Abstract 8832

CD377, a novel antiviral Fc-conjugate, demonstrates potent broad-spectrum activity in multiple *in vitro* assays against influenza A and B

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Background: AVCs (antiviral Fc-conjugates) 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 and pandemic influenza, comprising a novel neuraminidase inhibitor (NI) conjugated to IgG1 Fc, designed to provide broad-spectrum coverage of influenza A and B, including drug-resistant strains. CD377 has demonstrated efficacy in multiple lethal influenza mouse models. Herein, we characterize the activity of CD377 in multiple *in vitro* assays against influenza A and B strains including clinically relevant baloxavir- and NI–resistant mutants.

Materials/methods: CD377 was tested alongside oseltamivir, zanamivir, or baloxavir at concentrations ranging from 0.01 nM to 10,000 nM. Neuraminidase inhibition (NAI) activity was determined using a commercial NA-Fluor kit. Cytopathic effect (CPE) was determined against influenza A after 3 days and B strains after 5 days in MDCK SIAT1 cells. Activity in plaque reduction assay (PRA) was determined in MDCK cells after 48–72 h depending on virus strain tested.

Results: CD377 demonstrated potent NAI activity in a low nM range (IC50 0.01 – 23.55 nM) against influenza A/H1N1, influenza A/H3N2, and influenza B strains. The activity of CD377 did not shift against variants that confer resistance/reduced susceptibility to oseltamivir (H275Y, E119V), to oseltamivir and zanamivir (R292K), or to baloxavir (I38T/L/M) in NAI.

In the cell-based assays, CD377 demonstrated up to 100-fold increased potency than oseltamivir or zanamivir against influenza A and B wild-type strains. Notably, CD377 activity did not shift against H1N1 H275Y or H3N2 R292K mutants. The activity of CD377 in PRA or CPE was on par with or greater than that of baloxavir.

Conclusions: CD377 demonstrated potent, broad-spectrum antiviral activity *in vitro* against multiple seasonal and pandemic H1N1 and H3N2, and B strains. While CD377 shares a mechanism with approved NIs, its potency in cell-based assays was superior to oseltamivir or zanamivir, and comparable to or greater than baloxavir. This potent antiviral activity of CD377 in multiple *in vitro* assays, combined with efficacy in lethal mouse models of influenza infection support further development of CD377 for prevention and treatment of influenza infection.

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