INTERIM PHARMACOKINETIC ANALYSIS FROM THE SAATELLITE PHASE 2 CLINICAL TRIAL OF MEDI4893, AN EXTENDED HALF-LIFE MONOCLONAL ANTIBODY AGAINST *STAPHYLOCOCCUS AUREUS* ALPHA TOXIN

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Facts & Figures

Start date January 2014 - End date October 2019

Contributions IMI under grant agreement 115523 resources composed of financial contribution from the European Union Seventh Framework Program (FP7/2007-2013) and EFPIA contributions

IMI funding ..... 20M€

EFPIA in kind (MedImmune) ..... 16.5M€

Total Cost ..... 36.5M€

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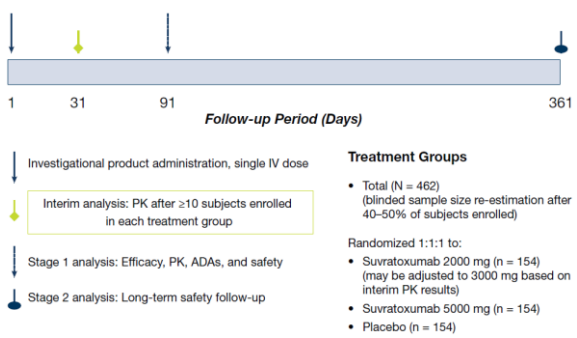
Challenge

- 23 to >60% of ventilator associated pneumonia cases are caused by *Staphylococcus aureus (SA)*
- *SA* is associated with widespread drug resistance
- **Suvratoxumab** (MEDI4893) is a human IgG1κ monoclonal antibody that neutralizes *SA*'s alpha toxin by blocking its binding and preventing oligomerization into its lytic heptameric conformation
- The ongoing phase 2 **SAATELLITE** (A Human Monoclonal antibody Against ***SA*** **A**lpha **T**oxin in M**e**chanica**ll**y Ventil**a**ted Adul**t** Subj**e**cts) trial was designed to evaluate the safety and efficacy of suvratoxumab as immuno-prophylactic in mechanically ventilated subjects colonized and at high risk of *SA* pneumonia (NCT02296320; EudraCT 2014-001097-34)

Here, Interim pharmacokinetic (PK) and antidrug antibody (ADA) data from subjects included are reported

Approach & Methodology



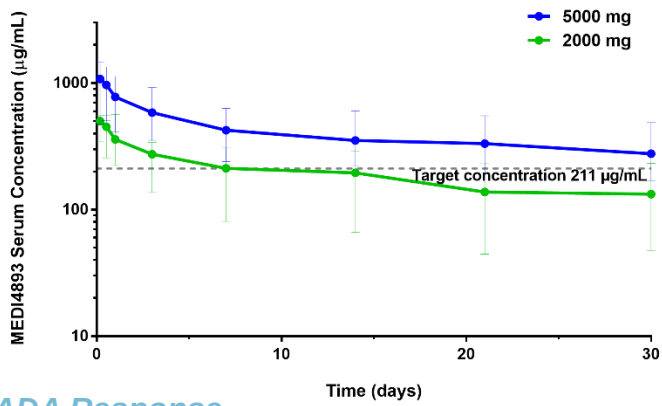
- If the mean serum concentration in the suvratoxumab 2000 mg group was <211µg/ml, dose adjustment to 3000 mg was to be considered
- PK samples were collected on days 1 (predose, end of infusion and 8h postdose) 2, 4, 8, 15, 22 and 31
- ADA samples were collected predose and on day 31

Results

	Suvratoxumab 2000 mg (n=10)	Suvratoxumab 5000 mg (n=10)	Placebo (n=10)
Age, years, mean (SD)	47 (14)	69 (6)	62 (17)
Male, n(%)	7 (70)	5 (50)	5 (50)

PK

Suvratoxumab Dose	C_{max} (µg/mL)	AUC_{0-30d} (day*µg/mL)	C_{30d} (µg/mL)
2000 mg (n=10)	489 ± 76	5542 ± 2095	126 ± 65
5000 mg (n=10)	1080 ± 358	11925 ± 3387	275 ± 100



ADA Response

- Two subjects tested positive for ADAs at predose on day 1 (1 subject receiving suvratoxumab 5000 mg and 1 receiving placebo)
- Two subjects receiving placebo tested positive for ADAs at postdose on day 31; no ADAs were detected postdose in the suvratoxumab-tested cohorts
- ADA response had no clear effect on the PK profile

Safety

To date, the independent data monitoring committee has recommended continuation of the trial without modification

Value of IMI collaboration

All recruiting sites were part of the COMBACTE CLIN-Net and LAB-Net research network.
The academic networking and close collaboration of academic experts on VAP and pre-emptive trials with MedImmune allowed scientific input from the early stages of protocol development. Accompaniment in organizational aspects has facilitated patient recruitment and project follow up

Impact & take home message

A single IV infusion of suvratoxumab 2000 mg or 5000 mg exhibited dose-proportional PK in mechanically ventilated subjects
In subjects who were dosed with suvratoxumab 5000 mg, mean serum exposure was maintained above target level of 211 µg/mL for 30 days
Based on these results, the 2000 mg dose of suvratoxumab was dropped, while the 5000 mg dose continued to be evaluated in the SAATELLITE study

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