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Safety and Tolerability of IV Omadacycline (OMC) and Tigecycline (TGC) in Healthy Subjects in a Study to Assess Intra-Pulmonary Steady-State Concentrations

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Background: OMC, a first-in-class aminomethylcycline antibiotic, is currently in phase 3 development for the treatment of community-acquired bacterial pneumonia (CABP). Tigecycline, a glycylcycline, is approved for the treatment of CABP. The primary objective of this open-label phase 1 study was to assess intra-pulmonary concentrations of OMC and TGC dosed IV to steady-state in healthy subjects. This is the first clinical study to directly compare IV OMC to IV TGC dosing.

Material/methods: A total of 63 healthy subjects received OMC (n=42, 100 mg IV every 12 h for 2 doses, then 100 mg IV daily) or TGC (n=21, 100 mg IV loading dose, then 50 mg IV every 12 h). Total treatment duration was 4 days. After the last dose, bronchoalveolar lavage (BAL) was performed once per subject for pharmacokinetic analysis. Blood samples for safety hematology and chemistry were collected and a 12-lead ECG was performed prior to dosing and at the study completion visit (1 day following the last dose). Vital signs (body temperature, blood pressure, pulse rate, and respiratory rate) were measured prior to treatment, daily (pre-dose) during treatment and at study completion. In addition, blood pressure, pulse rate and respiratory rate were measured just prior to, 30 min after and 60 min after the BAL procedure. Adverse events were recorded from the signing of informed consent through the final follow-up assessment 7-14 days after the last dose.

Results: The overall incidence and most common (>1 subject in either treatment group) treatment-emergent adverse events (TEAEs) are shown in the table below. All TEAEs were considered mild or moderate in severity.

Preferred Term	Omadacycline (N=42) n (%)	Tigecycline (N=21) n (%)	Overall (N=63) n (%)
Subjects with at Least One TEAE	12 (28.6)	11 (52.4)	23 (36.5)
Headache	5 (11.9)	3 (14.3)	8 (12.7)
Epistaxis	2 (4.8)	2 (9.5)	4 (6.3)
Nausea	1 (2.4)	10 (47.6)	11 (17.5)
Decreased Appetite	0	2 (9.5)	2 (3.2)
Vomiting	0	3 (14.3)	3 (4.8)

There were no serious adverse events reported in either treatment group during the study. Two TGC subjects discontinued study treatment and the study due to adverse events (both nausea which was considered related to study drug). No OMC subjects discontinued study treatment or the study due to adverse events. There were no clinically significant differences between the treatment groups in analyses of laboratory values, ECG parameters, or vital signs.

Conclusions: Over a 4-day treatment period in healthy subjects, IV OMC was associated with fewer gastrointestinal TEAEs than IV TGC.