Poster # A018

Preliminary Results for Solid Organ Transplant Patients Enrolled in CANOPY, a Phase 3 Study to Evaluate Efficacy and Safety of Pemivibart (VYD222), an IgG1 Monoclonal Antibody for Prevention of COVID-19

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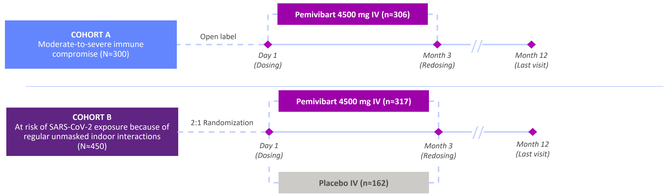
INTRODUCTION

- Given the emergence of SARS-CoV-2 variants that display resistance to monoclonal antibody (mAb) therapies, the development of next-generation mAbs with activity against circulating variants is needed to protect certain immuno-compromised populations
- Pemivibart (VYD222) is a recombinant human monoclonal IgG1λ antibody that targets the SARS-CoV-2 spike protein receptor-binding domain, thereby inhibiting virus attachment to the human angiotensin-converting enzyme 2 receptor on host cells[1]
- Pemivibart is an engineered version of adintrevimab; substitutions in the Fc region (M435L/N441A) of pemivibart extend its serum half-life[1–3]
- The US Food and Drug Administration granted pemivibart an emergency use authorization for pre-exposure prophylaxis of COVID-19 in certain adults and adolescents with moderate-to-severe immune compromise in March 2024[1]
- Here, we describe a subset of participants in Cohort A of CANOPY who were considered to have significant immune compromise because of a medical history of solid organ transplant

METHODS

Figure 1. Study Design



IV, intravenous.

Trial Design and Participants

- CANOPY (NCT06039449)[4] is an ongoing Phase 3 study that is evaluating the safety, tolerability, pharmacokinetics, and efficacy of pemivibart for pre-exposure prophylaxis of COVID-19 in adults aged ≥18 years (**Figure 1**)
- CANOPY includes Cohorts A and B
  - Cohort A is an open-label, single-arm cohort that enrolled adults with significant immune compromise to receive pemivibart
- All participants received a single dose of study drug via intravenous infusion on Day 1 and then another dose at Month 3
- For this subset analysis, data from participants in Cohort A who had a medical history of solid organ transplant and received pemivibart are reported

Endpoints and Assessment

- The primary endpoints for Cohort A included safety and calculated serum virus neutralizing antibody (sVNA) titers (pemivibart serum concentration/variant half-maximal inhibitory concentration [IC_{50}]) against relevant SARS-CoV-2 variants
- The primary analysis was based on an immunobridging approach to determine if calculated sVNA titers of pemivibart were consistent with titer levels associated with efficacy in prior clinical trials of other mAbs against SARS-CoV-2
- Secondary and exploratory endpoints evaluated presence of reverse transcription polymerase chain reaction (RT-PCR)–confirmed symptomatic COVID-19, severity and duration of COVID-19, presence of long COVID, and COVID-19–related hospitalization or death

Immunobridging

- All participants who received a full dose at the initial dosing and had a quantifiable serum concentration result at Day 28 were included in this analysis
- To demonstrate immunobridging, a protection titer threshold was determined for analysis
  - A protection titer threshold of 3514 at 3 months was chosen based on historical data from the EVADE study (NCT04859517), which demonstrated clinical efficacy (71% relative risk reduction verses placebo) of adintrevimab for pre-exposure prophylaxis against the Delta variant[3]
  - The protection titer threshold of 3514 at 3 months was back extrapolated to a titer of 8944 on day 28 based on the half-life of pemivibart
- sVNA titers at Day 28 were calculated based on serum pemivibart concentrations measured in participants on Day 28 divided by the IC_{50} against JN.1
- To determine if immunobridging was met, the ratio of geometric mean titers (GMTs) against selected SARS-CoV-2 variants at Day 28 following pemivibart administration was compared with the corresponding protection titer threshold of 8944, as described above
- Immunobridging was demonstrated if the lower limit of the 2-sided 90% CI of the ratio of the GMT value was greater than 0.8 among all participants who received a full dose at the initial dosing and had a quantifiable serum concentration result at Day 28
- JN.1 was chosen as it was the predominant variant in the United States at the time of analysis

Assessment of COVID-19

- Symptoms of COVID-19–like illness were self-reported by participants throughout the study
- Nasopharyngeal swab and saliva samples were collected from participants with qualifying symptoms and submitted for confirmatory testing at a central lab
- A participant was considered to have COVID-19 if they had RT-PCR–confirmed SARS-CoV-2 with onset of symptoms ≤14 days from the date of the positive sample collection or had a COVID-19–related hospitalization or all-cause death

RESULTS

Participants

- A total of 306 participants were enrolled in Cohort A; of these, 33 (11%) had a medical history of solid organ transplant (**Table 1**)
  - Types of transplant included 23 kidney, 2 heart, 2 lung, 4 liver, 1 kidney/pancreas, and 1 kidney/pancreas/islet cell
  - All 33 participants who had a solid organ transplant were actively taking immunosuppressants
  - 30 of 33 participants received the first full dose of pemivibart
    - 2 participants had IV infiltration; and 1 participant had tachycardia
  - 30 of 33 participants received the second dose of pemivibart
    - 1 participant withdrew
    - Site was unable to establish IV access
    - Physician decision because of tachycardia during first infusion
  - All 33 participants had received a prior vaccine for COVID-19; of those, the mean number of vaccinations was 5

Table 1. Baseline demographic characteristics of solid organ transplant subset

Characteristic	Pemivibart N = 33
Median age (range), years	64 (24–75)
≥55, n (%)	24 (72.7)
Female, n (%)	16 (48.5)
Race, n (%)	
White	28 (84.8)
Asian	2 (6.1)
Black or African American	2 (6.1)
Other	1 (3)
BMI, mean (SD), kg/m^2	30 (9.9)
Antibody serology N-protein status, n (%)	
Negative	23 (69.7)
Positive	10 (30.3)
Antibody serology S-protein status, n (%)	
Negative	1 (3)
Positive	32 (97)
Significant immune compromise,[a] n (%)	
Solid organ transplant recipient taking immunosuppressive therapy	33 (100)
Moderate or severe primary immunodeficiency	1 (3)
Advanced HIV infection (CD4 count <350 cells/mm^3)	1 (3)
Taking other immunosuppressive medications	26 (78.8)
Immunosuppressants,[b] n (%)	
Tacrolimus	24 (73)
Mycophenolate	26 (79)
Belatacept	7 (21)
Select risk factors for disease progression (other than immune compromise)[a], n (%)	
Obesity (BMI ≥30 kg/m^2)	11 (33.3)
Diabetes (type 1 or type 2)	13 (39.4)
Cardiac disease	20 (60.6)
Chronic lung disease	5 (15.2)
Chronic kidney disease	15 (45.5)
Number of prior COVID-19 vaccinations received by participants	
Mean (SD)	5.4 (1.97)
Median (range)	5.5 (1–9)

[a]Participants may be in more than one category. [b]Other immunosuppressants administered (1 participant each): cyclosporin, everolimus, leflunomide, sirolimus, ustekinumab, vedolizumab.
BMI, body mass index.

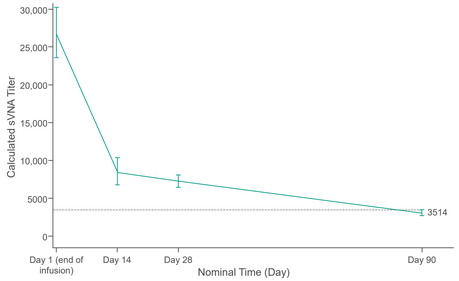
Assessment of COVID-19 for solid organ transplant subset

No cases of RT-PCR–confirmed symptomatic COVID-19 were reported in this subgroup of participants through Month 3; 3 cases were reported overall in Cohort A through Month 3

Immunobridging for solid organ transplant subset

- 28 of 33 participants were included in the analysis set for immunobridging
- The immunobridging results are as follows: GMT ratio for JN.1 variant using IC_{50} determined by authentic virus neutralization assay was 0.8 (90% CI, 0.71–0.90)
- Similar to overall Cohort A, the range of titers achieved with pemivibart in this subset for 3 months following administration of 4500 mg IV were consistent with the titer levels associated with clinical efficacy in prior clinical trials evaluating certain mAbs for prevention of COVID-19[5] **(Figure 2)**

Figure 2. Calculated serum neutralizing antibody titer against JN.1 in participants with a medical history of solid organ transplant



The plot displays GMT and 90% CI at each time point. The sVNA titers are calculated based on the serum concentration of pemivibart divided by IC_{50} value against JN.1 (63.6 ng/mL; authentic virus neutralization assay). The dotted line represents the protection threshold.

Safety and tolerability

- In this subset of participants
  - 52% of participants reported a treatment-emergent adverse event (TEAE; **Table 2**)
  - The most common TEAEs occurring in >5% of participants were influenza-like illness, infusion related reactions, infusion site extravasation, rhinovirus infection
  - 3 participants experienced TEAEs considered study drug related
    - 2 participants had infusion related reactions
    - 1 participant experienced tachycardia and tremor which led to permanent study drug discontinuation
  - Serious AEs (all with severity grade ≥3) included pneumonia, cholangitis, and pyelonephritis
  - There were no serious study drug–related TEAEs
  - In the overall Cohort A (n=306), 4 cases of anaphylaxis occurred, while no cases of anaphylaxis were noted in this subset

Table 2. Safety for solid organ transplant subset

Description, n (%)	Pemivibart (n=33)
Participants with any TEAE	17 (51.5)
Any TEAE grade ≥3	3 (9.1)
Any serious TEAE	2 (6.1)
Any TEAE leading to death	0
Any TEAE leading to permanent study treatment discontinuation	1 (3)
Any TEAE leading to study treatment interruption	4 (12.1)
Any study drug–related TEAE	3 (9.1)
Any study drug–related TEAEs leading to death	0

KEY FINDINGS for subset of participants with solid organ transplant

Cohort A of CANOPY comprised participants who were moderately to severely immunocompromised; 11% of those participants had a solid organ transplant

Geometric mean titer ratio for this subset of participants was 0.8

No cases of RT-PCR–confirmed symptomatic COVID-19 were reported in this subset of participants through 3 months post dosing

CONCLUSIONS for subset of participants with solid organ transplant

- **There were no serious study drug–related adverse events reported in this subset of participants receiving pemivibart 4500 mg IV; there were 4 cases of anaphylaxis in the overall cohort (n=306)**
- **Pemivibart produced high calculated neutralizing titer levels against JN.1**

REFERENCES

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2. Ison MG, et al. *Open Forum Infect Dis.* 2023;10:ofad279.
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5. Stadler E, et al. *Nat Commun.* 2023;14:4545.

DISCLOSURES

MP, KM, KT, DG, YL, and PH are all employees of Invivyd, Inc. and may own stock.
NB and PS were employees of Invivyd, Inc. at the time of this analysis.

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

Acknowledgments

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