Efficacy of Omadacycline versus Moxifloxacin in Treating Subjects from Different Geographic Regions with Community-acquired Bacterial Pneumonia (CABP)

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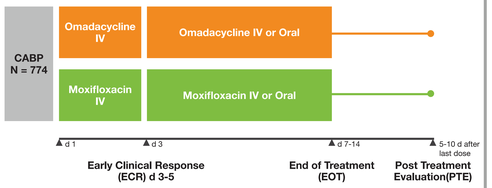
BACKGROUND

- Omadacycline (OMC) is the first late-stage aminomethylcycline in clinical development
  - Aminomethylcyclines are semi-synthetic antibiotics related to the tetracyclines[1,2]
- OMC demonstrates potent, *in vitro* activity against common Gram-positive aerobes (including methicillin- and penicillin-resistant strains), many Gram-negative aerobes, anaerobes, and atypical bacterial pathogens[3,4]
- OMC demonstrated non-inferiority to linezolid in two Phase 3 studies in acute bacterial skin and skin structure infection (ABSSSI)[5,6]
- OMC demonstrated non-inferiority to moxifloxacin (MOX) in the treatment of adults with community-acquired bacterial pneumonia (CABP) in the global Phase 3 **O**madacycline for **P**neumonia **T**reatment **I**n the **C**ommunity (OPTIC) study[7]
- Here we report efficacy outcomes in the OPTIC study by geographic region (Western Europe/North America, Eastern Europe, Rest of Word), which was a randomization stratification factor

METHODS

Figure 1. OPTIC Study Design



- Study Design: Multicenter, randomized (1:1), double-blind, comparator controlled study comparing OMC and MOX in adults with CABP
  - NCT02531438, EudraCT #2013-004071-13
- Treatment: 7-14 days
  - OMC: 100 mg intravenous (iv) q12h for 2 doses, then 100 mg iv q24h, with an option to transition at 3+ days to OMC 300 mg oral (po) q24h
  - MOX: 400 mg iv q24h, with an option to transition at 3+ days to 400 mg po q24h
- Subjects: Adults ≥ 18 years of age with 3+ symptoms (cough, production of purulent sputum, dyspnea, or pleuritic chest pain), 2+ abnormal vital signs (fever/hyperthermia, systolic BP < 90 mmHg, HR > 90 beats per min, RR > 20 breaths/min), and 1+ clinical sign or laboratory finding associated with CABP. Individuals were excluded if they used a systemic antibacterial treatment within 72 hours of the first dose of study drug, or if they had hospital-acquired pneumonia. Up to 25% of subjects were allowed a prior single dose of short-acting antibiotic

METHODS

- Randomization: Stratified by PORT Risk Class (II vs III/IV), geographic region, and receipt of an allowed prior antibiotic
- Analysis populations:
  - Intent-to-treat (ITT): All randomized subjects
  - microITT: All ITT subjects who had ≥1 bacterial pathogen identified
  - Clinically evaluable (CE): All ITT subjects who received study drug, had qualifying CABP, an assessment of outcome, and met all other criteria for evaluation
  - Microbiologically evaluable (ME): All subjects who met the microITT and CE criteria
- Microbiological analysis: Respiratory and blood cultures, and Gram stains were performed at screening to identify baseline pathogens; urine antigen testing and serology was performed to identify atypical pathogens at baseline
- Efficacy endpoints:
  - Primary – Early clinical response (ECR): Success defined as survival with improvement in ≥ 2 of 4 subject symptoms and no worsening of any symptom at 72 to 120 hours after first dose of study drug; ITT population
  - Secondary – Investigator-assessed clinical response at post-therapy evaluation (PTE; 5 to 10 days after last dose): Success defined as investigator-determined resolution of infection signs and symptoms such that further antibacterial treatment is not needed; ITT and CE populations

RESULTS

Table 1. Subjects by Geographic Region and Country (ITT Population)

Region	Omadacycline n (%)	Moxifloxacin n (%)	All, n (%)
OVERALL, n	386	388	774
All Europe	339 (87.8)	337 (86.9)	676 (87.3)
Western Europe/North America	91 (24)[a]	92 (24)	183 (24)
Czech Republic	17 (18.7)[b]	10 (10.9)	27 (14.8)
Spain	1 (1.1)	0	1 (0.5)
Greece	10 (11.0)	20 (21.7)	30 (16.4)
Croatia	38 (41.8)	43 (46.7)	81 (44.3)
Mexico	0	1 (1.1)	1 (0.5)
Poland	24 (26.4)	16 (17.4)	40 (21.9)
United States	1 (1.1)	2 (2.2)	3 (1.6)
Eastern Europe	249 (65)	248 (64)	497 (64)
Bulgaria	48 (19.3)	57 (23.0)	105 (21.1)
Georgia	10 (4.0)	16 (6.5)	26 (5.2)
Hungary	42 (16.9)	39 (15.7)	81 (16.3)
Latvia	19 (7.6)	18 (7.3)	37 (7.4)
Romania	31 (12.4)	30 (12.1)	61 (12.3)
Russia	12 (4.8)	14 (5.6)	26 (5.2)
Slovakia	4 (1.6)	0	4 (0.8)
Ukraine	83 (33.3)	74 (29.8)	157 (31.6)
Rest of World	46 (12)	48 (12)	94 (12)
Brazil	2 (4.3)	2 (4.2)	4 (4.3)
Israel	10 (21.7)	9 (18.8)	19 (20.2)
Peru	2 (4.3)	6 (12.5)	8 (8.5)
Philippines	16 (34.8)	15 (31.3)	31 (33.0)
Turkey	1 (2.2)	1 (2.1)	2 (2.1)
Taiwan	0	1 (2.1)	1 (1.1)
South Africa	15 (32.6)	14 (29.2)	29 (30.9)

[a]Percentage of overall population; [b]Percentage of regional population; These rules apply to all data cells in the table

RESULTS

Table 2. Subjects with Pathogens Identified at Baseline, by Geographic Region (microITT Population)

Region	microITT/ITT, n/N (%)[a]		
	Omadacycline	Moxifloxacin	All
microITT, n	204	182	386
All Europe	184/339 (54.3)	165/337 (49.0)	349/676 (51.6)
Western Europe/North America	49/91 (53.8)	35/92 (38.0)	84/183 (45.9)
Eastern Europe	135/249 (54.2)	130/248 (52.4)	265/497 (53.3)
Rest of World	20/46 (43.5)	17/48 (35.4)	37/94 (39.4)

[a]Percentage of ITT population for which at least 1 causative pathogen was identified through culture of a baseline blood specimen, respiratory specimen, urinary antigen test, and/or serology

Table 3. Baseline Pathogen by Geographic Region (microITT Population)

Baseline Pathogen, n (%)	Western Europe/ North America		Eastern Europe		Rest of World	
	OMC N = 49	MOX N = 35	OMC N = 135	MOX N = 130	OMC N = 20	MOX N = 17
Gram-positive bacteria	21 (42.9)	14 (40.0)	34 (25.2)	35 (26.9)	6 (30.0)	7 (41.2)
Streptococcus pneumoniae	15 (30.6)	11 (31.4)	25 (18.5)	21 (16.2)	3 (15.0)	2 (11.8)
Staphylococcus aureus	2 (4.1)	1 (2.9)	9 (6.7)	9 (6.9)	0	1 (5.9)
Gram-negative bacteria	12 (24.5)	7 (20.0)	60 (44.4)	56 (43.1)	7 (35.0)	6 (35.3)
Haemophilus influenzae	6 (12.2)	1 (2.9)	25 (18.5)	14 (10.8)	1 (5.0)	1 (5.9)
Haemophilus parainfluenzae	0	0	18 (13.3)	17 (13.1)	0	0
Klebsiella pneumoniae	3 (6.1)	1 (2.9)	7 (5.2)	10 (7.7)	3 (15.0)	2 (11.8)
Atypical pathogens	28 (57.1)	23 (65.7)	81 (60.0)	76 (58.5)	9 (45)	7 (41.2)
Mycoplasma pneumoniae	14 (28.6)	15 (42.9)	53 (39.3)	36 (27.7)	3 (15.0)	6 (35.3)
Legionella pneumophilia	8 (16.3)	4 (11.4)	26 (19.3)	32 (24.6)	3 (15.0)	1 (5.9)
Chlamydophilia pneumoniae	9 (18.4)	4 (11.4)	15 (11.1)	22 (16.9)	4 (20.0)	2 (11.8)

- Clinical success rates were high and comparable across OMC and MOX in different regions
  - Small sample sizes and heterogeneity in countries included in Rest of the World make it difficult to draw conclusions about the numeric differences

RESULTS

Figure 2. ECR at 72 to 120 Hours, with Difference (95% Confidence Interval) (ITT Population)

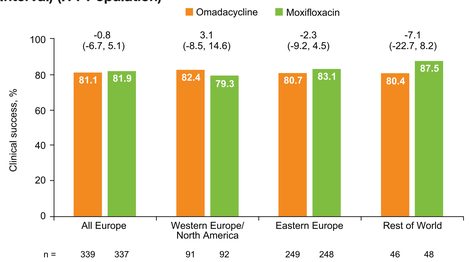


Figure 3. Investigator-assessed Clinical Response at PTE (ITT Population)

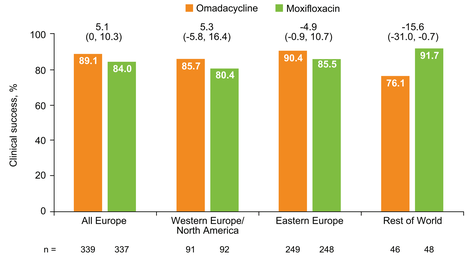
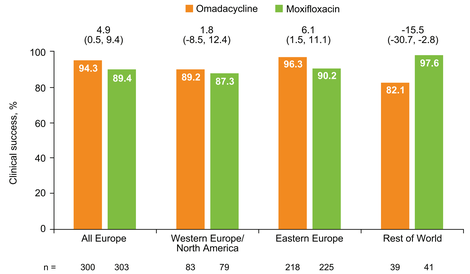


Figure 4. Investigator-assessed Clinical Response at PTE (CE Population)



CONCLUSIONS

- OMC showed comparable efficacy to MOX in the treatment of adults with CABP in Europe, where the majority of subjects were enrolled
- MOX showed higher clinical success rates than OMC in the Rest of World region, however small sample sizes make it difficult to draw any conclusions from this numeric difference
- The distribution of pathogens in all regions was as expected with *S pneumoniae* being the most commonly identified pathogen

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