ECCMID 2023 | Poster #P2173

In vitro Activity of Novel Compound RG6006 Against Clinical Isolates of *Acinetobacter baumannii-calcoaceticus* complex in the Presence of 20% Human Serum

Dee Shortridge[1], Paul Rhomberg[1], Michael Huband[1], Mariana Castanheira[1], Séverine Louvel[2], Claudia Zampaloni[2].

[1]JMI Laboratories, North Liberty, Iowa, USA; [2]Roche Pharma Research and Early Development, Immunology, Infectious Diseases and Ophthalmology, Roche Innovation Center Basel, F. Hoffmann-La Roche Ltd, Grenzacherstrasse 124, 4070 Basel, Switzerland.

Introduction

- RG6006 is the first representative of a novel class of tethered macrocyclic peptide antibiotics active against *Acinetobacter* spp., including carbapenem-resistant *Acinetobacter baumannii-calcoaceticus* complex (ABC) organisms.
- ABC is often multidrug-resistant, presenting serious treatment challenges.
- In this study, we determined the *in vitro* activity of RG6006 against 100 isolates of ABC: 59 clinical isolates from the 2015–2018 SENTRY Antimicrobial Surveillance program and 41 isolates from the CDC Antimicrobial Resistance Bank.

Materials and Methods

- Clinical ABC isolates were collected from hospitalized patients in 50 medical centres from 26 countries.
- Susceptibility testing was performed using broth microdilution with cation-adjusted Mueller-Hinton broth (CAMHB) for the comparators colistin and meropenem.
  - The comparator breakpoints used CLSI/EUCAST (2022) criteria.
- RG6006 minimum inhibitory concentrations (MIC) and minimum bactericidal concentrations (MBC) were determined in CAMHB + 20% pooled human serum, both non-heat inactivated and heat-inactivated.

Results

- MIC distributions for RG6006 and its comparators plus MBC distributions for RG6006 for all isolates are shown in Table 1 and Figure 1.
- Isolates were mostly carbapenem-resistant, with 73% resistant to meropenem (CLSI/EUCAST). Susceptibility to colistin was 84.0% (EUCAST).
- MIC and MBC distributions for RG6006 and comparators against meropenem-resistant ABC are shown in Table 2, and colistin resistant isolates are shown in Table 3.
- RG6006 activity was not affected by colistin or meropenem resistance (Tables 2 and 3).
- RG6006 was active against ABC isolates, with $MIC_{50/90}$ values of 0.5/1 mg/L in both non-heat inactivated and heat-inactivated serum.
- 93% of isolates were inhibited by ≤1 mg/L, with an MIC range of ≤0.015–4 mg/L.
- The $MBC_{50/90}$ values of RG6006 were 1/4 mg/L in both non-heat inactivated and heat-inactivated serum.

Conclusions

- RG6006 tested in the presence of 20% human serum showed potent activity against a challenging set of ABC, including meropenem-resistant and colistin-resistant isolates.
- Activity was similar in non-heat inactivated serum compared to heat-inactivated serum, indicating that human complement does not contribute to compound activity.
- Accordingly, these *in vitro* results support the development of RG6006 as a treatment for infections caused by ABC, including carbapenem-resistant ABC.

Acknowledgements

This project has been funded in whole or in part with Federal funds from the Department of Health and Human Services; Administration for Strategic Preparedness and Response; Biomedical Advanced Research and Development Authority, under OT number: HHS0100201600038C.

Table 1. Antimicrobial activity of RG6006 in various media, with comparators colistin, and meropenem tested against *Acinetobacter baumannii-calcoaceticus* complex isolates

References

1. CLSI. M26-A, Methods for determining bactericidal activity of antimicrobial agents; approved guideline. Wayne, PA, Clinical and Laboratory Standards Institute, 1999.
2. CLSI. M07Ed11. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard: eleventh edition. Wayne, PA, Clinical and Laboratory Standards Institute, 2018.
3. CLSI. M100Ed32. Performance standards for antimicrobial susceptibility testing: 29th informational supplement. Wayne, PA, Clinical and Laboratory Standards Institute, 2022.
4. European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters Version 12.0, 2022.