Poster 1113

Clinical and virologic outcomes with early adintrevimab monoclonal antibody therapy in mild and moderate COVID-19

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INTRODUCTION

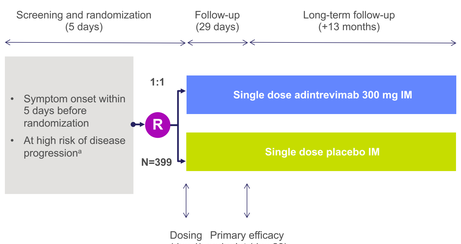
- Peak SARS-CoV-2 viral replication occurs in the upper respiratory tract in early symptomatic phases of infection[1,2]
- Administration of a monoclonal antibody (mAb) may be most beneficial in the early stages of infection, immediately after symptom onset, especially for patients who are at high risk of disease progression[3,4]
- Adintrevimab is a fully human immunoglobulin G1 mAb designed to have an extended half-life and improved potency and broad neutralization against SARS-CoV, SARS-CoV-2, and other SARS-like CoVs with pandemic potential[5,6]
- Adintrevimab can be administered intramuscularly (IM) and has been evaluated in 2 separate phase 2/3 clinical trials: the STAMP trial for treatment of COVID-19 and the EVADE trial for prevention of COVID-19 in both post-exposure and pre-exposure settings[7,8]
- In the STAMP trial, treatment with a single IM dose of adintrevimab significantly reduced the risk of COVID-19–related hospitalization or all-cause death through day 29 compared with placebo in high-risk ambulatory patients with mild to moderate COVID-19 due to non-Omicron SARS-CoV-2 (NCT04805671)[9]
- Here, we report clinical, virological, and safety outcomes in a subset of participants who received early treatment within 3 days of symptom onset in the STAMP trial

METHODS

STAMP Trial Design and Participants

- Multicenter, randomized, double-blind, placebo-controlled, phase 2/3 trial
- Eligible participants were non-hospitalized adults aged ≥18 years or adolescents aged 12 to 17 years weighing ≥40 kg at screening who had not received a SARS-CoV-2 vaccine, mAb, or convalescent plasma and who had a positive SARS-CoV-2 diagnostic assay within 5 days before randomization and at least 1 risk factor for disease progression based on age or comorbidities (**Figure 1**)
- Participants had mild or moderate COVID-19 not requiring oxygen supplementation at baseline (severity categorizations were adapted from the US Food and Drug Administration COVID-19 Guidance for Industry[10])
- Dosing was initiated in August 2021. Enrollment was suspended on January 11, 2022, because adintrevimab demonstrated lower in vitro potency against Omicron compared with other variants. Primary efficacy data are presented for the non-Omicron population. Long-term follow-up for safety is ongoing

Figure 1. STAMP study design

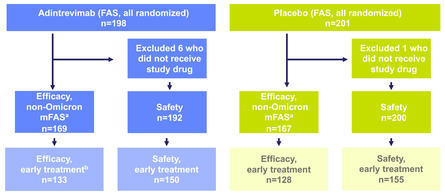


[a]At high risk defined as age >55 years or age 18 to ≤55 years with 1 or more of the following pre-existing medical conditions: obesity (body mass index [BMI] ≥30 kg/m^2), diabetes (type 1 or type 2), chronic kidney disease, chronic lung disease, cardiac disease, sickle cell disease or thalassemia, solid organ or blood stem cell transplant, other immunodeficiency due to underlying illness or immunosuppressant medication, Down syndrome, stroke or cerebrovascular disease, substance use disorder. R, randomization.

Analysis Population

- The full analysis set (FAS) included all randomized participants (n=399), regardless of whether they received study drug (**Figure 2**)
  - The non-Omicron modified FAS (mFAS) included all randomized participants with COVID-19 due to whole genome sequencing (WGS)-confirmed or suspected non-Omicron SARS-CoV-2 variants, regardless of whether the participant received study drug
- The safety population included all randomized participants who received a single IM dose of adintrevimab or placebo (**Figure 2**)
- A subgroup of participants received early treatment within 3 days of symptom onset

Figure 2. Patient disposition



[a]If baseline WGS data were missing, WGS data from post-baseline nasopharyngeal or saliva sample were used. Any participants with a missing WGS result were classified as suspected non-Omicron. [b]Early treatment denotes treatment administration within 3 days of symptom onset.

Endpoints and Assessments

- The primary endpoint was COVID-19–related hospitalization (for ≥24 hours) or all-cause death through day 29 in the non-Omicron mFAS population
- A population-level standardized risk was estimated using a logistic regression model predicted by treatment and baseline prognostic factors including continuous (age, BMI, and baseline viral load) and categorical (sex, baseline serostatus) variables[11]
- Secondary endpoints included symptom resolution/improvement and reduction in viral load (log_{10} copies/mL) from baseline assessed by reverse transcription-quantitative polymerase chain reaction (RT-qPCR) from saliva samples
- Safety and tolerability were also assessed (data cutoff date: March 28, 2022)

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DISCLOSURES

KM, KN, NB, YL, DG, PH, PS, and MP are employees of Invivyd, Inc. and may own stock or shares of Invivyd, Inc.

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RESULTS

Baseline Characteristics

Of 336 participants who comprised the non-Omicron mFAS efficacy analysis population, 261 received adintrevimab (n=133) or placebo (n=128) within 3 days of symptom onset

- Baseline characteristics were generally balanced between treatment groups (**Table 1**)

Table 1. Baseline characteristics of participants treated within 3 days of symptom onset (efficacy subgroup; early treatment)

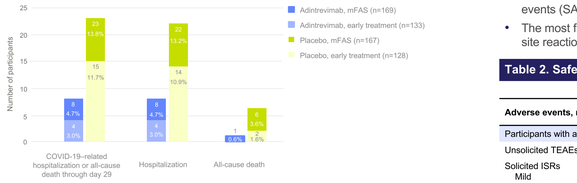
Characteristic	Adintrevimab n=133	Placebo n=128
Median age (range), years >70, n (%)	57 (22–93) 24 (18.0)	56 (21–85) 17 (13.3)
Female, n (%)	80 (60.2)	68 (53.1)
Race, n (%) White Black or African American	 132 (99.2) 1 (0.8)	 128 (100) 0
BMI, mean (SD), kg/m^2	29.25 (4.7)	30.71 (4.9)
Antibody serology status,[a] n (%) Negative Positive Missing	 118 (88.7) 15 (11.3) 0	 109 (85.2) 18 (14.1) 1 (0.8)
Disease severity, n (%) Mild Moderate	 78 (58.6) 55 (41.4)	 62 (48.4) 66 (51.6)
Select risk factors for disease progression, n (%) Age > 55 years Obesity (BMI ≥30 kg/m^2) Diabetes (type 1 or type 2)	 71 (53.4) 79 (59.4) 20 (15.0)	 68 (53.1) 76 (59.4) 15 (11.7)
Days from symptom onset to drug administration 0 1 2 3	 14 (10.5) 21 (15.8) 54 (40.6) 44 (33.1)	 17 (13.3) 19 (14.8) 49 (38.3) 43 (33.6)

[a]Measures total antibodies to SARS-CoV-2 "N" antigen.

Interim Analysis of Efficacy

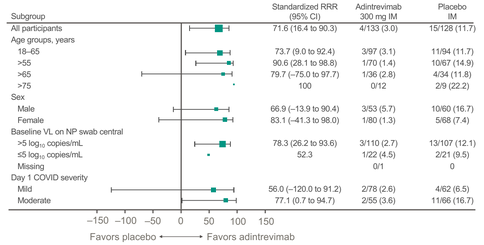
- In the overall non-Omicron mFAS population, the study met the primary endpoint, demonstrating a 66% relative risk reduction (RRR) in COVID-19–related hospitalization or all-cause death through day 29 with adintrevimab compared with placebo (**Figure 3**)[9]
  - A standardized risk difference of –8.7% (95% CI, –14.71 to –2.67; *P*=0.0047)
- Among the subgroup of participants who received early treatment, adintrevimab was associated with a clinically significant reduction in the risk of COVID-19–related hospitalization or all-cause death through day 29 compared with placebo (4 [3.0%] vs 15 [11.7%]), a 74% RRR in favor of adintrevimab. There were no deaths in the adintrevimab group (**Figure 3**)
  - A standardized risk difference of –8.0% (95% CI, –14.11 to –1.86; nominal *P*<0.05)

Figure 3. COVID-19–related hospitalization or all-cause death through day 29 (mFAS and early treatment)



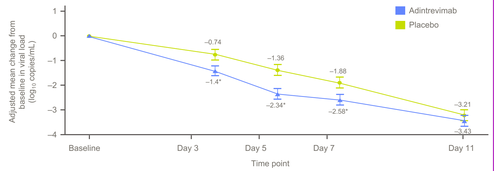
- For the early treatment subgroup
  - COVID-19–related hospitalization or all-cause death through day 29 was lower with adintrevimab vs placebo across all key prespecified subgroups (**Figure 4**)
  - Median time to sustained symptom resolution was shorter with adintrevimab (11 days; 95% CI, 10 to 14) vs placebo (15 days; 95% CI, 12 to 18)
  - Reduction in SARS-CoV-2 viral load from baseline in saliva samples was significantly greater in the adintrevimab group (adjusted least squares means difference, –0.97 (95% CI, –1.546 to –0.398; *P*=0.0010 at day 5; **Figure 5**)

Figure 4. COVID-19–related hospitalization or all-cause death through day 29 across key subgroups in participants treated within 3 days of symptom onset (early treatment)



Subgroups with fewer than 5 total events are summarized descriptively. The size of the square marker is proportional to the total number of participants meeting the criteria for the composite endpoint. NP, nasopharyngeal; VL, viral load.

Figure 5. Adjusted mean change from baseline in SARS-CoV-2 viral load (log_{10} copies/mL) assessed by RT-qPCR from saliva samples in participants treated within 3 days of symptom onset (early treatment)



Baseline is defined as last non-missing measurement prior to dosing. The bars represent standard error. *P<0.05.

Interim Analysis of Safety and Tolerability

- In the safety subgroup (as of March 28, 2022), no study drug–related serious adverse events (SAEs), including deaths, and no hypersensitivity reactions were reported (**Table 2**)
- The most frequently reported treatment emergent adverse events (TEAEs) were injection-site reactions (ISRs), all of which were mild or moderate in severity (**Table 2**)

Table 2. Safety summary of participants treated within 3 days of symptom onset

	Safety subgroup (non-Omicron mFAS)	
Adverse events, n (%)	**Adintrevimab (n=150)**	**Placebo (n=155)**
Participants with any TEAE	38 (25.3)	50 (32.3)
Unsolicited TEAEs	25 (16.7)	39 (25.2)
Solicited ISRs Mild Moderate Severe or life threating Non-graded	19 (12.7) 12 (8.0) 6 (4.0) 0 1 (0.7)	14 (9.0) 9 (5.8) 3 (1.9) 0 2 (1.3)
Study drug–related TEAEs (including ISRs)	20 (13.3)	14 (9.0)
Participants with any SAE	6 (4.0)	18 (11.6)
Study drug–related SAEs	0	0
SAEs leading to death	0	0
Any hypersensitivity reactions	0	0

KEY FINDINGS

In high-risk ambulatory patients with mild to moderate COVID-19 due to non-Omicron SARS-CoV-2, treatment with adintrevimab reduced the relative risk of COVID-19–related hospitalization or all-cause death by 66% compared with placebo

Among a subgroup of patients who received therapy within 3 days of symptom onset, adintrevimab reduced the relative risk of COVID-19–related hospitalization or all-cause death by 74% compared with placebo

Early therapy within the first 3 days also led to a greater reduction in viral load compared with placebo and shorter time to sustained symptom resolution in patients who are at high risk of disease progression

Adintrevimab was well tolerated.
The most frequently reported adverse events were mild to moderate injection-site reactions, which occurred in 12.7% and 9% of patients who received adintrevimab or placebo, respectively

CONCLUSIONS

- Early therapy with a single dose of adintrevimab 300 mg IM provided a statistically significant reduction in the risk of COVID-19–related hospitalization or all-cause death through day 29 compared with placebo in high-risk unvaccinated ambulatory patients with mild to moderate COVID-19 due to non-Omicron SARS-CoV-2
- Patients treated within 3 days of symptom onset had a lower relative risk of COVID-19–related hospitalization or all-cause death than the entire trial population

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