Single-Dose and Repeat Single-Dose Ascending Dose Study Evaluating Safety, Tolerability, and Pharmacokinetics of Subcutaneous and Intramuscular CD388, a Novel Long-acting Drug-Fc Conjugate for Universal Prevention of Seasonal and Pandemic Influenza

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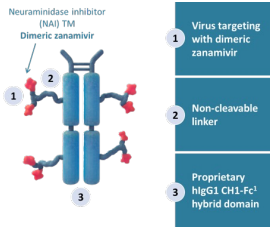
BACKGROUND

CD388 is a novel multivalent conjugate of a dimeric zanamivir stably linked to a proprietary human IgG1 Fc fragment engineered for extended half-life (**Figure 1**). CD388 is being developed for universal prevention of seasonal and pandemic influenza.

- Potent in vitro and in vivo activity against all tested seasonal and pandemic strains of influenza A and B
- Maintains potency against NAI-resistant strains
- Similar exposure and protection via intravenous (IV), subcutaneous (SQ), or intramuscular (IM) routes
- Equivalent protection in immune-competent and immune–compromised mouse models

Figure 1. CD388



METHODS

CD388 for injection (100 mg/mL) was administered IM or SQ at doses of 50, 150, and 450, and 900 mg (SQ only). Subjects in the 150-mg or 450-mg dose groups received a second single dose after a washout period of approximately 5 half-lives ($t_{1/2}$). Plasma CD388 concentrations and anti-CD388 antibody analysis were determined for subjects randomized to receive CD388 using validated methods. Safety was monitored throughout the study.

RESULTS

CD388 was absorbed rapidly and eliminated slowly with similar results following IM or SQ routes of administration (**Figure 2**). Pharmacokinetic (PK) parameters of CD388 are shown in **Table 1**. Increases in CD388 exposures were approximately dose proportional (**Figure 3**). Exposures were similar following a second single dose administration. Formation of anti-drug antibodies (ADAs) were rare, at low titers when present, and did not affect PK.

Most treatment emergent adverse events (TEAEs) were mild in intensity, and there were no deaths, or serious AEs. Overall, no dose-dependent trend was observed for TEAEs, and the proportion of participants that experienced ≥1 TEAE or drug-related TEAE was similar for both administration routes (IM and SQ). The most common TEAE overall was headache.

Figure 2. Mean Plasma Concentrations of CD388 Administered by IM or SQ Injection

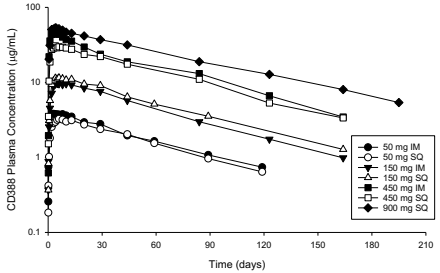


Figure 3. Single Dose Mean Plasma CD388 AUC for CD388 Administered by IM or SQ Injection

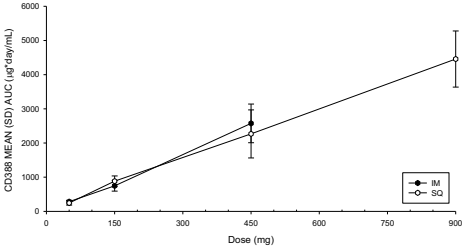


Table 1. CD388 PK Parameters Following a Single IM or SQ Administration

Dose	Parameter, mean (CV%) except where noted			
	$AUC_{0-\infty}$, µg•day /mL	C_{max}, µg/mL	T_{max}, days median (min, max)	$t_{1/2}$, days
50 mg				
IM	282.9 (14.3)	4.1 (18.1)	4.0 (2, 10)	51.4 (11.3)
SQ	244.6 (25.1)	3.57 (26.4)	9.5 (3, 13)	44.6 (20.2)
150 mg				
IM	745.8 (20.3)	10.4 (23.5)	5.5 (3, 13)	49.7 (19.8)
SQ	883.3 (17.3)	12.0 (27.8)	5.5 (2, 13)	52.7 (17.7)
450 mg				
IM	2575 (22.0)	48.6 (24.1)	3.3 (1, 6)	41.9 (31.2)
SQ	2266.7 (31.0)	32.7 (28.8)	4.0 (2, 10)	44.4 (22.5)
900 mg				
SQ	4458.3 (18.4)	58.8 (29.8)	4.0 (2, 8)	57.7 (20.4)

$AUC_{0-\infty}$=area under the concentration-time curve from time 0 extrapolated to infinity; C_{max}=maximum concentration; T_{max}=time to maximum concentration; $t_{½}$=terminal elimination half-life.

CONCLUSIONS

- CD388 absorption by both routes was rapid and elimination was slow, indicating that seasonal influenza prevention could be achieved with one dose per season.
- Lack of significant ADA formation with repeat administration supports annual use.
- No safety concerns were noted in this study.

ACKNOWLEDGMENTS and DISCLOSURES

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