

Supplementary Material

A statistical immune correlates of protection model for predicting efficacy from neutralizing antibody titers to establish immunobridging of monoclonal antibodies for prevention of COVID-19

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Model development:

Consistent with prior analyses, this Cox model evaluates the relationship between clinical efficacy and calculated neutralizing titers attributable to pemivibart alone and does not account for pre-existing baseline neutralizing antibodies in participants (1-3). Baseline sVNA titers were measured in only a subset of CANOPY participants to optimize study efficiency and costs, and the available data were insufficient for reliable incorporation into the model. In clinical practice, baseline neutralizing titers are rarely known at the time of vaccine or monoclonal antibody administration, similar to other factors that may influence SARS-CoV-2 infection risk, such as crowd exposure, air travel frequency, or occupational setting.

To evaluate the impact of prior-study vaccination status, age, baseline body mass index (BMI), and sex on the model, we incorporated continuous variables as covariates. Prior-study vaccination status was included enabling their baseline hazards vary in a stratified Cox regression analysis. None of these variables meaningfully altered the hazard ratio estimates. The adjusted β for non-immunocompromised participants was -0.435 (95% CI: -0.630, -0.240) compared to the unadjusted estimate of -0.438 (95% CI: -0.633, -0.244). For the immune-compromised participants, the adjusted β was -0.278 (95% CI: -0.457, -0.099) compared to the unadjusted estimate of -0.257 (95% CI: -0.417, -0.096).

Therefore, by focusing exclusively on Pemivibart-derived sVNA titers, this Cox model provides a practical framework for establishing target neutralizing antibody thresholds and predicting efficacy for current and next-generation SARS-CoV-2-targeting monoclonal antibodies.

Model Diagnostics for Proportional Hazards Assumption:

The proportional hazards assumption was evaluated using scaled Schoenfeld residuals. Visual inspection of the residual plots suggested a potential time-varying pattern in the log10 titer coefficient (as biologically expected), with antibody-mediated protection appearing stronger during the earlier follow-up period compared to later periods for both non-IC (Figure S1) and IC (Figure S2) participants. Despite this visual trend, the formal global test for proportional hazards did not reach statistical significance (non-IC: Chi-square = 0.51, df = 1, p = 0.47; IC: Chi-square = 1.17, df = 1, p = 0.28). To formally evaluate potential time-dependent effects, we fit models including a $\log_{10}(\text{time}) \times \log_{10}(\text{sVNA})$ interaction term. For non-IC participants, the interaction term had p = 0.14 with negligible improvement in model fit (difference in AIC = 0.3), providing weak evidence for a time-varying coefficient. For IC participants, the interaction term had p = 0.053 with modest improvement in fit (difference in AIC = 1.3), suggesting possible waning of antibody protection over time. Given the modest evidence for time-dependency and for consistency across groups, we report time-averaged hazard ratios from the constant-effect proportional hazards model.

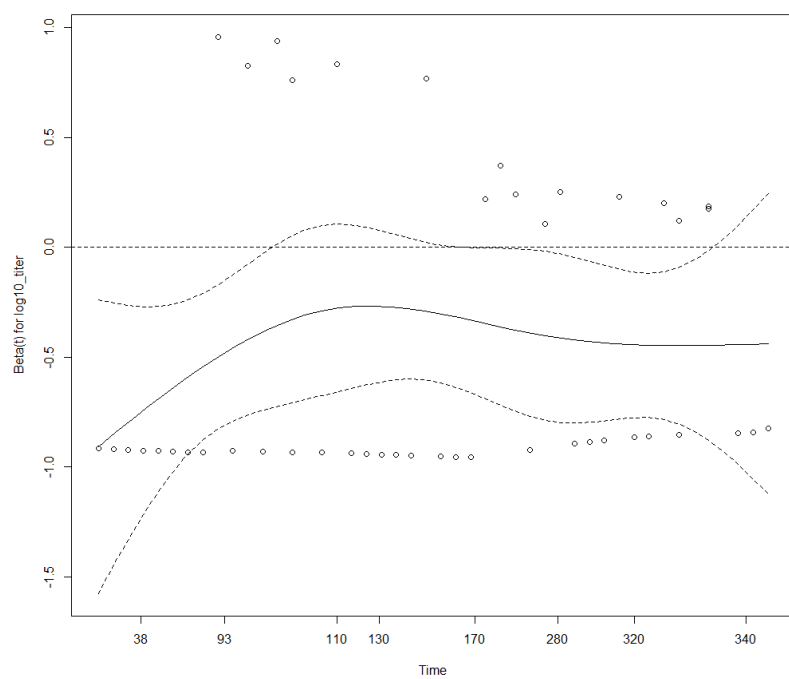


Figure S1: Scaled Schoenfeld residuals for non-IC participants

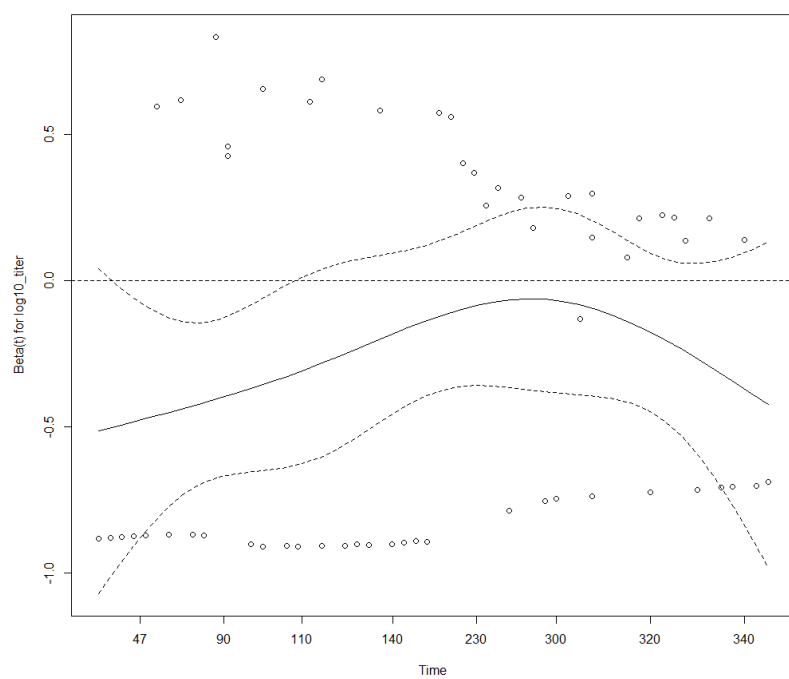


Figure S2: Scaled Schoenfeld residuals for non-IC participants

References

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2. Schmidt P, Li Y, Popejoy M. Immunobridging for Pemivibart, a Monoclonal Antibody for Prevention of Covid-19. *N Engl J Med.* 2024;391(19):1860–2.
3. Wolfe CR, Cohen J, Mahoney K, et al. Safety and Efficacy of Pemivibart, a Long-Acting Monoclonal Antibody, for Prevention of Symptomatic COVID-19: Interim Results From a Phase 3 Randomized Clinical Trial (CANOPY). *Clin Infect Dis.* 2025;81(3):439-450. doi:10.1093/cid/ciaf265