Poster 226

Higher Doses of Adintrevimab, an Extended Half-Life Monoclonal Antibody, for the Treatment and Prevention of COVID-19: Preliminary Results from a Phase 1 Single Ascending-Dose Study

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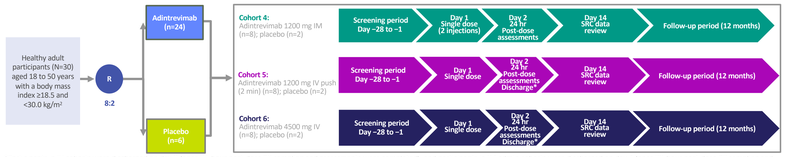
INTRODUCTION

- Adintrevimab is an extended half-life, fully human IgG1 monoclonal antibody (mAb) engineered to have high potency and broad neutralization against SARS-CoV-2 and other SARS-like CoVs with pandemic potential[1,2]
- *In vitro*, adintrevimab has demonstrated potent neutralizing activity against most variants and sublineages of SARS-CoV-2. Adintrevimab displays reduced *in vitro* activity against Omicron BA.1/BA.1.1 and lacks activity against BA.2, BA.3, BA.4, and BA.5[2-6]
- Adintrevimab is being assessed in two separate phase 2/3 clinical trials: the EVADE and STAMP trials for prevention and treatment of COVID-19[7,8]
- We previously reported preliminary results from the 300 mg IM, 600 mg IM, and 500 mg IV cohorts in an ongoing Phase 1 single ascending-dose study evaluating the safety, tolerability, and pharmacokinetics (PK) of a single dose of adintrevimab in healthy adults[9]
- Here, we report results from higher doses of adintrevimab assessed in this study, given that emerging SARS-CoV-2 variants may have varying susceptibilities to adintrevimab

METHODS

Figure 1. Phase 1 study design (cohorts 4, 5, & 6)



*Participants in IV cohorts were discharged on day 2 (once 24-hour post-dose PK sampling and assessments were completed), and participants in IM admin cohorts were discharged on day 4 (once 72-hour post-dose PK sampling and assessments were completed). IM, intramuscular; IV, intravenous; R, randomization; SRC, safety review committee.

Study design and objectives

- Randomized, double-blind, placebo-controlled, single ascending-dose study conducted at a single center in the United States
- Follow-up through 12 months is ongoing and the study remains blinded
- Eligible participants were healthy adults aged 18 to 55 years and had a negative SARS-CoV-2 RT-PCR test on day prior to dosing
  - Participants were dosed regardless of serostatus
- 3 cohorts (n=10 per cohort) were randomized (8:2) to receive adintrevimab or placebo (**Figure 1**)
- Participants could receive a vaccine at least 14 days prior to dosing at any point during the follow-up period
- Objective of this analysis was to:
  - Evaluate the safety and tolerability of all cohorts
  - Evaluate PK of a single dose of adintrevimab in cohorts 4 and 5 up to 21 days post dose*
  - Evaluate serum viral neutralizing antibody (sVNA) titer samples for up to 3 months for cohorts 4 and 5*

*Analysis was not complete for cohort 6 at time the data for poster was analyzed

Endpoints and assessments

- Adverse event (AE) monitoring, clinical laboratory and vital sign assessments, and physical examinations were performed throughout the study
  - Injection site tolerability was assessed through Day 4 in the IM cohort
  - Hypersensitivity reactions were monitored throughout the duration of the study
- Serum PK samples were collected at specified visits for up to 3 months
- Serum adintrevimab concentrations were determined using a validated hybrid ligand binding liquid chromatography–mass spectrometry (LC-MS)/MS assay
- PK parameters were estimated using standard non-compartmental methods (WinNonlin) and summarized using descriptive statistics
- As an exploratory research analysis for cohorts 4 and 5, the 50% neutralization (MN50) sVNA titers were determined using a plaque reduction assay against SARS-CoV-2 strain D614G (BavPat) and Omicron BA.1

RESULTS

Participants

- Overall, 30 participants were randomized to adintrevimab (n=24) or placebo (n=6)
- Baseline characteristics were well balanced among cohorts (**Table 1**)

Table 1

Baseline characteristics	Adintrevimab		
Characteristic	Cohort 4 (n=10)	Cohort 5 (n=10)	Cohort 6 (n=10)
Age, years			
Median (range)	34.5 (24-46)	28.5 (20-48)	35.0 (21-47)
≥50, n (%)	0 (0)	0 (0)	0 (0)
Female, n (%)	5 (50.0)	3 (30.0)	5 (50.0)
Race, n (%)			
Asian	1 (10)	0 (0)	2 (20)
Black or African American	1 (10)	4 (40)	2 (20)
White	8 (80)	6 (60)	6 (60)
Other	0 (0)	0 (0)	0 (0)
Ethnicity, n (%)			
Hispanic or Latinx	3 (30)	5 (50)	3 (30)
Not Hispanic or Latinx	7 (70)	5 (50)	7 (70)
Mean (SD) body mass index at baseline, kg/m²	23.95 (2.1)	25.56 (1.8)	25.62 (1.5)

SD, standard deviation

Safety and tolerability

- No study drug-related AEs, serious AEs, discontinuations, deaths, injection-site reactions, or hypersensitivity reactions were reported

PK profile

- The observed PK profiles through Day 21 for 1200 mg IM and 1200 mg IV of adintrevimab are shown in **Figure 2**
- The median time to maximum concentration (T_{max}) was 0.33 days (range: 0.042-1) for 1200 mg IV versus 6 days (range: 3-6) after a single 1200 mg IM injection **(Table 2)**
- IM and IV comparison of 1200 mg from lower dose 600 mg IM and 500 mg IV cohorts indicates dose proportionality of C_{max} and exposure AUC_{Day21} [9]

Figure 2. Mean adintrevimab concentration over time

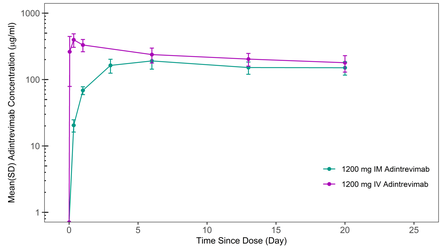


Table 2. Non-compartmental analysis of observed data

Treatment	T_{max}, median (range), days	C_{max}, mean (SD), µg/mL	$AUC_{Day\ 0\text{-}21}$, mean (SD), day*µg/mL
Adintrevimab 1200 mg IM (n=8)[a]	6 (3-6)	191 (48.2)	3040 (602)
Adintrevimab 1200 mg IV (n=8)[a]	0.33 (0.042-1)	423 (105)	4610 (105)

[a]Includes only participants who received ADG20. AUC, area under the curve; C_{max}, maximum serum concentration

sVNA titers

- Participants enrolled had a range of preexisting titers due to previous infections and/or COVID-19 vaccination
- The addition of adintrevimab boosted titers rapidly from baseline with peak titers achieved for 1200 mg IV at Day 1 (BavPat) and Day 2 (BA.1) and for 1200 mg IM at Day 7 (BA.1 and BavPat) (**Figure 3**)
- Adintrevimab-boosted geometric mean titers remained above baseline at Day 90 for 1200 mg IV: 136% (BA.1) and 1175% (BavPat); 1200 mg IM: 128% (BA.1) and 321% (BavPat) while geometric mean titers for placebo participants dropped below baseline by Day 90 for both variants (placebo: 50% [BA.1] and 65% [BavPat]) **(Figure 4)**

Figure 3. Adintrevimab-associated sVNA titers for BavPat and Omicron BA.1

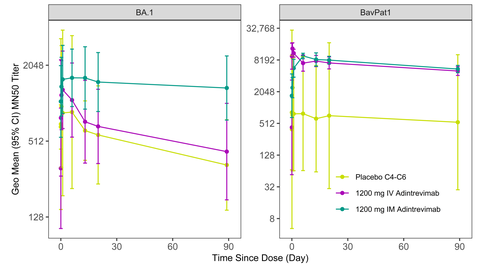
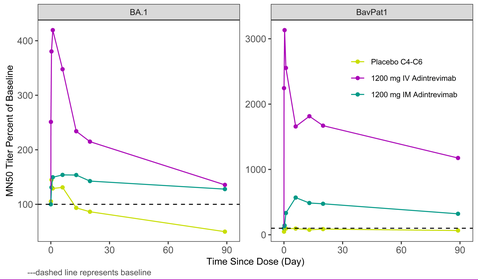


Figure 4. Adintrevimab-associated sVNA percent change from baseline



---dashed line represents baseline

KEY FINDINGS

A single dose of adintrevimab, up to 4500 mg IV, was well tolerated by healthy adults with no study drug-related AEs, serious AEs, or injection-site or hypersensitivity reactions reported

The preliminary PK profile was dose proportional compared with previous cohorts and consistent with the method of administration

Adintrevimab provided a boost to neutralizing titers compared to participants receiving placebo and maintained titers above baseline out to 90 days for Omicron BA.1

CONCLUSIONS

- A single dose of adintrevimab 1200 mg IV or IM provided rapid development of neutralizing titers that persisted against omicron BA.1 above baseline out to 90 days
- A single dose of adintrevimab up to 4500 mg was well tolerated. These preliminary safety and PK data support the potential use of higher doses of adintrevimab as needed to address emerging SARS-CoV-2 variants

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DISCLOSURES

XP, JG, EC, KN, DG, AC, and PS employees of Invivyd. FE has received consulting fees from Invivyd

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