Pharmacokinetics of CW002, a Novel Neuromuscular Blocking Agent in the Initial Cohorts of a Phase 1 Clinical Trial

J. S. Owen 1, P. M. Heerdt 2, J. K. Malhotra 2, M. T. Murrell 2, N. M. Trepanier 3, C. A. Lien 2
1 Union University, 2 Cornell University, 3 Charles River Laboratories

Purpose
CW002 Injection is a novel intravenously (IV) administered neuromuscular blocking (NMB) agent for use as an adjunct to general anesthesia to facilitate both rapid sequence and routine endotracheal intubation and to provide skeletal muscle relaxation during surgery or mechanical ventilation. Nonclinical pharmacology studies suggest that CW002 will produce profound and rapid NMB. Pharmacokinetic analysis of the first 3 cohorts of this ongoing study has been conducted.

Methods
18 healthy volunteers in 3 initial cohorts of this first-in-man study received doses of 0.04, 0.06, and 0.08 mg/kg CW002. Noncompartmental (NCA) and compartmental PK analysis was performed for 6 subjects in each cohort.

Results
Concentrations in each cohort are seen to decline in a multi-exponential fashion with a very rapid distribution phase followed by slower distribution and elimination phases. Mean (SD) dose-normalized AUC(0-inf) by NCA was 2550 (364), 2577 (582), and 2629 (288) min*ng/mL/mg, across cohorts, respectively. A 3-compartment mammillary model adequately described the individual CW002 PK profiles. Mean (SD) clearance was 295 (62), 336 (105), and 316 (59) mL/min, with Vss of 5.3 (2.8), 6.3 (2.8), and 6.5 (2.5) L, across dose levels, respectively. Mean terminal half-life (26 – 28 minutes) was not different across cohorts.

Conclusion
Three initial cohorts of this ascending dose study suggest the PK of CW002 may be well described by a 3-compartment model with linear elimination properties in this dose range.