28th ECCMID EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES
Madrid, Spain
21 – 24 April 2018

P2212 Interim pharmacokinetic analysis from the SAATELLITE Phase 2 Clinical Trial of Suvratoxumab (MEDI4893), an extended half-life monoclonal antibody against Staphylococcus aureus alpha toxin

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Background: Suvratoxumab (MEDI4893) is an IgG1 monoclonal antibody that specifically binds to and neutralises *Staphylococcus aureus* (*Sa*) alpha toxin (AT). A murine model demonstrated that a serum level of 211 µg/mL, designated to be the target serum exposure in humans, correlated with protection against lethal *Sa* pneumonia. Suvratoxumab has a triple mutation M252Y/S254T/T256E (YTE) that was engineered into the Fc region to extend the terminal half-life. This analysis describes interim pharmacokinetics (PK) from an ongoing SAATELLITE study (NCT02296320): a Phase 2, randomised, double-blind, placebo-controlled study conducted within the Public-Private COMBACTE-NET consortium, in mechanically ventilated (MV) subjects that are colonized with *Sa* and at high-risk for *Sa* pneumonia.

Materials/methods: Subjects were randomised in a 1:1:1 ratio to receive 2000 mg suvratoxumab, 5000 suvratoxumab or placebo as a single intravenous infusion. Serum samples were tested for PK analysis on Days 1 (pre-dose, end of infusion and 8 hours post-dose), 2, 4, 8, 15, 22 and 31 and were also tested for anti-drug antibodies (ADA) to suvratoxumab on Days 1 (pre-dose), 15 and 31. Interim PK analysis was conducted when at least 10 subjects were randomized in each arm and followed through Day 31. An independent Data Monitoring Committee (DMC) reviews the study data on an ongoing basis.

Results: Non-compartmental analysis showed dose-proportional suvratoxumab mean maximum observed serum concentration (C_{max}) of 489 µg/mL (2000 mg) and 1080 µg/mL (5000 mg); area under the concentration-time curve from time 0 to 30 days post-dose (AUC_{0-30}) of 5542 µg*day/mL (2000 mg) and 11925 µg*day/mL (5000 mg); and mean Day 31 serum concentration of 126 µg/mL (2000 mg) and 275 µg/mL (5000 mg). ADA were detected in 3 subjects pre-dose (2 in placebo and 1 in 5000 mg suvratoxumab cohort); no ADA were detected post-dose up to Day 31. ADA had no apparent impact on PK. The DMC has had no concerns with the safety data collected to date.

Conclusions: Single intravenous infusion of 5000 mg suvratoxumab demonstrated dose-proportional concentrations and maintained serum exposure above the target level through Day 31. These results support continued development of suvratoxumab.