Poster # 750

A Phase 3 study to evaluate efficacy and safety of pemivibart, an IgG1 monoclonal antibody for prevention of COVID-19 (CANOPY): Subset analysis of participants with chronic lymphocytic leukemia

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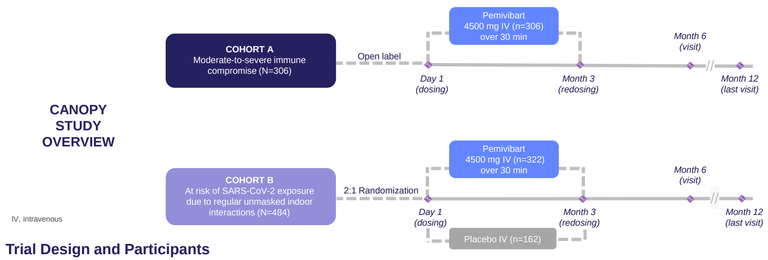
INTRODUCTION

- Given the emergence of SARS-CoV-2 variants that displayed resistance to monoclonal antibody (mAb) therapies, the development of next-generation mAbs with activity against circulating variants was needed to protect certain immunocompromised 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 with improved binding to omicron variants; both contain substitutions in the Fc region (M435L/N441A) to extend serum half-life[1–3]
- A phase 3 study investigating pemivibart (CANOPY; NCT06039449) for pre-exposure prophylaxis of COVID-19 in immunocompromised participants (Cohort A) and in immunocompetent participants at risk of exposure to SARS-CoV-2 (Cohort B) was conducted[4, 5, 6]
- The US Food and Drug Administration issued 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 the single-arm, open-label Cohort A of CANOPY, who were considered to have significant immune compromise due to chronic lymphocytic leukemia (CLL)

METHODS

Figure 1. CANOPY, a phase 3 study to evaluate efficacy and safety of pemivibart for the prevention of COVID-19



Trial Design and Participants

- CANOPY was a 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**)[4, 5, 6]
- CANOPY Cohort A was an open-label, single-arm cohort that enrolled adults with significant immune compromise to receive pemivibart
- CANOPY Cohort B was a randomized placebo-controlled cohort of immunocompetent participants at risk of acquiring SARS-CoV-2
- All participants received a dose of study drug via intravenous infusion on Day 1 and then another equivalent dose at Month 3 over 30 minutes
  - Infusion time changed to 60 minutes for 31 participants in Cohort A that received 2nd dose
  - Participants were followed through Month 12; no additional doses were administered following the Month 3 dose
- Data from participants in Cohort A who had a medical history of CLL and received pemivibart are reported in this subset analysis

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 (results previously reported)[5]
- The primary efficacy 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, COVID-19–related hospitalization or death, and emergence of pemivibart resistance

Assessment of COVID-19

- Symptoms of COVID-19–like illness were self-reported by participants throughout the study
- Nasopharyngeal (NP) swab and saliva samples were collected from participants with qualifying symptoms and submitted for confirmatory testing at a central lab; next generation sequencing of the spike gene was performed on positive NP samples to determine SARS-CoV-2 variant and monitor for mutations associated with resistance
- 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

REFERENCES

1. Fact Sheet for Healthcare Providers: Emergency Use Authorization for Pemivibart. Last updated September 2024.
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6. Wolfe C, et al, medRxiv 2024.11.11.24317127.

DISCLOSURES

PH, KN, AP, DG, AH are employees of Invivyd, Inc, and may own stock. YL was an employee at the time the study was conducted. DW is a paid consultant of Invivyd, Inc.

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.

RESULTS

Participants

- A total of 306 participants were enrolled in Cohort A; of these, 29 (9.5%) were included in the CLL subset (**Table 1**)
- All 29 CLL participants received both the first and second doses of pemivibart
- Median age was 66 years, 52% were female
- Median number of prior COVID-19 vaccinations received in the CLL subset was 6
- 31% of participants were actively taking antineoplastic agents: venetoclax (3), acalabrutinib (2), fluorouracil (2), ibrutinib (2), cetuximab (1), obinutuzumab (1), pembrolizumab (1), rituximab (1), ruxolitinib phosphate (1), zanubrutinib (1)
- 28 participants completed the study; 1 participant was unable to make final visit due to hospitalization due to hematoma

Table 1. Baseline Demographic Characteristics CLL Subset

Characteristic	Pemivibart (n=29)
Median age (range), years	66 (39–83)
≥55, n (%)	25 (86.2)
Female, n (%)	15 (51.7)
Race,[a] n (%)	
White	28 (96.6)
Black or African American	0 (0)
American Indian or Alaska Native	1 (3.4)
Multiple	1 (3.4)
Other	1 (3.4)
BMI, mean (SD), kg/m^2	26.2 (4.2)
Antibody serology SARS-CoV-2 N-protein status, n (%)	
Negative	21 (72.4)
Positive	7 (24.1)
Missing	1 (3.4)
Antibody serology SARS-CoV-2 S-protein status, n (%)	
Negative	0
Positive	28 (96.6)
Missing	1 (3.4)
Select risk factors for disease progression (other than immune compromise),[a] n (%)	
Age ≥55	25 (86.2)
Obesity (BMI ≥30 kg/m^2)	7 (24.1)
Diabetes (type 1 or type 2)	4 (13.8)
Cardiac disease	12 (41.4)
Chronic lung disease	5 (17.2)
Chronic kidney disease	1 (3.4)
Stroke or cerebrovascular disease	1 (3.4)
Number of prior COVID-19 vaccinations received by participants	
Median (range)	6 (2–7)

[a]Participants may be in more than one category
BMI, body mass index; N-protein, nucleocapsid protein, S-protein, spike protein

Assessment of COVID-19 for CLL subset

- The predominant variants circulating during CANOPY were SARS-CoV-2 Omicron sublineages HV.1 (mean IC_{50}=41.2 ng/mL), JN.1 (mean IC_{50}=74.6 ng/mL), and KP.3.1.1 (mean IC_{50}=239.3 ng/mL) (**Figure 2**)
- No cases of RT-PCR–confirmed symptomatic COVID-19 were reported in this subgroup of CLL participants through Month 6 (**Table 2**)
  - 6 cases were reported in the follow-up period (Month 6-12) when no additional doses of pemivibart were given
- For the cases that developed between Month 6 and Month 12, the time from most recent dosing to symptom onset was a median of 224 days (min 123, max 235)
- SARS-CoV-2 spike sequence was obtained from 3 of 6 confirmed NP samples. None demonstrated mutations within close proximity of the pemivibart binding site potentially associated with resistance. SARS-CoV-2 variants observed included KP.3.3 and KP.3.1.1, consistent with infections occurring late in CANOPY during the follow up phase.

Figure 2. CDC proportions of tracked variants during CANOPY trial (Cohort A)

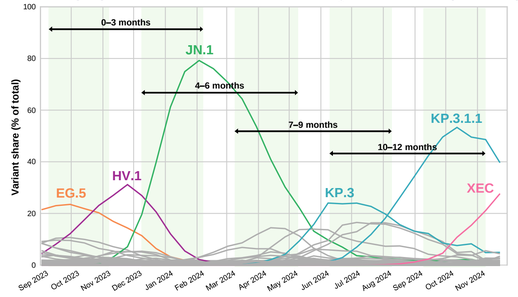

Table 2. Incidence of RT-PCR–confirmed symptomatic COVID-19, COVID-19–related hospitalizations, and all-cause mortality among adults with CLL

n (%)	Outcomes	Active Dosing Period through Month 6, n (%)	Follow Up Period (no additional doses) through Month 12, n (%)
Pemivibart (n=29)	Composite RT-PCR–confirmed COVID-19	0 (0)	6 (20.7)
	Symptomatic COVID-19	0 (0)	6 (20.7)
	COVID-19–related hospitalizations	0 (0)	0 (0)
	All-cause mortality	0 (0)	0 (0)

RT-PCR, reverse transcription polymerase chain reaction

Safety and tolerability

- In this subset of participants:
  - 76% of participants reported a treatment-emergent adverse event (TEAE; **Table 3**)
  - The most common TEAEs occurring in >5% of participants were upper respiratory tract infection, back pain, fatigue, gastritis, hypertension, and urinary tract infection
  - 5 participants experienced TEAEs considered study drug related
    - 4 participants had events considered infusion related reactions within 24 hours of study drug administration (fatigue, nausea, headache, tachycardia, flushing)
  - There were no serious study drug related TEAEs
- Overall in Cohort A (n=306) 4 cases of anaphylaxis occurred; no cases occurred in this subset

Table 3. Safety for CLL subset

Description, n (%)	Pemivibart (n=29)
Participants with any TEAE	22 (75.9)
Any TEAE grade ≥3	2 (6.9)
Any serious TEAE	1 (3.4)
Any TEAE leading to death	0
Any TEAE leading to permanent study treatment discontinuation	0
Any TEAE leading to study treatment interruption	1 (3.4)
Any study drug–related TEAE	5 (17.2)
Any study drug–related serious TEAE	0

KEY FINDINGS

for Subset of Participants with CLL

Cohort A of the CANOPY trial enrolled participants who were moderately to severely immune compromised; 9.5% (n=29) of those participants had CLL

Following a dose of pemivibart given on Day 1 and Month 3, no cases of RT-PCR–confirmed symptomatic COVID-19 were reported in this subset of CLL participants through Month 6

In 6 participants who developed COVID-19 during the follow up period (Month 6 to 12), median time to onset of symptoms from most recent dose (at Month 3) was approximately 7.5 months

CONCLUSIONS

for Subset of Participants with CLL

- **In the CLL subset of the CANOPY study, the protection provided by pemivibart was observed during circulation of contemporary variants**
- **There were no serious study drug–related adverse events reported in this subset of participants receiving pemivibart 4500 mg IV**

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