Poster #6

Assessment of Effect of Adintrevimab on COVID-19 Vaccine Response

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INTRODUCTION

- Monoclonal antibodies (mAbs) have been studied and administered as pre-exposure prophylaxis for COVID-19
- Many of the patients who were administered mAbs for prevention of COVID-19 would likely also have received primary series vaccination(s) as well as boosters
- Bamlanivamab, a mAb used for COVID-19, has previously been shown to not impact antibody response to vaccination[1]
- Impact of receptor binding domain (RBD)-directed COVID-19 mAbs on immune response to COVID-19 vaccines is critical to understand as both are key parts of a preventive strategy
- Adintrevimab is a fully human immunoglobulin (Ig) G1 mAb derived from a survivor of the SARS 2003 epidemic that targets the RBD
- Adintrevimab has shown potent activity through the Delta variant but reduced in vitro neutralization against Omicron BA.1/BA1.1 sublineages and no neutralizing activity against other Omicron sublineages
- Adintrevimab was studied in both a Phase 1 first in human study and a Phase 2/3 study in the prevention of COVID-19 (EVADE, NCT04859517)
- As part of these studies, the effect of adintrevimab on the vaccine response was assessed; here, we report those findings

METHODS

Study design and participants

- Participants receiving 300 mg intramuscular (IM) dose of adintrevimab were pooled across phase 1 and phase 2/3 prevention studies
  - Phase 1: Randomized, double-blind, single ascending-dose study evaluating the safety and tolerability, pharmacokinetics, and immunogenicity of ascending intravenous (IV) or IM doses of adintrevimab
  - EVADE: Multicenter, double-blind, placebo-controlled phase 2/3 trial for prevention of COVID-19
- Participants had to be seronegative prior to start of both studies but were allowed to receive a COVID-19 vaccine during the follow-up period
- Assessments were performed prior to vaccination and 2 weeks after final vaccine dose, including the collection of blood samples to measure serum virus neutralizing antibody (sVNA) titers
- sVNA titers were determined against SARS-CoV-2 D614G (BavPat1/2020) using a validated microneutralization method at Viroclinics, B.V. (Rotterdam, The Netherlands)
- These were reported using a measure of maximum serum dilution that reduced the plaque number by 80% (MN80) using methodology by Zielinska et al.[2]
- Additionally, vaccine-derived sVNA titers were measured by blocking adintrevimab activity in serum using a specific anti-idiotype (anti-ID) reagent prior to microneutralization
  - A maximum adintrevimab serum concentration of 100 µg/mL (observed across doses in the phase 1 and EVADE studies) was assumed for all samples
  - To block adintrevimab, a 10-fold excess of anti-ID blocking antibody was spiked into starting dilutions of serum, from participants that received adintrevimab or placebo.
  - Control testing demonstrated the 10-fold excess of anti-ID completely blocked the SARS-CoV-2 neutralizing activity of adintrevimab without nonspecific inhibition of other neutralizing antibodies
- Descriptive statistics are used to describe demographics, total sVNA titers and vaccine-derived sVNA titers

REFERENCES

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2. Zielinska E, et al. Virology Journal. 2005;2:84.
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5. ADG20-DOF-013. Invivyd, Inc. 2023.

DISCLOSURES

KT, DG, AH, YL, PH, PS, and KN are all employees of Invivyd and may own stock

Adintrevimab is an investigational product candidate that is not approved for use in any country. The safety and efficacy of adintrevimab have not been established.

RESULTS

Baseline Characteristics[3]

- A total of 52 participants were included in the analysis (n=21 adintrevimab, n=31 placebo)
- Baseline characteristics were balanced between groups (**Table 1**)
- Participants received 1-2 doses of COVID-19 vaccine, including Pfizer, Moderna, or J&J
- Median time to first vaccination following study dosing was 24.5 weeks (min, max: 9, 36) for the adintrevimab treated group and 10 weeks (min, max: 4, 37) for the placebo group

Table 1. Baseline characteristics

Characteristic	Adintrevimab n=21	Placebo n=31
Median age (range), years	40 (28–64)	41 (18–62)
Female, n (%)	12 (57.1)	15 (48.4)
Race, n (%)		
White	15 (71.4)	24 (77.4)
Black or African American	5 (23.8)	2 (6.5)
Native Hawaiian or Other Pacific Islander	1 (4.8)	0
Other	0	2 (6.5)
American Indian or Alaskan Native	0	1 (3.2)
Multiple	0	2 (6.5)
BMI, mean (SD), kg/m^2	30.85 (10.1)	29.68 (7.99)

Neutralizing antibody titers[4,5]

- Prior to vaccination, geometric mean MN80 titers were higher in the adintrevimab group (75.9) compared to the placebo group (11.1)
- Post-vaccination geometric mean MN80 titers were comparable across groups, adintrevimab group (201.3) vs placebo group (101.6), consistent with no impact on vaccine response by adintrevimab (**Figure 1**)
- Pre-treatment of serum with a specific anti-ID reagent to block adintrevimab activity demonstrated comparable neutralizing antibody responses due to vaccination in adintrevimab and placebo groups (**Figure 2**)

Figure 1. Pre- and Post-Vaccination sVNA Titers*

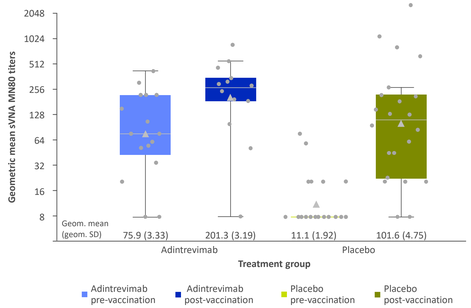
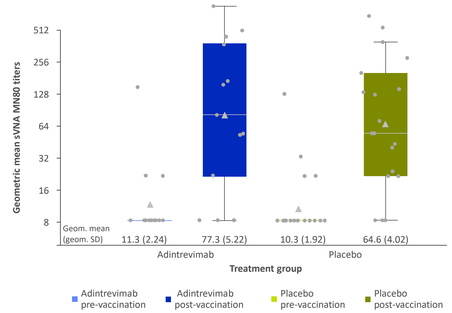


Figure 2. Vaccine-derived sVNA Titers*



*Box and triangle denote median, interquartile range (IQR), and geometric mean, respectively. Whisker end points are equal to the maximum and minimum values below or above the median ±1.5 times the IQR. Closed circle points indicate actual data.

KEY FINDINGS

Adintrevimab, a monoclonal antibody targeting the RBD on SARS-CoV-2, did not impact neutralizing antibody response to COVID-19 primary vaccination

Targeted blocking of adintrevimab with anti-idiotype reagent in vitro demonstrated comparable neutralizing antibody response to vaccination in both adintrevimab and placebo groups

CONCLUSIONS

- **Adintrevimab and bamlanivamab have both demonstrated minimal impact on neutralizing antibody response to vaccination**
- **Taken together, RBD-directed COVID-19 mAbs do not appear to inhibit the development of neutralizing antibodies after vaccination**
- **These data support the use of mAbs as part of a COVID-19 prevention plan in patients who may have impaired responses to vaccination and/or require additional protection**

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