

### CD377, a novel antiviral Fc-conjugate, demonstrates a lower resistance potential than baloxavir and oseltamivir against pandemic influenza A(H1N1)

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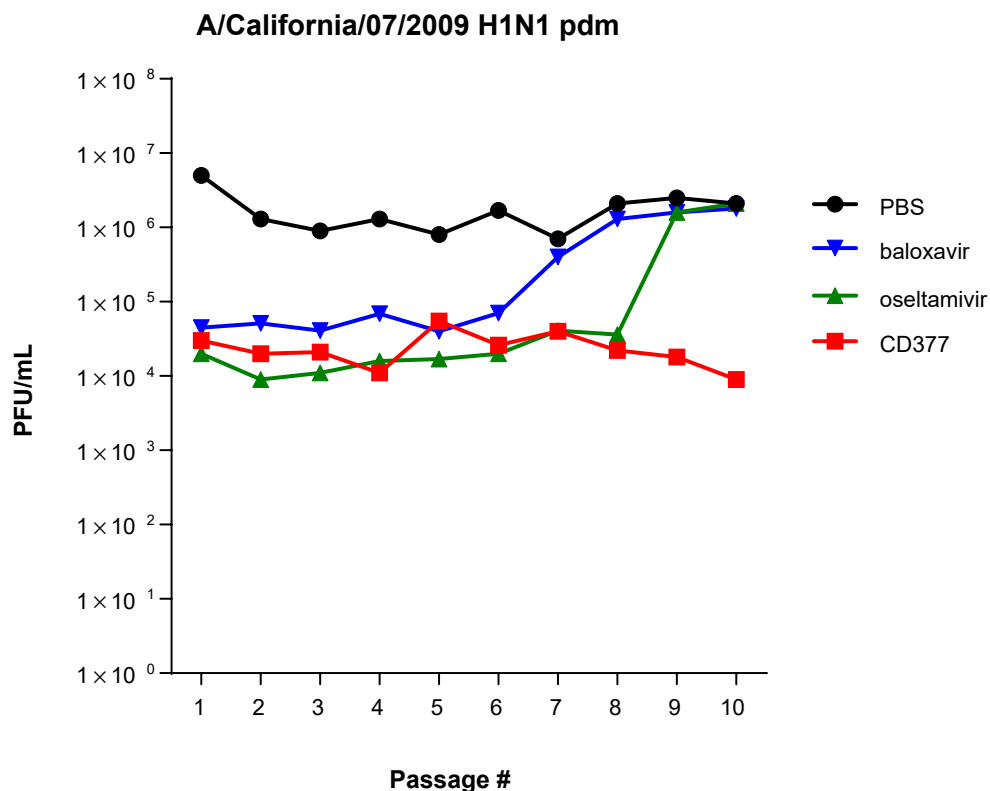
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**Background:** AVCs (antiviral Fc-conjugates) developed by Cidara Therapeutics are novel, long-acting immunotherapeutic conjugates of potent antivirals and the Fc domain of human IgG1. CD377 is an AVC development candidate for the prevention and treatment of seasonal influenza, comprising a neuraminidase-targeting small molecule conjugated to IgG1 Fc. CD377 was designed to provide broad-spectrum coverage of influenza A and B, including drug-resistant strains. Herein, the resistance potential of this agent was assessed by *in vitro* serial passage in comparison to standard of care agents baloxavir and oseltamivir.

**Materials/methods:** Serial passage was conducted in Madin-Darby canine kidney (MDCK) cells infected at an MOI of 0.01 with A/California/07/09 H1N1 pdm. Selecting agent concentrations were optimized as required for maximum virus inhibition, while maintaining sufficient virus for subsequent passages [CD377 - 4 nM, baloxavir - 4 nM, oseltamivir - 200 nM]. A PBS no-drug control group was also included. Following the addition of drugs, cells were incubated for 24 hours. Next, viral supernatants were collected and used to quantify viral titer by plaque assay. Finally, freshly seeded cells were re-infected in the presence of compounds. The process was repeated for 10 passages.

**Results:** Over the course of 10 passages, A/California/07/2009 H1N1 pdm did not show any increase in viral titer in the presence of CD377 (Fig. 1). In contrast, viral titers in the baloxavir and oseltamivir selection groups increased to levels similar to those observed in the PBS control after passages 6 and 8, respectively, indicating reductions in susceptibility.

Figure 1. Viral titers for A/California/07/2009 passaged in MDCK cells with sub-inhibitory concentrations of CD377, baloxavir, or oseltamivir



**Conclusions:** CD377 demonstrated a low resistance potential as compared to baloxavir and oseltamivir in serial passage with a pandemic H1N1 influenza strain. Follow-up studies on plaque-purified viruses from each passage group will characterize any changes in genotype, phenotype, or fitness. Future serial passage studies will investigate the resistance profile of CD377 against other clinically relevant influenza strain types, such as H3N2 and B.

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