Efficacy of CD377, a novel antiviral Fc-conjugate, against influenza A(H1N1) in a lethal mouse model of Severe Combined Immunodeficiency (SCID)

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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. These long-acting AVCs directly inhibit viral replication while simultaneously engaging the immune system. CD377 is an AVC development candidate being evaluated for seasonal and pandemic influenza, including in immune-deficient populations who are unable to benefit from vaccination. We evaluated CD377 in SCID mice to determine the impact of compromised immune status on its efficacy.

Materials/methods: Efficacy was evaluated in female BALB/c or BALB/c *scid* mice challenged intranasally with 3x the LD_{95} of influenza A/Puerto Rico/8/1934 (H1N1) (3E2 or 2E2 pfu/mouse respectively) . Mice were treated with a single subcutaneous dose of CD377 (between 0.01 and 10 mg/kg) two hours after viral challenge. The SCID study included baloxavir as comparator, at 3 or 10 mg/kg, bid x 1 day. Body weights (BW) were monitored daily for 14 or 28 days, with 20% BW loss recorded as mortality.

Results: In a benchmark study with immune-competent mice, CD377 was protective at 0.1 mg/kg (P=0.0031 relative to vehicle) accompanied by a transient drop in BW of less than 7%. Full recovery to starting BW was observed by study end (Day 14). Groups treated with vehicle or Fc-only control fully succumbed to infection by Day 6.

In a similar study with immune-compromised *scid* mice challenged with the same virus, CD377 dosed at 0.1 mg/kg was fully protective for 21 days. At 0.3 mg/kg, mice were fully protected for the entire study (28 days) (P=0.0020). In contrast, mice treated with 6 mg/kg (total dose) of baloxavir were only protected until Day 13, reaching 40% mortality by study end on Day 28. The potency of CD377 was further supported by BW data; *scid* mice treated at 0.3 mg/kg demonstrated only a transient BW drop of <3% (Day 4).

Conclusions: CD377 demonstrated robust efficacy in immune-competent and severely immunodeficient mouse infection models. The dose necessary to protect lethally challenged mice from both studies for 14 days was equivalent. This result supports further development of CD377 as a novel antiviral for prevention against influenza, including high-risk patients with immunodeficiencies.

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