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SINGLE ASCENDING DOSE 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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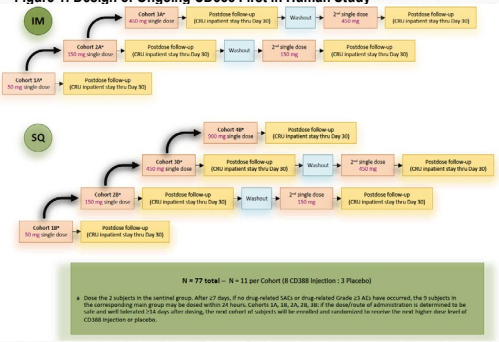
BACKGROUND

CD388 is a novel, long-acting, antiviral drug-Fc conjugate (DFC) designed to deliver universal prevention of seasonal and pandemic influenza. Nonclinical studies have shown CD388 to be effective prophylactically against seasonal and pandemic influenza A and B strains in lethal and nonlethal mouse models of infection.

METHODS

The design of the ongoing blinded CD388 First in Human study (NCT05285137), which is being conducted in healthy subjects is shown in Figure 1. CD388 for injection (100 mg/mL) was administered by intramuscular (IM) or subcutaneous (SQ) route. Safety and tolerability data were obtained in all subjects. Single dose CD388 pharmacokinetics were determined for subjects in the 50, 150, and 450 mg cohorts of each dosing route at protocol specified nominal time points; alias subject numbers were used to maintain blind. 900 mg SQ cohort still ongoing. Plasma CD388 concentrations were determined for subjects randomized to receive CD388 using a validated hybrid immunoassay LC-MS method with lower limit of quantitation (LLOQ) of 0.1 µg/mL. Noncompartmental pharmacokinetics were determined using Phoenix WinNonlin (Certara NC, USA).

Figure 1: Design of Ongoing CD388 First in Human Study



RESULTS

Safety and Tolerability

- Overall profile: well-tolerated up to 900 mg single dose; study in progress with limited follow up at highest doses
- No treatment-emergent SAEs and no withdrawals due to safety findings
- Most TEAEs were Grade 1 (90%), few Grade 2, all resolved within the exposure time-frame
- Incidence of TEAE not dose-dependent
- No hypersensitivity reactions were observed
- Few injection site events (pain, IM route mainly), Grade 1, all resolved spontaneously
- No clinically relevant ECG, vital signs or physical exam abnormalities

Pharmacokinetics

- IM or SQ CD388 was well absorbed
- Time of maximum plasma concentrations (T_{max}) appeared from 2 to 13 days post dose, and quantifiable concentrations (>LLOQ) lasted for months (Figure 2)
- CD388 AUC increased approximately dose proportional for both routes (Figure 3)
- Mean apparent half-life of elimination was ~ 6 to 7 weeks (Table 1)

Figure 2: Single Dose Mean Plasma CD388 Concentrations versus Time for 50, 150, or 450 mg CD388 Administered by Intramuscular or Subcutaneous Injection (Semi-logarithmic Scale)

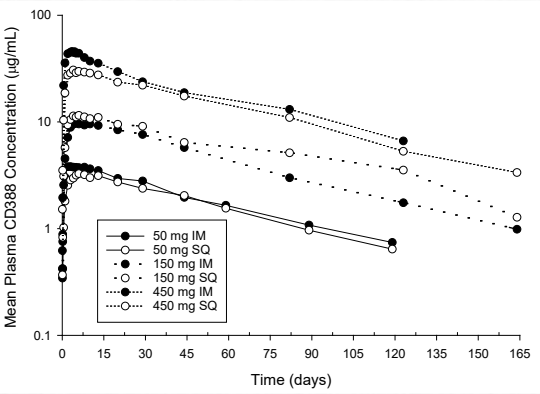


Figure 3: Mean CD388 AUC Versus Intramuscular or Subcutaneous Dose

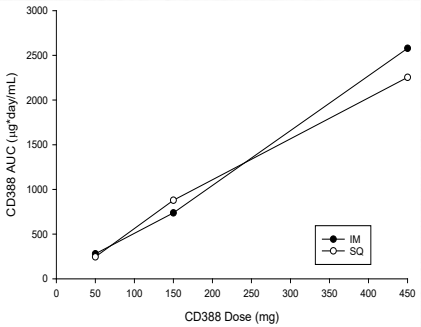


Table 1: Plasma CD388 PK Parameter Estimates

Group	T_{max} (day)	C_{max} (µg/mL)	$AUC_{0-\infty}$ (µg•day/mL)	$t_{1/2}$ (day)
IM 50 mg	4.0, 2-10	4.1 (18.1%)	280 (15.9%)	50.4 (18.4%)
SQ 50 mg	9.5, 3-13	3.6 (26.4%)	246 (25.6%)	46.3 (18.1%)
IM 150 mg	5.5, 3-13	10.4 (23.4%)	738 (18%)	47.5 (23.2%)
SQ 150 mg	5.5, 2-13	12 (27.8%)	879 (18.6%)	53.3 (19%)
IM 450 mg	3.3, 1-6	48.6 (24.2%)	2579 (22.5%)	43.8 (25.2%)
SQ 450 mg	4.0, 2-10	32.7 (28.7%)	2254 (31.7%)	45.0 (23.2%)

Data are presented as mean (standard deviation) for N= 8 subjects per group, except T_{max}= Median, Range.

CONCLUSIONS

- CD388 was generally well tolerated with no significant safety concerns in this ongoing study at single doses of up to 900 mg
- Plasma concentrations and pharmacokinetics of CD388 were similar following IM or SQ routes of administration
- Sustained plasma CD388 concentrations due to its long half-life indicate potential for season-long protection with a single dose

DISCLOSURES / ACKNOWLEDGMENTS

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