute bacterial skin and skin structure infections (ABSSSI) in the phase 3 OASIS-1 trial.[2] Oral-only regimens of omadacycline and linezolid were studied in the phase 3 OASIS-2 trial in ABSSSI.[3]

Methods

In OASIS-1 and OASIS-2, patients with ABSSSI were randomized 1:1 to omadacycline or linezolid for a total treatment duration of 7 to 14 days (**Figure 1**). In OASIS-1, IV therapy could be switched to PO therapy after 3 days. Patients with sole gram-negative pathogens at baseline were excluded from efficacy analyses.

Patients taking selective serotonin reuptake inhibitors were excluded from the studies.

Figure 1: Source Study Analysis Populations



IV, intravenous; mITT, modified intention-to-treat; PO, oral

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Clinical response was assessed at post-treatment evaluation (7 to 14 days after the last dose of study drug), with success defined as survival with resolution or improvement in signs and symptoms of infection to the extent that further antibacterial therapy was unnecessary.

Treatment groups were pooled and stratified as IV-start (OASIS-1) or PO-start (OASIS-2), and success rates were compared overall and for subgroups at risk for clinical failure (obesity, liver disease, lesion size) and with an inflammatory response. Efficacy analyses were conducted on the modified intent-to-treat population (randomized patients without solely gram-negative ABSSSI pathogens at baseline).

Results

The pooled dataset included 645 IV-start inpatients and 735 PO-start outpatients. Roughly one-third of patients in each cohort were obese (BMI >30 kg/m^2) (**Table 1**).

Table 1: Demographic and Baseline Characteristics (Safety Population)

	IV-start (n=645)	PO-start (n=735)
Median age, years (range)	47 (18, 90)	44 (18, 86)
Male, n (%)	416 (64.5)	462 (62.9)
Race, n (%)		
White	594 (92.1)	668 (90.9)
Non-White	51 (7.9)	67 (9.1)
Ethnicity, n (%)		
Hispanic or Latino	175 (27.1)	310 (42.2)
Not Hispanic or Latino	464 (71.9)	425 (57.8)
Missing/Unknown	6 (0.9)	0
Region, n (%)		
US	405 (62.8)	735 (100.0)
Non-US	240 (37.2)	0
Categorical BMI, kg/m^2, n (%)		
<25	227 (35.2)	278 (37.8)
25–30	225 (34.9)	239 (32.5)
>30	192 (29.8)	218 (29.7)
PWID, n (%)	322 (49.9)	500 (68.0)
History of liver disease[a], n (%)	184 (28.5)	242 (32.9)
History of diabetes, n (%)	58 (9.0)	47 (6.4)
Lesion size, n (%)		
≤300 cm^2	314 (48.7)	358 (48.7)
>300 cm^2	331 (51.3)	377 (51.3)
Inflammatory response		
Leukopenia/leukocytosis[b]	286 (44.3)	251 (34.1)
Fever/hypothermia[c]	141 (21.9)	42 (5.7)
Pathogen(s), n (%); micro-mITT population	**(n=455)**	**(n=563)**
Gram-positive aerobes	439 (96.5)	548 (97.3)
Staphylococcus aureus	307 (67.5)	453 (80.5)
Gram-positive anaerobes	31 (6.8)	34 (6.0)
Gram-negative aerobes	51 (11.2)	54 (9.6)
Gram-negative anaerobes	30 (6.6)	23 (4.1)

[a]Liver disease defined as a medical history of any hepatitis B, any hepatitis C, hepatic steatosis, alcoholic liver disease, hepatic cirrhosis, nonalcoholic steatohepatitis, or hepatic failure.
[b]Leukopenia/leukocytosis defined as white blood cell count ≤4000 or ≥10,000 cells/μL.
[c]Fever/hypothermia defined as body temperature >38.0°C or <36.0°C.
BMI, body mass index; IV, intravenous; micro-mITT, microbiological modified intention-to-treat; PO, oral; PWID, people who inject drugs.

Comparable clinical efficacy of oral and IV antibiotic therapy for the treatment of acute bacterial skin and skin structure infections

Objective

To compare clinical response rates between patients who were started on IV therapy and patients who were treated exclusively with PO therapy using pooled data from the OASIS-1 and OASIS-2 trials.

Conclusions

Oral therapy is equally efficacious to IV therapy when a bioequivalent agent such as omadacycline or linezolid is used to treat acute bacterial skin and skin structure infections, and as such, may reduce the need to provide IV therapy in many situations.

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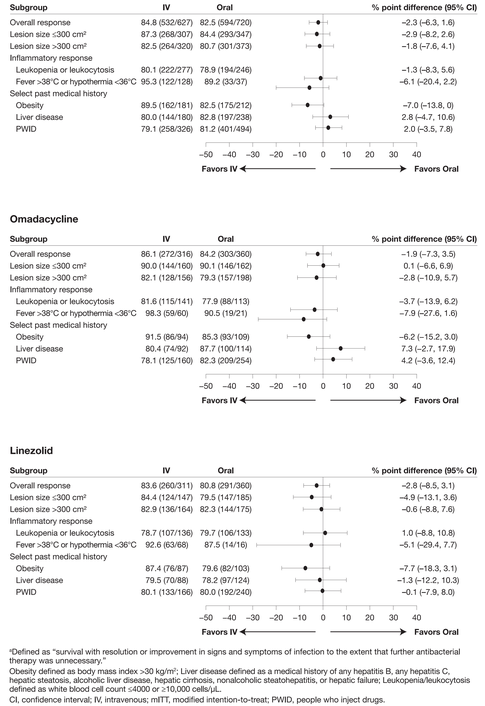
Results (continued)

Clinical success rates were similar overall between the pooled IV-start and PO-start cohorts and also when analyzed among subgroups by characteristics such as lesion size, inflammatory response, obesity (BMI >30 kg/m^2), liver disease, and people who inject drugs. Results were also consistent when stratified by individual drug (omadacycline or linezolid) (**Figure 2**).

Overall, the incidence of treatment-emergent adverse events was similar between the IV-start and PO-start cohorts (**Table 2**), although there were expected differences between groups in the incidence of events associated with particular methods of administration (nausea/vomiting, infusion site extravasation).

Figure 2: Clinical Success[a] at Post-treatment Evaluation for IV-to-Oral and Oral-Only Formulations, for Pooled Treatment Groups, Omadacycline Only, and Linezolid Only, mITT Population



[a]Defined as "survival with resolution or improvement in signs and symptoms of infection to the extent that further antibacterial therapy was unnecessary."
Obesity defined as body mass index >30 kg/m^2; Liver disease defined as a medical history of any hepatitis B, any hepatitis C, hepatic steatosis, alcoholic liver disease, hepatic cirrhosis, nonalcoholic steatohepatitis, or hepatic failure; Leukopenia/leukocytosis defined as white blood cell count ≤4000 or ≥10,000 cells/μL.
CI, confidence interval; IV, intravenous; mITT, modified intention-to-treat; PWID, people who inject drugs.

Table 2: Adverse Events (≥2% in Pooled Treatment Group), Safety Population

	IV-start (n=645)	PO-start (n=735)
Any adverse event	303 (47.0)	334 (45.4)
Any treatment-related adverse event	117 (18.1)	191 (26.0)
Serious adverse event	20 (3.1)	10 (1.4)
Adverse event leading to treatment discontinuation	13 (2.0)	9 (1.2)
Most common adverse events		
Nausea	72 (11.2)	139 (18.9)
Infusion site extravasation	47 (7.3)	0
Subcutaneous abscess	36 (5.6)	14 (1.9)
Vomiting	33 (5.1)	73 (9.9)
Cellulitis	30 (4.7)	21 (2.9)
Headache	23 (3.6)	21 (2.9)
ALT increase	23 (3.6)	30 (4.1)
AST increase	20 (3.1)	29 (3.9)
Diarrhea	17 (2.6)	25 (3.4)
Wound infection	13 (2.0)	39 (5.3)

All values are shown as n (%).
ALT, alanine aminotransferase; AST, aspartate aminotransferase; IV, intravenous; PO, oral.

References

1. Stevens, DL, et al. *CID*. 2014;59:149–159.
2. O'Riordan W, et al. *N Engl J Med*. 2019;380:528–538.
3. O'Riordan W, et al. *Lancet Infect Dis*. 2019;10:1080–1090.

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