Omadacycline *p*-Toluenesulfonate Tablets and Injection

For the Treatment of

Acute Bacterial Skin and Skin Structure Infections (ABSSSI) and Community-Acquired Bacterial Pneumonia (CABP)

Erratum to Briefing Document for:

Antimicrobial Drugs Advisory Committee (AMDAC)

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ADVISORY COMMITTEE BRIEFING MATERIALS:
AVAILABLE FOR PUBLIC RELEASE

OVERVIEW OF ERRATUM

Paratek has identified an error in the comparison of individual patient blood urea nitrogen (BUN) values to the CURB-65 BUN criteria due to incorrect unit conversion resulting in CURB-65 mis-classification. In addition, the modified ATS scores are also being updated due to incorrect numbers resulting from the same BUN conversion errors.

The revisions resulting from these changes are shown on the following pages in tracked changes, and these pages should be considered replacement pages for Page 58 to 60 of the Briefing Book dated 01-Jul-2018.

The number and percentage of patients with resolution of all clinical symptoms that were present at Baseline was evaluated for each visit throughout the study. At the PTE visit, a majority of patients had complete resolution with rates that were similar between treatment groups (74.5% omadacycline, 75.4% moxifloxacin). Of the patients who did not have complete resolution of symptoms at the PTE visit, a majority (76.1% omadacycline, 73.3% moxifloxacin) was determined to be clinical successes by the investigators at PTE with residual or minimal clinical symptoms of CABP at PTE that did not require further systemic antimicrobial therapy.

3.5.2.6 Subgroup Analyses

Subgroup analyses of ECR and IACR at the PTE visit were conducted for descriptive purposes by PORT Risk Class, and CURB-65 score (Table 27). Post hoc subgroup analyses of ECR and IACR at the PTE visit were also conducted for descriptive purposes for age, asthma/COPD and smoking status, and modified ATS severity criteria.

PORT Risk Class was a stratification factor for OPTIC and a validated classification schema for estimating risk of mortality. Clinically, it guides site of care decisions. CURB-65 is a similar classification schema with mostly bedside criteria validated and used for similar purposes as the PORT Risk Class. The modified minor ATS criteria (based upon physiological criteria) is a validated screening tool for identifying patients with a higher severity of illness and potential need for increased level of care. These classification schemes were used to categorize patients to analyze efficacy at the ECR and PTE endpoints in patients with a higher risk of mortality or higher severity at baseline.

ECR and IACR at the PTE assessment were similar by PORT Risk Class. Since age is a major component of the PORT Risk Class and a driver of the overall score, efficacy was examined partitioned by age. Among the oldest patients (age ≥ 65 or age ≥ 75 years), similar rates of clinical success were observed between treatment groups at ECR and for IACR at the PTE assessment. Similar results were observed for CURB-65 strata < 2 and ≥ 2.

~~Similar results were observed between different CURB-65 scores, with the exception of patients who had a CURB-65 score of 2, for which a higher percentage of patients in the moxifloxacin group had clinical success compared to omadacycline patients. However, by PTE, omadacycline and moxifloxacin patients had similar efficacy.~~

For the modified ATS minor criteria classification and the SMART-COP which are principally used to assess for severity of CAP, patients with ≥ 3 ATS minor criteria or ≥~~>~~ 3 SMART-COP criteria represent the severe patients. For patients meeting these criteria, clinical success at ECR and PTE are similar between omadacycline and moxifloxacin. SIRS and qSOFA are used to define patients with sepsis criteria. Similar efficacy at ECR and PTE for both treatment groups were observed.

Table 27. Clinical Response at ECR and PTE by Subgroups in OPTIC (ITT Population)

Parameter		Omadacycline	Moxifloxacin	Difference	LCL(95%)	UCL(95%)
Actual PORT Risk Class[a]						
ECR	II	43/57(75.4)	41/56(73.2)	2.2	-14	18.4
	III	191/227(84.1)	187/216(86.6)	-2.4	-9.1	4.2
	IV	79/102(77.5)	93/116(80.2)	-2.7	-13.8	8.1
PTE	II	47/57(82.5)	47/56(83.9)	-1.5	-15.7	12.8
	III	206/227(90.7)	190/216(88.0)	2.8	-3	8.7
	IV	85/102(83.3)	93/116(80.2)	3.2	-7.4	13.4
Age category						
ECR	<65	190/223(85.2)	177/205(86.3)	-1.1	-7.8	5.6
	≥ 65	123/163(75.5)	144/183(78.7)	-3.2	-12.2	5.6
	≥ 75	65/85(76.5)	68/88(77.3)	-0.8	-13.5	11.8
PTE	< 65	197/223(88.3)	176/205(85.9)	2.5	-3.9	9
	≥ 65	141/163(86.5)	154/183(84.2)	2.4	-5.3	9.9
	≥ 75	76/85(89.4)	72/88(81.8)	7.6	-3.1	18.4
No. of Curb-65 Score Criteria						
ECR	< 2	231/275 (84.0) 276/333 (82.9)	214/257 (83.3) 270/331 (81.6)	0.7 1.3	-5.6 -4.5	7.1 2.7
	≥ 2	82/111 (73.9) 37/53 (69.8)	107/131 (81.7) 51/57 (89.5)	-7.8 -19.7	-18.5 -34.7	2.7 -4.8
PTE	< 2	248/275 (90.2) 293/333 (88.0)	220/257 (85.6) 281/331 (84.9)	4.6 3.1	-1.0 -2.1	10.3 8.4
	≥ 2	90/111 (81.1) 45/53 (84.9)	110/131 (84.0) - 49/57 (86.0)	-2.9 -1.1	-12.8 -15.1	6.7 12.6
No. of SIRS Criteria Met						
ECR	< 2	82/98(83.7)	85/102(83.3)	0.3	-10.2	10.8
	= 2	127/150(84.7)	138/163(84.7)	0	-8.2	8.1
	= 3	74/96(77.1)	78/97(80.4)	-3.3	-15	8.3
	= 4	30/42(71.4)	20/26(76.9)	-5.5	-25.6	17.2
PTE	< 2	88/98(89.8)	91/102(89.2)	0.6	-8.4	9.5
	= 2	137/150(91.3)	136/163(83.4)	7.9	0.5	15.4
	= 3	78/96(81.3)	81/97(83.5)	-2.3	-13.2	8.7
	= 4	35/42(83.3)	22/26(84.6)	-1.3	-18.7	19.2
No. of qSOFA Criteria						
ECR	< 2	68/86(79.1)	70/87(80.5)	-1.4	-13.5	10.7
	≥ 2	245/296(82.8)	251/301(83.4)	-0.6	-6.7	5.4
PTE	< 2	74/86(86.0)	78/87(89.7)	-3.6	-13.9	6.4
	≥ 2	264/296(89.2)	252/301(83.7)	5.5	0	11

Table 27. Clinical Response at ECR and PTE by Subgroups in OPTIC (ITT Population)

Parameter		Omadacycline	Moxifloxacin	Difference	LCL(95%)	UCL(95%)
No. of Modified ATS Criteria						
ECR	< 3	271/324(83.6) ~~265/317(83.6)~~	264/317(83.3) ~~257/307(83.7)~~	0.4 ~~0.1~~	-5.4 ~~6~~	6.2 ~~5.7~~
	>= 3	31/44(70.5) ~~35/49(71.4)~~	42/53(79.2) ~~47/62(75.8)~~	-8.8 ~~4.4~~	-26.4 ~~21.2~~	8.5 ~~12~~
PTE	< 3	291/324(89.8) ~~284/317(89.6)~~	271/317(85.5) ~~263/307(85.7)~~	4.3 ~~3.9~~	-0.8 ~~1.3~~	9.5 ~~9.2~~
	≥ 3	34/44(77.3) ~~39/49(79.6)~~	44/53(83) ~~50/62(80.6)~~	-5.7 ~~1.1~~	-22.4 ~~16.8~~	10.2 ~~13.8~~
No. of SMART-COP Risk Criteria						
ECR	< 3	167/200(83.5)	167/201(83.1)	0.4	-7	7.8
	≥ 3	138/173(79.8)	150/182(82.4)	-2.6	-10.9	5.5
PTE	<3	178/200(89.0)	174/201(86.6)	2.4	-4.1	9
	≥ 3	152/173(87.9)	153/182(84.1)	3.8	-3.5	11.1

ATS = American Thoracic Society, ECR = early clinical response, ITT = intent-to-treat, LCL = lower confidence limit, PORT = Pneumonia Outcomes Research Team, PTE = post therapy evaluation, qSOFA = quick sequential organ failure assessment, SIRS = systemic inflammatory response syndrome, UCL = upper confidence limit.

[a] Patients with PORT Risk categories I and V were thought to have a qualified PORT Risk Class of II, III, or IV at enrollment (based on the inclusion criteria), but were later determined to be PORT Risk I or V.

Asthma and/or COPD are common co-morbidities in hospitalized patients with CABP. In addition, asthma/COPD are clinically important co-morbidity demographics associated with a potentially more severe presentation and associated with potentially worse outcomes in CABP patients.[31] Table 28 demonstrates that the presence or absence of Asthma or COPD did not impact overall clinical success rates in these patient populations across all efficacy assessments.

Smoking impairs the mucocilliary apparatus, decreases mucous clearance and pre-disposes patients to pneumonia. Evaluation of smoking status and efficacy is shown in Table 29. Past or present smoking did not impact overall efficacy with clinical success rates that were similar for both omadacycline and moxifloxacin treated patients. High and similar efficacy rates were observed between patients with a smoking history and those who were reported as a non-smoker.