Disclosures. All authors: No reported disclosures.

734. Modeling the Pharmacokinetics and Pharmacodynamics of Intravenous and Oral Omacystacine with and without a Loading Dose
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Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
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Background. Omacystacine (OMC) is an intravenous (IV) and oral aminomethylcycline antibiotic in the tetracycline class approved in the United States to treat acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia (CAPB) in adults. The approved dosing regimens of OMC include a loading dose designed to achieve steady-state exposures early in the course of therapy. We assessed the impact on OMC exposure and subsequent pharmacodynamics (PD) on Day 2 and at steady state (Day 5) in the situation where a loading dose may not be given.

Methods. Phase 1 pharmacokinetic (PK) data were used to determine OMC exposure on Day 2 and at steady state (Day 5) for the following: IV regimens 100 mg IV q12h on Day 1 then 100 mg IV QD (load), 100 mg IV QD (no load); and oral regimens 450 mg oral QD on Days 1 and 2 then 300 mg QD (load) and 300 mg oral QD (no load). AUC on Day 2 and Day 5 for no-load regimens were compared with the regimens with loading doses. Additionally, AUC/MIC ratios were calculated using OMC MICs for two main pathogens of interest in ABSSSI and CAPB, respectively, Staphylococcus aureus (0.25 mg/L) and Streptococcus pneumoniae (0.12 mg/L). In vivo AUC/OMC targets for stasis and 1-log kill were used as 21.9 and 31.2 and 65.8 (S. pneumoniae).

Results. Day 2 and 5 AUCs are shown in the Figure. AUCs on Day 2 were lower for the two regimens without loading doses and were 72% (IV) and 73% (oral) of those with a loading dose. However, at steady state on Day 5, no-load regimen AUCs were essentially the same at 98% for both the IV and oral regimens. Despite lower AUCs on Day 2 for the no-load regimens, the AUC/MIC ratio would still be expected to exceed the stasis threshold for both pathogens and the 1-log kill threshold for S. pneumoniae (figure). This same pattern was also noted on Day 5.

Conclusion. Exposure as assessed using AUC was lower early on in therapy on Day 2 for both IV and oral regimens. However, exposures were not different on Day 5 at steady state. Despite lower exposure on Day 2, OMC would still be expected to meet or exceed PK/PD thresholds associated with stasis for S. aureus and S. pneumoniae. The 1-log kill threshold was exceeded for S. pneumoniae. Further studies are needed to confirm any clinical impact of the omission of OMC loading doses.

735. Bacteriophage Therapy Improves Survival of Galleria mellonella Larvae Injected with Vancomycin-Resistant Enterococcus faecium
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Background. Vancomycin-resistant Enterococcus faecium (VRE) is a major multidrug-resistant organism which may cause infection or colonization in hematopoietic cell transplant (HCT) patients. The use of VRE-specific bacteriophages (phages) may potentially help eradicate VRE colonization and subsequent infections. To test the efficacy and safety of phages against VRE in vivo, a cocktail combining four phages was used in a VRE-infected larva model.

Methods. The pre-screening model Greater Wax Galleria mellonella larva was used in this study. Larvae were infected with VRE by injecting a VRE strain isolated from stools of a VRE-colonized HCT patient at a concentration of 10^9 colony-forming units/10 μL. A single phage (MDA1) or a phage cocktail (MDA1, MDA2, MDA3, and MDA4) were also injected at a concentration of 10^6 colony-forming units/10 μL. Two model groups were tested; a prevention group (PG) and a treatment group (TG). For the PG, phages were administered 1 hour before bacterial injection whereas the TG were injected with phages 1 hour post bacterial injection. Control groups included larvae injected with bacteria alone, phages alone (to measure toxicity due to phage administration), sterile media (to measure any lethal effects due to physical trauma from the injection), or without any manipulation. Every group was composed of 5 larvae. The insect’s health state was observed and scored after 8 hours of incubation at 37°C using a published health index scoring system.

Results. Phages improved survival of VRE-infected larvae (table). Only 32% of the VRE-infected larvae survived after 8 hours of infection whereas more than 80% survived when adding phages, whether phages were administered before or after VRE infection. The phage cocktail was shown to be more effective than the single phage MDA1 in improving survival (66% vs. 82% survival). Injecting larvae with phages alone was as safe as the same survival rate was observed when compared with those injected with sterile media or those without manipulation.

Conclusion. The use of larva model G. mellonella allows for rapid and efficient screening of the bacterial virulence and phage efficacy and safety. Such results highlight the feasibility and the potential impact of phage therapy on VRE colonization and infections.

Table. Efficacy of phages (MDA1 or phage cocktail MDA1, MDA2, MDA3 and MDA4) to improve survival of VRE-infected larvae.

| Phage Regimen | % of Larvae Survival | Median |
|---------------|---------------------|--------|
| Control       | 88                  | 90     |
| Sterile media | 84                  | 90     |
| VRE           | 32                  | 0      |
| MDA1 alone    | 88                  | 90     |
| Phage cocktail alone | 88 | 90     |
| VRE+MDA1 (TG) | 84                  | 90     |
| VRE+Phage cocktail (TG) | 86 | 90     |
| MDA1+VRE (PG) | 66                  | 80     |
| Phage cocktail+VRE (PG) | 82 | 90     |

Abbreviations: VRE, Vancomycin-resistant Enterococcus faecium; TG, treatment group; PG, prevention group

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736. The Use of Bacteriophages to Inhibit Different Strains of Vancomycin-Resistant or Susceptible Enterococci
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Background. Vancomycin-resistant Enterococci (VRE) is a well-known infectious complication among immunocompromised patients, especially hematopoietic
737. Novel Glycans Reduce Carbapenem-Resistant Enterobacteriaceae and Vancomycin-Resistant Enterococci Colonization in an Ex Vivo Assay by Supporting Growth and Diversity of Commensal Microbiota at the Expense of MultiDrug-Resistant Organisms (MDRO)

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**Background.** Infections with Carbapenem-resistant Enterobacteriaceae (CRE) and vancomycin-resistant Enterococci (VRE) are major health implications for humans and agriculture. At our center, isolates of CRE and VRE strains in culture, nor of other pathogens frequently encountered in critically ill patients receiving broad-spectrum antibiotics.

**Results.** One major risk factor for clinical infection is intestinal colonization with CRE or VRE. There are currently no FDA-approved compounds to decolonize these carriers. A major risk factor for clinical infection is intestinal colonization with CRE or VRE. There are currently no FDA-approved compounds to decolonize these carriers.

**Conclusion.** Our results highlight the feasibility and the potential success of these phages in inhibiting VRE in vitro. These VRE-specific phage cocktails may be used in future studies to reduce VRE colonization and subsequent infections in HCT recipients.

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