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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* (CRAB) pose a significant global challenge, because of its virulence, resistance, and limited treatment options, leading to **severe nosocomial infections[1].**
- 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

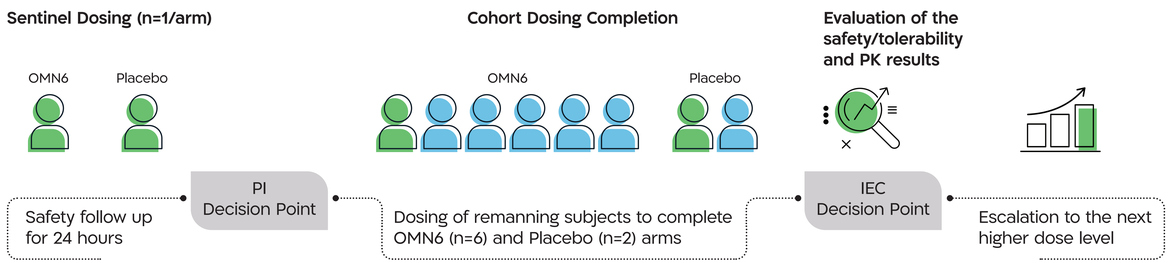
- The **First in Human Phase 1** OMN6 clinical trial was a single Phase 1 unite center, double-blind, placebo-controlled, randomized, single ascending total daily dose study, conducted in healthy volunteers.
- Five single ascending total daily doses were tested; **5 cohorts adults aged 18-59, and 1 cohort 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) |
| **Female (%)** | 2 (33.33 %) | 2 (33.33 %) | 4 (66.67 %) | 3 (50 %) | 4 (66.67 %) | 2 (33.33 %) | 5 (41.67 %) |
| **Hight (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 (8.859) | 75.63 (7.415) | 77.43 (11.056) | 72.95 (6.168) | 72.18 (9.823) |
| **BMI (Kg/m$^2$), 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 (1.883) |

**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) |
| | **COVID-19**** | 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

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**Abbreviations**

*Acinetobacter baumannii* (*A. baumannii*), Area under the curve from zero to infinity ($AUC_{inf}$), Carbapenem-resistant Acinetobacter baumannii (CRAB), Clearance (CL), Max plasma concentration ($C_{max}$), Healthy volunteer (HV), Independent ethics committee (IEC), Intravenously (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. Loretelli C, et al. Front Immunol. 2020;11:601614.
3. Tacconelli E et al., Lancet Infect Dis. (2018), 18(3):318-327.
4. Mandel S, et al. Sci Rep. (2021), 11(1):6403.
5. Michaeli J, et al. Antibiotics (2022), 11(9):1201.

### 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

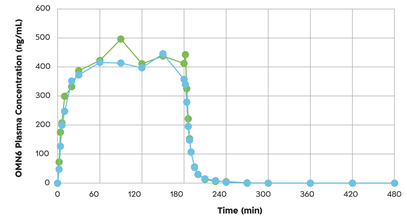


**TABLE 5:**
Pharmacokinetics Parameters of Adults and Older Adults Cohorts

| 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 1 clinical trial suggest that OMN6, once approved, will be a major anti-infective product which will save lives of **both adults and older adults patients.**

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