

Efficacy of CD377, a novel antiviral Fc-conjugate against seasonal influenza in lethal mouse models

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Background: Cidara's AVCs (antiviral Fc-conjugates) are novel, immunotherapeutic conjugates of potent, antiviral agents with the Fc domain of human IgG1. CD377 is an AVC development candidate for prevention and treatment of influenza that has demonstrated broad anti-neuraminidase activity in both enzymatic and cell-based assays, and the ability to engage the immune system through its Fc domain. These attributes, coupled with an exceptional PK profile, underscore the potential of CD377 for the long-term prevention of seasonal influenza.

Materials/methods: Efficacy studies were conducted in female BALB/c mice lethally challenged intranasally at 3x the LD₉₅ with influenza A virus (H1N1, H3N2) and influenza B (Victoria, Yamagata lineages). CD377 was administered as a single dose subcutaneously (SC) at various concentrations 2 hours after viral challenge. Body weights (BW) and health scores were monitored daily, with 20% BW loss recorded as a mortality.

Results: In mice challenged with a lethal dose of a pandemic H1N1 strain (A/California/07/09), a single dose of CD377 (0.1 to 3 mg/kg) administered 2 hours post-challenge was fully protective (P=0.0026 relative to vehicle). This result was accompanied by only a transient drop in BW that was greatest on Day 4 before full recovery to starting BW by Day 9. In a similar study against a mouse-adapted H3N2 subtype (A/Hong Kong/1/68), a single dose of CD377 at 0.3 mg/kg was fully protective (P=0.0025).

The activity of CD377 was also evaluated against both lineages of influenza B. Against influenza B/Malaysia/8/34 (Victoria), a single CD377 dose of 0.1 mg/kg was fully protective (P=0.0027) while the Fc-only control dosed at 1 mg/kg was not (P=0.3173), as expected. Against the Yamagata lineage (B/Florida/4/06), CD377 demonstrated even greater potency, achieving full protection from lethal challenge at 0.03 mg/kg (P=0.0023).

Conclusions: CD377 was protective against lethal challenge with several seasonal influenza subtypes at single doses of 0.3 mg/kg or less. The exceptional PK profile of CD377 combined with its ability to engage the immune system highlight its potential for use as a long-term preventative against seasonal influenza.

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