# Safety and Efficacy of Pemivibart, a Long-acting Monoclonal Antibody, for Prevention of Symptomatic COVID-19: Final Analysis From a Phase 3 Randomized Clinical Trial (CANOPY)

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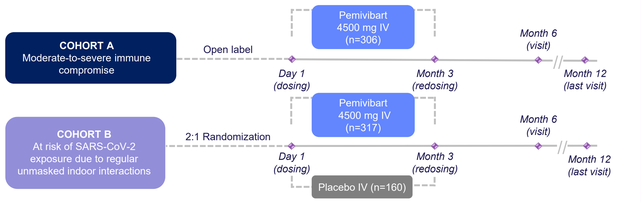
## INTRODUCTION

- Emerging variants of SARS-CoV-2 remain a significant clinical threat, with acute infection associated with severe outcomes, including hospitalization and death. Post-acute sequelae, such as Long COVID, may occur irrespective of initial disease severity and contribute to ongoing impairment in daily activity[1-3]
- Previous natural exposure and/or vaccination is imperfect for preventing future SARS-CoV-2 infections[4]
- Monoclonal antibodies targeted to SARS-CoV-2 spike protein represent an alternative preventive strategy against COVID-19[5]
- Here we summarize the 12-month analysis of safety and efficacy of pemivibart in individuals with (Cohort A) or without (Cohort B) significant immunocompromise in the phase 3 CANOPY trial

## METHODS

**Figure 1. CANOPY, a Phase 3 Study to Evaluate Efficacy and Safety of Pemivibart for the Prevention of COVID-19[a]**




*[a]Of 482 participants randomized, 480 (99.6%; 320 pemivibart, 160 placebo) comprised the full analysis set (FAS) and 477 (99.0%; 317 pemivibart, 160 placebo) the safety analysis set (SAS). Cohort B modified FAS (mFAS) includes all randomized participants without SARS-CoV-2 infection at baseline who received any amount of pemivibart or placebo.*

### Study Design

- CANOPY (NCT06039449) was a Phase 3, randomized, placebo-controlled trial (conducted in the United States during 2023-2024) that evaluated the safety, tolerability, pharmacokinetics, and efficacy of pemivibart for pre-exposure prophylaxis of COVID-19 in adults aged ≥18 years (**Figure 1**)
- **CANOPY Cohort A:** open-label, single-arm cohort that enrolled adults with significant immune compromise to receive pemivibart
- **CANOPY Cohort B:** randomized, double-blind, placebo-controlled cohort of non-immunocompromised participants at risk of acquiring SARS-CoV-2 due to regular unmasked face-to-face interactions in indoor settings (e.g., workplace, gym facility, public transportation). Participants were randomized (2:1) to receive either pemivibart or placebo.
- Participants received a dose of study drug via intravenous infusion on Day 1 and then another equivalent dose at Month 3
  - Participants were followed through Month 12; no additional doses were administered following the Month 3 dose

### Objectives and Assessments

***Cohort A Primary Objectives:***

- Evaluation of safety and tolerability of pemivibart in all treated participants
- Evaluation of protection against symptomatic COVID-19 based on sVNA titers against SARS-CoV-2 after receiving pemivibart (immunobridging data reported previously[6])

***Cohort B Primary Objective:***

- Evaluation of safety and tolerability of pemivibart compared with placebo in all treated participants

***Additional Objectives Include:***

- Evaluation of sVNA titers against SARS-CoV-2 after receiving pemivibart via csVNA and measured sVNA titers against relevant SARS-CoV-2 variants (i.e., pseudotyped JN.1 SARS-CoV-2 variant) (Cohort A and B)
- Evaluation of pemivibart in the prevention of reverse transcriptase polymerase chain reaction (RT-PCR)-confirmed symptomatic COVID-19 (Cohort A)
- Evaluation of the clinical efficacy of pemivibart compared with placebo in the prevention of severe/critical COVID-19 via a composite of RT-PCR-confirmed symptomatic COVID-19 with onset of symptoms ≤14 days from positive sample collection, COVID-19-related hospitalization, or all-cause mortality (Cohort B)

- Data were analyzed through 365 days
- TEAEs were recorded through the last follow-up visit before data cutoff

## RESULTS

### Participants

- The 12-month analysis included 306 participants in Cohort A and 480 in Cohort B (320 pemivibart, 160 placebo; **Table 1**)
- In Cohort B, baseline characteristics between pemivibart (n=320) and placebo (n=160) arms were generally well balanced

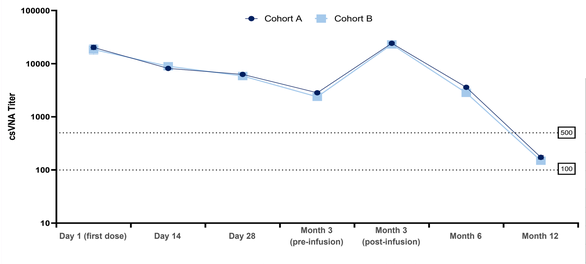
### Safety and Tolerability

- Treatment emergent adverse events (TEAEs) were reported in 74.8% of Cohort A participants. TEAEs reported in Cohort B-pemivibart and Cohort B-placebo arms were 45.1% and 46.3%, respectively
  - There were 5 all cause deaths reported in Cohort A
  - There was 1 all cause death reported in Cohort B
- The most common study drug-related TEAEs were infusion-related reactions (Cohort A: 12/306 [3.9%]; Cohort B: 7/320 [2.2%] pemivibart, 0/160 placebo; **Table 2**)
  - Four of 626 (0.6%) pemivibart-receiving participants in Cohort A experienced an anaphylactic reaction (2 serious in Cohort A; study drug was permanently discontinued in both instances. Both anaphylaxis reactions were resolved within 24 hours)

### Pemivibart neutralization by sVNA titers against relevant SARS-CoV-2 variants

- Following pemivibart dosing, csVNA titers across both cohorts were elevated to historical levels associated with protection against COVID-19 (**Figure 2**)

**Figure 2. csVNA Titer Against JN.1[a] in CANOPY**




*[a]JN.1 variant was a predominant variant in the United States during the conduct of CANOPY; The plot displays geometric mean titer (GMT) and 90% confidence interval at each time point. The sVNA titers were calculated based on the serum concentration of pemivibart divided by $IC_{50}$ value against JN.1 (74.6 ng/mL; pseudotyped VLP neutralization assay). A time-varying Cox proportional hazards model developed using total CANOPY efficacy and csVNA titer data demonstrated a titer threshold of 500 and 100 was associated with a predicted efficacy of 50% & 40% (immunocompromised) and 70% & 58% (non-immunocompromised) for the protection against symptomatic COVID-19.[7]*

### COVID-19 Assessments

*Risk of RT-PCR-confirmed COVID-19 through day 365 (**Figure 3**)*

- Cohort A: 10.1% (95% CI, 6.6%-14.5%)
- Cohort B:
  - **Pemivibart:** 5.3% (95% CI, 3.1%-8.7%)
  - **Placebo:** 19.0% (95% CI, 13.2%-26.9%)

*Incidence of RT-PCR-confirmed symptomatic COVID-19 through day 365 **(Table 3)***

- Cohort A: 25 (8.4%) had confirmed COVID-19 and 4 (1.3%) had all-cause death
- Cohort B:
  - **Pemivibart:** 14 (4.4%) confirmed COVID-19, 1 (0.3%) death not related to COVID-19
  - **Placebo:** 28 (17.8%) confirmed COVID-19
  - **SRR with pemivibart:** 74.1% (95% CI: 53.1–85.7, p<0.0001)

**Table 1: Demographic and Baseline Characteristics in Cohorts A and B**

| Characteristic | Cohort A (SAS) Pemivibart n=306 | Cohort B (FAS) Pemivibart n=320 | Cohort B (FAS) Placebo n=160 |
|---|---|---|---|
| **Median age (range), years** | 59 (22–83) | 47.0 (18–84) | 48.0 (19–78) |
| **Female, n (%)** | 187 (61.1) | 166 (51.9) | 91 (56.9) |
| **BMI, mean (SD), kg/m²** | 29.5 (7.8) | 29.4 (6.6) | 29.5 (6.7) |
| **Negative baseline SARS-CoV-2 central RT-PCR test, n (%)** | 302 (98.7) | 312 (97.5) | 157 (98.1) |
| **Baseline serology, (%)** | | | |
| N-protein positive | 49.0 | 84.7 | 85.6 |
| N-protein negative | 49.3 | 14.4 | 14.4 |
| S-protein positive | 97.7 | 98.4 | 99.4 |
| S-protein negative | 0.7 | 0.6 | 0.6 |
| **Immunocompromising condition[a], n (%)** | | | |
| Taking other immunosuppressive medications[b] | 202 (66.0) | - | - |
| Acute leukemia, CLL, NHL, multiple myeloma | 40 (13.1) | - | - |
| Moderate/severe primary immunodeficiency | 37 (12.1) | - | - |
| SOT recipient taking immunosuppressive therapy | 33 (10.8) | - | - |
| Advanced HIV (CD4 <350 cells/mm³) | 27 (8.8) | - | - |
| Actively treated solid tumor or hematologic malignancies | 20 (6.5) | - | - |
| **Risk factor for COVID-19 progression,[a] n (%)** | 306 (100) | 212 (66.3) | 99 (61.9) |
| Age ≥55 years | 179 (58.5) | 117 (36.6) | 59 (36.9) |
| Cardiac disease | 129 (42.2) | 68 (21.3) | 40 (25.0) |
| Obesity (BMI >30 kg/m²) | 116 (37.9) | 128 (40.0) | 65 (40.6) |
| Chronic lung disease | 58 (19.0) | 8 (2.5) | 7 (4.4) |
| Diabetes (type 1 or 2) | 54 (17.6) | 29 (9.1) | 15 (9.4) |
| Solid organ or blood stem cell transplant recipient | 33 (10.8) | 0 | 0 |
| Chronic kidney disease | 31 (10.1) | 1 (0.3) | 2 (1.3) |
| Stroke or cerebrovascular disease | 9 (2.9) | 0 | 1 (0.6) |
| Substance use disorder | 6 (2.0) | 4 (1.3) | 3 (1.9) |
| Sickle cell disease or thalassemia | 1 (0.3) | 0 | 0 |

*Abbreviations: BMI, body mass index; CLL, chronic lymphocytic leukemia; COVID-19, coronavirus disease 2019; FAS, full analysis set; HIV, human immunodeficiency virus; NHL, non-Hodgkin lymphoma; RT-PCR, reverse-transcription polymerase chain reaction; SAS, safety analysis set; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation; SOT, solid organ transplant.*
*[a]Participants may have >1 immunocompromising condition or medication or risk factor for COVID-19 progression.*
*[b]Taking high-dose corticosteroids (≥20 mg of prednisone or equivalent per day for ≥2 weeks), B-cell-depleting agents (within the past year), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, TNF blockers, or other immunosuppressive/immunomodulatory biologic agents.*

**Table 2. Summary of Treatment-Emergent Adverse Events (SAS)***

| Adverse Event Category, n (%) | Cohort A Pemivibart n = 306 | Cohort B Pemivibart n = 317 | Cohort B Placebo n = 160 |
|---|---|---|---|
| Any TEAEs | 229 (74.8) | 143 (45.1) | 74 (46.3) |
| Serious TEAEs | 47 (15.4) | 6 (1.9) | 3 (1.9) |
| Any TEAEs leading to death | 5 (1.6) | 1 (0.3) | 0 |
| Any study drug-related TEAEs[a] | 34 (11.1) | 15 (4.7) | 0 |
| Study drug-related serious TEAEs | 2 (0.7) | 0 | 0 |
| Study-drug related TEAEs leading to death | 0 | 0 | 0 |
| Study drug-related TEAEs leading to study treatment interruption[b] | 14 (4.6) | 4 (1.3) | 0 |
| Study drug-related TEAEs leading to study treatment discontinuation[c] | 7 (2.3) | 3 (0.9) | 0 |

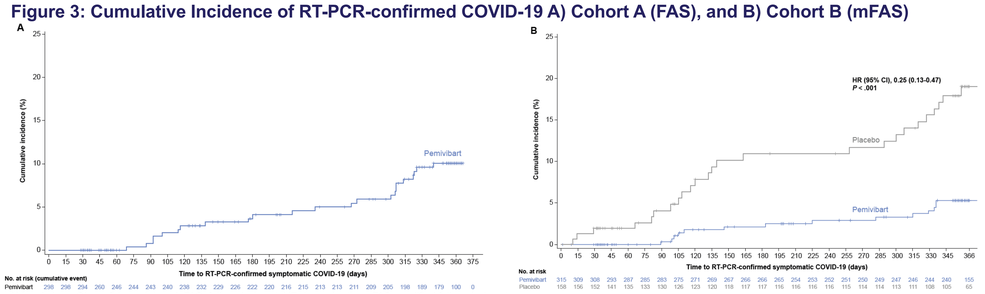
*SAS, safety analysis set.*
**Data cutoff February 3, 2025.*
*[a]Missing relationship assessments were assumed to be "Related."*
*[b]Treatment interruption included any participant who received a partial dose or who had a dose interrupted but restarted and completed the dose.*
*[c]Study treatment discontinuation included any participant who began dosing on day 1 but did not finish and was not re-dosed at month 3, or received a full dose on day 1 but was not re-dosed at month 3, or received a full dose on day 1 and began redosing at month 3 but did not finish. Does not include participants who had a dose interrupted but restarted and completed the dose or had the day 1 dose interrupted/discontinued but was subsequently re-dosed fully at month 3.*

**Table 3. RT-PCR-Confirmed Symptomatic COVID-19[a]**

| Cohort A[b] | Pemivibart (n = 298) |
|---|---|
| **Composite RT-PCR-confirmed symptomatic COVID-19 through day 365, n (%)** | 29 (9.7) |
| Symptomatic COVID-19 | 25 (8.4) |
| All-cause death[c] | 4 (1.3) |
| **Cohort B[d]** | **Pemivibart (n = 315)** / **Placebo (n = 158)** |
| **Composite RT-PCR-confirmed symptomatic COVID-19 through day 365, n (%)** | 15 (4.8) / 29 (18.4) |
| Observed risk difference, % | –13.6 |
| SRR (95% CI), %; 2-sided P-value | 74.1 (53.1–85.7); <0.0001 |
| Symptomatic COVID-19 | 14 (4.4) / 29 (18.4) |
| All-cause death through day 365[e], n (%) | 1 (0.3) / 0 |

*CI, confidence interval; FAS, full analysis set; mFAS, modified full analysis set; SRR, standardized relative risk reduction.*
*[a]Central laboratory conducted confirmatory testing using RT-PCR on nasopharyngeal swabs and saliva samples collected from participants with self-reported symptoms of COVID-19-like illness*
*[b]Cohort A FAS includes all participants who received a full dose of pemivibart at initial dosing.*
*[c]Due to suicide (n=1), unknown cause (n=1), cerebrovascular accident (n=1), and cardiac arrest (n=1), as assessed by the investigator. The participant who died after day 365 in cohort A did not contribute to composite COVID-19 endpoint through 365 days.*
*[d]Cohort B mFAS includes all randomized participants without SARS-CoV-2 infection at baseline who received any amount of pemivibart or placebo.*
*[e]Due to congestive heart failure, as assessed by the investigator.*

**Figure 3: Cumulative Incidence of RT-PCR-confirmed COVID-19 A) Cohort A (FAS), and B) Cohort B (mFAS)**




*Abbreviations: CI, confidence interval; FAS, full analysis set; HR, hazard ratio; mFAS, modified full analysis set.*

## KEY FINDINGS

**Two intravenous infusions of pemivibart administered 90 days apart were well tolerated; the majority of drug-related TEAEs with pemivibart (in both cohorts) were mild/moderate in severity. Anaphylaxis was an important identified safety risk.**

**csVNA titers were elevated to protective levels from symptomatic COVID-19 through 12 months**

**There was a 74.1% standardized relative risk reduction in composite COVID-19 incidence through 12 months with pemivibart (4.8%) versus placebo (18.4%)**

## CONCLUSIONS

- **Pemivibart was well tolerated and provided prophylactic efficacy against contemporary COVID-19 variants in individuals with or without immune compromise**
- **Overall, these data further support the durability of pemivibart as a preventive option against COVID-19 for individuals with or without immune compromise**

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## DISCLOSURES

Funding for this research was provided by Invivyd, Inc.

ML, KN, and IY are employees of Invivyd, Inc. and may own stock. DW is a paid consultant of Invivyd, Inc. CW was on an Invivyd Advisory Board.

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