CD377, a Novel Antiviral Fc-conjugate, Demonstrates Potent Viral Burden Reduction Against Influenza A (H1N1) in Mouse and Ferret Models

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Abstract 162
Disclosures

All authors are employees and stockholder of Cidara Therapeutics, Inc.
Conventional approaches to prevent and treat influenza

- **Vaccine**: Limited VE
- **Monoclonal Antibody**: Limited to Influenza A
- **Small Molecule**: Limited to Treatment

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Vaccines have limited vaccine effectiveness (VE) against influenza

Source: CDC
Vaccines have limited vaccine effectiveness (VE) - especially in the elderly - against influenza

%VE in high-risk group of >65 is only 30%

Source: CDC
Annual disease burden by influenza in the US (2019-20)

- **39-56M** flu illnesses
- **410-740K** hospitalizations
- **24-62K** deaths

*Source: CDC*
Antiviral Fc-conjugate (AVC) are a novel approach for prevention and treatment of influenza
CD377, the first development candidate of the Cloudbreak® AVC platform, for prevention and treatment of influenza

**Antiviral activity**

Potent, universal activity against influenza A and B

**Neuraminidase inhibitor**

Fc domain of human IgG1
CD377, the first development candidate of the Cloudbreak® AVC platform, for prevention and treatment of influenza

- **Fc-mediated functions**
  - Allows for engagement of immune effector cells
  - Long $T_{1/2}$

- Neuraminidase inhibitor
- Fc domain of human IgG1
CD377 has ideal attributes for prevention and treatment of influenza

| Attribute | Description |
|-----------|-------------|
| Broad-spectrum, universal coverage |  |
| Superior resistance profile |  |
| Protection for High-Risk Populations |  |
| Expanded efficacy window |  |
| Long duration of action |  |
| Rapid onset of activity |  |
| Flexible administration |  |
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CD377 has universal activity against influenza A and B in vitro

Neuraminidase inhibition assay (median IC$_{50}$ nM)

| Influenza subtype | CD377 | Oseltamivir | Zanamivir |
|-------------------|-------|-------------|-----------|
| A (H1N1, n=9)     | 1.5   | 1.5         | 0.6       |
| A (H3N2, n=6)     | 4.5   | 0.4         | 1         |
| B (n=7)           | 3.1   | 28.5        | 5.9       |
CD377 has universal activity against influenza A and B \textit{in vitro}

**Neuraminidase inhibition assay (median IC$_{50}$ nM)**

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**Cell-based cytopathic effect assay (median EC$_{50}$ nM)**

| Influenza subtype | CD377 | Oseltamivir | Zanamivir | Baloxavir |
|-------------------|-------|-------------|-----------|-----------|
| A (H1N1, n=10)    | 1     | 925         | 343       | 3         |
| A (H3N2, n=6)     | 1     | 3,190       | 112       | 2         |
| B (n=6)           | 3.9   | 654.8       | 67        | 11.5      |
Lethal challenge with influenza A (H1N1) in mouse model

- Infection with Influenza
- Treatment (SC) t=+2 h
- Health check for 14 days
CD377 has potent efficacy against influenza A (H1N1) in mice

![Graph showing efficacy of CD377 against influenza A (H1N1) in mice. The x-axis represents days post infection, and the y-axis represents % survival. Different treatments include PBS, hIgG1 Fc (1 mg/kg), CD377 (0.3 mg/kg), CD377 (0.1 mg/kg), CD377 (0.03 mg/kg), and CD377 (0.01 mg/kg). The graph shows that CD377 at various doses significantly improves survival compared to the control groups.]
CD377 has potent efficacy against influenza A (H1N1) in mice

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**Graph 1:**
- **Y-axis:** % Survival
- **X-axis:** Days post infection
- **Legend:**
  - PBS
  - hlgG1 Fc (1 mg/kg)
  - CD377 (1 mg/kg)
  - CD377 (0.3 mg/kg)
  - CD377 (0.1 mg/kg)
  - CD377 (0.03 mg/kg)
  - CD377 (0.01 mg/kg)

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**Graph 2:**
- **Y-axis:** % Body Weight
- **X-axis:** Days post infection
- **Legend:**
  - PBS
  - hlgG1 Fc (1 mg/kg)
  - CD377 (1 mg/kg)
  - CD377 (0.3 mg/kg)
  - CD377 (0.1 mg/kg)
  - CD377 (0.03 mg/kg)
  - CD377 (0.01 mg/kg)
CD377 has potent efficacy against influenza A (H1N1) in mice

**Single dose at 0.1 mg/kg of CD377 is fully protective**
CD377 is superior to oseltamivir against influenza A (H1N1) in mice

Human equivalent dose of oseltamivir = 5 mg/kg BID x 5
CD377 is superior to oseltamivir against influenza A (H1N1) in mice

Comparison of survival and body weight of mice infected with A/PR/8/1934 (H1N1) treated with different doses of oseltamivir and CD377.

Human equivalent dose of oseltamivir = 5 mg/kg BID x 5
CD377 is superior to oseltamivir against influenza A (H1N1) in mice

**Survival**

- PBS
- hIgG1 Fc (1 mg/kg)
- CD377 (0.3 mg/kg)
- Oseltamivir (5 mg/kg BID x 5)
- Oseltamivir (50 mg/kg BID x 5)

**Body Weight**

- PBS
- hIgG1 Fc (1 mg/kg)
- CD377 (0.3 mg/kg)
- Oseltamivir (5 mg/kg BID x 5)
- Oseltamivir (50 mg/kg BID x 5)

*CD377 is superior to oseltamivir at < 1/1,000 the total dose of oseltamivir*
Viral burden and cytokine analysis on day 4 after lethal challenge with influenza A (H1N1) in mice.
CD377 demonstrates dose-dependent viral burden reduction against influenza A (H1N1)

| Test article [mg/kg] | Log reduction |
|----------------------|---------------|
| PBS [0]              | 0.00          |
| hlgG1 Fc [3]         | -0.5          |
| Oseltamivir [5]      | 0.8           |
| Oseltamivir [50]     | 0.8           |
| CD377 [0.1]          | 1.1           |
| CD377 [0.3]          | 2.1           |
| CD377 [1]            | 3.2           |
| CD377 [3]            | 3.6           |
Dose-dependent reduction in inflammation by CD377 correlates with viral burden reduction
High-challenge dose, transient infection with influenza A/CA/07/2009 (H1N1)pdm in ferret model
CD377 reduces viral burden in dose-dependency against influenza A (H1N1)

Day 2

| Test article [mg/kg] | Log reduction |
|---------------------|--------------|
| PBS [0]             | 0            |
| hlgG1 Fc [15]       | -0.3         |
| Oseltamivir [5]     | 0.5          |
| CD377 [0.3]         | 0.3          |
| CD377 [1]           | 0.5          |
| CD377 [3]           | 1.3          |
| CD377 [10]          | 1.9          |
| CD377 [30]          | 1.9          |
CD377 reduces viral burden in dose-dependency against influenza A (H1N1)
Summary of AVCs against influenza

- CD377 has universal, broad-spectrum activity against influenza A and B
- CD377 at 0.3 mg/kg or lower is protective in lethal mouse models against influenza A and B (Talk #159 presented by James Levin, PhD)
- CD377 has superior efficacy as compared SOC, Oseltamivir, in mice
- CD377 demonstrates dose-dependent reduction in viral burden and inflammation in mice
- CD377 demonstrates dose-dependent reduction in viral burden in ferrets

→ CD377 has true universal activity against influenza with potential to transform the prevention and treatment of influenza
Cidara Cloudbreak® AVC platform: Expansion to other viruses
Cidara Cloudbreak® AVC platform: Expansion to other viruses

- Influenza
- RSV
- HIV
- hCoV
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- Link to Website https://www.cidara.com/cloudbreak/