A Phase 3 Randomized, Double-Blind, Multi-Center Study to Compare the Safety and Efficacy of Oral and IV Omadacycline to Linezolid for Treating Adult Subjects With ABSSSI (The OASIS Study)

Evan Loh, MD

President, Chief Operating Officer, Chief Medical Officer

Paratek Pharmaceuticals, Inc

Presented at ECCMID, 24 April 2017, Vienna, Austria. Abstract 630.

Acknowledgments and Disclosures

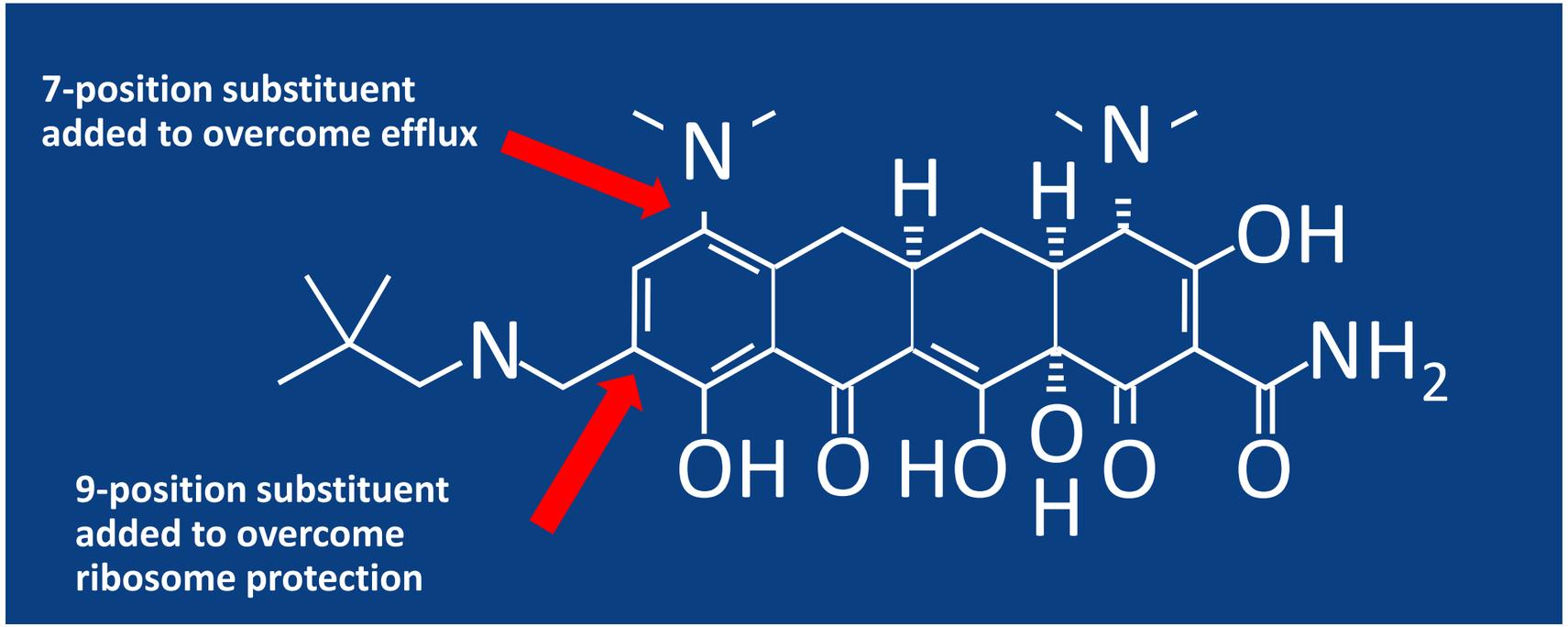
William O'Riordan, MD[1]
Sinikka Green, MD[1]
J. Scott Overcash, MD[1]
Ivan Puljiz, MD, PhD[2]
Symeon Metallidis, MD[3]
Janis Gardovskis, MD[4]
Lynne Garrity-Ryan[5]
Anita Das, PhD[5]
Evan Tzanis[5]
Paul Eckburg, MD[5]
Amy Manley[5]
Stephen Villano, MD[5]
Judith Steenburgen, PhD[5]

Special thanks to the subjects and investigators that participated in this study

This study was sponsored by Paratek Pharmaceuticals, Inc.

[1]eStudySite, San Diego, CA, USA.
[2]University Hospital for Infectious Diseases "Dr. F. Mihaljević", Zagreb, Croatia.
[3]AHEPA University Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece.
[4]Paula Stradins Clinical Hospital, Riga, Latvia.
[5]Paratek Pharmaceuticals, Inc., King of Prussia, PA, USA.

Potent New Class of Antibiotics — *Aminomethylcyclines*
Restoring Broad-Spectrum Tetracycline Activity by Overcoming Resistance



- ***Omadacycline*** is the first antibiotic in a new class, the aminomethylcyclines[1,2]
- In late-stage development as a once-daily oral and IV monotherapy for acute bacterial skin and skin structure infection (ABSSSI) and community-acquired bacterial pneumonia (CABP)

1. Villano S, et al. *Future Microbiol*. 2016;11:1421-1421; 2. Honeyman L, et al. *Antimicrob Agents Chemother.* 2015;59:7044-7053.

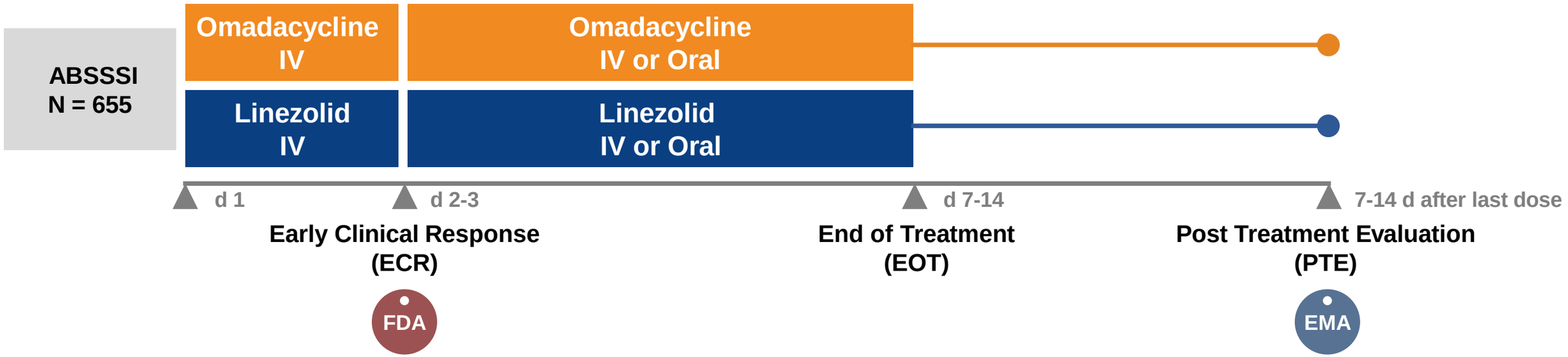
Omadacycline

Potent Broad-Spectrum In Vitro Activity Against ABSSSI Pathogens[1]

Pathogen	N	MIC_{50}	MIC_{90}
Staphylococcus aureus	4215	0.12	0.25
MRSA	1438	0.12	0.25
Streptococcus pyogenes	448	0.06	0.12
Streptococcus anginosus group	107	0.06	0.12
Enterococcus faecalis	677	0.12	0.25
Enterococcus faecium	390	0.06	0.12
Escherichia coli	3541	0.5	2
ESBL phenotype	733	1	2

[1]JMI 2016 US and EU Surveillance; Data on file

Design of the Phase 3 OASIS Study
IV to Once-Daily Oral Omadacycline vs Twice-Daily IV/Oral Linezolid (1:1)



FDA Primary Endpoint

- Early Clinical Response: ≥20% reduction in lesion size 48 to 72 hours after first dose of study drug in the modified intent-to-treat (mITT) population

EMA Co-Primary Endpoints

- Clinical response at post treatment evaluation (PTE) in the mITT population
- Clinical response at post treatment evaluation (PTE) in the clinically evaluable (CE) population

Clinicaltrials.gov: NCT02378480.
EudraCT Number: 2013-003644-23.

Subject Selection and Analysis Populations

Key inclusion criteria

- Qualifying ABSSSI ≥ 75 cm^2 total surface area of contiguous involved tissue
  - Classification of qualifying infections
- Evidence of a systemic inflammatory response within 24 h prior to randomization

Key exclusion criteria

- Received 1 or more doses of a potentially effective systemic or topical antibacterial treatment within the 72-h period prior to first dose of test article
- Taking medications with associated risks when co-administered with linezolid (eg, MAOIs)

Population	Omadacycline n (%)[a]	Linezolid n (%)[a]
ITT	329	326
Safety	323 (98.2)	322 (98.8)
mITT	316 (96.0)	311 (95.4)
micro-mITT	228 (69.3)	227 (69.6)
CE-PTE	269 (81.8)	260 (79.8)

[a] Percentage of ITT population.

ABSSSI, acute bacterial skin and skin structure infection; CE, clinically evaluable; ITT, intent-to-treat; MAOI, monoamine oxidase inhibitor, micro-mITT, microbiological modified intent-to-treat; mITT, modified intent-to-treat; PTE, post treatment evaluation.

Demographic Characteristics — Safety Population

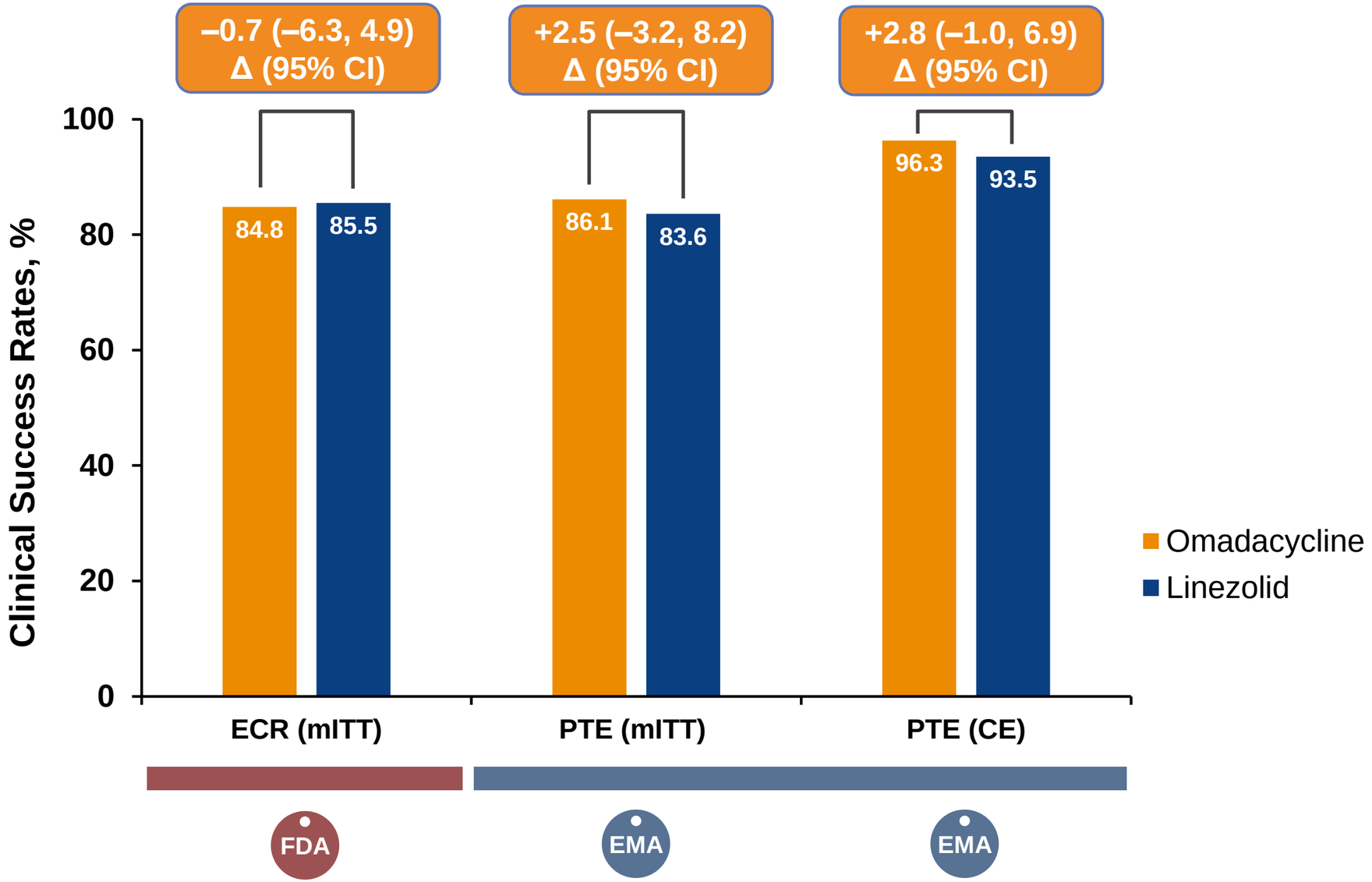
Balanced Demographics Between Treatment Arms

Characteristic	Omadacycline	Linezolid
Gender (%)		
Male	62.8	66.1
Female	37.2	33.9
Median age (years)	48	46
Median BMI[a] (kg/m^2)	27	27[b]
Infection type (%)[c]		
Wound infection	30.7	33.2
Cellulitis/erysipelas	40.6	38.2
Major abscess	28.8	28.6
Median primary lesion area [cm^2 (range)]	300 (77-4100)	314 (88-6739)

[a] BMI = body mass index.
[b] Weight not available for 1 linezolid subject.
[c] Randomization stratification factor.

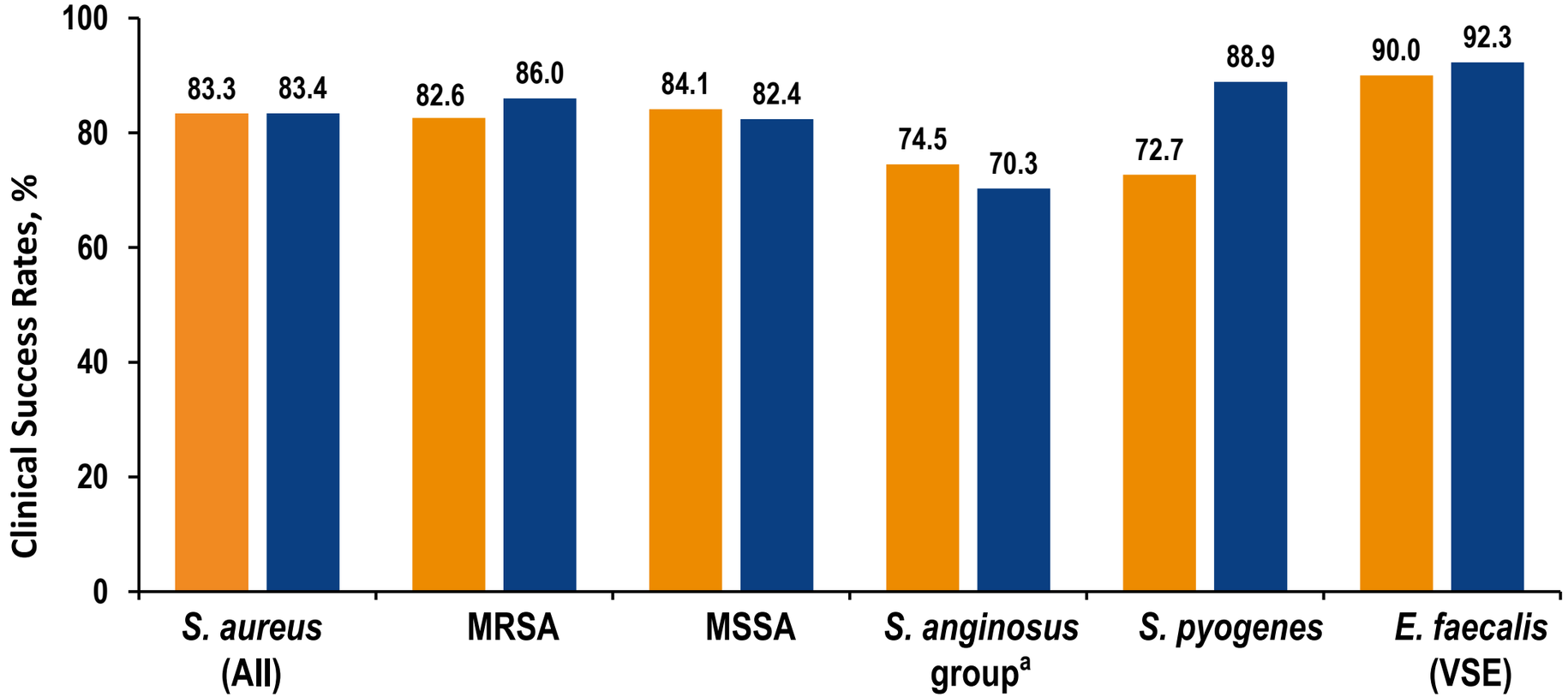
Omadacycline Effective in ABSSSI

Met Non-Inferiority for Both FDA and EMA Efficacy Endpoints



Clinical Response by Pathogen at PTE — Micro-mITT Population

Microbiological Responses Similar to Clinical Responses



	S. aureus (All)	MRSA	MSSA	*S. anginosus* group[a]	*S. pyogenes*	*E. faecalis* (VSE)
Omadacycline, n	156	69	88	47	11	10
Linezolid, n	151	50	102	37	18	13

[a] *S. anginosus* group consists of *S. anginosus, S. intermedius,* and *S. constellatus.*

Overview of Adverse Events — Safety Population
Consistent Between Treatment Groups

Subjects with at least one, n (%)	Omadacycline (N = 323)	Linezolid (N = 322)
TEAE	156 (48.3)	147 (45.7)
Drug-related TEAE	58 (18.0)	59 (18.3)
Severe TEAE	6 (1.9)	10 (3.1)
Serious TEAE	11 (3.4)	8 (2.5)
Drug-related serious TEAE	0	0
Serious TEAE leading to death	1[a]	2 (0.6) [b]
TEAE leading to discontinuation of study drug [c]	6 (1.9)	7 (2.2)

TEAE, treatment-emergent adverse event.
[a] Death due to opioid overdose reported 7 months after database lock.
[b] Deaths due to cardiac arrest and cardiac failure.
[c] Only 1 Omadacycline and 1 Linezolid discontinuation was due to a GI TEAE.

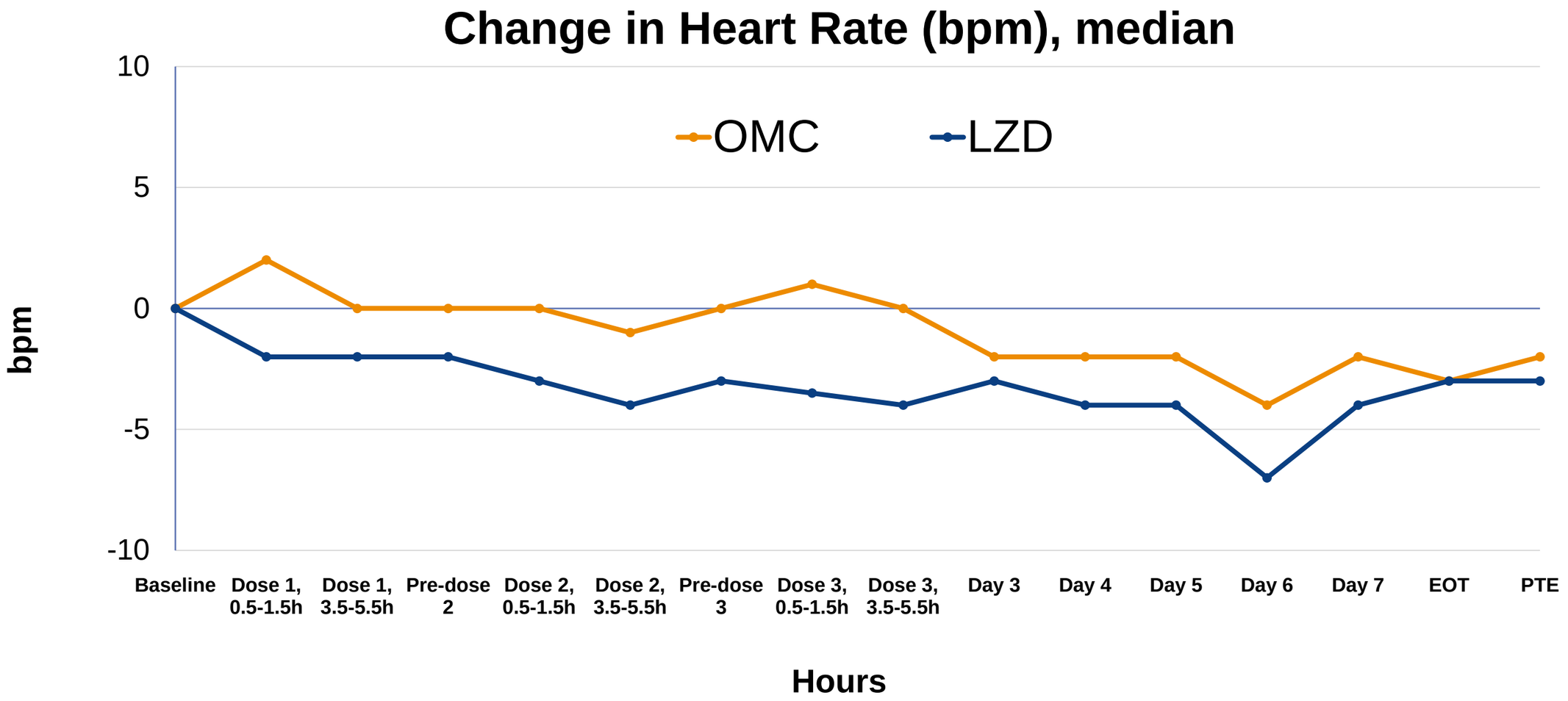
Most Common Adverse Events — Safety Population

Omadacycline Was Generally Safe and Well Tolerated

Most frequent TEAEs (≥3%), n (%)	Omadacycline (N = 323) n (%)	Linezolid (N = 322) n (%)
Subjects with any TEAE	**156 (48.3)**	**147 (45.7)**
Nausea[a]	40 (12.4)	32 (9.9)
Infusion site extravasation[b]	28 (8.7)	19 (5.9)
Subcutaneous abscess	17 (5.3)	19 (5.9)
Vomiting	17 (5.3)	16 (5.0)
Cellulitis	15 (4.6)	15 (4.7)
Headache	10 (3.1)	13 (4.0)
ALT increased	9 (2.8)	14 (4.3)
AST increased	8 (2.5)	12 (3.7)
Diarrhea[c]	7 (2.2)	10 (3.1)

[a] All nausea was mild or moderate: Omadacycline = 87.5% mild,12.5% moderate; Linezolid = 78.1% mild, 21.9% moderate.
[b] Typically due to difficulty in finding reliable venous access sites. All events were mild; none caused treatment discontinuation.
[c] No *C. difficile* infection identified in either arm.

Cardiac Safety
No Clinically Meaningful Difference in Heart Rate



Cardiac Safety
No Clinically Meaningful Change in Heart Rate or Blood Pressure

	Omadacycline (N = 323) n (%)	Linezolid (N = 322) n (%)
Subjects with HR value at any post-Baseline visit		
HR ≥ 120 bpm	5 (1.5)	6 (1.9)
Subjects with HR value at Baseline and any post-Baseline visit		
HR ≥ 120 bpm and increase of ≥ 15 bpm	5 (1.5)	6 (1.9)
Systolic BP ≥ 180 mmHg	5 (1.5)	12 (3.7)
Subjects with systolic BP value at Baseline and any post-Baseline visit		
Systolic BP ≥ 180 mmHg and increase of ≥ 20 mmHg	4 (1.2)	11 (3.4)
Subjects with diastolic BP value at Baseline and any post-Baseline visit		
Diastolic BP ≥ 105 mmHg and increase of ≥ 15 mmHg	6 (1.9)	9 (2.8)

Other Safety Assessments — Safety Population
Low Incidence of Elevated LFTs

Liver Chemistry Analysis	Omadacycline (N = 323) n (%)	Linezolid (N = 322) n (%)
ALT: n = normal at BL	**240**	**251**
Worst post-BL: >3 × ULN	3 (1.3%)	5 (2.0%)
>5 × ULN	3 (1.3%)	2 (0.8%)
>10 × ULN	1 (0.4%)	1 (0.4%)
AST: n = normal at BL	**263**	**281**
Worst post-BL: >3 × ULN	3 (1.1%)	6 (2.1%)
>5 × ULN	2 (0.8%)	3 (1.1%)
>10 × ULN	0	0
Total bilirubin: n = normal at BL	**296**	**296**
Worst post-BL: >1.5 × ULN	2 (0.7%)	1 (0.3%)
>2 × ULN	1 (0.3%)	1 (0.3%)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BL, baseline; ULN, upper limit normal.

No subject met laboratory criteria for Hy's Law.

OASIS Study
Omadacycline Is Effective in ABSSSI; Generally Safe and Well-tolerated

- In the phase 3 OASIS trial, omadacycline was effective and non-inferior to linezolid for treatment of ABSSSI
  - ✓ Met **both** FDA and EMA primary endpoints
  - ✓ High clinical response rates for the most common ABSSSI pathogens, including MRSA
- Omadacycline was generally safe and well-tolerated following both IV and oral dosing, with a safety profile similar to that of linezolid

Omadacycline Is Clinically Effective as an IV to Once-daily Oral Antibiotic With Activity Against the Most Common ABSSSI Pathogens Including MRSA

Additional Omadacycline Presentations at ECCMID 2017

Session	Topic	Abstract No., First Author	Title
Poster Session: New Data on New Tetracyclines **Monday, 24 April 12:30-13:30**	OASIS: Efficacy by Infection Type and Pathogen	889 O'Riordan	Efficacy of Oral and IV Omadacycline vs. Linezolid for Treating Adult Subjects With ABSSSI: Analyses by Infection Type and Pathogen in the OASIS Study
	OASIS: Treatment Effects on Lesion Size and Local Signs of ABSSSI	4089 Overcash	Effects of IV/Oral Omadacycline Versus IV/Oral Linezolid on Lesion Size and Local Signs of ABSSSI in the Phase 3 OASIS Trial
	OASIS: Efficacy by Geographic Region	4114 O'Riordan	Efficacy of Omadacycline Versus Linezolid in Treating ABSSSI Patients From Different Geographic Regions (OASIS Trial)
	Safety in Healthy Subjects (Ph 1 study)	5737 Gotfried	Safety and Tolerability of IV Omadacycline (OMC) and Tigecycline (TGC) in Healthy Subjects in a Study to Assess Intra-Pulmonary Steady-State Concentrations
Oral Session: PK/PD: New and Old-Revived Antibiotics **Tuesday, 25 April 13:30-15:30 Hall K**	PK/PD after IV Administration / Lung Concentrations (Ph 1 study)	3760 Horn	Comparison of Omadacycline (OMC) and Tigecycline (TGC) Pharmacodynamics (PD) in the Plasma, Epithelial Lining Fluid (ELF), and Alveolar Macrophages (AM) in Healthy Subjects