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Early Clinical Response of Omadacycline Versus Moxifloxacin in the Treatment of Community-acquired Bacterial Pneumonia by PORT Risk Class: Results From the OPTIC Study

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Acknowledgments and Disclosures

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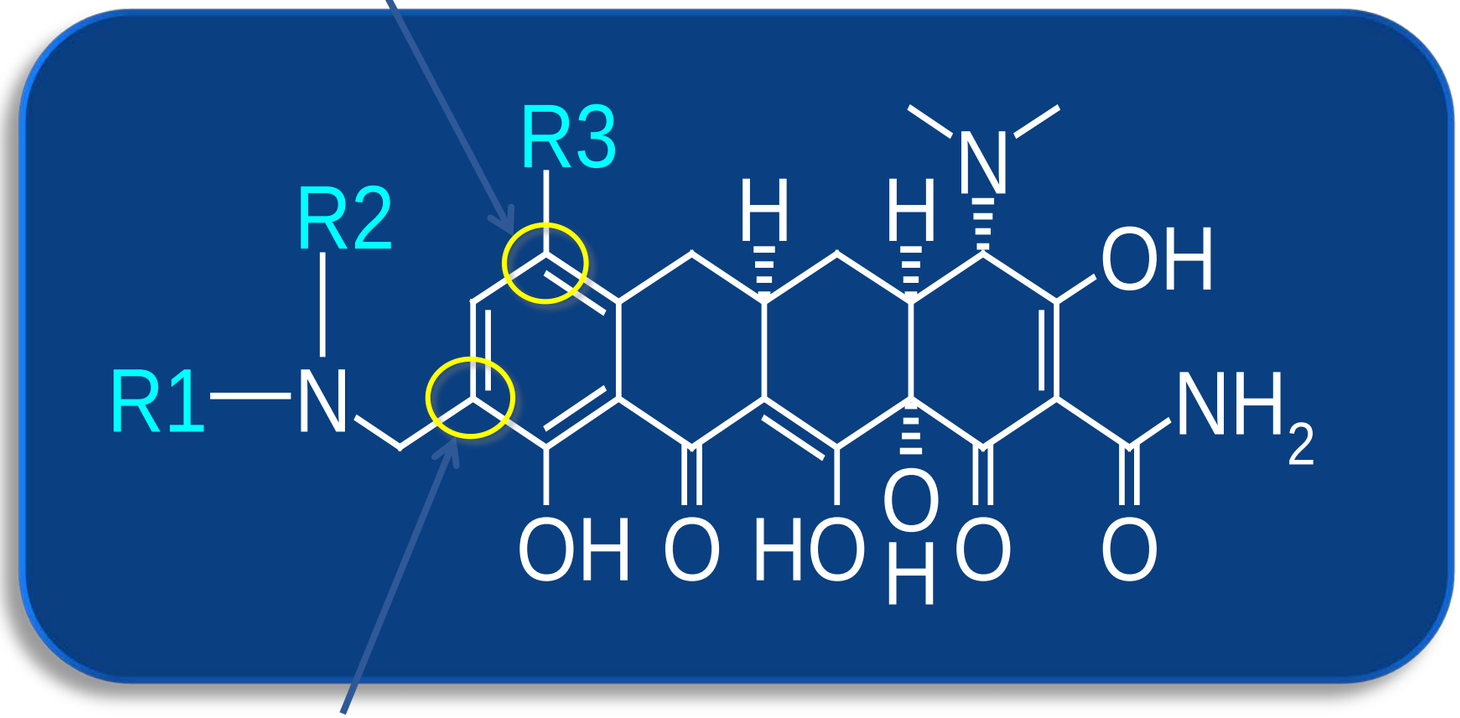
Background: CABP

- Omadacycline (OMC) demonstrated non-inferiority to moxifloxacin (MOX) in the treatment of adults with community-acquired bacterial pneumonia (CABP) in the phase 3 Omadacycline for Pneumonia Treatment in the Community (OPTIC) Study.
- The Food and Drug Administration (FDA) considers early clinical response (ECR) as a primary outcome in patients with CABP.
- ECR is influenced by patient's severity of disease at time of hospitalization.
- The primary objective of this study was to evaluate ECR and the secondary objective was to evaluate post therapy clinical response (PTCR) by Pneumonia Research Outcomes Team (PORT) Risk Class and other measures of mortality and severity.

Omadacycline

Aminomethylcycline

7-Position Modification:
Overcomes Efflux Pump



9-Position Modification:
Overcomes Ribosomal Protection

Activity Against Common CABP Pathogens*		
	N	MIC_{90}
S. pneumoniae	1,314	0.12
Pen-R (≥2)	152	0.12
Tetracycline-R	263	0.12
Macrolide-R	413	0.12
H. influenzae	803	1
β-lactamase +	201	1
β-lactamase -	602	1
M. catarrhalis	408	0.25
L. pneumophila	90	0.25
C. pneumoniae	15	0.25
M. pneumoniae	20	0.25

*** 2016 SENTRY data, Pfaller et al. AAC 2018; J Dubois et al. 2016 abstract 1284 ECCMID Amsterdam, The Netherlands; M Hammerschlag, SUNY Downstate Medical Center, Data on File; Waites KB, et al. 2016. Antimicrob Agents Chemother 60:7502–7504**

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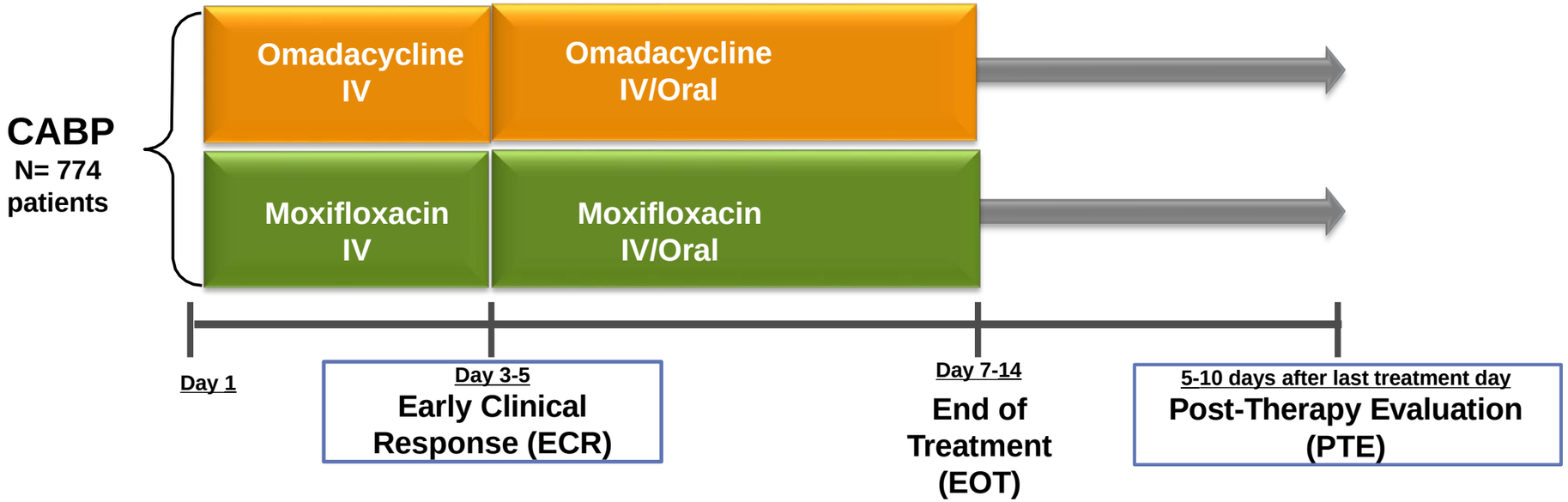
Methods: CABP (OPTIC) Study Design



	Day 1		Day 2	Day 3	After Day 3
	0h	12h	24h	48h	
Omadacycline	100 mg IV	100 mg IV	100 mg IV	100 mg IV	100 mg IV or 300 mg PO once daily
Moxifloxacin	400 mg IV		400 mg IV	400 mg IV	400 mg IV or 400 mg PO once daily

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ECR and PTE Endpoint Definitions

- **FDA Primary Endpoint**
  - **ECR evaluated 72 to 120 hours after first dose of study drug**
  - **Determined programmatically with clinical success defined as:**
    - **Survival**
    - **Improvement of at least 1 level (e.g., severe to moderate) compared to Screening in at least 2 CABP symptoms (cough, sputum production, pleuritic chest pain and dyspnea) with no worsening by at least 1 level in the other inclusion CABP symptoms**
    - **Does not meet any criteria for Clinical Failure or Indeterminate**
- **FDA Secondary Endpoints (ITT and CE Population)**
  - **PTE evaluated 5-10 days after the last dose of study drug**
  - **Investigator assessment of clinical response with clinical success defined as:**
    - **Survival**
    - **No systemic antibacterial therapy other than test article**
    - **Resolution of signs and symptoms of the infection present at Screening, with no new symptoms or complications attributable to CABP and no need for further antibacterial therapy.**

Results: OPTIC Demographics – ITT Population

	Omadacycline (N=386)	Moxifloxacin (N=388)	All Subjects (N=774)
Gender, n (%)			
Male	208 (53.9)	219 (56.4)	427 (55.2)
Age			
Mean (SD)	60.9 (15.2)	62.1 (15.2)	61.5 (15.2)
Categorical Age (years), n(%)			
18 – 45	62 (16.1)	61 (15.7)	123 (15.9)
>45 – 65	172 (44.6)	155 (39.9)	327 (42.2)
>65[a]	152 (39.4)	172 (44.3)	324 (41.9)
BMI (kg/m^2)			
Mean (SD)	27.23 (5.746)	27.42 (5.791)	27.33 (5.765)

Table 14.1.2.2

[a] 20.4% of all subjects were > 75 years old

Demographics – ITT Population

	Omadacycline (N=386) n (%)	Moxifloxacin (N=388) n (%)	All Subjects (N=774) n (%)
PORT Risk Class (actual)[a]			
II (51≤Port Score≤70)[b]	55 (14.2)	54 (13.9)	109 (14.1)
III (71≤Port Score≤90)	227 (58.8)	216 (55.7)	443 (57.2)
IV (91≤Port Score≤130)	102 (26.4)	115 (29.6)	217 (28.0)
CURB-65 ≥2	53 (13.9)	57(14.7)	110 (14.2)
SIRS Criteria (≥ 2 criteria)	288 (74.6)	286 (73.7)	574 (74.2)
Modified ATS Severity (≥3 minor criteria)	49 (13.4)	62 (16.8)	111 (15.1)
qSOFA (≥ 2 criteria)	296 (76.7)	301 (77.6)	597 (77.1)
SMART-COP (≥ 3 criteria)	173 (44.8)	182 (46.9)	355 (45.9)
COPD or Asthma[c]	85 (22.3)	76 (19.6%)	161 (20.9)
Multilobar infiltrates	93 (24.1)	113 (29.1)	206 (26.6)
Pleural Effusion	60 (15.5)	65 (16.8)	125 (16.1)
Bacteremia	15 (3.9)	18 (4.6)	33 (4.3)

Table 14.1.4.1, Table 14.1.9.1, Table 14.1.13.1, Table 14.2.1.1.1.IR1

[a] excludes 5 subjects with Port Risk Class I and V (2 on omadacycline and 3 on moxifloxacin)
[b] PORT Risk Class II capped at 15% by protocol design
[c] defined as asthma, COPD, emphysema, or chronic bronchitis

Overall Efficacy Results

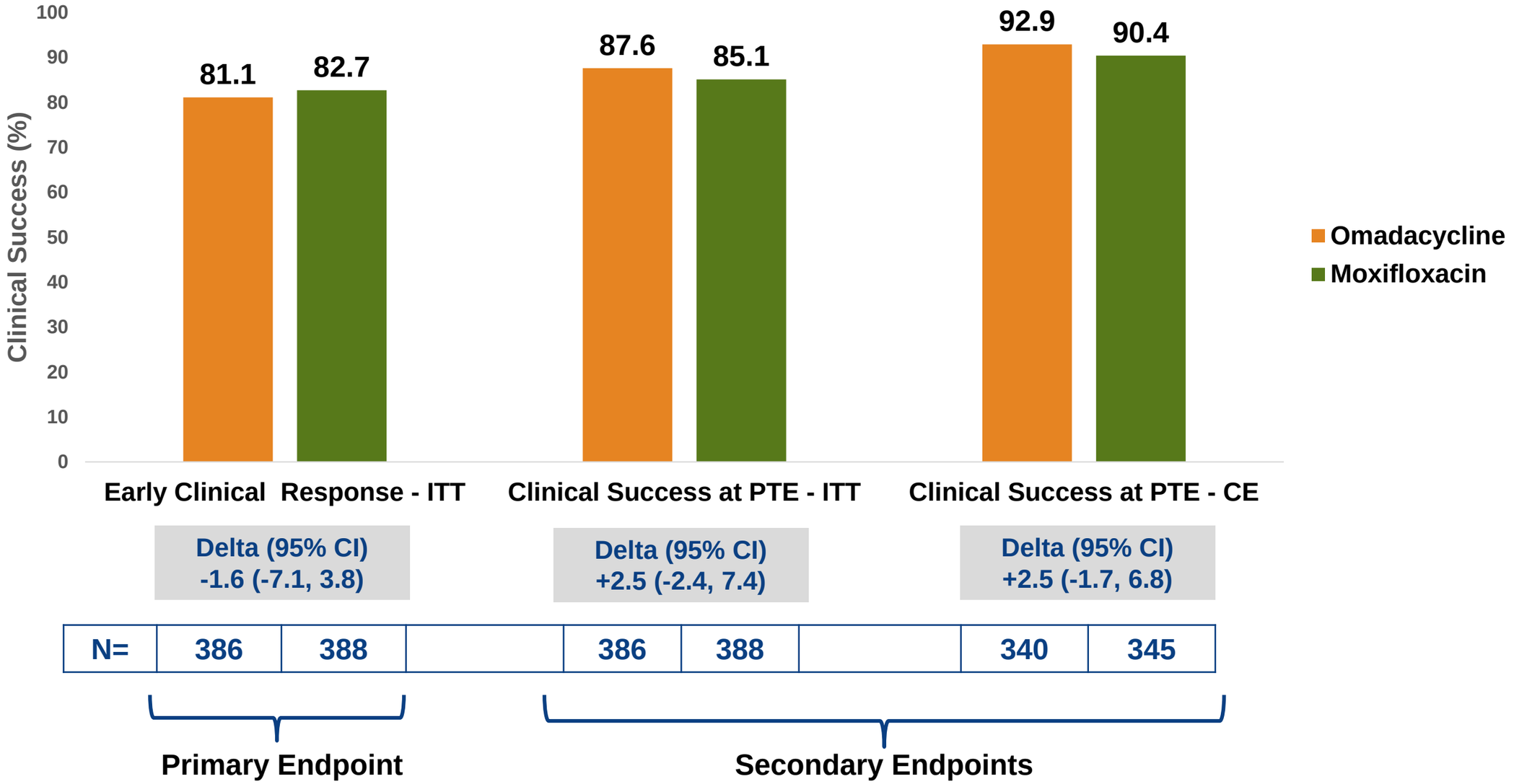

Table 14.2.1.1.1, Table 14.2.2.1.1

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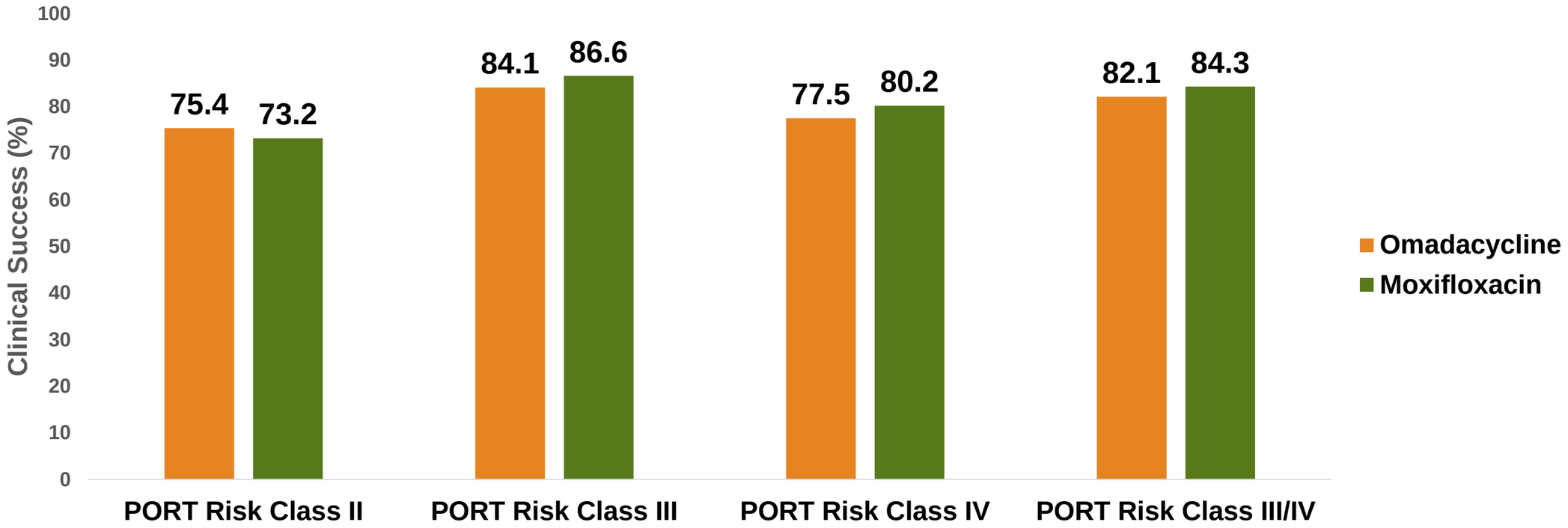
Clinical Response at ECR by PORT Risk Class
ITT Population



N=	57	56		227	216		102	116		329	331

Delta (95% CI)	Delta (95% CI)	Delta (95% CI)	Delta (95% CI)
+2.2 (-14.0, 18.4)	-2.4 (-9.1, 4.2)	-2.7 (-13.8, 8.1)	-2.2 (-8.0, 3.5)

Table 14.2.1.3.1

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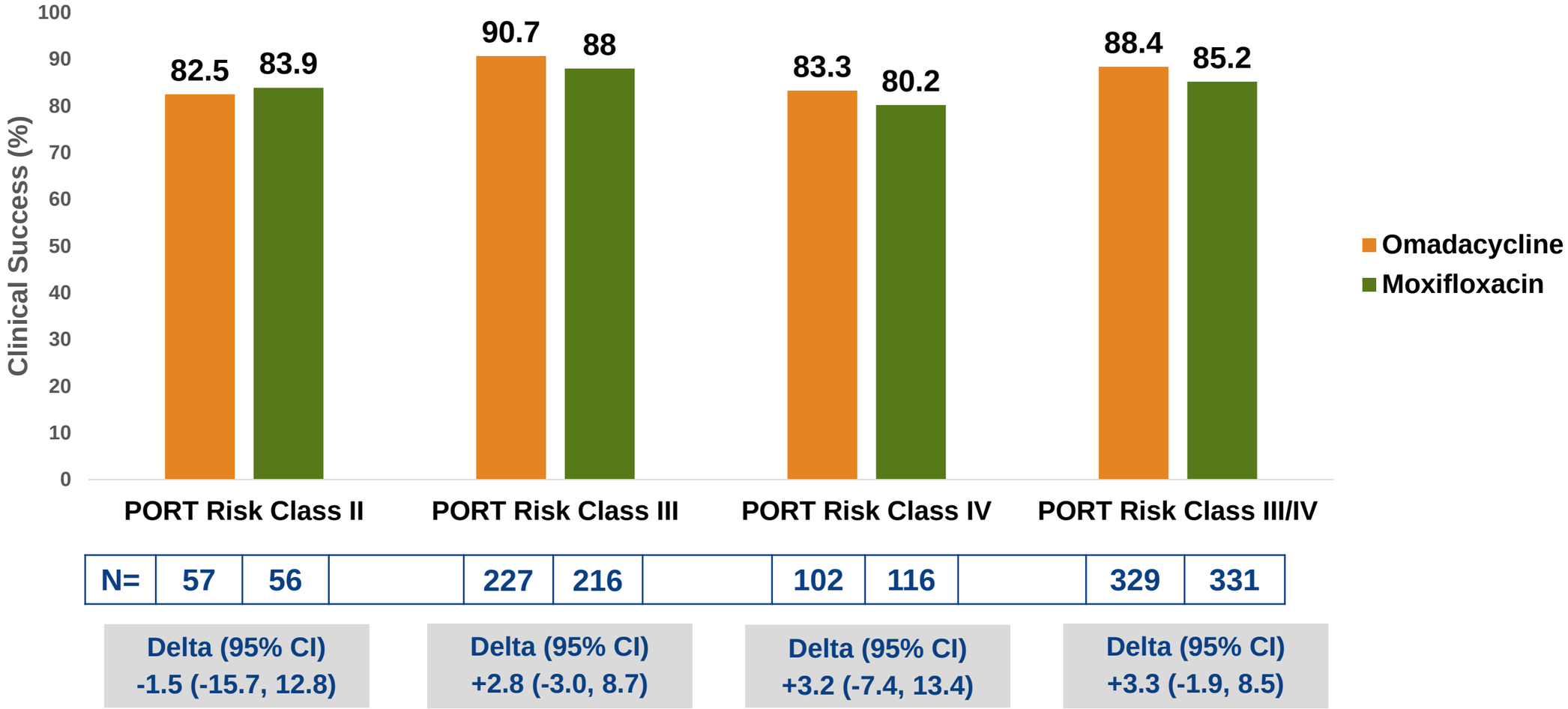
Clinical Response at PTE by PORT Risk Class
ITT Population



N=	57	56		227	216		102	116		329	331

Delta (95% CI)	Delta (95% CI)	Delta (95% CI)	Delta (95% CI)
-1.5 (-15.7, 12.8)	+2.8 (-3.0, 8.7)	+3.2 (-7.4, 13.4)	+3.3 (-1.9, 8.5)

Table 14.2.2.3.1

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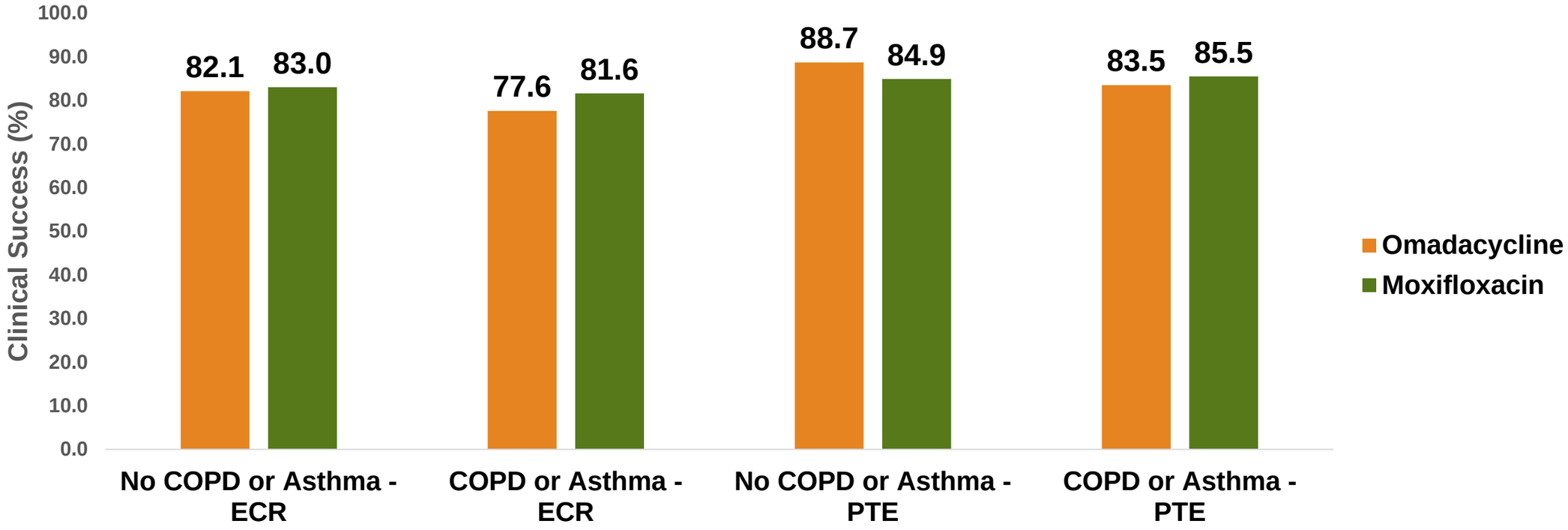
Clinical Response at PTE by Age
ITT Population

	Omadacycline n/N (%)	Moxifloxacin n/N (%)	Difference (95% CI)
Age < 65 - ECR	190/223 (85.2)	177/205 (86.3)	-1.1 (-7.8, 5.6)
Age ≥ 65 - ECR	123/163 (75.5)	144/183 (78.7)	-3.2 (-12.2, 5.6)
Age ≥ 75 - ECR	65/85 (76.5)	68/88 (77.3)	-0.8 (-13.5, 11.8)
Age < 65 - PTE	197/223 (88.3)	176/205 (85.9)	+2.5 (-3.9, 9.0)
Age ≥ 65 - PTE	141/163 (86.5)	154/183 (84.2)	+2.4 (-5.3, 9.9)
Age ≥ 75 - PTE	76/85 (89.4)	72/88 (81.8)	+7.6 (-3.1, 18.4)

Listings 16.2.6.2.1 and 16.2.4.6

Clinical Response by COPD or Asthma[a]
ITT Population



N=	301	312		85	76		301	312		85	76

Delta (95% CI)	Delta (95% CI)	Delta (95% CI)	Delta (95% CI)
-1.0 (-7.0, 5.1)	-3.9 (-16.4, 8.8)	+3.8 (-1.6, 9.2)	-2.0 (-13.4, 9.7)

Table 14.2.1.1.1.IR3, Table 14.2.2.1.1.IR3

[a] defined as asthma, COPD, emphysema, or chronic bronchitis

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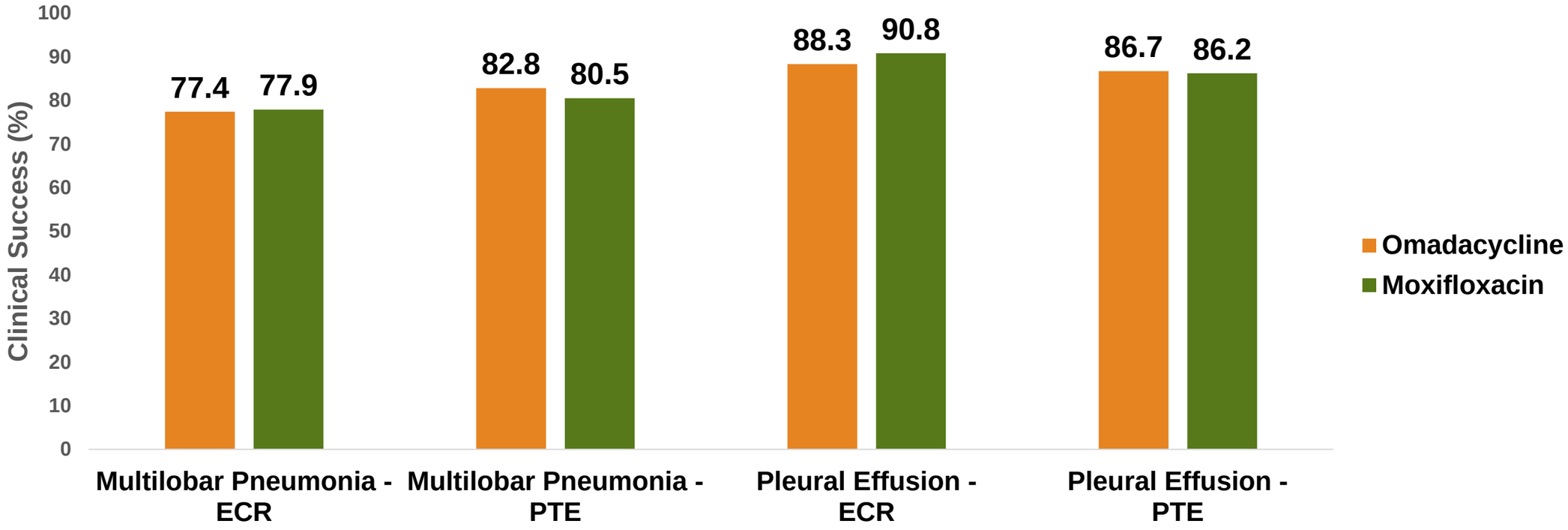
Clinical Response by Radiographic Abnormality
ITT Population



N=	93	113		93	113		60	65		60	65

Delta (95% CI)	Delta (95% CI)	Delta (95% CI)	Delta (95% CI)
-0.5 (-12.2, 10.9)	+2.3 (-8.7, 12.8)	-2.4 (-14.3, 8.9)	+0.5 (-12.3, 13.0)

Table 14.2.1.1.1.IR4, Table 14.2.1.1.1.IR5, Table 14.2.2.1.1.IR4, Table 14.2.2.1.1.IR5M

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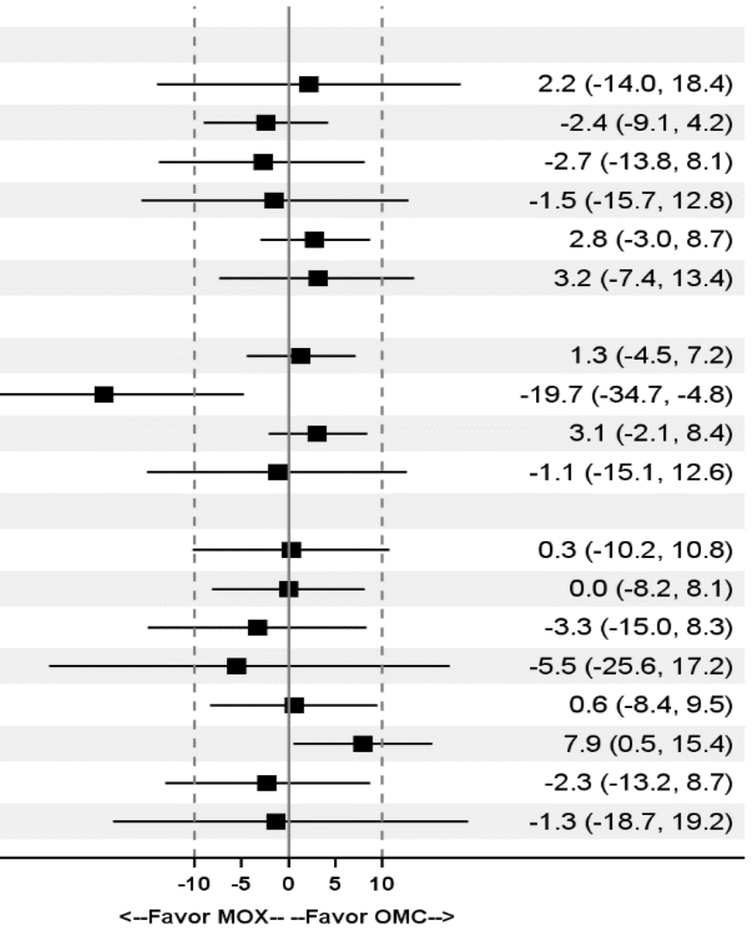
ECR and PTE by Mortality and Severity Scores – ITT Population

Subgroup	Omadacycline *No. of events/total no.(%)*	Moxifloxacin *No. of events/total no.(%)*	Percentage-Point Difference (95% CI)
Actual PORT Risk Class (ITT)			
II- ECR	43/57(75.4)	41/56(73.2)	2.2 (-14.0, 18.4)
III - ECR	191/227(84.1)	187/216(86.6)	-2.4 (-9.1, 4.2)
IV - ECR	79/102(77.5)	93/116(80.2)	-2.7 (-13.8, 8.1)
II - IACR-PTE	47/57(82.5)	47/56(83.9)	-1.5 (-15.7, 12.8)
III - IACR-PTE	206/227(90.7)	190/216(88.0)	2.8 (-3.0, 8.7)
IV - IACR-PTE	85/102(83.3)	93/116(80.2)	3.2 (-7.4, 13.4)
CURB-65 Score (ITT)			
< 2 criteria - ECR	276/333(82.9)	270/331(81.6)	1.3 (-4.5, 7.2)
>=2 criteria - ECR	37/53(69.8)	51/57(89.5)	-19.7 (-34.7, -4.8)
< 2 criteria - IACR-PTE	293/333(88.0)	281/331(84.9)	3.1 (-2.1, 8.4)
>=2 criteria - IACR-PTE	45/53(84.9)	49/57(86.0)	-1.1 (-15.1, 12.6)
SIRS Criteria (ITT)			
Met <2 criteria - ECR	82/98(83.7)	85/102(83.3)	0.3 (-10.2, 10.8)
Met 2 criteria - ECR	127/150(84.7)	138/163(84.7)	0.0 (-8.2, 8.1)
Met 3 criteria - ECR	74/96(77.1)	78/97(80.4)	-3.3 (-15.0, 8.3)
Met 4 criteria - ECR	30/42(71.4)	20/26(76.9)	-5.5 (-25.6, 17.2)
Met <2 criteria - IACR-PTE	88/98(89.8)	91/102(89.2)	0.6 (-8.4, 9.5)
Met 2 criteria - IACR-PTE	137/150(91.3)	136/163(83.4)	7.9 (0.5, 15.4)
Met 3 criteria - IACR-PTE	78/96(81.3)	81/97(83.5)	-2.3 (-13.2, 8.7)
Met 4 criteria - IACR-PTE	35/42(83.3)	22/26(84.6)	-1.3 (-18.7, 19.2)



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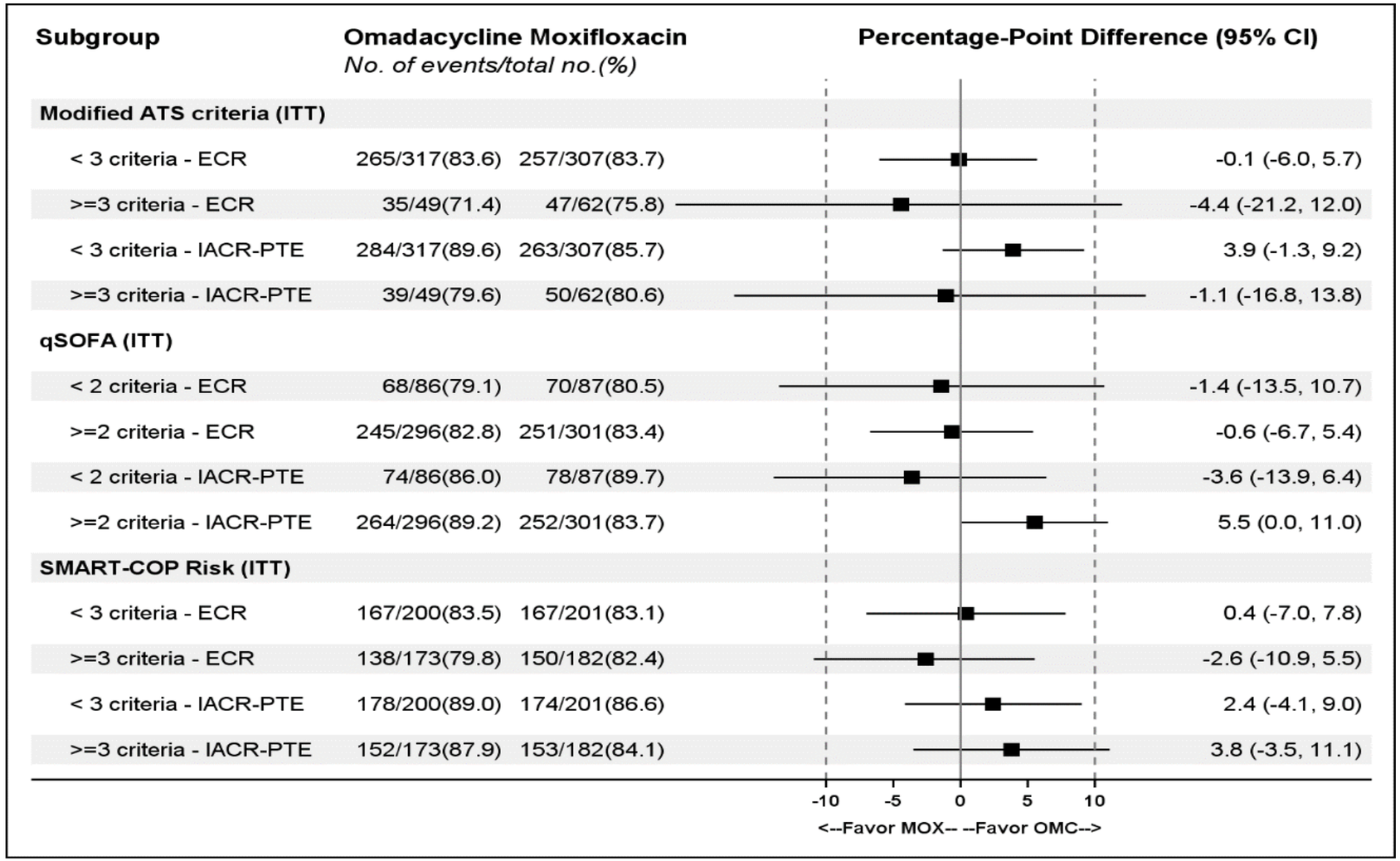
ECR and PTE by Mortality and Severity Scores – ITT Population



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Conclusions

- Regardless of severity of disease (PORT Risk Class), patients with CABP treated with omadacycline or moxifloxacin have comparable success rates at ECR and PTE
- A high percentage of patients in both treatment arms (75 to 80%) reached the FDA endpoint of ECR in each PORT Risk Class.
- Additional analyses in subgroups with higher mortality risk or higher severity are consistent with the PORT Risk Class clinical success at ECR and PTE
- In clinical practice, reaching ECR is likely to translate into an early switch from intravenous to oral antibiotics and early hospital discharge