A PHASE I FIRST-IN-HUMAN STUDY IN HEALTHY VOLUNTEERS WITH INTRAVENOUSLY ADMINISTERED OMN6, A NOVEL ANTIMICROBIAL PEPTIDE TARGETING *ACINETOBACTER BAUMANNII*

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INTRODUCTION

- Serious Gram-negative bacterial infections pose a significant global health threat due to an increased antibiotic resistance. There is a critical unmet-need for new antibiotics[2-3]
- ***Acinetobacter baumannii*** *(A. baumannii),* an opportunistic nosocomial Gram-negative bacterium, has been ranked first on the World Health Organization (WHO) Priority Pathogen list as it is an antibiotic-resistant pathogen causing lethal infections in hospitalized patients[1]
- **OMN6 is a novel, biochemically-engineered antimicrobial peptide** with a unique and new mechanism of action (MoA), selective for Gram-negative bacteria with a minimal potential to develop resistance[4-5]. The proposed MoA for OMN6 is that it selectively attaches to bacterial membranes, creates pores and promotes lysis and cell death (Figure 1)
- OMN6 is intended for the treatment of **severe infections** involving *A. baumannii,* including carbapenem-resistant *A. baumannii* (CRAB) and multi-drug-resistant (MDR) *A. baumannii*

FIGURE 1A:
OMN6 Structure

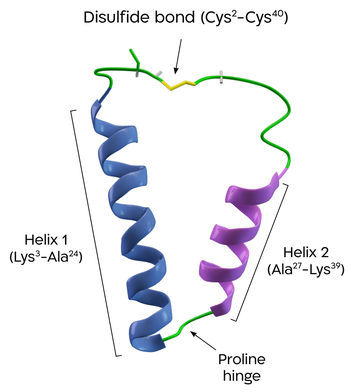
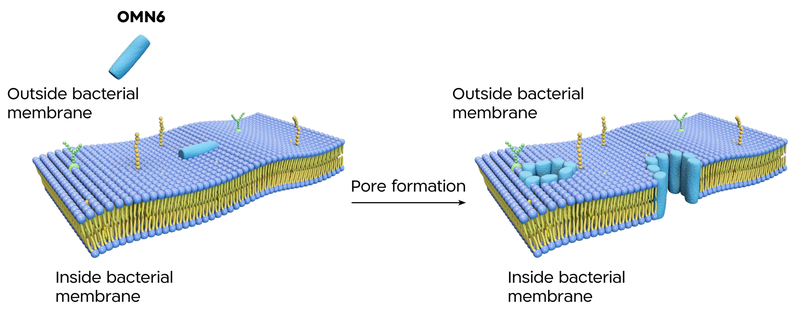


FIGURE 1B:
Illustration of the suggested MoA of OMN6



METHODS

- The First in Human (FIH) Phase 1 OMN6 clinical trial was a single-center, double-blind, placebo-controlled, randomized, single ascending total daily dose study
- Nine ascending total daily doses were tested in 9 cohorts of 8 subjects each, aged 18 to 59, with a randomized 3:1 active to placebo (0.9% Saline solution) ratio among healthy male and female adult volunteers
- Subjects received daily doses ranging from 7.5 to 300 mg OMN6 as 3-hour infusion with a 5 hours wash-out period between subsequent infusions (Q8h). Cohorts 1 to 5 received a single 3-hour intravenous (IV) infusion, cohorts 6-7 received two 3-hour IV infusions, and cohorts 8-9 received three 3-hour IV infusions (Figure 2)
- Safety and tolerability assessments, and pharmacokinetic (PK) blood sampling occurred at pre-defined timepoints. All blood samples for the PK evaluation were analyzed with a validated LC/MS/MS assay. All safety, tolerability and PK results were descriptively analyzed

STUDY OBJECTIVES

- Primary objective: Safety and tolerability of IV doses of OMN6
- Secondary objective: Plasma PK following IV doses of OMN6

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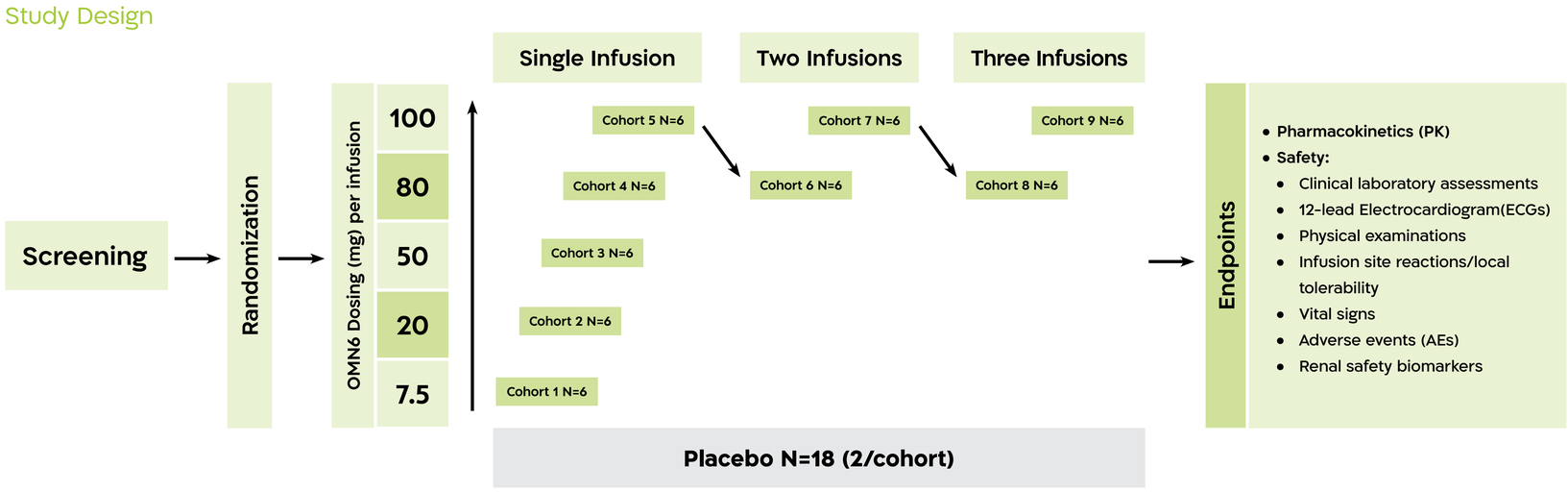
FIGURE 2:
Study Design



RESULTS

- A total of **72 healthy participants** were screened
- All study participants completed the study per protocol with no major protocol deviations, and with no premature drop-outs

Baseline Characteristics

- The study population consisted of healthy young male and female adult volunteers between 18-59 years old (mean age varied from 22.0 to 28.7 years old within OMN6 dosing cohorts)
- In each cohort, at least 2 subjects were male and at least 2 subjects were female

Primary Objective: Safety and Tolerability of IV Doses of OMN6

TABLE 1:
Summary of Treatment-Emergent Adverse Events (TEAEs)

AEs, N of subjects		Cohort 1 7.5 mg/day N = 6	Cohort 2 20 mg/day N = 6	Cohort 3 50 mg/day N = 6	Cohort 4 80 mg/day N = 6	Cohort 5 100 mg/day N = 6	Cohort 6 160 mg/day N = 6	Cohort 7 200 mg/day N = 6	Cohort 8 150 mg/day N = 6	Cohort 9 300 mg/day N = 6	Pooled Placebo N = 18
Subjects with Any TEAE		0	1	5	4	3	3	4	4	3	6
Subjects with Any Drug-Related TEAE		0	1	4	4	0	0	3	2	1	4
Any Drug-Related TEAE Intensity	Mild	0	1	4	4	0	0	3	2	1	4
	Moderate	0	0	0	0	0	0	0	0	0	0
	Severe	0	0	0	0	0	0	0	0	0	0
Outcome	Recovered	0	1	5	4	3	3	4	4	3	6

TABLE 2:
Incidence of Drug-Related Treatment-Emergent Adverse Events (TEAEs)

Drug-related AEs, N of subjects	Cohort 1 7.5 mg/day N = 6	Cohort 2 20 mg/day N = 6	Cohort 3 50 mg/day N = 6	Cohort 4 80 mg/day N = 6	Cohort 5 100 mg/day N = 6	Cohort 6 160 mg/day N = 6	Cohort 7 200 mg/day N = 6	Cohort 8 150 mg/day N = 6	Cohort 9 300 mg/day N = 6	Pooled Placebo N = 18
Abdominal pain	0	0	0	0	0	0	1	0	0	0
Chest discomfort	0	0	1	1	0	0	1	0	0	0
Dizziness	0	1	0	1	0	0	0	0	0	0
Dysaesthesia	0	0	0	0	0	0	0	0	0	1
Epistaxis	0	0	1	0	0	0	0	0	0	0
Feeling hot	0	0	0	0	0	0	0	0	1	0
Headache	0	0	2	3	0	0	2	2	0	3
Injection site reaction	0	0	0	0	0	0	0	0	0	0
Malaise	0	0	1	0	0	0	0	0	0	0
Myalgia	0	0	0	0	0	0	0	0	0	1
Nausea	0	0	0	1	0	0	0	0	0	0
Ocular hyperaemia	0	0	1	0	0	0	0	0	0	0

- **No serious AEs (SAEs) were reported in the study**
- All mean values for safety parameters; vital signs, ECG, safety labs in blood and urine, physical examinations and local tolerability; were within normal limits
- **All drug-related treatment-emergent AEs (TEAEs) were of mild intensity**
- All AEs resolved within the study, and exhibited no dose or time dependent effect

Secondary Objective: Plasma PK Following IV Doses of OMN6

FIGURE 3:
Mean Concentration of Single and Multiple Infusions within 24 hours (Q8h)

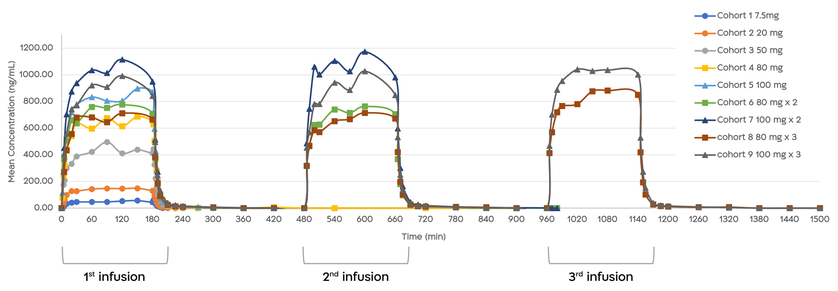
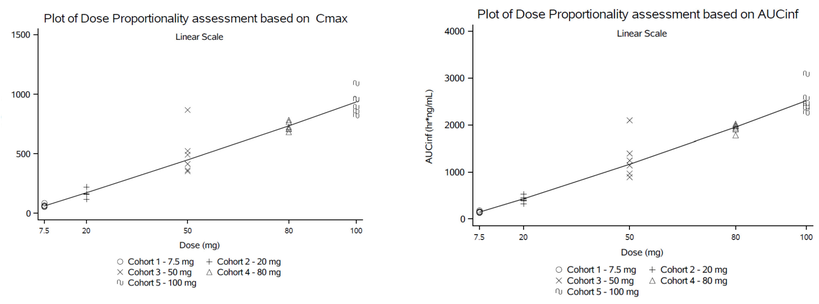


TABLE 3:
PK Parameters of Single Infusion Cohorts

Mean (SD)	Cohort 1 7.5 mg x 1 N = 6	Cohort 2 20 mg x 1 N = 6	Cohort 3 50 mg x 1 N = 6	Cohort 4 80 mg x 1 N = 6	Cohort 5 100 mg x 1 N = 6
AUC_{inf} (h*ng/mL)	147 (15)	416 (70)	1289 (437)	1937 (85)	2529 (296)
C_{max} (ng/mL)	64 (11)	163 (33)	502 (192)	729 (39)	931 (96)
$T_{1/2}$ (h)	0.08 (0.02)	0.09 (0.04)	0.3 (0.28)	0.94 (0.72)	0.83 (0.39)
CL (L/h)	11.01 (4.7)	6.91 (2.24)	7.86 (2.96)	8.43 (2.26)	9.14 (3.11)

FIGURE 4:
Dose Proportionality Assessments based on C_{max} and AUC_{inf}



- Within the single infusion cohorts, mean C_{max} results demonstrated dose proportionality
- For AUC_{inf}, near dose-proportionality was demonstrated
- The model parameter R-squared for C_{max} and AUC_{inf} was comparable (0.97 and 0.98, respectively)

TABLE 4:
PK Parameters of Multiple infusions Cohorts

Mean (SD)	Cohort 6 80 mg x 2 N = 6		Cohort 7 100 mg x 2 N = 6		Cohort 8 80 mg x 3 N = 6			Cohort 9 100 mg x 3 N = 6		
# Infusion	1st	2nd	1st	2nd	1st	2nd	3rd	1st	2nd	3rd
AUC_{inf} (h*ng/mL)	2210 (442)	2160 (417)	3081 (656)	3267 (1061)	2094 (448)	2043 (391)	2526 (494)	2701 (561)	2771 (447)	3076 (452)
C_{max} (ng/mL)	816 (176)	784 (148)	1155 (211)	1209 (423)	796 (155)	740 (140)	932 (195)	1056 (238)	1079 (247.84)	1131 (182)
$T_{1/2}$ (h)	0.44 (0.31)	0.86 (0.42)	1.42 (1.09)	1.36 (0.59)	0.46 (0.35)	0.53 (0.38)	0.79 (0.35)	0.72 (0.19)	1.29 (0.48)	1.21 (0.11)
CL (L/h)	6.33 (2.01)	7.26 (0.91)	6.75 (2.64)	6.28 (1.50)	6.83 (2.06)	7.28 (2.14)	5.96 (0.55)	7.54 (1.77)	8.34 (2.91)	6.63 (1.45)

- There are no indications of an accumulation of OMN6 upon two or three infusion periods, with a wash-out period of 5 hours between them
- There are no indications that the PK behavior of OMN6 is affected by the number of infusions
- There are no indications of a gender dependent effect on the PK of OMN6

CONCLUSIONS

- The novel biochemically-engineered antimicrobial peptide, OMN6, has a favorable safety, tolerability, and pharmacokinetic profile in healthy volunteers, up to a maximum total daily dose of 300 mg
- Pharmacokinetics parameters of OMN6 were linear across the administrated dose range
- Taken together with the efficacy data demonstrated in pre-clinical models[5], the results support further clinical development of OMN6 as a potential therapeutic option for life-threatening infections involved with *A. baumannii*

Acknowledgments

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References

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Abbreviations

Acinetobacter baumannii (A. baumannii); World Health Organization (WHO), Mechanism of action (MoA); Multi-drug-resistant (MDR); Carbapenem-resistant *A. baumannii* (CRAB); First in Human (FIH); Intravenous (IV); Pharmacokinetics (PK); Electrocardiogram (ECG); Adverse events (AEs); Treatment-emergent adverse event (TEAE); Serious AEs (SAEs); Max plasma concentration (C_{max}); Area under the curve from zero to infinity (AUC_{inf}).

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