Poster # 2532

A Phase 3 Study to Evaluate Efficacy and Safety of Pemivibart (VYD222), an IgG1 Monoclonal Antibody for Prevention of COVID-19 (CANOPY): Subset Analysis of Participants With Significant Immune Compromise in the Setting of Solid Tumor or Hematologic Malignancies

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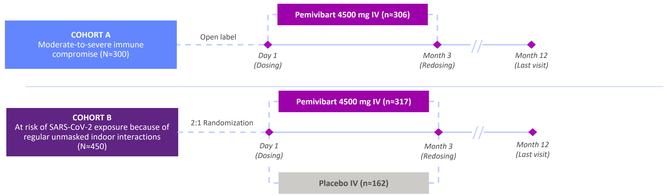
INTRODUCTION

- 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 in the setting of solid tumor or hematologic malignancies

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 with active treatment for solid tumor or hematologic malignancies or a diagnosis of acute leukemia, chronic lymphocytic leukemia (CLL), non-Hodgkin lymphoma, or multiple myeloma (regardless of treatment) 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 immune-compromised participants were enrolled in Cohort A
  - Of those, 55 (18%) were included in the solid tumor or hematologic malignancy subset (**Table 1**)
- 20 (36%) participants were being actively treated for solid tumor or hematologic malignancy, and 40 (73%) had a hematologic cancer diagnosis
  - The most common diagnosis was CLL, which was reported in 28 (51%) participants
- 55 participants received the first full dose of pemivibart, with 2 participants having the initial infusion interrupted
  - 54 of 55 participants received the second dose of pemivibart
- Most participants (87%) reported receipt of a COVID-19 vaccine at some time prior to study entry
  - The mean number of prior COVID-19 vaccinations was 5

Table 1. Baseline Demographic Characteristics of Solid Tumor or Hematologic Malignancy Subset

Characteristic	Pemivibart n=55
Median age (range), years	65 (35–83)
≥55, n (%)	44 (80)
Male, n (%)	30 (54.5)
Race,[a] n (%)	
White	50 (90.9)
Black or African American	4 (7.3)
American Indian or Alaska Native	1 (1.8)
Multiple	1 (1.8)
Other	1 (1.8)
BMI, mean (SD), kg/m^2	28.1 (6.2)
Antibody serology N-protein status, n (%)	
Negative	30 (54.5)
Positive	24 (43.6)
Missing	1 (1.8)
Antibody serology S-protein status, n (%)	
Negative	0
Positive	54 (98.2)
Missing	1 (1.8)
Significant immune compromise,[a] n (%)	
Actively treated for solid tumor or hematologic malignancy	20 (36.4)
Acute leukemia, CLL, non-Hodgkin lymphoma, or multiple myeloma	40 (72.7)
Moderate or severe primary immunodeficiency	2 (3.6)
Advanced HIV infection (CD4 count <350 cells/mm^3)	1 (1.8)
Taking other immunosuppressive medications	9 (16.4)
Select risk factors for disease progression (other than immune compromise),[a] n (%)	
Obesity (BMI ≥30 kg/m^2)	20 (36.4)
Diabetes (type 1 or type 2)	9 (16.4)
Cardiac disease	27 (49.1)
Chronic lung disease	11 (20)
Chronic kidney disease	3 (5.5)
Stroke or cerebrovascular disease	4 (7.3)
Number of prior COVID-19 vaccinations received by participants	
Mean (SD)	5.4 (1.61)
Median (range)	6 (2–8)

[a]Participants may be in more than one category.
BMI, body mass index.

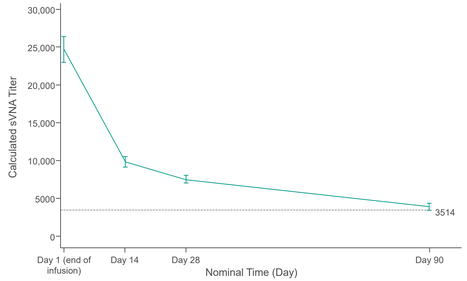
Assessment of COVID-19 for Solid Tumor/Hematologic Malignancy Subset

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

Immunobridging for Solid Tumor/Hematologic Malignancy Subset

- 54 of 55 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 at Day 28 was 0.84 (90% CI, 0.79–0.90), consistent with the result in the overall population of Cohort A
- GMT for JN.1 variant using IC_{50} determined by authentic virus neutralization assay stayed above the 3-month protection threshold of 3514 at Day 90 in this subset of participants (**Figure 2**), consistent with the result in the overall population of Cohort A
- 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 Solid Tumor or Hematologic Malignancy Subset



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
  - 51% of participants reported a treatment-emergent adverse event (TEAE; **Table 2**)
  - The most common TEAEs occurring in >2% of participants were upper respiratory tract infection, diarrhea, fatigue, hypertension, influenza-like illness, infusion-site extravasation, nausea, and viral infection
  - 4 participants experienced TEAEs considered study drug related
    - Nausea, headache, fatigue and tachycardia were reported by one participant each and considered infusion-related; one participant also reported night sweats
    - All were mild in severity; none led to permanent study drug discontinuation
  - Serious AEs (all with severity grade ≥3) included cholecystitis (2), colon cancer, basilar artery aneurysm, and death (unknown cause). None were considered related to study drug
- 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 Tumor or Hematologic Malignancy Subset

Description, n (%)	Pemivibart (n=55)
Participants with any TEAE	28 (50.9)
Any TEAE grade ≥3	5 (9.1)
Any serious TEAE	5 (9.1)
Any TEAE leading to death	1 (1.8)
Any TEAE leading to permanent study treatment discontinuation	0
Any TEAE leading to study treatment interruption	3 (5.5)
Any study drug–related TEAE	4 (7.3)
Any study drug–related TEAE leading to death	0

REFERENCES

1. Fact Sheet for Healthcare Providers: Emergency Use Authorization for Pemivibart. https://www.fda.gov/media/177067/download?attachment. Last updated March 22, 2024
2. Ison MG, et al. *Open Forum Infect Dis*. 2023;10:ofad279.
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4. ClinicalTrials.gov. https://classic.clinicaltrials.gov/ct2/show/NCT06039449. Accessed May 1, 2024.
5. Stadler E, et al. *Nat Commun*. 2023;14:4545.

DISCLOSURES

MP, KM, KN, AP, DG, YL, PH, GGL, and AH are all employees of Invivyd, Inc. and may own stock.

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

The study was funded by Invivyd, Inc.

KEY FINDINGS for Subset of Participants with Solid Tumor or Hematologic Malignancies

Cohort A of the CANOPY trial enrolled participants who were moderately to severely immunocompromised; 18% (n=55) of those participants had solid tumor or hematologic malignancies

The geometric mean neutralizing titers in this subset were above the predefined protection threshold at Day 90

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 Tumor or Hematologic Malignancies

- **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**

Poster presented at the American Society of Clinical Oncology Annual Meeting; May 31–June 4, 2024; Chicago, IL

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