Pemivibart for COVID-19 prevention: CANOPY subgroup analysis of older adults

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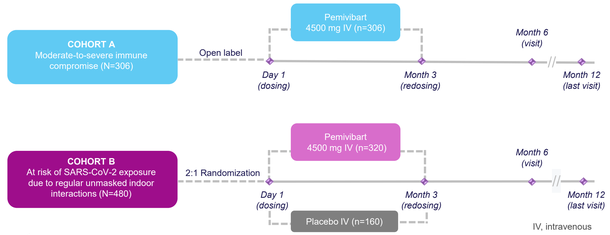
INTRODUCTION

- COVID-19 remains a significant threat for older adults (OA), particularly those living in long-term care facilities
  - The immunosenescence that defines older age combined with comorbidities that accrue across the lifespan compounds their vulnerability to severe infection outcomes[1,2]
  - For many OAs, exposure risk is year-round with COVID-19 now endemic within retirement or long-term care settings[3]
  - Inconsistent or suboptimal COVID-19 vaccine response is also consequential in this population, with disproportionate levels of breakthrough infection reported[4]
- 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[5]
- 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 (IC)[6,7,8]
- Here we describe a post hoc analysis of pemivibart receipt amongst OA participants (≥65 years) in open-label, single-arm Cohort A (immunocompromised) and placebo-controlled arm Cohort B (non-immunocompromised)

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 evaluated the safety, tolerability, pharmacokinetics, and efficacy of pemivibart for pre-exposure prophylaxis of COVID-19 in adults aged ≥18 years (**Figure 1**)[6,7,8]
- CANOPY Cohort A: an open-label, single-arm cohort that enrolled adults with significant immune compromise to receive pemivibart
- CANOPY Cohort B: randomized placebo-controlled cohort of non-immunocompromised 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 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
- Data from OA participants in Cohort A and Cohort B are reported in this post hoc subgroup analysis. Data from underpinning Cohorts have been reported elsewhere[8]
- Data were analyzed through Month 6

Endpoints and Assessments

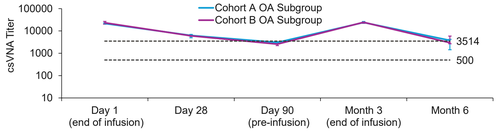
- Primary Objectives:
  - Both Cohort A & Cohort B: evaluation of safety and tolerability via study drug-related treatment emergent adverse events (TEAEs), serious adverse events (SAEs), and treatment interruption/discontinuation
  - Cohort A: evaluation of protection against symptomatic COVID-19 based on sVNA titers against SARS-CoV-2 after receiving pemivibart, using an immunobridging approach[7]
- Secondary Analysis: pemivibart neutralization by calculated (csVNA) titers against relevant SARS-CoV-2 variants
- Exploratory Endpoint: composite incidence of RT-PCR-confirmed symptomatic COVID-19, including COVID-related hospitalization and all-cause mortality, with standardized relative risk reduction (sRRR) between placebo and pemivibart Cohort B recipients also reported
- 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

RESULTS

Participants

- Participants were enrolled from September 2023 – November 2023
- A total of 306 participants were enrolled in Cohort A
  - 95 (31.0%) were included in the OA subgroup (**Table 1**)
- A total of 480 participants were enrolled in Cohort B
  - 88 (18.3%) were included in the OA subgroup (**Table 1**)
    - 61 (12.7%) in Cohort B-pemivibart arm; 27 (5.6%) in Cohort B-placebo arm

Figure 2: csVNA Titer Against JN.1[a] in CANOPY Cohort A and Cohort B Older Adult Subgroups



[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 represents the 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.[7,10] 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.[11]

Table 1. Baseline Demographic Characteristics Of Older Adult Subgroups

Parameter	Cohort A OA Subgroup n=95	Cohort B OA Subgroup n = 88	Cohort B OA Subgroup Pemivibart n=61	Cohort B OA Subgroup Placebo n=27
Median age [range], years	69 [65-83]	69 [65-84]	68 [65-84]	69 [65-78]
Female, n (%)	53 (55.8)	41 (46.6)	29 (47.5)	12 (44.4)
BMI, mean (SD), kg/m^2	28.2 (6.8)	29.4 (5.9)	29.2 (5.6)	29.8 (6.5)
Participants with prior COVID-19 vaccinations, n (%)	81 (85.3%)	60 (68.2%)	37 (60.7%)	23 (85.2%)
Number of prior COVID-19 vaccinations, median (range)	6 (1-9)	3 (1-6)	3 (1-6)	3 (1-5)
≥1 Concomitant medication	100%	79.5%	77.0%	85.2%
Risk Factor for COVID-19[a]				
Obesity (BMI > 30 kg/m^2)	31.6%	40.9%	37.7%	48.1%
Diabetes (T1 or T2)	22.1%	20.5%	21.3%	18.5%
Chronic kidney disease	11.6%	2.3%	0.0%	7.4%
Chronic lung disease	22.1%	11.4%	9.8%	14.8%
Cardiac disease	56.8%	56.8%	55.7%	59.3%
Sickle cell disease	0.0%	0.0%	0.0%	0.0%
Stroke or cerebrovascular disease	1.1%	0.0%	0.0%	0.0%
Substance use disorder	1.1%	0.0%	0.0%	0.0%
Baseline serology, (%)				
N-protein positive	46.3	78.4	77.0	81.5
N-protein negative	52.6	20.5	21.3	18.5
S-protein positive	98.9	97.7	96.7	100
S-protein negative	0.0	1.1	1.6	0.0
Baseline measured SARS-CoV-2 sVNA titers (%[b])				
sVNA titers against B.1.617.2	85.3	43.2	41.0	48.1
sVNA titers against BA.4/5	72.6	39.8	37.7	44.4
sVNA titers against XBB1.5	48.4	22.7	16.4	37.0

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

Assessment of COVID-19 for the Older Adult Subgroups

- Both OA subgroup sVNA titers were boosted to levels associated with protection against COVID-19[9] (**Figure 2**)
- No cases of RT-PCR–confirmed symptomatic COVID-19 were reported in the Cohort A OA subgroup through Month 6 (**Table 2**)
- Three cases of RT-PCR–confirmed symptomatic COVID-19 were reported in the Cohort B OA subgroup through Month 6 (**Table 2**)
  - 1 amongst pemivibart recipients, 2 amongst placebo recipients
- Through Month 6, there were two reports of all-cause mortality (1 in Cohort A OA subgroup) (**Table 2**)
- In Cohort B, sRRR in the overall population was 84.2% (95% CI: 61.1 – 93.5%, p<0.001) in favor of pemivibart
- In the Cohort B OA subgroup, the estimated sRRR was 77.9%, (95% CI: -133.8 – 97.9, p=0.21)

Safety and Tolerability

- Through Month 6, 63.2% of Cohort A OA participants reported a TEAE (**Table 3**)
  - 11 (11.6%) were SAEs
  - 9 (9.5%) were study drug-related
  - Treatment interruption was warranted in 3 instances (3.2%); treatment was never discontinued
- Through Month 6, 37.5% of Cohort B OA participants reported a TEAE (**Table 3**)
  - 1 (1.1%) were SAEs
  - 2 (3.3%) were study drug-related
  - There was no treatment interruption and/or discontinuation
- There were no instances of anaphylaxis in either OA subgroup; 4 cases were reported in overall cohorts through Month 6[9]

Table 2. Incidence of RT-PCR–confirmed Symptomatic COVID-19, COVID-related Hospitalizations, and All-cause Mortality Among CANOPY Cohorts A&B and Older Adult Subgroups Through Month 6

Parameter	Overall Cohort A n=298	Cohort A OA Subgroup n=95	Overall Cohort B n = 453	Cohort B OA Subgroup n = 85	Overall Cohort B Pemivibart n=306	Cohort B OA Subgroup Pemivibart n=59	Overall Cohort B Placebo n=147	Cohort B OA Subgroup Placebo n=26
COVID-19 composite event, n (%)	11 (3.7)	1 (1.1)	25 (5.5)	3 (3.5)	6 (2.0)	1 (1.7)	19 (12.9)	2 (7.7)
PCR-confirmed case, n (%)	9 (3.0)	0 (0.0)	25 (5.5)	3 (3.5)	6 (2.0)	1 (1.7)	19 (12.9)	2 (7.7)
All-cause mortality	2 (0.7)[a,b]	1 (1.1)[a]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0	0 (0.0)	0 (0.0)

[a]Cause: Suicide (n=1); [b]Cause: Unknown (n=1)

Table 3. Safety for CANOPY Cohorts A&B, and Older Adult Subgroups through Month 6[a]

Parameter	Overall Cohort A n=306	Cohort A OA Subgroup n=95	Overall Cohort B n = 477	Cohort B OA Subgroup n = 88	Overall Cohort B Pemivibart n=317	Cohort B OA Subgroup Pemivibart n=61	Overall Cohort B Placebo n=160	Cohort B OA Subgroup Placebo n=27
TEAE, n (%)	204 (66.7)	60 (63.2)	217 (45.5)	33 (37.5)	143 (45.1)	22 (36.1)	74 (46.3)	11 (40.7)
SAE, n (%)	35 (11.4)	11 (11.6)	9 (1.9)	1 (1.1)	6 (1.9)	1 (1.6)	3 (1.9)	0 (0.0)
Study drug related TEAEs, n (%)	34 (11.1)	9 (9.5)	15 (3.1)	2 (2.3)	15 (4.7)	2 (3.3)	0 (0.0)	0 (0.0)
-leading to death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
-leading to interruption	14 (4.6)	3 (3.2)	4 (0.8)	0 (0.0)	4 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)
-leading to discontinuation	7 (2.3)[a]	0 (0.0)	3 (0.6)[b]	0 (0.0)	3 (0.9)[b]	0 (0.0)	0 (0.0)	0 (0.0)

[a]The safety analysis set included all participants who received any amount of the study drug; [b]Overall 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]Overall Cohort B pemivibart-related causes of study discontinuation included eye pain (n =1), hypersensitivity (n = 2)

KEY FINDINGS

for Subgroup of Older Adult Participants

CANOPY enrolled participants with (Cohort A) and without (Cohort B) immunocompromise; among these, 95 participants (31.0%) in Cohort A and 88 participants (18.3%) in Cohort B were in the OA subgroup

Pemivibart was well-tolerated in both OA subgroups; those with additional risk conferred through active immunocompromise (Cohort A) experienced more adverse events

Overall, sRRR data supports the advantage of pemivibart over placebo in terms of COVID-19 prevention. sRRR did not reach statistical significance in the Cohort B OA subgroup, likely due to limited sample size

CONCLUSIONS

for Subgroup of Older Adult Participants

- **Pemivibart was well tolerated amongst OAs with or without immune compromise**
- **In the OA subgroups, pemivibart provided calculated neutralizing titers associated with protection against COVID-19**
- **These data may be of particular interest in long-term care, where exposure is common and outbreaks could be mitigated through prophylaxis**
- **Future studies focused on the feasibility and effectiveness of the use of pemivibart as prophylaxis in long-term care settings are warranted**

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DISCLOSURES

ML, KN, KT, IY, MW are employees of Invivyd, Inc, and may own stock. DW is a paid consultant of Invivyd, Inc. MK has grant support from AHRQ and CDC, is a consultant for Skinclique and for legal firms as an expert witness.

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