

3rd and 4th doses of vaccines broaden and stabilize immunity to SARS-CoV-2 in immunocompromised patients with immune-mediated inflammatory diseases

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Introduction

Patients with **immune-mediated inflammatory diseases (IMID)** are immunocompromised due to maintenance treatment with immunosuppressive drugs and have increased risk of severe outcomes following infection with SARS-CoV-2.¹ The effect of **immunomodulatory therapies** on the immunogenicity of SARS-CoV-2 mRNA vaccine-induced immunity has not been extensively studied. As such, the **Immune response after COVID-19 vaccination during maintenance Therapy (IMPACT) in immune-mediated inflammatory diseases** study was established.^{2,3}

Objective

To assess the immunogenicity of one to four doses of mRNA vaccine (BNT162b2 Pfizer and mRNA-1273 Moderna) in IMID patients.

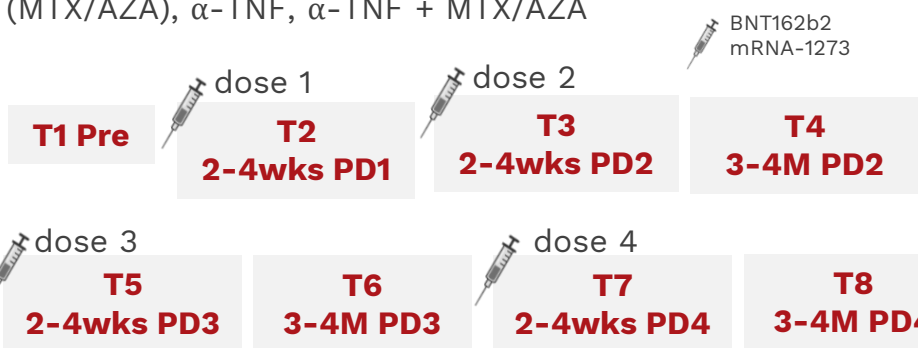
Methods IMPACT observational cohort study

January 2021 - October 2022



Cohort: healthy controls & IMID patients (inflammatory bowel disease, rheumatic or psoriatic disease)

Untreated or treated with immunosuppressive drugs: α-IL-17, α-IL-12/23, α-IL-23, methotrexate/azathioprine (MTX/AZA), α-TNF, α-TNF + MTX/AZA



Blood collection for immunogenicity assessment:

- (1) Anti-Spike and anti-RBD IgG
- (2) Neutralization of Wildtype (WT) SARS-CoV-2 and variants of concern (VOC)
- (3) T cell responses to WT and VOC

Results

▲ Vaccine dose
 ■ Healthy Controls ■ TNF IMID ■ Non-TNF IMID
 — Median of Convalescents — Seropositivity Threshold (IgG) — Lower Limit of Detection

Figure 1. Humoral responses pre and post one to four vaccine doses.

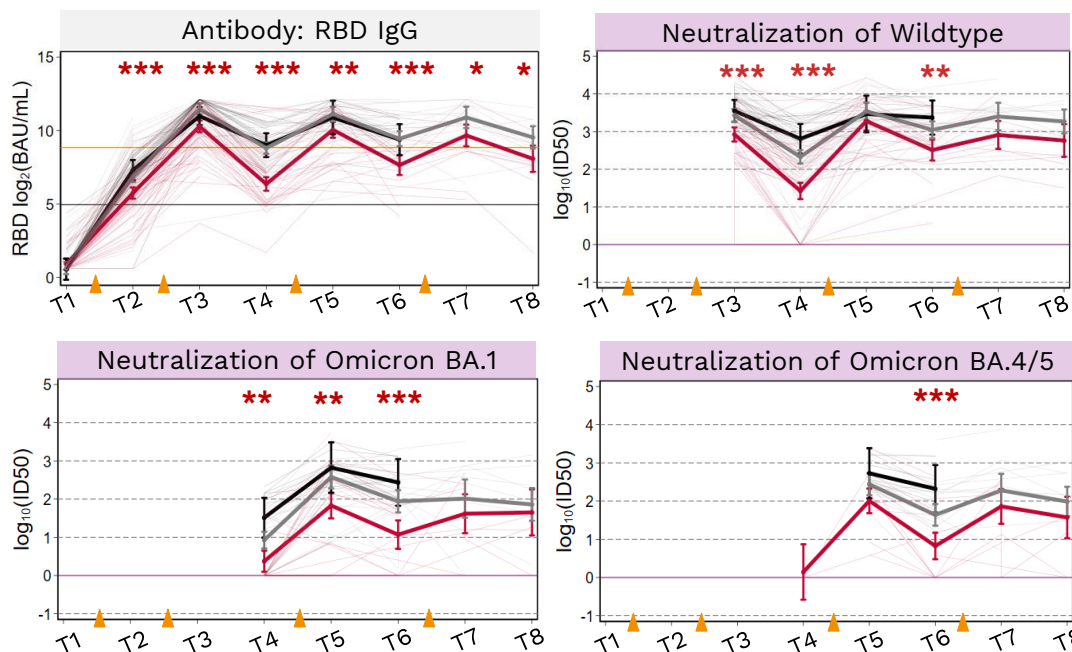
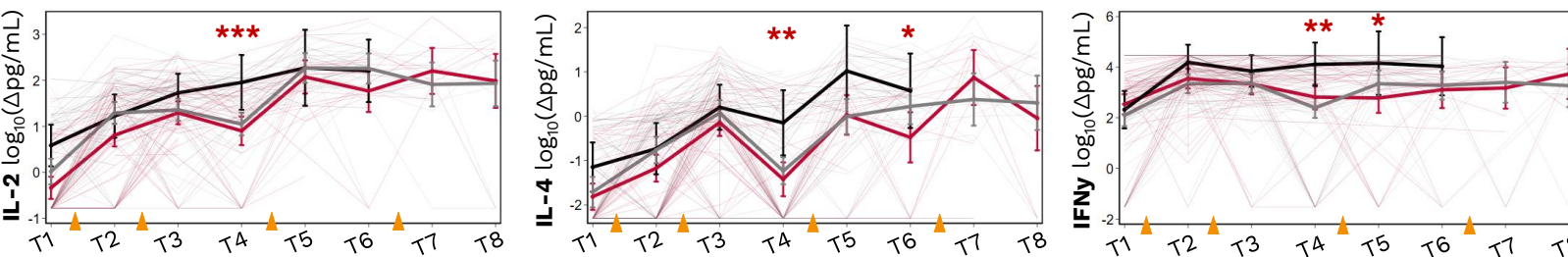


Figure 2. T cell cytokine responses pre and post one to four vaccine doses.



Conclusions

- ▶ **IMID patients exhibit accelerated waning** of humoral and cellular immunity by 3 months post dose 2, with the greatest **deficits in TNF treated patients**, highlighting the importance of booster doses.
- ▶ The **3rd dose** corrects waning immunity, and maximizes, stabilizes, and broadens immunity to SARS-CoV-2 in IMID patients; **4th dose** has subtle effects on the magnitude of responses and further stabilizes responses.

Figure 3. Waning of antibody responses after two, three, and four vaccine doses.

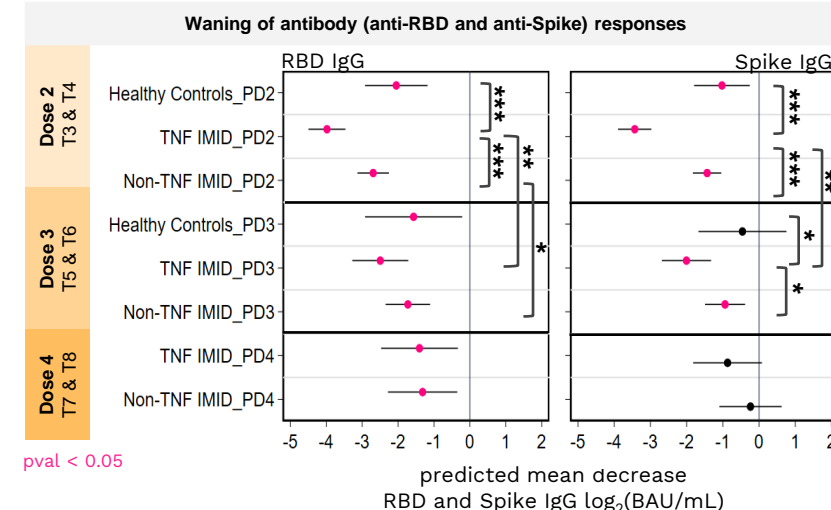
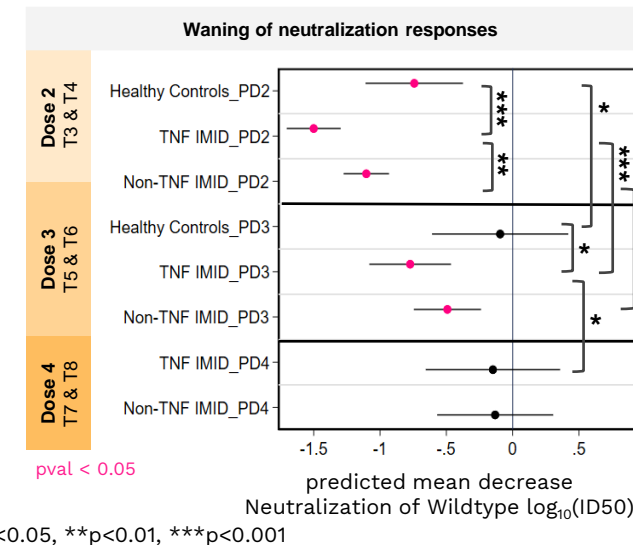


Figure 4. Waning of neutralization activity against Wildtype SARS-CoV-2 after two, three, and four vaccine doses.



References

1. MacKenna, B. *et al.* Risk of severe COVID-19 outcomes associated with immune-mediated inflammatory diseases and immune-modifying therapies: a nationwide cohort study in the OpenSAFELY platform. *Lancet Rheumatol.* **4**, e490–e506 (2022).
2. Dayam, R. M. *et al.* Accelerated waning of immunity to SARS-CoV-2 mRNA vaccines in patients with immune-mediated inflammatory diseases. *JCI Insight* **7**, (2022).
3. Cheung, M. W. *et al.* Third dose corrects waning immunity to SARS-CoV-2 mRNA vaccines in immunocompromised patients with immune-mediated inflammatory diseases. *RMD Open* **8**, e002622 (2022).

