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1060. Pritelivir in Immunocompromised Patients with Mucocutaneous Acyclovir-Resistant Herpes Simplex Virus-Infections – First Case Series

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Session: P-61. Novel Agents

Background. HSV recurrences are usually managed effectively with existing antiviral drugs (nucleoside analogs such as acyclovir). However, in immunocompromised patients (e.g., malignancy, HIV, transplant), if lesions persist or recur while receiving antiviral treatment, acyclovir resistance should be suspected. In this population, there are limited treatment options. The helicase-primase inhibitor pritelivir is a novel oral antiviral, with a new mode of action and is active against both HSV-1 and HSV-2, including acyclovir and foscarnet-resistant strains. In this case series, we report the first clinical experiences with pritelivir in the treatment of immunocompromised patients with acyclovir resistant HSV infection.

Methods. All patient reported in this case series received pritelivir in a Phase 2 study. There were treated in an open-label design with a 400 mg pritelivir oral loading dose followed by a 100 mg oral maintenance dose daily for up to 28 days.

Results. Of the 23 patients, 11 had HIV infection and 12 had malignancy, transplant or an autoimmune disease. Of this cohort, 19 patients showed full resolution of their HSV-related lesions during the 28 day treatment period, while in 4 subjects lesions improved but did not completely heal during the observation period. Pritelivir was well tolerated without significant adverse effects.Reasons for incomplete lesion resolution during the 28 day treatment period, were extensive lesions in one patient, one patient with resistance development, and one patient with lesions in the oral cavity. Three patients subsequently experienced full resolution, while one patient required foscarnet due to CMV reactivation, necessitating early discontinuation.

Conclusion. Pritelivir is a promising novel treatment option for patients with severe mucocutaneous HSV-1/2 infections that are resistant to acyclovir and foscarnet. An international Phase 3 study is underway to evaluate pritelivir efficacy in immunocompromised patients.

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1061. Clinical Phage Microbiology: Evaluating Phages for Biofilm-associated Prosthetic Valve Endocarditis

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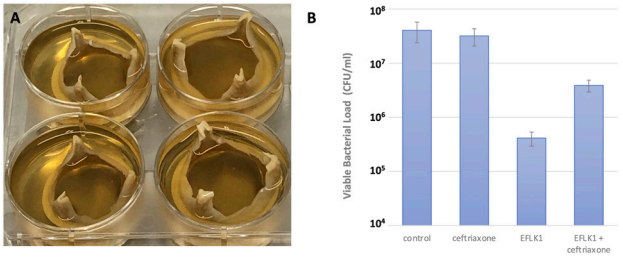
Session: P-61. Novel Agents

Background. **Prosthetic valve endocarditis (PVE)** is a major treatment challenge associated with biofilm formation. It requires intensive infectious diseases consultations and prolonged therapy. Nevertheless, high mortality rates are reported even with timely diagnosis and optimal management. *Bacteriophage (phage) therapy*, the use of bacterial viruses as antimicrobial agents, has been suggested as a potential adjunctive treatment for PVE. This is due to the ability of lytic phages to synergize with antibiotics and to destroy biofilms. However, due to their high specificity, it is crucial to match the phages by *in-vitro* evaluations that simulate the clinical settings.

Methods. In this study we demonstrate this matching using an *in-vitro* PVE model of vancomycin-resistant *Enterococcus faecalis* (VRE). We have looked at the ability of the phage EFLK1, alone or in combination with antibiotics, to destroy mature biofilms from a commonly used bioprosthetic valve. In addition, we tried to predict these effects using several *in-vitro* phage susceptibility assays.

Results. We found that the phage EFLK1 presents a significant inhibitory effect against planktonic cultures of VRE, both alone or in combination with ampicillin or ceftriaxone. We then tested the effect of these combinations on mature biofilm grown on a standard 96-well plates. We found that the phage, or its combination with ceftriaxone, led to a two-log reduction in the bacterial viability. In contrast, the addition of ampicillin to the phage caused interference with this antibacterial effect. When tested against biofilm grown on a pericardial patch, the combination of EFLK1 and ceftriaxone was found most efficient. Finally, when tested on the whole bioprosthetic aortic valve, we found that the phage EFLK1 alone was even more efficient than its combination with ceftriaxone.

Biofilm Eradication from Bioprosthetic Aortic Valve



(A) Representation of E. faecalis biofilm formation on bioprosthetic valves. (B) Following 48-hours of growth, the valves were treated for five days by the phage EFLK1,