



PTK0796-CABP-1200 Study Design and Results

April 3, 2017

Omadacycline for **P**neumonia **T**reatment **I**n the **C**ommunity - The **OPTIC** Study

A Phase 3 Randomized, Double-Blind, Multi-Center Study to Compare the Safety and Efficacy of Omadacycline IV/PO to moxifloxacin IV/PO for Treating Adult Subjects with Community Acquired Bacterial Pneumonia (CABP)

Safe Harbor Statement

This presentation contains “forward-looking” statements that are within the meaning of federal securities laws and are based on our management’s beliefs and assumptions and on information currently available to management. Forward-looking statements include information concerning our possible or assumed future results of operations, business strategies, financing plans, competitive position, industry environment, potential growth opportunities, potential market opportunities and the effects of competition.

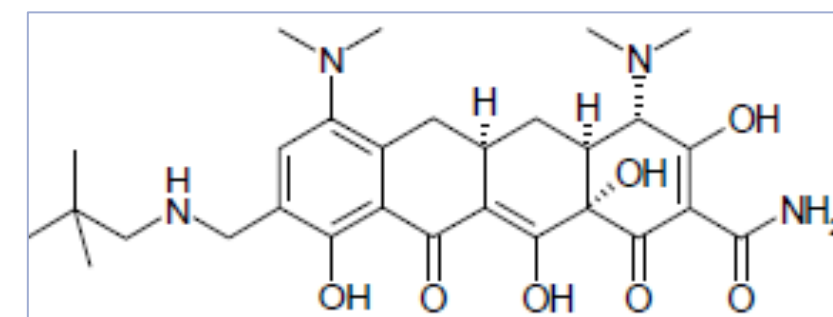
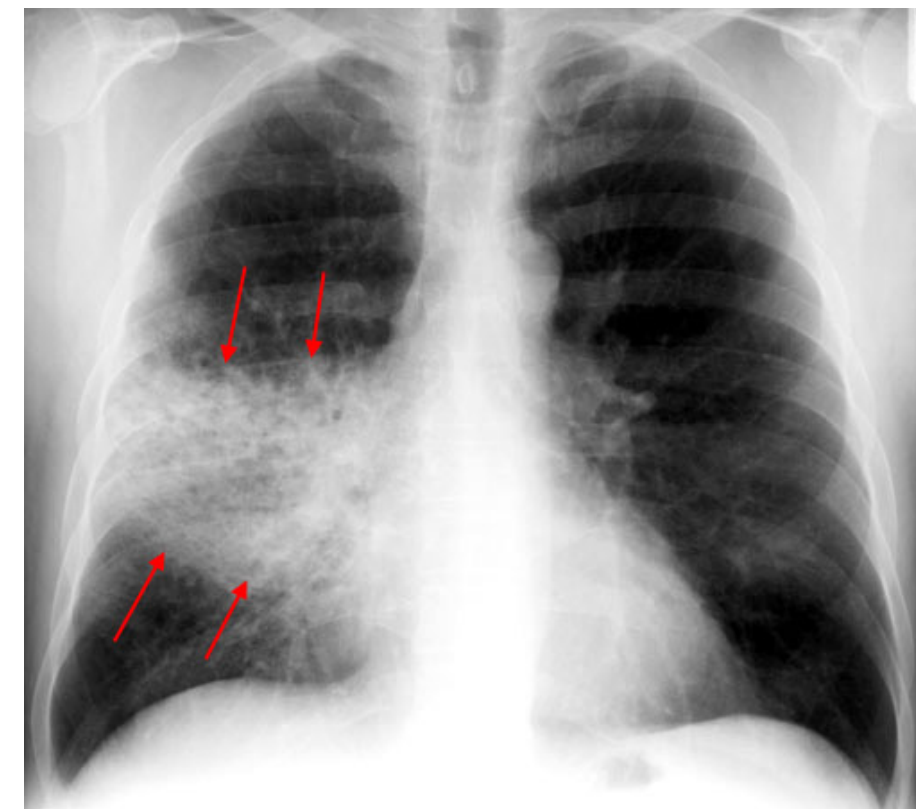
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You may get copies of our Annual Report on Form 10-K, Quarterly Report on Form 10-Q and our other SEC filings for free by visiting EDGAR on the SEC website at <http://www.sec.gov>.

CABP Epidemiology & Potential for Omadacycline

A Novel Broad-Spectrum Oral and IV Antibiotic that Addresses Resistance

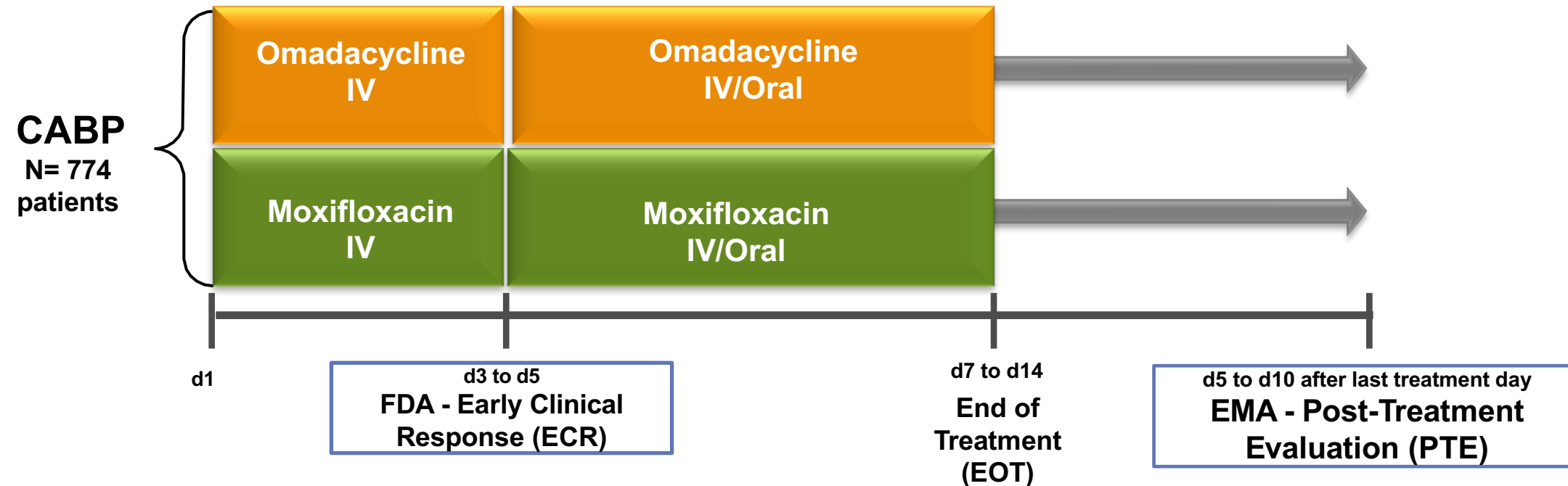
- Most common cause of infectious hospitalization
- 4th most common cause of death globally
 - Mortality rate exceeding 5%
 - Highest mortality rates in those over the age of 60
- Once-Daily Oral and IV Omadacycline
 - Potent *in vitro* activity against common CABP pathogens
 - Atypical (*Mycoplasma*, *Chlamydia*, *Legionella*)
 - Gm Negatives (*H. influenzae*)
 - Gm Positives (*S. pneumoniae*, *S. aureus*)
 - Circumvents known mechanisms of tetracycline resistance
- Potential treatment option for patients who can't receive standard therapy with β -lactams, fluoroquinolones, or macrolides (e.g., drug resistance or intolerance)



Chemical structure of omadacycline

Phase 3 CABP Study Design

SPA Approved: IV to Once-Daily Oral



📦 FDA Primary Endpoint (PORT Risk II, III, and IV)

- **Intent-to-Treat (ITT) Population (n=774):** Early Clinical Response = improvement in ≥ 2 of 4 subject symptoms 72 to 120 hours after first dose of study drug without receipt of an antibiotic

📦 EMA Co-Primary Endpoints (PORT Risk III and IV)

- **ITT Population (n=685):** Clinical Success = Resolution of infection signs and symptoms at PTE
- **Clinically Evaluable (CE) Population (n=669):** Clinical Success = Clinical response at PTE

Subject Disposition – ITT population

Low Discontinuation Rates from Treatment

Parameter/ Category	Omadacycline (N=386) n (%)	Moxifloxacin (N=388) n (%)	All Subjects (N=774) n (%)
Randomized	386 (100.0)	388 (100.0)	774 (100.0)
Completed Study Treatment	352 (91.2)	346 (89.2)	698 (90.2)
Prematurely Discontinued from Study Treatment	34 (8.8)	42 (10.8)	76 (9.8)

Demographics – Safety Population

Balanced Demographics Between Treatment Arms

	Omadacycline (N=382)	Moxifloxacin (N=388)	All Subjects (N=770)
Gender, n (%)			
Female	177 (46.3)	169 (43.6)	346 (44.9)
Male	205 (53.7)	219 (56.4)	424 (55.1)
Age			
Mean (SD)	60.9 (15.1)	62.1 (15.2)	61.5 (15.2)
Categorical Age (years)			
18 – 45	61 (16.0)	61 (15.7)	122 (15.8)
>45 – 65	171 (44.8)	155 (39.9)	326 (42.3)
>65 – 75	150 (39.3)	172 (44.3)	322 (41.8)
>75 – 97	74 (19.4)	83 (21.4)	157 (20.4)
Weight (kg)			
Mean (SD)	77.6 (18.0)	78.0 (17.8)	77.8 (17.9)

PORT Risk Class – Safety Population

Represents High Severity of Pneumonia

PORT Risk Class (actual)	Omadacycline (N=382)	Moxifloxacin (N=388)	All Subjects (N=770)
II (51<=Port Score<=70)	54 (14.1)	54 (13.9)	108 (14.0)
III (71<=Port Score<=90)	226 (59.2)	216 (55.7)	442 (57.4)
IV (91<=Port Score<=130)	100 (26.2)	115 (29.6)	215 (27.9)

Excludes 5 subjects with Actual Port Risk Scores of I and V (2 on omadacycline and 3 on moxifloxacin)

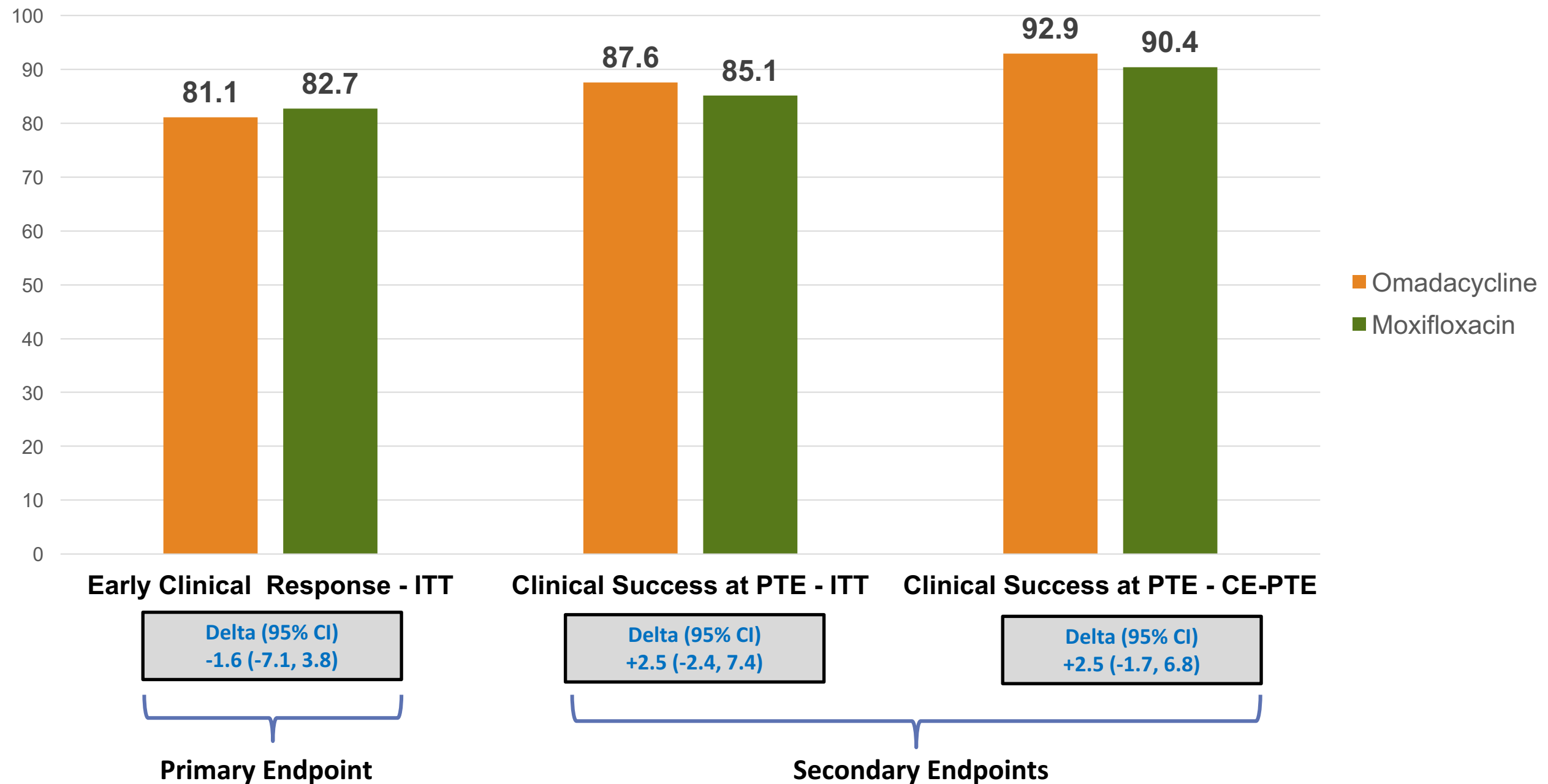


OPTIC Study

Efficacy Data

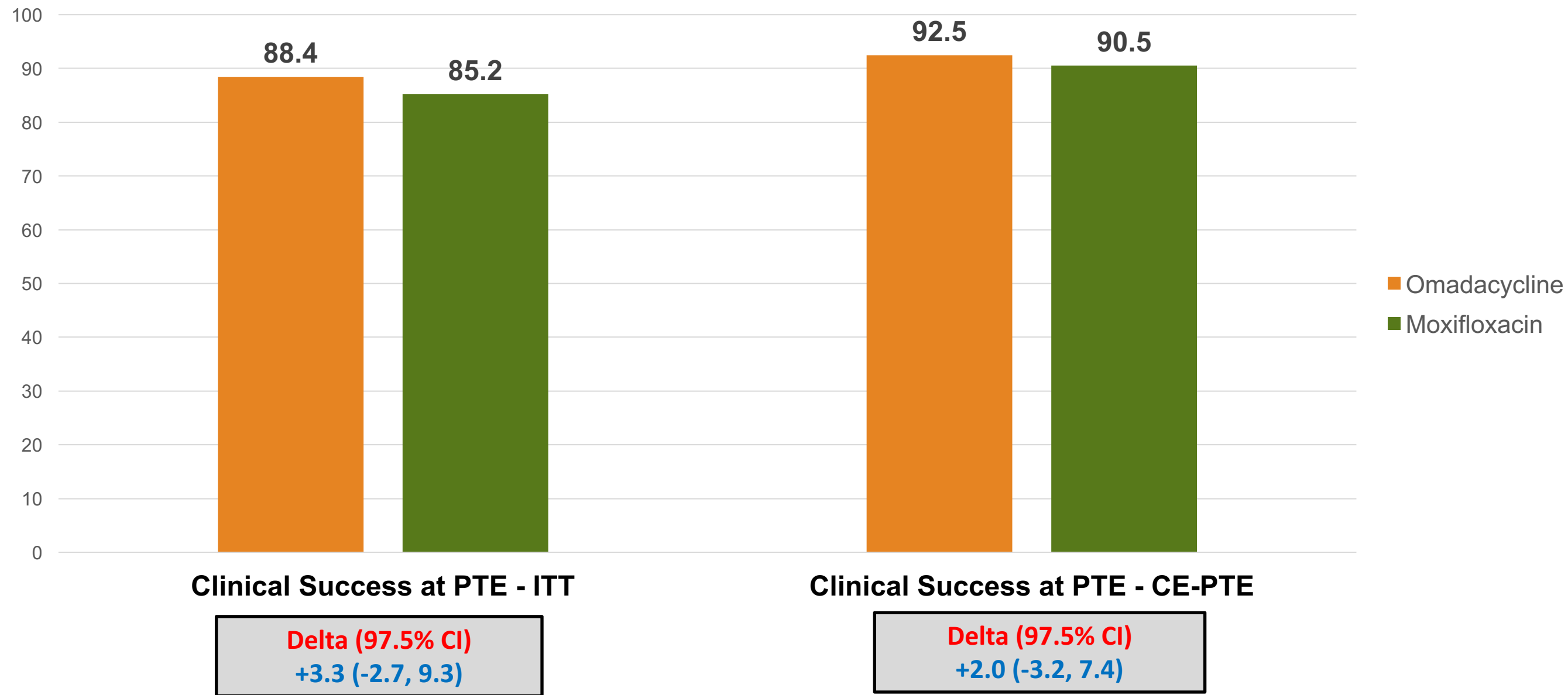
OPTIC Study - Efficacy Results

Omadacycline Meets Both FDA Primary and Secondary Efficacy Endpoints



OPTIC Efficacy Results – (PORT Risk III and IV)

Omadacycline Meets EMA Co-Primary Endpoints (97.5% Confidence Level)



Clinical Success at PTE by Baseline Pathogen*

Broad Representation of Pathogens Associated with CABP

Baseline Pathogen	Omadacycline (N=204)		Moxifloxacin (N=182)	
	N	Clinical Success n (%)	N1	Clinical Success n (%)
Atypical Pathogens	118	109 (92.4)	106	97 (91.5)
<i>Mycoplasma pneumoniae</i>	70	66 (94.3)	57	50 (87.7)
<i>Chlamydophila pneumoniae</i>	28	25 (89.3)	28	25 (89.3)
<i>Legionella pneumophila</i>	37	35 (94.6)	37	36 (97.3)
Gram-Negative Bacteria (aerobes)	79	67 (84.8)	68	55 (80.9)
<i>Haemophilus influenzae</i>	32	26 (81.3)	16	16 (100.0)
<i>Haemophilus parainfluenzae</i>	18	15 (83.3)	17	13 (76.5)
<i>Klebsiella pneumoniae</i>	13	10 (76.9)	13	11 (84.6)
Gram-Positive Bacteria (aerobes)	61	52 (85.2)	56	49 (87.5)
<i>Streptococcus pneumoniae</i>	43	37 (86.0)	34	31 (91.2)
PSSP	26	23 (88.5)	22	21 (95.5)
Macrolide Resistant	10	10 (100.0)	5	5 (100.0)
<i>Staphylococcus aureus</i>	11	8 (72.7)	11	9 (81.8)

*10 or More Isolates for Omadacycline



OPTIC Study

Safety and Tolerability Data

Reasons for Premature Discontinuation from Study Treatment

Low Rates of Treatment Discontinuation

Parameter/ Category	Omadacycline (N=386) n (%)	Moxifloxacin (N=388) n (%)	All Subjects (N=774) n (%)
Completed Study Treatment	352 (91.2)	346 (89.2)	698 (90.2)
Prematurely Discontinued from Study Treatment	34 (8.8)	42 (10.8)	76 (9.8)
Reason For Premature Discontinuation from Study Treatment			
Adverse Event	17 (4.4)	28 (7.2)	45 (5.8)
Lost to Follow-up	0	1 (0.3)	1 (0.1)
Withdrawal by Subject	4 (1.0)	3 (0.8)	7 (0.9)
Physician Decision	3 (0.8)	9 (2.3)	12 (1.6)
Death	4 (1.0)	1 (0.3)	5 (0.6)
Other	6 (1.6)	0	6 (0.8)

Subjects randomized but not treated (total n=4) are counted in the Other category

Overview of Adverse Events – Safety Population

Consistent Between Treatment Groups

	Omadacycline (N=382)	Moxifloxacin (N=388)
Subjects with at least one		
Adverse Events (AE)	170 (44.5)	200 (51.5)
TEAE	157 (41.1)	188 (48.5)
Drug-Related TEAE	39 (10.2)	69 (17.8)
Severe TEAE	25 (6.5)	26 (6.7)
Serious TEAE	23 (6.0)	26 (6.7)
Drug-Related Serious TEAE	2 (0.5)	2 (0.5)
Serious TEAE Leading to Death	8 (2.1)	4 (1.0)
TEAE Leading to Premature D/C on of Test Article	21 (5.5)	27 (7.0)
TEAE Leading to Premature Discontinuation of Study	7 (1.8)	9 (2.3)
Serious TEAEs Leading to Premature Discontinuation of Test Article	10 (2.6)	11 (2.8)

TEAEs > 2% for Omadacycline – Safety Population

Generally Safe and Well Tolerated

	Omadacycline (N=382) n (%)	Moxifloxacin (N=388) n (%)	All Subjects (N=770) n (%)
Subjects with at Least One TEAE	157 (41.1)	188 (48.5)	345 (44.8)
ALT Increased	14 (3.7)	18 (4.6)	32 (4.2)
Hypertension	13 (3.4)	11 (2.8)	24 (3.1)
GGT Increased	10 (2.6)	8 (2.1)	18 (2.3)
Insomnia	10 (2.6)	8 (2.1)	18 (2.3)
Vomiting	10 (2.6)	6 (1.5)	16 (2.1)
Constipation	9 (2.4)	6 (1.5)	15 (1.9)
Nausea	9 (2.4)	21 (5.4)	30 (3.9)
AST Increased	8 (2.1)	14 (3.6)	22 (2.9)
Headache	8 (2.1)	5 (1.3)	13 (1.7)

Treatment Emergent Adverse Events of Interest

Generally Safe and Well Tolerated

	Omadacycline (N=382)	moxifloxacin (N=388)	All Subjects (N=770)
Preferred Term (PT)	n (%)	n (%)	n (%)
Diarrhea	4 (1.0)	31 (8.0)	35 (4.5)
Clostridium Difficile Colitis	0	1 (0.3)	1 (0.1)
Clostridium Difficile Infection	0	6 (1.5)	6 (0.8)
Pseudomembranous Colitis	0	1 (0.1)	1 (0.1)
Dizziness	0	4 (1.0)	4 (0.5)
Blood Pressure Increased	3 (0.8)	1 (0.3)	4 (0.5)
Hypersensitivity	1 (0.3)	4 (1.0)	5 (0.6)
Tachycardia	4 (1.0)	3 (0.8)	7 (0.9)

Liver Chemistry - Safety Population

Low Incidence of Elevated LFTs

Lab Parameter			Omadacycline (N=382) n (%)	Moxifloxacin (N=388) n (%)
ALT (U/L)	Worst post-baseline (Highest)	n	281	295
		> 3x ULN	7 (2.5)	11 (3.7)
		> 5x ULN	2 (0.7)	1 (0.3)
		>10x ULN	2 (0.7)	0
AST (U/L)	Worst post-baseline (Highest)	n	323	328
		> 3x ULN	5 (1.5)	5 (1.5)
		> 5x ULN	3 (0.9)	1 (0.3)
		>10x ULN	1 (0.3)	0
Total Bilirubin (umol/L)	Worst post-baseline (Highest)	n	333	343
		>1.5x ULN	1 (0.3)	6 (1.7)
		> 2x ULN	1 (0.3)	4 (1.2)

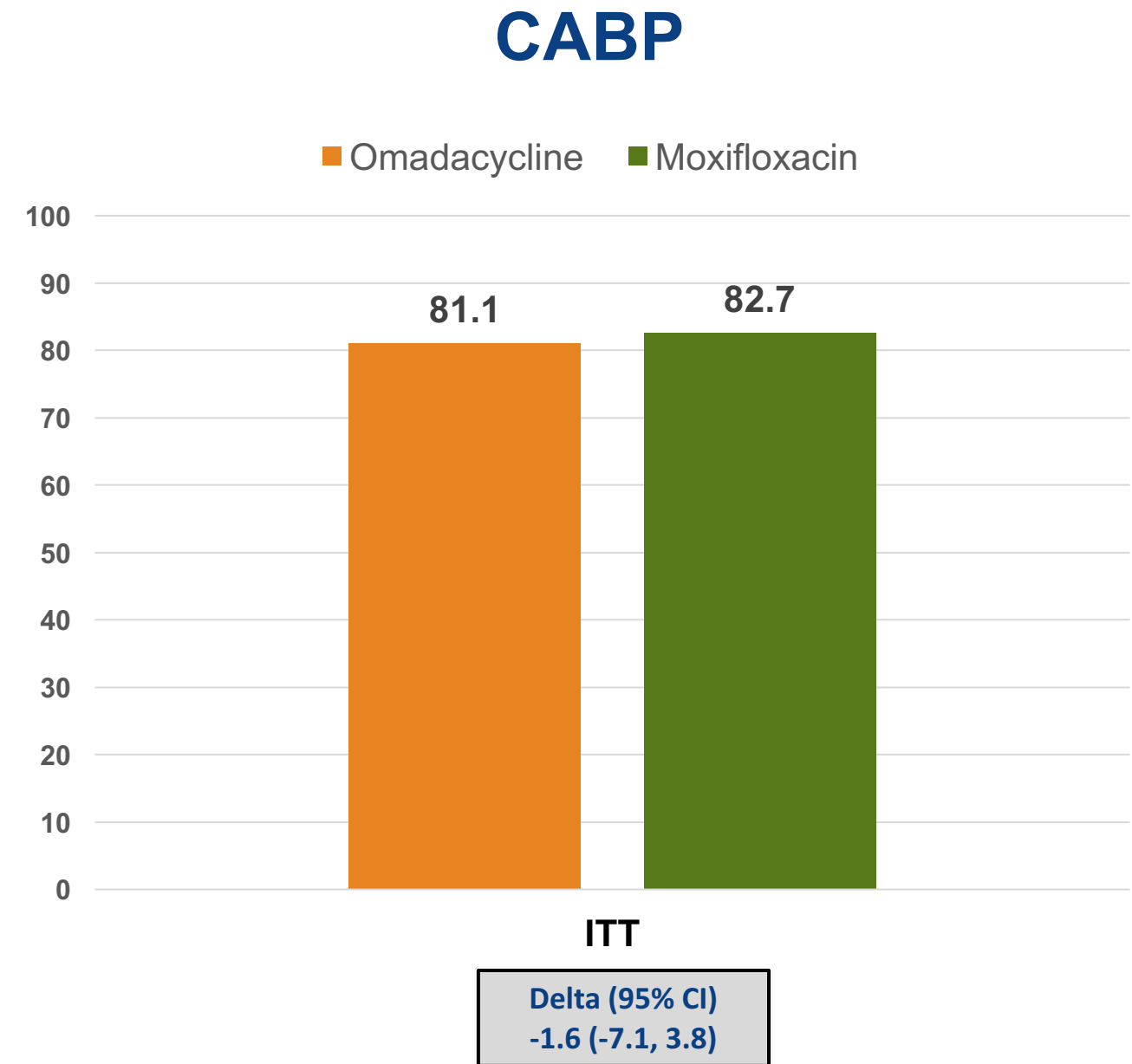
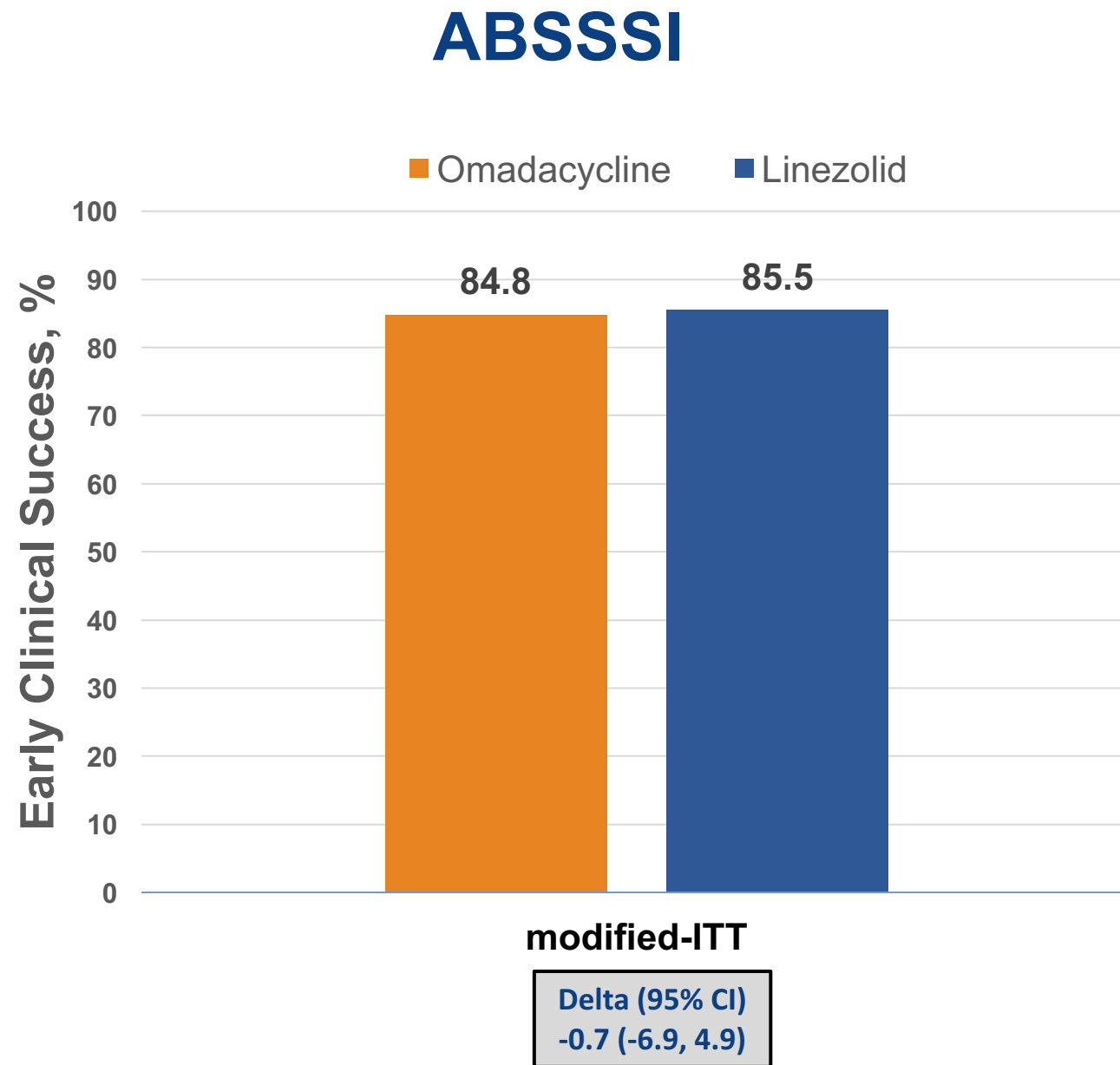
No subjects met laboratory criteria for Hy's Law



Establishing the Safety and Efficacy of Once-Daily Oral and IV Omadacycline in ABSSI and CABP

Omadacycline Efficacious in ABSSSI and CABP (IV to Oral)

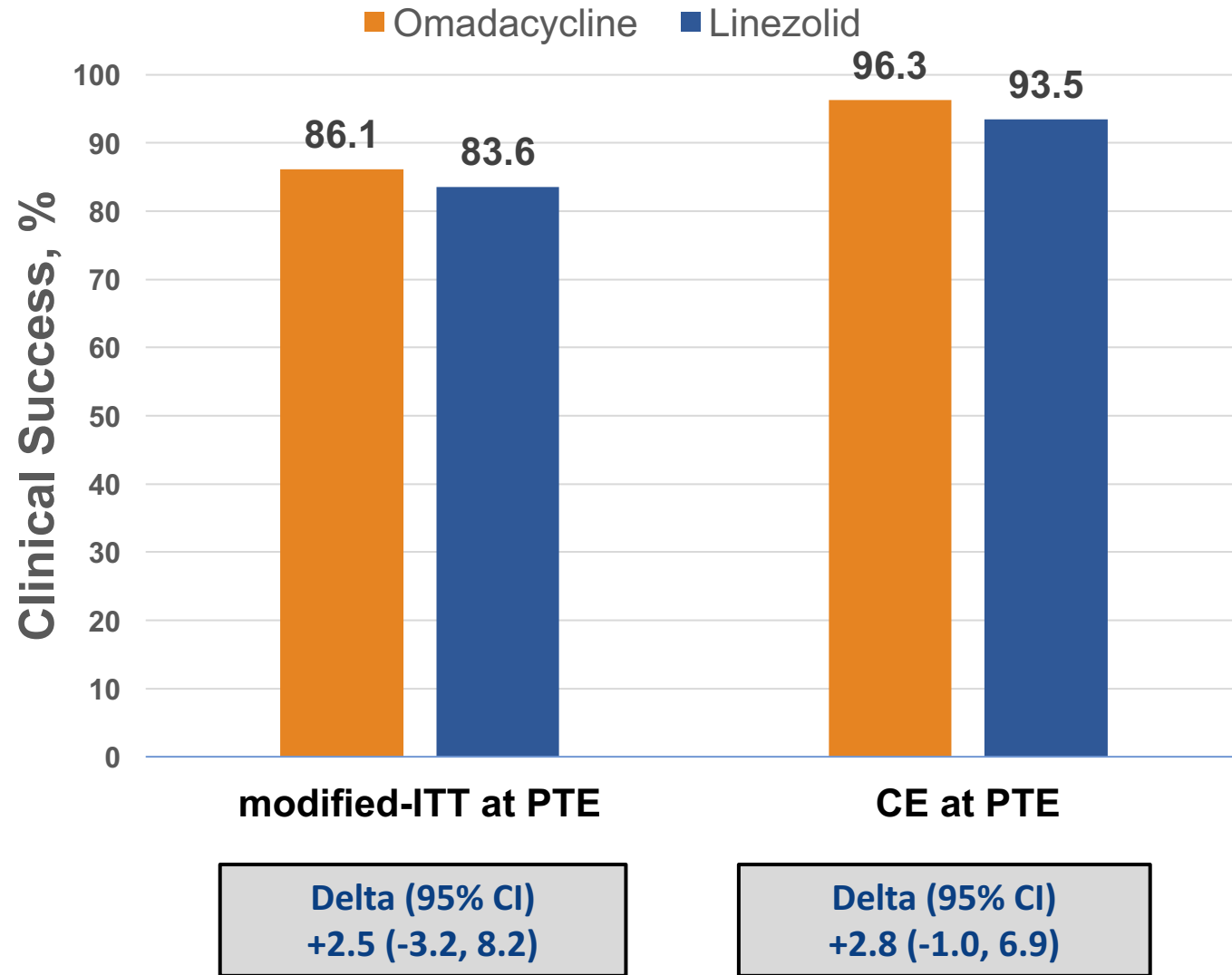
Robust & Consistent Efficacy (Early Clinical Response - FDA Primary Endpoint)



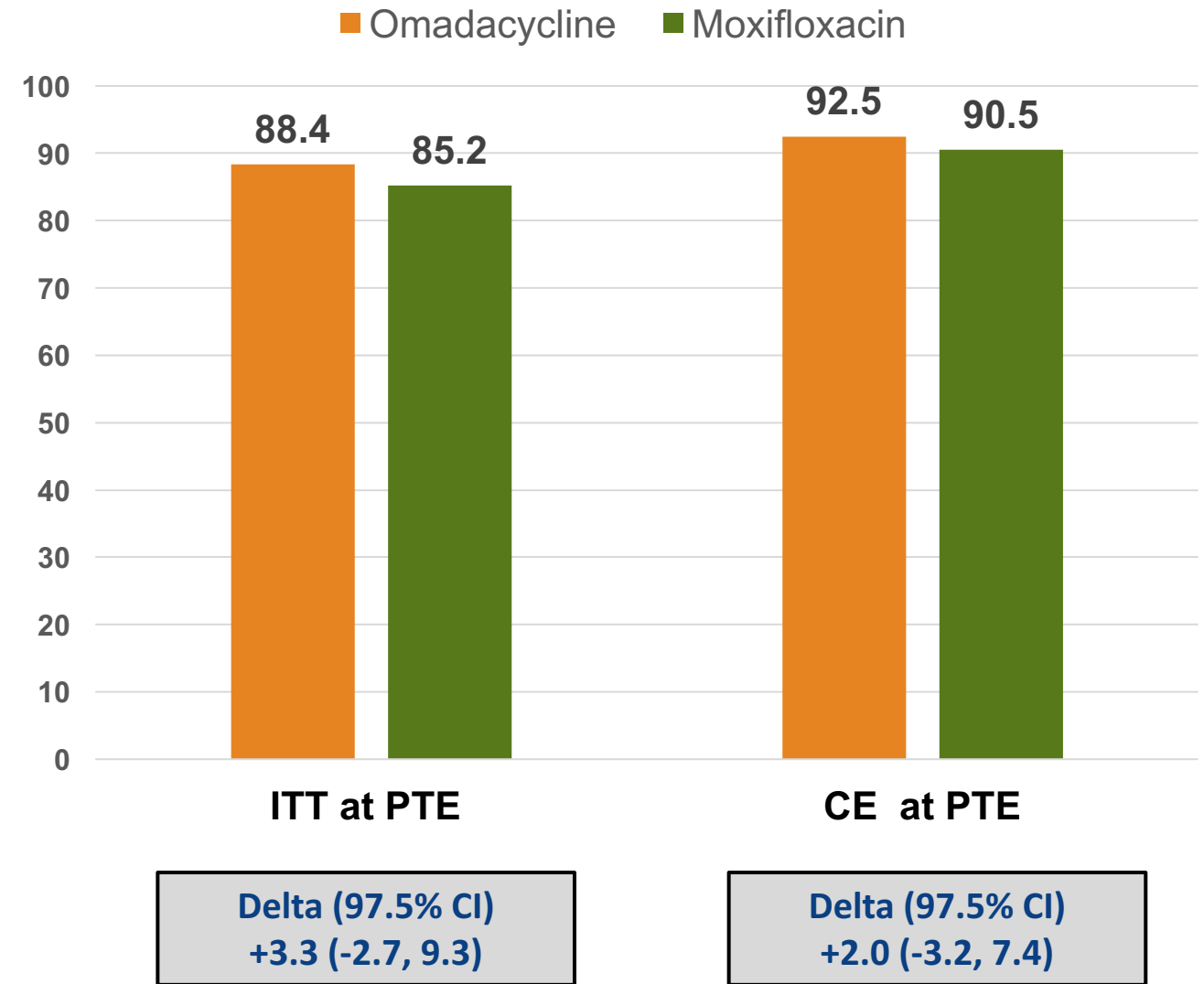
Omadacycline Efficacious in ABSSSI and CABP (IV to Oral)

Robust & Consistent Efficacy (PTE - EMA Primary Endpoint)

ABSSSI



CABP



Omadacycline is Generally Safe and Well Tolerated – Adverse Events $\geq 3\%$ in ABSSSI or CABP

PTK0796-ABSI-1108 (OASIS)

	Omadacycline (N=323) n (%)	Linezolid (N=322) n (%)
Subjects with any TEAE	156 (48.3)	147 (45.7)
Nausea	40 (12.4)	32 (9.9)
Infusion site extravasation ^a	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	7 (2.2)	10 (3.1)
Hypertension	6 (1.9)	4 (1.2)

PTK0796-CABP-1200 (OPTIC)

	Omadacycline (N=382) n (%)	Moxifloxacin (N=388) n (%)
Subjects with any TEAE	157 (41.1)	188 (48.5)
Nausea	9 (2.4)	21 (5.4)
Infusion site related events	4 (1.0)	9 (2.3)
Subcutaneous abscess	0	0
Vomiting	10 (2.6)	6 (1.5)
Cellulitis	1 (0.3)	0
Headache	8 (2.1)	5 (1.3)
ALT increased	14 (3.7)	18 (4.6)
AST increased	8 (2.1)	14 (3.6)
Diarrhea	4 (1.0)	31 (8.0)
Hypertension	13 (3.4)	11 (2.8)

^a Events were reported as IV site infiltration, typically due to difficulty in finding reliable venous access sites. All events were mild.

Among these subjects, 79% in each treatment group had ABSSSI considered related to intravenous drug use.

Omadacycline Regulatory Pathway

Pursuing FDA and EMA Approval in Both ABSSSI and CABP

- ❏ Successful ABSSSI and CABP IV to once-daily oral Phase 3 studies satisfy the FDA SPA agreement and support omadacycline submission for both indications.
- ❏ The oral only skin study TLD readout as early as June 2017. This study will be included in the NDA to support an oral only dosing regimen.
- ❏ FDA and EMA discussions planned for the second half of this year.
- ❏ NDA submission as early as the first quarter of 2018
- ❏ EMA submission to follow later in 2018