Clinically Meaningful Influenza and SARS-CoV-2 Vaccine Responses Following Treatment-Free Window of Obexelimab in Patients with IgG4-RD

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Background

- Obexelimab is a humanized, bifunctional monoclonal antibody designed to inhibit B-cell activity through co-engagement of CD19 and the inhibitory receptor FcγRIIb **(Figure 1)**[1,2,3]
- B-cell inhibition by obexelimab is reversible, with B-cell activity returning within weeks of obexelimab cessation, supporting the feasibility of a planned treatment-free window **(Figure 2)**[2,4]
- Seasonal vaccination is particularly important for older patients and patients receiving immunosuppressive therapy
- A planned treatment-free window may facilitate vaccination when clinically indicated

Figure 1. Co-engagement of CD19 and FcγRIIb

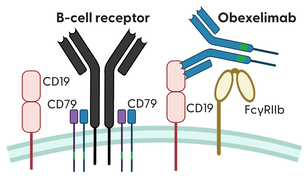
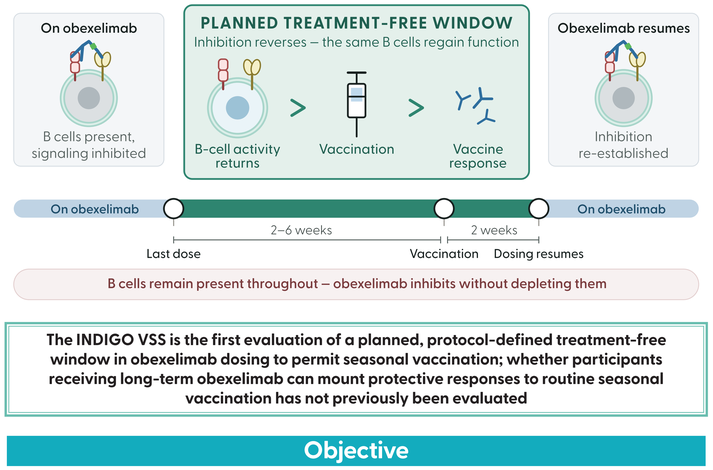


Figure 2. Treatment-free window concept in the vaccine sub-study (VSS)



The INDIGO VSS is the first evaluation of a planned, protocol-defined treatment-free window in obexelimab dosing to permit seasonal vaccination; whether participants receiving long-term obexelimab can mount protective responses to routine seasonal vaccination has not previously been evaluated

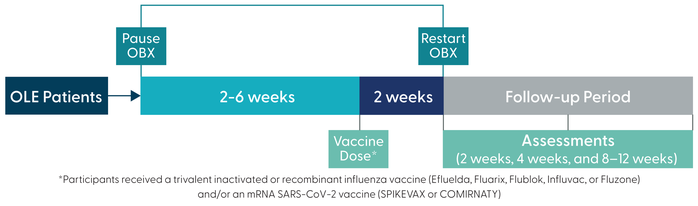
Objective

To evaluate humoral immune responses following influenza and SARS-CoV-2 vaccination administered during a short, protocol-defined treatment-free window

Methods

- INDIGO VSS: conducted during the OLE of the Phase 3 INDIGO trial in IgG4-RD, at sites in the US and EU **(Figure 3)**
- All patients who enrolled in the VSS were included in the analysis
- Vaccine responses, including seroresponse (≥2-fold titer rise), seroconversion (≥ 4-fold titer rise), and seroprotection, were evaluated using two functional neutralization assays (HAI for influenza and MNT for SARS-CoV-2) and one assay to quantitate antigen-specific IgG levels.

Figure 3. INDIGO OLE Vaccine Sub-Study design schematic



*Participants received a trivalent inactivated or recombinant influenza vaccine (Efluelda, Fluarix, Flublok, Influvac, or Fluzone) and/or an mRNA SARS-CoV-2 vaccine (SPIKEVAX or COMIRNATY)

Key eligibility criteria

- In OLE and flare-free for ≥ 3 months
- Judged by the investigator able to safely tolerate a 2–6-week treatment-free window pre-vaccination and at low risk of flare
- Eligible for an mRNA SARS-CoV-2 vaccine and/or inactivated influenza vaccine per standard guidelines
- No confirmed COVID-19 or influenza infection within 3 months before enrollment

Results

Baseline Characteristics and Disposition

- As of the May 2026 data cutoff, titer data were available for 11 vaccinations in 7 participants aged 52-76 years across US and EU sites **(Table 1)**

Table 1. Baseline characteristics and disposition

Baseline Characteristics	Participants (N = 7)
Age, years, range	52–76
Male, n (%)	5 (71.4)
RCP treatment assignment, n	Obexelimab 3; Placebo 4
Influenza vaccination, n (%)	7 (100)
SARS-CoV-2 vaccination, n (%)	4 (57.1)
Time from first obexelimab dose to vaccination, days, range	97–629
Obexelimab exposure before treatment-free window, days, range	77–615
Pre-vaccination treatment-free window, days, range	14–26
Post-vaccination treatment-free window, days, range	14–22
Total treatment-free window, mean days	34.6

RCP treatment assignment is the arm to which participants were randomized during the RCP; all participants received obexelimab during the OLE.
Age is at informed consent during the RCP.

Participants Mounted Humoral Immune Responses to Influenza Vaccination

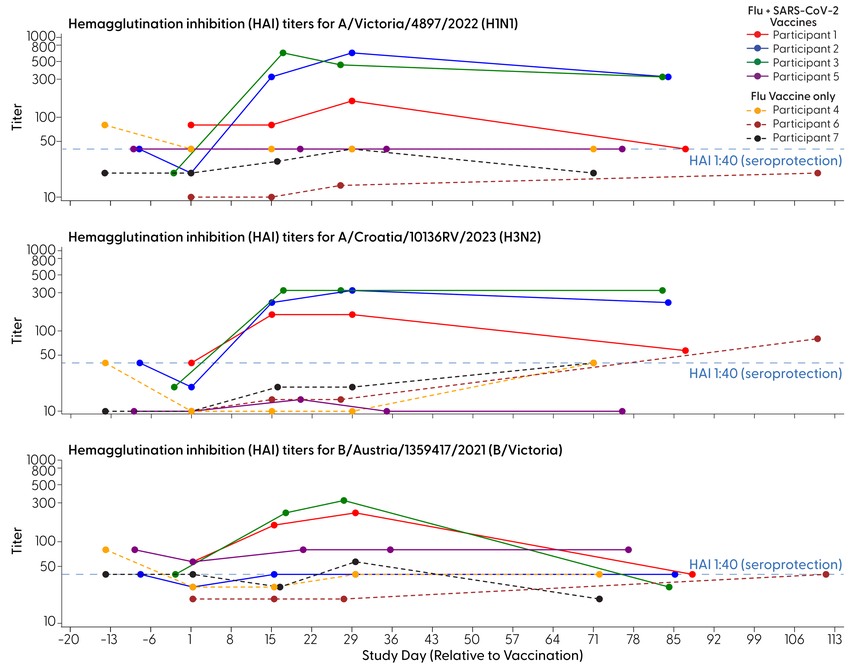
- All 7 participants achieved seroprotection to ≥1 influenza vaccine strain by Week 8–12; 6/7 achieved both a ≥ 2-fold seroresponse and ≥ 4-fold seroconversion at any post-baseline visit **(Table 2, Figure 4)**

Table 2. Fold Rise and Seroprotection of at least one HAI titer (H1N1, H3N2, or B/Victoria) over time

Visit	N	Seroresponse (≥ 2-fold), n (%)	Seroconversion (≥ 4-fold), n (%)	Seroprotection (≥ 1:40), n (%)
Baseline	7	–	–	5 (71.4)
Week 2	7	4 (57.1)	3 (42.9)	5 (71.4)
Week 4	7	4 (57.1)	3 (42.9)	6 (85.7)
Week 8–12	7	5 (71.4)	5 (71.4)	7 (100)
Any post-baseline	7	6 (85.7)	6 (85.7)	7 (100)

Seroprotection was defined as an HAI titer ≥ 1:40 to ≥ 1 influenza vaccine strain. [5] Seroresponse and seroconversion were defined as ≥ 2-fold and ≥ 4-fold increases from baseline, respectively.

Figure 4. Individual HAI titers over time by influenza vaccine strain



Participants Mounted Humoral Immune Response to SARS-CoV-2 Vaccination

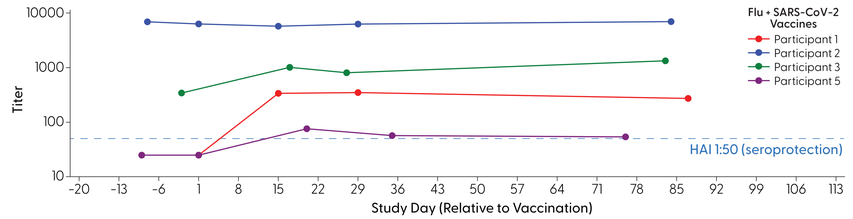
- All 4 SARS-CoV-2 vaccine recipients achieved seroprotective JN.1 neutralizing antibody titers by Week 2 and remained seroprotected through Week 8–12. Three of 4 achieved a ≥2-fold seroresponse **(Table 3, Figure 5)**

Table 3. JN.1 neutralizing antibody responses by visit in the 4 participants who received SARS-CoV-2 vaccine

Visit	N	Seroresponse, n (%)	Seroconversion, n (%)	Seroprotection (≥ 1:50), n (%)*
Baseline	4	–	–	2 (50.0)
Week 2	4	3 (75.0)	1 (25.0)	4 (100)
Week 4	4	3 (75.0)	1 (25.0)	4 (100)
Week 8–12	4	3 (75.0)	1 (25.0)	4 (100)
Any post-baseline	4	3 (75.0)	1 (25.0)	4 (100)

Seroprotection was defined as an MNT titer ≥ 1:50, derived from published correlates of protection.[6–8] Seroresponse was defined as a ≥ 2-fold, and seroconversion as a ≥ 4-fold rise from the pre-vaccination baseline titer.
*The participant without a seroresponse had a baseline JN.1 titer of 6298. JN.1 is the variant closest to the current vaccine strain.

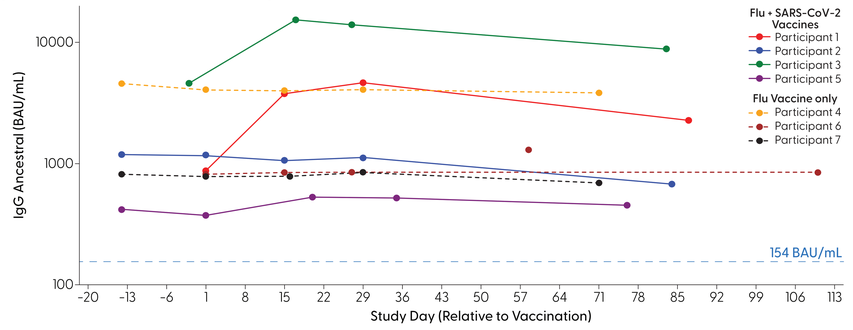
Figure 5. Individual JN.1 neutralizing antibody titers over time in the 4 participants who received SARS-CoV-2 vaccine



Participants Retained Pre-existing Immunity

- All 7 participants maintained anti-Spike IgG above the protection threshold (≥ 154 BAU/mL*) at all visits, including the 3 who did not receive SARS-CoV-2 vaccination during the sub-study **(Figure 6)**

Figure 6. SARS-CoV-2 ancestral Spike IgG over time in all 7 participants



*154 BAU/mL derived from published correlates of protection[5–8]

Safety

- No flares, and no signs or suspicion of flare, were observed in any of the 7 participants during the treatment-free window
- No adverse events of interest were reported

Limitations

- Small sample (n = 7), no control group; 4 received SARS-CoV-2 vaccine
- Heterogeneous prior vaccination and baseline titers; analyses were descriptive
- Routine influenza and SARS-CoV-2 testing was not required; testing was performed at the investigator's discretion

Conclusions

- **Participants mounted vaccine responses following a short treatment-free window**
- **Seroprotective immunity was maintained during long-term obexelimab treatment**
- **Disease control was maintained despite the treatment-free window as no flares were observed during follow-up**

n=7 received influenza vaccine; n=4 also received SARS-CoV-2 vaccine. All analyses descriptive.

Obexelimab is investigational and has not been approved by the US Food and Drug Administration or any regulatory body worldwide.

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Abbreviations: AE = adverse event; BAU = binding antibody unit; HA = hemagglutinin; HAI = hemagglutination inhibition; IgG4-RD = IgG4-related disease; MNT = microneutralization; OLE = open-label extension; RCP = randomized controlled period; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VSS = vaccine sub-study.

References: 1) Chu et al. *Mol Immunol.* 2008;45(15):3926–3933 & Zenas data on file. **2)** Abeles et al. *Annu Rev Immunol.* 2024;42:103-126. **3)** Verbeek et al. *Front Immunol.* 2019;10:2061. **4)** Perugino et al. *Lancet Rheumatol.* 2023;5:e442 Supplement. **5)** Coudeville et al. *BMC Med Res Methodol.* 2010;10:18. **6)** Khoury et al. *Nat Med.* 2021;27(7):1205–1211. **7)** Goldblatt et al. *Vaccine.* 2022;40(2):306–315. **8)** Plotkin. *Front Immunol.* 2023;13:1081107.