Poster 633

Preliminary Results From a Phase 1 Single Ascending-Dose Study Assessing Safety, Pharmacokinetic Profile, and Serum Viral Neutralizing Antibody Titers of ADG20: an Extended Half-Life Monoclonal Antibody Being Developed for the Treatment and Prevention of COVID-19

Helen Paguntalan,[1] Zoltán Magyarics,[2] Lynn E. Connolly,[2] Ellie Hershberger,[2] Kristin Narayan,[2] Deepali Gupta,[2] Paul G. Ambrose,[2] Frank Engler,[3] Ed Campanaro,[2] Anita F. Das,[2] Pete Schmidt[2]

[1]WCCT Global, Cypress, CA, USA; [2]Adagio Therapeutics, Inc., Waltham, MA, USA; [3]Clinical Pharmacology, Certara, Buffalo, NY, USA

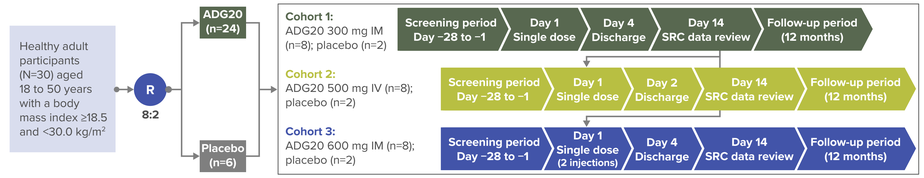
Pete Schmidt
303 Wyman Street Suite 300
Waltham, MA, 02451
E-mail: pschmidt@adagiotx.com
Phone: (510) 745-1251

INTRODUCTION

- ADG20 is a fully human IgG1 monoclonal antibody engineered to have high potency and broad neutralization against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and other SARS-like CoVs with pandemic potential by binding to a highly conserved epitope in the receptor-binding domain of the spike protein[1]
- The Fc region of ADG20 has been modified to provide an extended half-life[1]
- ADG20 is in clinical development for the treatment and prevention of COVID-19[2,3]
- The spread of SARS-CoV-2 and the emergence of new variants of concern represent ongoing global public health issues; the search for therapies to treat or prevent COVID-19 remains a matter of urgency[4,5]
- In vitro, ADG20 displays high binding affinity and potent neutralization against all SARS-CoV-2 variants tested, including variants of concern (B.1.1.7/Alpha, B.1.351/Beta, P.1/Gamma, B.1.617.2/Delta)[6-8]
- Here, we report preliminary results (up to 6 months of follow-up) from an ongoing Phase 1 single ascending-dose study evaluating the safety, tolerability, and pharmacokinetics (PK) of a single dose of ADG20 in healthy adults

METHODS

Figure 1. Phase 1 study design



IM, intramuscular; IV, intravenous; R, randomization; SRC, safety review committee.

Study design and participants

- Randomized, double-blind, placebo-controlled, single ascending-dose study initiated at a single center in the United States in March 2021
- Follow-up through 12 months (March 2022) is ongoing and the study remains blinded
- Eligible participants were healthy adults aged 18 to 50 years at low risk of SARS-CoV-2 infection and with no evidence of prior or current SARS-CoV-2 infection (negative SARS-CoV-2 quantitative reverse transcription polymerase chain reaction and serology tests [nucleocapsid as antigen, detecting both IgG and IgM] at screening)
- 3 cohorts (n=10 per cohort) were randomized (8:2) to receive ADG20 or placebo (**Figure 1**)
- The primary objective was to evaluate the safety and tolerability of a single dose of ADG20

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 self-assessed using a diary through Day 4
- Serum PK samples were collected at specified visits for up to 6 months
- Serum ADG20 concentrations were determined using a validated hybrid ligand binding liquid chromatography–mass spectrometry (MS)/MS assay
- PK parameters were estimated using standard non-compartmental methods (WinNonlin) and summarized using descriptive statistics
- Serum viral neutralizing antibody (sVNA) titer samples were collected at specified visits for up to 6 months
- As a non-prespecified exploratory research analysis, the 50% neutralization (MN50) sVNA titers were determined using a plaque reduction assay against SARS-CoV-2 strain D614G (BavPat). sVNA titers following administration of ADG20 were compared with peak responses following AZD1222 and mRNA-1273 vaccination

RESULTS

- This study is ongoing, and data are presented in a blinded manner

Participants

- Overall, 30 participants were randomized to ADG20 (n=24) or placebo (n=6)
- Baseline characteristics were well balanced among cohorts (**Table 1**)

Table 1. Baseline characteristics

Characteristic	Cohort 1 (n=10)	Cohort 2 (n=10)	Cohort 3 (n=10)
Age, years			
Median (range)	37.5 (18.0–48.0)	40.5 (20.0–54.0)	34.0 (18.0–55.0)
>50, n (%)	0	2 (20.0)	2 (20.0)
Male, n (%)	4 (40.0)	4 (40.0)	6 (60.0)
Female, n (%)	6 (60.0)	6 (60.0)	4 (40.0)
Race, n (%)			
Asian	1 (10.0)	0	0
Black or African American	1 (10.0)	1 (10.0)	1 (10.0)
White	6 (60.0)	9 (90.0)	8 (80.0)
Native Hawaiian or other Pacific Islander	2 (20.0)	0	0
Multiple	0	0	1 (10.0)
Ethnicity			
Hispanic or Latino	1 (10.0)	6 (60.0)	5 (50.0)
Not Hispanic or Latino	9 (90.0)	4 (40.0)	5 (50.0)
Mean (SD) body mass index, kg/m²	23.5 (3.1)	23.7 (1.8)	24.9 (3.4)

SD, standard deviation.

Safety and tolerability

- No study drug–related AEs, serious AEs, discontinuations, deaths, injection-site reactions, or hypersensitivity reactions were reported
- Through a minimum of 12 weeks post dose, 11 AEs were reported in 7 participants (2/10 [20%] Cohort 1; 3/10 [30%] Cohort 2; 2/10 [20%] Cohort 3); all were mild in severity and considered unrelated to study drug

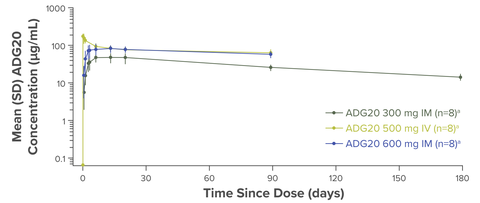
PK profile

- The observed PK profile through Day 180 for a single 300 mg IM injection of ADG20 and through Day 90 for 500 mg IV and 600 mg IM doses of ADG20 was dose proportional and consistent with an extended half-life monoclonal antibody (**Figure 2**)
- The median time to maximum concentration (T_{max}) was 13 days (range: 6–20) after a single 300 mg IM injection
- Based on 6-month data collected from participants who received 300 mg IM, the estimated half-life of ADG20 was 96.8 days. The observed mean ADG20 concentration at 6 months was 4990 µg/mL
- At 6 months, ADG20 serum concentration was highly predictive of the MN50 sVNA titer (**Figure 3**)

sVNA titers

- The MN50 sVNA titer (geometric mean [coefficient of variation, %]) was 1382 (32.7) by Study Day 14 (13 days [median T_{max}] following administration of a single 300 mg IM injection of ADG20 [Cohort 1] **Figure 3**)
- By Study Day 2 (the day following administration of a single 300 mg IM injection of ADG20 [Cohort 1]), MN50 sVNA titers significantly exceeded peak titers associated with AZD1222 and were similar to peak titers associated with mRNA-1273 (**Figure 4**)
- By Study Day 7, MN50 sVNA titers associated with ADG20 were significantly higher than peak titers associated with AZD1222 and mRNA-1273 and were maintained at comparable levels through Study Month 6 (**Figure 4**)

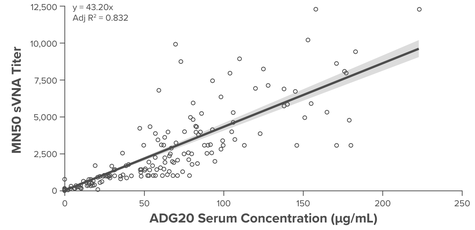
Figure 2. Mean ADG20 concentration over time (non-compartmental analysis observed data)



Treatment	T_{max}, median (range), days	C_{max}, mean (SD), µg/mL	$AUC_{Day\ 0-31}$, mean (SD), day*µg/mL	$AUC_{Day\ 0-84}$, mean (SD), day*µg/mL	$AUC_{Day\ 0-180}$, mean (SD), day*µg/mL	$T_{1/2}$ (SD), days
ADG20 300 mg IM (n=8)[a]	13 (6–20)	50.0 (14.9)	843 (259)	3260 (836)	4990 (1140)	96.8 (13.8)
ADG20 500 mg IV (n=8)[a]	0.0417 (0.0417–0.0417)	169 (29.1)	1870 (294)	6360 (1230)	–	–
ADG20 600 mg IM (n=8)[a]	13 (3–20)	85.6 (19.2)	1480 (371)	6060 (1160)	–	–

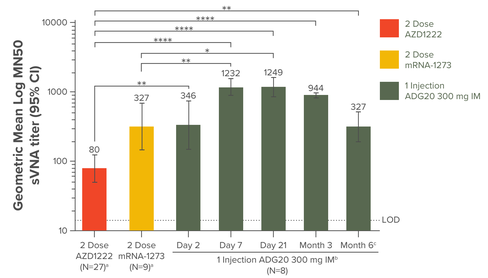
[a]Includes only participants who received ADG20. AUC, area under the curve; C_{max}, maximum serum concentration; $t_{1/2}$, half-life.

Figure 3. 6-month ADG20 serum concentration/sVNA relationship



Gray line = mean linear regression; gray shading = 95% CI; black circles = individual time matched ADG20 serum concentration and MN50 sVNA titer measurements. Linear regression excluded samples that were taken following SARS-CoV-2 vaccination from participants who received vaccination during the trial.

Figure 4. ADG20-associated sVNA titers compared with peak responses following AZD1222 and mRNA-1273 vaccination



*P <0.05; **P <0.01; ****P <0.0001 (2-tailed Mann–Whitney U test).
[a]Vaccine time point: 7 to 31 days post second dose. [b]Includes only participants who received ADG20. [c]Excludes samples that were taken following SARS-CoV-2 vaccination from participants who received vaccination during the trial.
LOD, limit of detection.

KEY FINDINGS

These data support evaluation of ADG20 in the ongoing Phase 2/3 trials for the treatment and prevention of COVID-19

A single dose of ADG20, up to 600 mg IM, 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 and consistent with an extended half-life monoclonal antibody. The observed geometric mean sVNA titer at 6 months was 327

ADG20-associated sVNA titers the day following dosing were similar to or higher than titers achieved by a full dose regimen of AZD1222. By Day 7, ADG20 sVNA titers significantly exceeded peak titers associated with AZD1222 and mRNA-1273 and were maintained at comparable levels through Study Month 6

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CONCLUSIONS

- Taken together, ADG20 was well tolerated and the preliminary PK and sVNA titer data support the potential for a single 300 mg IM injection of ADG20 to provide protection from symptomatic COVID-19 for a minimum of 6 months
- Ongoing clinical trials are evaluating the safety and efficacy of ADG20 at a single 300 mg IM injection for the prevention of COVID-19 (EVADE, ClinicalTrials.gov identifier: NCT04859517) and treatment of ambulatory patients with mild to moderate COVID-19 (STAMP, ClinicalTrials.gov identifier: NCT04805671)

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DISCLOSURES

LEC, EH, KN, DG, PGA, EC, and PS are employees of Adagio Therapeutics, Inc. ZM, AFD, and FE have received consulting fees from Adagio Therapeutics, Inc. HP has no conflicts to disclose.

Acknowledgments

The authors would like to thank the study participants and their families; Chengzi I. Kaku and Laura M. Walker (Adimab LCC, Lebanon, NH, USA) for providing AZD1222 and mRNA-1273 sVNA titer data; WCCT Global LLC (Cypress, CA, USA) for clinical monitoring; and Quartesian LLC (Princeton, NJ, USA) for programming and data management. This study was funded by Adagio Therapeutics, Inc. Writing assistance was provided by Russell Craddock, PhD, of Parexel, and was funded by Adagio Therapeutics, Inc.