

IMS-P22 **Discovery of Amenamevir (ASP2151), a Helicase-Primase Inhibitor as an Antiviral Drug against Varicella-Zoster Virus and Herpes Simplex Virus Types 1 and 2**

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Varicella-zoster virus (VZV), herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) are members of human herpesvirus family. Herpes helicase-primase is essential for a viral DNA replication. Helicase-primase is therefore the potential therapeutic target for a novel antiherpesvirus agent.

We discovered a series of novel tetrahydrothiopyran derivatives as a helicase-primase inhibitor (HPI) that demonstrated potent antiviral activities against VZV as well as HSV-1 and HSV-2 in vitro. Interestingly, other known HPIs showed anti-viral activity against HSV-1 and HSV-2, but not VZV. Amenamevir (ASP2151; 1.0–30 mg/kg, p.o.) significantly inhibited the development of skin lesion in hairless mice cutaneously infected with HSV-1. These results indicate that amenamevir is useful for the treatment of infectious diseases related to VZV, HSV-1, and HSV-2 such as zoster, herpes labialis, and genital herpes. In this presentation, we will show the synthesis and SAR of this novel series of HPIs, and pharmacological profiles of amenamevir.