Poster 0363

In Vitro Neutralisation of Pemivibart (VYD222) against Omicron sublineages

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KEY FINDINGS

- Pemivibart (VYD222) is an IgG1 monoclonal antibody (mAb) and is a re-engineered version of adintrevimab
- Pemivibart neutralised SARS-CoV-2 variants tested in both pseudovirus and authentic virus assays
- The neutralising activity demonstrated in these assays supports the continued development of pemivibart

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 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 ACE2 receptor on host cells.
- Amino acid substitutions in the Fc region (M435L/N441A) of pemivibart extend serum half-life.
- CANOPY is an ongoing, Phase 3 clinical trial investigating the pre-exposure prophylaxis of COVID-19 with pemivibart, an extended half-life monoclonal antibody, in immunocompromised participants (Cohort A) and in participants at risk of exposure to SARS-CoV-2 (Cohort B) (NCT06039449).[1,2]
- The US Food & Drug Administration (FDA) granted pemivibart an emergency use authorization (EUA) in certain patients with moderate-to-severe immune compromise in March 2024.[3]
- Here, we characterize the in vitro neutralising potency of pemivibart against a panel of SARS-CoV-2 variants.

METHODS

Pseudovirus

- SARS-CoV-2 pseudovirus neutralisation assays were performed using the PhenoSense SARS-CoV-2 Neutralising Antibody Assay (LabCorp Monogram Biosciences).
- Pseudovirus testing was done by co-transfecting HEK293 cells with a codon-optimized spike sequence expression vector and an HIV genomic vector with a firefly luciferase reporter gene replacing the HIV envelope gene.
- To test antibody neutralisation, a predetermined amount of pseudovirus was incubated with titrating amounts of test mAb for 1 hour at 37 °C before adding to HEK293 cells transiently expressing hACE2 and TMPRSS2.
- For each variant tested, the WT (D614G) reference was tested in parallel.
- Pseudovirus infection was allowed to occur for 3 days before cells were assessed for luciferase activity.
- Neutralization IC_{50} values were determined based on a four parameter logisitic regression of mAb dilution versus % inhibition of luciferase activity.

Authentic Virus

- To evaluate the neutralising capacity of pemivibart against SARS-CoV-2, two different authentic virus neutralization assays were performed, both using Vero hTMPRSS2 cells.
  - In the first, cells were fixed 18 hours after infection, stained with antibodies targeting the SARS-CoV nucleoprotein, and quantified using an analyzer to determine the number of stained foci
  - In the second, an immuno-detection assay was performed to determine expression of viral nucleoprotein (NP) in infected cells using staining with a SARS-CoV-2 NP specific antibody, followed by a colorimetric readout.
- To compute the neutralization IC50 values, logistic regression (sigmoidal) curves were fit to the data using GraphPad Prism version 9.5.1.

RESULTS

- Pemivibart neutralised variants tested in both pseudovirus and authentic virus assays.[4,5,6,7]
- Pemivibart retained neutralising activity for all pseudovirus variants tested (**Figure 1**), including wild-type D614G, Delta, and Omicron types BA.1, XBB.1.5, XBB.1.5.10, XBB.1.16, HK.3, HV.1, BA.2.86, and JN.1.
- Pemivibart also potently neutralized all authentic variants tested, including wild-type D614G, Delta, and Omicron types BA.1, XBB.1.5, XBB.1.16, HV.1, and JN.1.
- Mean 50% inhibitory concentrations of pemivibart against pseudovirus and authentic viruses are listed in **Table 1.**

Figure 1: Pemivibart Neutralization of SARS-CoV-2 Pseudoviruses

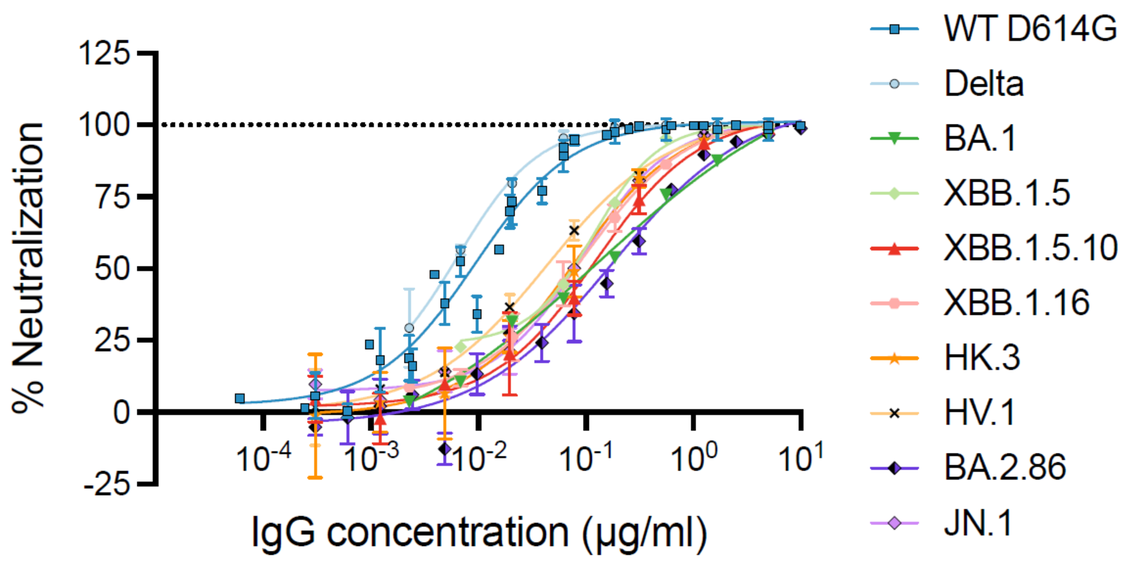

Table 1: Pemivibart Half Maximal Inhibitory Concentration (IC_{50}) Values against SARS-CoV-2 Authentic & Pseudovirus variants

Variant	Mean IC_{50} (µg/ml) Pseudovirus	Mean IC_{50} (µg/ml) Authentic Virus
WT D614G	0.0084	0.0243 - 0.034
Delta	0.0052	0.011
BA.1 (Omicron)	0.1214	0.0142
XBB.1.5 (Omicron)	0.1043	0.290 - 0.4799
XBB.1.5.10 (Omicron)	0.1081	-
XBB.1.16 (Omicron)	0.0776	0.118 - 0.6612
HK.3 (Omicron)	0.0723	-
HV.1 (Omicron)	0.0412	0.5294
BA.2.86 (Omicron)	0.1677	-
JN.1 (Omicron)	0.0746	0.0636

CONCLUSIONS

- **Pemivibart (VYD222) neutralised SARS-CoV-2 variants tested in both pseudovirus and authentic virus assays**
- **The neutralising activity demonstrated in these assays support the continued development of pemivibart**

DISCLOSURES

Funding for this research was provided by Invivyd, Inc.
Brandyn West, Pamela Hawn, and Robert Allen are employees of Invivyd and may own stock.
Peter Halfmann is receiving funding from Invivyd, Inc for research.

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REFERENCES

1. CANOPY (VYD222-PREV-001) Protocol. Version 3.0. 29Nov2023.
2. Invivyd Press Release, Invivyd Announces Positive Initial Results from Ongoing CANOPY Phase 3 Pivotal Clinical Trial Investigating VYD222 for the Prevention of COVID-19, Dec 18, 2023.
3. Invivyd Press Release, Invivyd Announces FDA Authorization for Emergency Use of PEMGARDA™ (formerly VYD222) for Pre-exposure Prophylaxis (PREP) of COVID-19, March 22, 2024.
4. VYD-DOF-007
5. VYD-DOF-008
6. VYD-DOF-018
7. VYD-DOF-019

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