Pemivibart for Prevention of COVID-19: Phase III CANOPY Subset in Advanced HIV Infection

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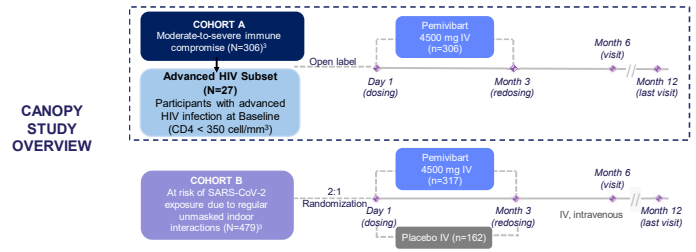
INTRODUCTION

- People living with HIV remain at increased risk of severe outcomes from COVID-19 due to underlying immunologic vulnerability and comorbidities[1,2]
- Pemivibart is a recombinant human monoclonal IgG1λ antibody that targets the SARS-CoV-2 spike protein receptor binding domain, thereby inhibiting virus attachment to host cells[3]
- Based on Phase 3 CANOPY data (NCT06039449), pemivibart was granted emergency use authorization (Mar 2024) for pre-exposure prophylaxis of COVID-19 in certain adults and adolescents with moderate-to-severe immune compromise[4,5,6]

Here we describe a post hoc analysis of participants with advanced HIV infection in the CANOPY open-label, single-arm immunocompromised Cohort A.

METHODS

Figure 1. CANOPY, A Phase 3 Study To Evaluate Efficacy and Safety of Pemivibart for the Prevention Of COVID-19



Trial Design and Subset Analysis

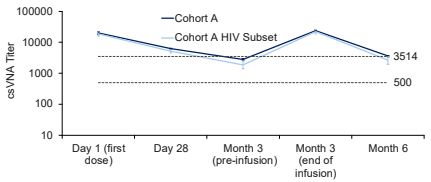
- CANOPY was a Phase 3 study that evaluated the safety, tolerability, pharmacokinetics, and efficacy of pemivibart for pre-exposure prophylaxis of COVID-19 in adults aged ≥18 years (**Figure 1**)[4,5,6]
- CANOPY Cohort A: open-label, single-arm cohort that enrolled adults with significant immune compromise to receive pemivibart (**Figure 1 dashed box**)
- Primary and secondary objectives from CANOPY Cohort A included the following:
  - Primary
    - Evaluation of safety via study drug-related treatment emergent adverse events (TEAEs), serious adverse events (SAEs), and treatment interruption/discontinuation
    - Evaluation of protection against symptomatic COVID-19 based on calculated serum virus neutralizing antibody (csVNA) titers against SARS-CoV-2 after receiving pemivibart (immunobridging data reported previously[4])
  - Secondary
    - Evaluation of sVNA titers against SARS-CoV-2 after receiving pemivibart via csVNA and measured sVNA titers against relevant SARS-CoV-2 variants
    - Evaluation of pemivibart in the prevention of RT-PCR-confirmed symptomatic COVID-19 via RT-PCR-confirmed symptomatic COVID-19
    - Evaluation of the immunogenicity and PK of pemivibart
- 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 increased to 60 minutes with 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
- The advanced HIV subset included Cohort A participants with advanced HIV infection at baseline (CD4 < 350 cell/mm³)
- Data are presented for both Cohort A and Cohort A advanced HIV subset that were analyzed through Month 6

RESULTS

Participants

- CANOPY participants were enrolled from September 2023 – November 2023
- A total of 306 participants were enrolled in Cohort A
  - 27 (8.8%) were included in the advanced HIV subset (**Table 1**)
- Twenty-six (96.3%) participants in the advanced HIV subset reported drug-management via antiviral/antiretroviral treatment
- Prior to enrollment, 85.2% participants in the advanced HIV subset received ≥ 1 COVID-19 vaccine; majority were seropositive to N (74.1%) and S (96.3%) antigens but < 50% had measurable sVNA titers against historical/concurrent variants (**Table 1**).

Figure 2: csVNA Titer Against JN.1[a] in CANOPY Cohort A and Advanced HIV Subset Through Month 6



[a]JN.1 variant was the predominant variant in the United States at the time of analysis; The plot displays GMT and 90% confidence interval at each time point. The sVNA titers were calculated based on the serum concentration of pemivibart divided by IC50 value against JN.1 (74.6 ng/mL; pseudotyped VLP neutralization assay). The dotted lines represent protection titer thresholds. A threshold of 3514 is based on historical data from the EVADE study (NCT04859517), which demonstrated clinical efficacy (71% relative risk reduction vs. placebo) of adintrevimab for pre-exposure prophylaxis against the Delta variant through 3 months.[7,8] A time-varying Cox proportional hazards model developed using total CANOPY efficacy and csVNA titer data demonstrated a threshold of 500 was associated with an estimated efficacy of 50% (immunocompromised) and 70% (non-immunocompromised) for the protection against symptomatic COVID-19.[9]

Table 1. Baseline Characteristics in CANOPY Cohort A and Advanced HIV Subset

Parameter	Cohort A n=306[6]	Cohort A Advanced HIV Subset n =27
Median age [range], years	59 [22-83]	60 [39-77]
Female, n (%)	187 (61.1)	4 (14.8)
BMI, mean (SD), kg/m²	29.5 (7.8)	28.6 (9.6)
Participants with prior COVID-19 vaccinations, n (%)	269 (87.9)	23 (85.2%)
Number of prior COVID-19 vaccinations, median (range)	5 (1-11)	3 (1-6)
≥1 Concomitant medication	305 (99.7)	26 (96.3)
Risk Factor for COVID-19[a] (%)		
Age (≥55 years)	58.5	66.7
Obesity (BMI > 30 kg/m²)	37.9	25.9
Diabetes (T1 or T2)	17.6	7.4
Chronic kidney disease	10.1	3.7
Chronic lung disease	19.0	18.5
Cardiac disease	42.2	37.0
Sickle cell disease	0.3	0.0
Solid organ transplant recipient	10.8	3.7
Stroke or cerebrovascular disease	2.9	11.1
Substance use disorder	2.0	7.4
Baseline serology, (%)		
N-protein positive	49.0	74.1
N-protein negative	49.3	25.9
S-protein positive	97.7	96.3
S-protein negative	0.7	3.7
Baseline measured SARS-CoV-2 sVNA titers (%[b])		
msVNA titers against B.1.617.2	85.3	48.1
msVNA titers against BA.4/5	69.0	44.4
msVNA titers against XBB1.5	41.2	22.2

[a]Participants may be in more than one category;
[b]Baseline msVNA titer above detectable threshold
BMI, body mass index; N-protein, nucleocapsid protein, S-protein, spike protein; msVNA, measured serum virus neutralizing antibody

Safety and Tolerability

- Through Month 6, 66.7% of Cohort A advanced HIV participants reported a TEAE (**Table 2**)
  - 7 (25.9%) were SAEs
  - 2 (7.4%) were study-drug related, 1 (3.7%) of which required treatment interruption but was not considered an SAE
- Two all-cause mortalities were reported (**Table 3**)
- There were no instances of anaphylaxis in the advanced HIV subset; 4 cases of anaphylaxis were reported in the overall Cohort A

Assessment of COVID-19 for Cohort A and Advanced HIV Subset

- Following pemivibart dosing, advanced HIV subset csVNA titers were elevated to levels associated with protection against COVID-19 and were comparable with the overall Cohort A6 (**Figure 2**)
- No cases of RT-PCR-confirmed symptomatic COVID-19 were reported in the Cohort A advanced HIV subset through Month 6 (**Table 3**)

Table 2. Safety for CANOPY Cohort A and Advanced HIV Subset Through Month 6[a]

Parameter	Overall Cohort A n=306	Cohort A Advanced HIV Subset n=27
TEAE, n (%)	204 (66.7)	18 (66.7)
SAE, n (%)	35 (11.4)	7 (25.9)
Study drug related TEAEs, n (%)	34 (11.1)	2 (7.4)
-leading to death	0 (0.0)	0 (0.0)
-leading to interruption	14 (4.6)	1 (3.7)[c]
-leading to discontinuation	7 (2.3)[b]	0 (0.0)

[a]Safety analysis set includes all participants who received any amount of study drug during the study
[b]Cohort A pemivibart-related causes of study discontinuation included: Hypersensitivity (n = 2), anaphylaxis (n = 2), infusion related reaction (n = 2), tachycardia (n = 1), tremor (n = 1).
[c]Cohort A advanced HIV subset pemivibart-related cause of study interruption included: infusion related reaction (n = 1)

Table 3. Incidence of RT-PCR–confirmed symptomatic COVID-19, COVID-19–related hospitalizations, and all-cause mortality among CANOPY Cohort A and Advanced HIV Subset Through Month 6[a]

Parameter	Overall Cohort A n=298	Cohort A Advanced HIV Subset n=27
COVID-19 composite event, n (%)[b]	11 (3.7)	2 (7.4)
PCR-confirmed case, n (%)	9 (3.0)	0 (0.0)
All-cause mortality	2 (0.7)[c]	2 (7.4)[c]

[a]Full analysis set includes all participants who received a full dose of study drug at the initial dosing
[b]Assessment of COVID-19: 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.
[c]Cause: Suicide (n=1), Unknown (n=1)

KEY FINDINGS

for Advanced HIV Subset

- **CANOPY enrolled participants with immune compromise (Cohort A); among these, 27 participants (8.8%) were in the advanced HIV subset**
- **Pemivibart was well-tolerated in the advanced HIV subset as measured by study drug-related TEAEs**
- **csVNA titers were elevated to levels associated with protection by pemivibart in the advanced HIV subset**
- **There were no cases of RT-PCR-confirmed symptomatic COVID-19 reported through Month 6 in the advanced HIV subset**

CONCLUSIONS

for Advanced HIV Subset

These data support pemivibart as a preventative option against COVID-19 in this high-risk clinical group

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DISCLOSURES

ML, KN, IY, MW are employees of Invivyd, Inc, and may own stock. DW is a paid consultant of Invivyd, Inc.

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