Pharmacokinetics and Safety of CD388 Following Subcutaneous Administration in Healthy Japanese Participants

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BACKGROUND

CD388 is a novel multivalent conjugate of a neuraminidase inhibitor stably linked to a proprietary human IgG1 Fc fragment engineered for extended half-life.

CD388 is being developed for seasonal pan-influenza prophylaxis. Here we describe pharmacokinetics (PK) and safety data in healthy volunteers of Japanese descent.

METHODS

Twenty-seven healthy study participants of Japanese descent (aged 20–65 yr) were randomized (7 CD388 and 2 placebo at each of three doses) to receive a single dose of CD388 (50, 150, or 450 mg) or placebo by subcutaneous (SQ) injection (NCT05619536). Blood samples were taken from all participants, and CD388 plasma concentrations were determined using a validated hybrid method with immune capture and LC-MS-MS detection in all who received CD388. Anti-drug antibody (ADA) results were also determined using a multi-tiered validated assay with screening, confirmatory immunodepletion, and titering as needed. Blinded safety assessments included an assessment of neuropsychiatric events, based on zanamivir USPI Warnings and Precautions.

RESULTS

Pharmacokinetics

CD388 absorption following SQ administration was rapid, exceeding efficacious levels in animal models within hours with monoexponential elimination (**Figure 1**). CD388 exposures increased approximately dose proportionally (**Table 1**). SQ clearance was slow, and volume approximated extracellular body water. Half-life values were long, averaging ~50 to 55 days. Overall PK parameters showed low to moderate variability across all dose levels. Similar PK results have been reported from a previous Phase 1 study in Western participants[1]. PK exposures of CD388 in Japanese participants were consistently higher than in Western participants at all doses (**Figure 2**), but these minor differences are likely attributed to lower body weights in Japanese participants.

Figure 1. Mean Plasma Concentration-Time Profiles of CD388 Following a Single SQ Administration of CD388 to Healthy Japanese Adult Participants (Semi-Log Scale)

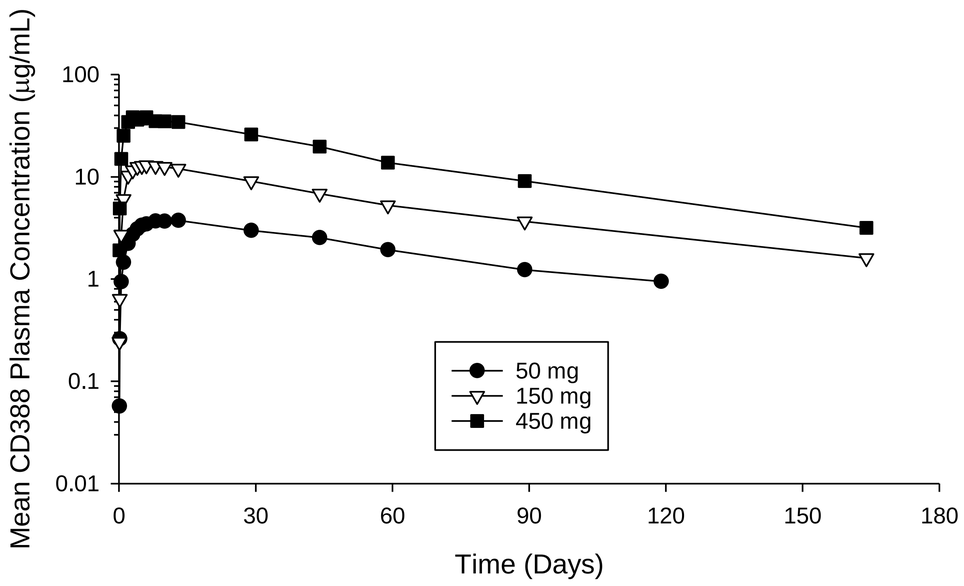


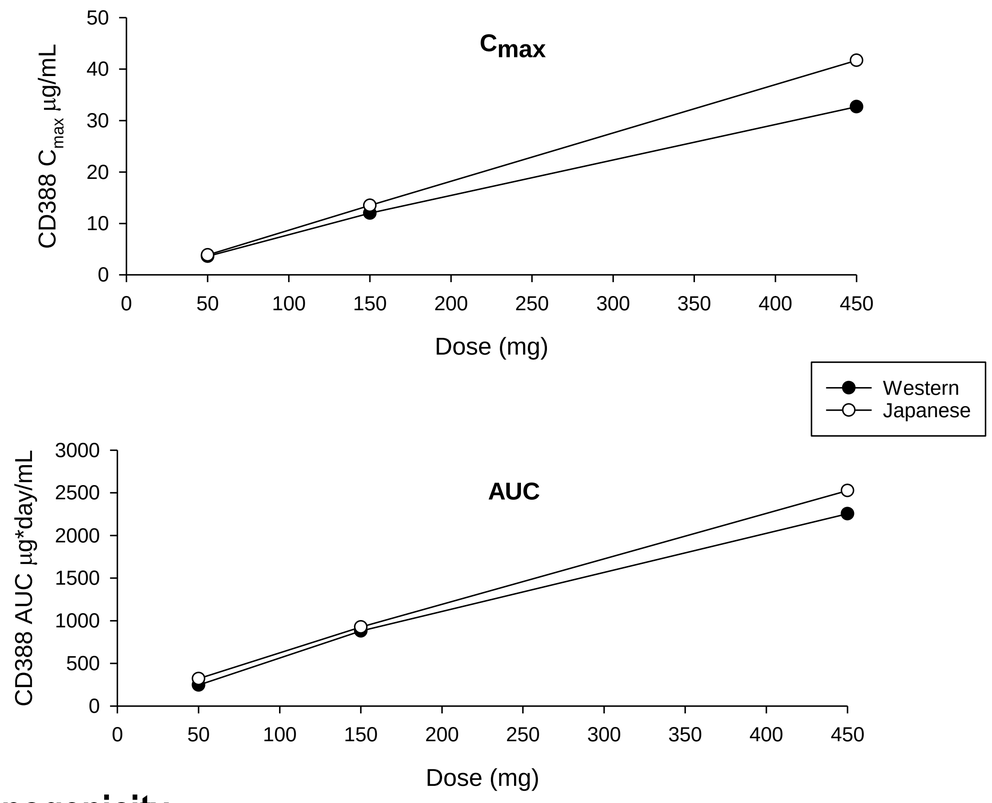
Table 1. Summary Statistics of Plasma PK Parameters of CD388 Following a Single SQ Administration of CD388 to Healthy Japanese Adult Participants

Parameter (Unit)	Mean (CV%) except where noted		
	Cohort 1: 50 mg (N=7)	Cohort 2: 150 mg (N=7)	Cohort 3: 450 mg (N=7)
T_{max} (days) median (min, max)	13 (8, 13)	4 (2, 13)	6 (3, 13)
C_{max} (µg/mL)	3.87 (20.1)	13.5 (30.4)	41.7 (22.2)
$AUC_{0\text{-}last}$ (µg*day /mL)	245 (10.5)	787.5 (30.3)	2120.8 (15.6)
$AUC_{0\text{-}\infty}$ (µg*day /mL)	380.8 (8.5)	925 (28.8)	2525 (17.7)
$t_{1/2}$ (days)	55.2 (21.8)	53.5 (30.3)	50.4 (16.0)
CL/F (L/day)	0.16 (8.1)	0.17 (27.7)	0.18 (18.8)
Vz/F (L)	12.5 (23.0)	12.6 (27.2)	13.3 (23.3)

$AUC_{0\text{-}last}$=area under the concentration-time curve from time 0 to time of last quantifiable sample; $AUC_{0\text{-}\infty}$=area under the concentration-time curve from time 0 extrapolated to infinity; CL/F=apparent clearance; C_{max}=maximum concentration; T_{max}=time to maximum concentration; $t_{½}$=terminal elimination half-life; Vz/F=apparent volume of distribution.

RESULTS (cont'd)

Figure 2. Mean CD388 C_{max} or $AUC_{0\text{-}\infty}$ Following Single Subcutaneous Dose to Japanese or Western Participants



Immunogenicity

The ADA screening results were negative for all but 4 participants. Confirmatory tests (immunodepletion assay) were carried out on these 4 participants (2 from the 50-mg dose group and 2 from the 450-mg dose group). Three participants exhibited negative results in these tests. One participant who received 50 mg CD388 exhibited positive confirmatory results post-dose (Days 14 and 30); however, the titration results were <25 (minimum detectable titer of the assay=25), indicating negligible ADA levels. The positive confirmatory results were transient, and the participant had negative ADA results on Days 45 and 60. The plasma exposures were not impacted, as evidenced by similar C_{max}, and AUC values for this participant were comparable to the rest of the participants in Cohort 1.

Safety

Overall, CD388 was well-tolerated at doses of up to 450 mg after single SQ injection in healthy adult Japanese participants with observations comparable across the study arms. There were no deaths, serious adverse events, and no clinically significant (CS) treatment-emergent adverse events (TEAEs). No participants were withdrawn from the study due to safety reasons. No CS abnormal findings in laboratory evaluations, vital signs, ECGs, or physical examinations were noted during the study, except for one elevated temperature finding associated with a COVID-19 infection. No influenza infections were reported during the study.

There were no injection site hypersensitivity reactions. All TEAE were Grade 1 and self-resolved. The most common TEAE was fatigue. There were no hallucinations, nervous system AEs, or psychiatric AEs. There were no study discontinuations due to TEAE.

CONCLUSIONS

- The PK profile of CD388 in Japanese participants were comparable to results from Western participants
- Overall, CD388 injection was safe and well tolerated in healthy participants of Japanese descent
- These data support further clinical studies with CD388 in Japanese populations for seasonal influenza prevention

REFERENCES

1. Flanagan S, Ong V, Baguet T, Rojas R, Wang S-S, Equils O. 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. Presented at ID Week 2023; Boston, MA; Oct 11-15, 2023.

ACKNOWLEDGMENTS

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