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INTERIM PHARMACOKINETIC ANALYSIS FROM THE EVADE PHASE 2 CLINICAL TRIAL OF MEDI3902, A BISPECIFIC MONOCLONAL ANTIBODY AGAINST PCRV AND PSL OF *PSEUDOMONAS AERUGINOSA*

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Facts & Figures

Start date January 2015 - End date October 2020

Contributions IMI under grant agreement 115737-4 resources composed of financial contribution from the European Union Seventh Framework Program (FP7/2007-2013) and EFPIA contributions

IMI funding ..... 18M€

EFPIA in kind (MedImmune) ..... 9M€

Total Cost ..... 27M€

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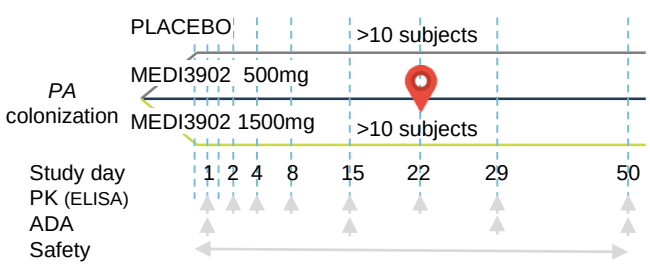
Challenge

- *Pseudomonas aeruginosa (PA)* is a leading cause of ventilator associated pneumonia and often exhibits antibiotic resistance
- **MEDI3902** is a bivalent, bispecific human IgG1κ monoclonal antibody that selectively binds to both PcrV and Psl of *PA,* inhibiting the pathogen's cytotoxicity and promoting opsonophagocytic killing
- The efficacy and safety of MEDI3902 as immuno-prophylactic against *PA* among mechanically ventilated subjects is being evaluated by the ongoing phase 2 **EVADE** (**E**ffort to Pre**v**ent Nosocomi**a**l Pneumonia caused by *Pseu**d**omonas aeruginosa* in Mechanically v**e**ntilated Subjects) trial

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

Approach & Methodology

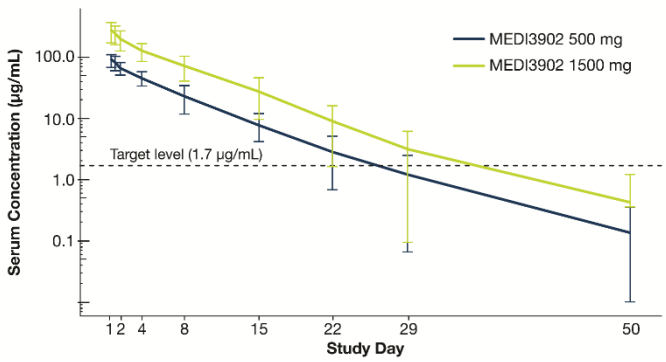


- If the mean serum concentration in the MEDI3902 1500mg group was <1.7µg/ml, dose adjustment to 3000 mg was to be considered

Results

	MEDI3902 (N=32)	
	500mg (n=14)	1500mg (n=18)
Age, years, mean (SD)	64.4 (8.1)	67.1 (13.1)
Female, n(%)	4 (28.6)	4 (22.2)
White, n (%)	14 (100)	18 (100)

PK



MEDI3902 Dose	Subjects with serum concentration > 1.7µg/mL (%)							
	Day 1	Day 2	Day 4	Day 8	Day 15	Day 22	Day 29	Day 50
500mg	100	100	100	92.9	91.7	58.3	33.3	0
1500mg	100	100	94.4	100	100	80	57.1	10

MEDI3902 Dose	Cmax (µg/mL)	AUC (day*µg/mL)	CL (mL/day)	$T_{1/2}$ (days)	Vss (mL)	Vz (mL)
500 mg (n=13)	91 ± 22	495 ±123	1140 ± 611	5.2 ± 2.2	5935 ± 2157	7906 ± 3211
1500 mg (n=17)	274 ± 91	1447 ± 520	1215 ± 580	5.0 ± 2.2	7542 ± 5969	8589 ± 5277

ADA Response

- Two subjects receiving 1500 mg tested positive for ADAs postdose
- Two subjects receiving 500 mg tested positive for ADAs pre and postdose
- One subject receiving placebo tested positive for ADAs at 3 time points
- The false-positive rate was 6.4%
  - Validation false-positive (4.7%)
- 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 are 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

ADA response had no clear effect on the PK profile
A single IV dose of MEDI1500mg maintained a mean serum concentration above the target level of 1.7µg/mL for 22 days postdose
The data monitoring committee recommended continuation of the trial with the MEDI3902 1500mg dose vs. placebo

imi innovative medicines initiative efpia

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