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A PHASE I FIRST-IN-HUMAN STUDY TO EVALUATE THE SAFETY AND PHARMACOKINETIC (PK) PROPERTIES OF THE INTRAVENOUSLY (IV) ADMINISTERED OMN6, A NOVEL ANTIMICROBIAL PEPTIDE TARGETING *ACINETOBACTER BAUMANNII (A. BAUMANNII)*, IN ADULTS INCLUDING OLDER HEALTHY VOLUNTEERS (HVs) SUBJECTS

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BACKGROUND

- ***Acinetobacter baumannii (A. baumannii)*** is an opportunistic Gram-negative pathogen that is listed as of critical priority on the World Health Organization (WHO) Priority Pathogen list.[1]
- Carbapenem-resistant *A. baumannii* resistance, virulence, its of because challenge, global significant a pose (CRAB) and limited treatment options, leading to **severe nosocomial infections.**[2]
- Given the accelerating pace of global population aging, the burden of diseases including CRAB infections is increasingly falling on **older adults** in intensive care units, with alarmingly high mortality rates.[1,2]
- Due to both elevated mortality rates associated with *A. baumannii* and the lack of effective treatments in older adults, there is a **critical unmet need** to develop new effective and safe anti-infectives.[3]
- OMN6 is a **novel, biochemically-engineered antimicrobial peptide,** with a unique mechanism of action, which is being developed for the treatment of severe *A. baumannii* infections including CRAB.[4,5]

METHODS

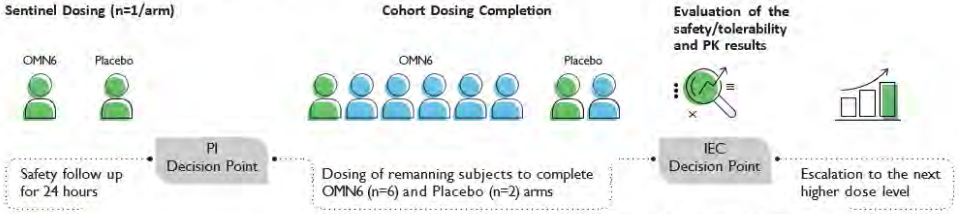
- The **First in Human Phase 1** OMN6 clinical trial was a single Phase I unite center, double-blind, placebo-controlled, randomized, single ascending total daily dose study, conducted in healthy volunteers.
- Five single ascending total daily doses were tested; **5 cohorts adults aged 18-59, and 1 cohort of older adults aged ≥60.** Adults aged 18-59 received doses ranging from **7.5 mg to 100 mg OMN6 as a 3-hour single IV infusion,** while 50 mg was administered to both adults and older adults (Table 1).
- **Safety and tolerability assessments, and pharmacokinetic (PK)** blood sampling occurred at pre-defined timepoints. All blood samples for PK evaluation were analyzed with a validated LC/MS/MS assay.
- PK parameters of 50 mg OMN6 in **adults and older adults were compared.**

TABLE 1:
Single Infusion Dose Escalation Cohorts

Single Infusion Cohorts	
Adults (18-59 years)	7.5 mg OMN6 (n=6) or placebo (n=2)
	20 mg OMN6 (n=6) or placebo (n=2)
	50 mg OMN6 (n=6) or placebo (n=2)
	80 mg OMN6 (n=6) or placebo (n=2)
	100 mg OMN6 (n=6) or placebo (n=2)
Older Adults (≥60 years)	50 mg OMN6 (n=6) or placebo (n=2)

STUDY DESIGN

FIGURE 1: Single Infusion Study Design



Abbreviations: independent ethics committee (IEC), Pharmacokinetics (PK), Principal Investigator (PI)

Study Endpoints:

Primary: To evaluate the safety and tolerability of single ascending IV doses of OMN6 in healthy adults and older adults.

Secondary: To evaluate OMN6 PK in plasma following single ascending IV doses of OMN6 in healthy adults and older adults.

RESULTS

Baseline Characteristics

- All cohorts consisted of **8 healthy subjects** (6 active, 2 placebo). In each cohort, at least 2 subjects were male and at least 2 subjects were female.
- **Mean age** of adults cohorts ranged between **22.0 to 28.7 years,** while the mean age of the older adults cohort was **66.3 years.**
- Demographic and baseline characteristics between the OMN6 and placebo cohorts within both adults and older adults were **similar** (Table 2).

Safety

- **No serious adverse events** (SAEs) were reported in either adults or older adults and all dose levels were considered safe and well tolerated.
- All Treatment-Emergent Adverse Events (TEAEs) recorded within the single infusion cohorts were mild, and **completely recovered** (Table 3). The TEAEs that occurred in more than 5% of the subjects are presented in Table 4.
- Among these TEAEs, drug-related TEAEs that were reported by more than 1 subject were **headache and dizziness.**
- All safety parameters; vital signs, ECG, safety labs in blood and urine, physical examinations and local tolerability, were within **normal limits** with no change from baseline.
- The tolerability of OMN6 was **similar between the age cohorts.**

TABLE 2:
Baseline Characteristics of Adults and Older Adults Cohorts

	Adults (18-59 years)					Older Adults (≥60 years)	Pooled Placebo
OMN6 dose (mg)	7.5 mg	20 mg	50 mg	80 mg	100 mg	50 mg	
Number of Subjects	6	6	6	6	6	6	12
Age (years), Mean (SD)	28.7 (7.99)	22.0 (1.79)	23.3 (2.34)	26.5 (7.82)	28.5 (8.29)	66.3 (4.13)	32.4 (19.18)
Females (%)	2 (33.33 %)	2 (33.33 %)	4 (66.67 %)	3 (50 %)	4 (66.67 %)	2 (33.33 %)	5 (41.67 %)
Height (cm), Mean (SD)	178.92 (7.119)	175.48 (10.240)	171.72 (13.491)	181.40 (10.692)	175.88 (8.694)	173.12 (6.760)	175.83 (7.551)
Weight (Kg), Mean (SD)	75.08 (8.047)	68.05 (10.382)	65.52 (8.059)	75.63 (7.415)	77.43 (11.056)	72.95 (6.168)	72.18 (9.823)
BMI (kg/m²), Mean (SD)	23.42 (1.620)	22.00 (1.747)	22.28 (2.560)	23.00 (1.566)	24.92 (1.308)	24.37 (2.285)	23.28 (1.885)

TABLE 3:
Summary of Treatment-Emergent Adverse Events (TEAEs)

		Adults (18-59 years)					Older Adults (≥60 years)	Pooled Placebo
OMN6 dose (mg)		7.5 mg	20 mg	50 mg	80 mg	100 mg	50 mg	
Number of Subjects		6	6	6	6	6	6	12
Any TEAE (n of subjects)		0	1	5	4	3	2	6
Any Drug-Related TEAE (n of subjects)		0	1	4	4	0	1	3
Any TEAE Intensity (n of subjects)	Mild	0	1	5	4	3	2	6
	Moderate	0	0	0	0	0	0	0
	Severe	0	0	0	0	0	0	0
Outcome (n of subjects)	Recovered	0	1	5	4	3	2	6

TABLE 4:
Incidence of Treatment-Emergent Adverse Events (TEAEs) (Preferred Term Over 5%)

		Adults (18-59 years)					Older Adults (≥60 years)	Pooled Placebo
OMN6 dose (mg)		7.5 mg	20 mg	50 mg	80 mg	100 mg	50 mg	
Number of Subjects		6	6	6	6	6	6	12
Number of Subjects with TEAE (%*)	Headache	0 (0)	0 (0)	2 (33.33)	3 (50)	0 (0)	0 (0)	3 (25.00)
	QTcF(D-DP)**	0 (0)	0 (0)	1 (16.67)	1 (16.67)	1 (16.67)	0 (0)	0 (0)
	Dizziness	0 (0)	1 (16.67)	0 (0)	1 (16.67)	0 (0)	1 (16.67)	0 (0)
	Fatigue**	0 (0)	0 (0)	0 (0)	0 (0)	1 (16.67)	2 (33.33)	0 (0)

Preferred term according to Medical Dictionary for Regulatory Activities (MedDRA) Version 25.1
* The TEAE incidence rate is defined as: 100% * The number of subjects with event / The number of subjects in the cohort
**Not a drug-related TEAE

Acknowledgments

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Abbreviations

Acinetobacter baumannii (A. baumannii), Area under the curve from zero to infinity ($AUC_{0-\infty}$), Carbapenem-resistant Acinetobacter baumannii (CRAB), Clearance (CL), Max plasma concentration (C_{max}), Healthy volunteer (HV), Independent ethics committee (IEC), Intravenous (IV), Pharmacokinetic (PK), Principal Investigator (PI), Serious adverse events (SAE), Terminal elimination half-life ($T_{1/2}$), Treatment-emergent adverse event (TEAE), Volume of distribution at steady state (Vss), World Health Organization (WHO).

References

1. WHO Bacterial Priority Pathogens List, 2024
2. Lansbaill C. et al. Front Immunol. 2022; 13:911414.
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Pharmacokinetics

- Upon a single infusion administration, mean **PK** results demonstrated dose-proportionality for C_{max} and near dose-proportionality for **AUC_{inf}.**
- The OMN6 **PK profiles in adults and older adults** at the 50 mg dose indicated **a similar pattern** (Figure 2).
- The mean AUC_{inf} and C_{max} for adults and older adults, were 1289 and 1211 h*ng/mL; and 502 and 470 ng/mL, respectively (Table 5).

FIGURE 2:
Mean OMN6 Plasma Concentration in Adults (18-59 years) and Older (≥60 years) Following Single Infusion of 50 mg OMN6

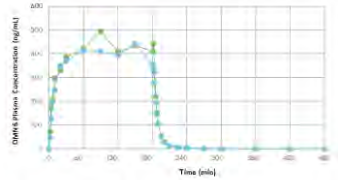

TABLE 5:
Pharmacokinetics Parameters of Adults and Older Adults Cohorts

Mean (SD)	Adults (18-59 years)					Older Adults (≥60 years)
OMN6 dose (mg)	7.5 mg	20 mg	50 mg	80 mg	100 mg	50 mg
Number of Subjects	6	6	6	6	6	6
AUC_{inf} (h*ng/mL)	147 (15)	416 (70)	1289 (437)	1937 (85)	2529 (296)	1211 (301)
C_{max} (ng/mL)	64 (11)	163 (33)	502 (192)	729 (39)	931 (96)	470 (141)
$T_{1/2}$ (h)	0.08 (0.02)	0.09 (0.04)	0.3 (0.28)	0.94 (0.72)	0.83 (0.39)	0.25 (0.10)
Vss (L)	11.01 (4.07)	6.91 (2.24)	7.86 (2.96)	8.43 (2.26)	9.14 (3.11)	7.74 (2.87)
CL (L/h)	51.55 (4.82)	49.15 (8.23)	41.92 (11.58)	41.37 (1.91)	39.94 (4.15)	43.67 (11.79)

CONCLUSIONS

- OMN6 is a **novel biochemically-engineered antimicrobial peptide,** that is being developed for the treatment of **severe *A. baumannii* infections** including CRAB.
- OMN6 had a **favorable safety and tolerability profile** with no SAEs in adults aged 18-59 and **older adults** aged 60 ≥years.
- **A dose response** was demonstrated for OMN6 doses in the single infusion cohorts.
- The PK behavior of OMN6 **was not affected by the age of the subjects.**
- The positive results obtained across the different age range **support advancing OMN6 to Phase 2** clinical trials.
- Taken together, the safety/tolerability and PK results and from Phase I clinical trial suggest that OMN product infective-anti major a be will approved, once ,6 of lives save will which**both adults and older adults patients.**

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