

University of Groningen

Use of TNF- α -antagonists and systemic steroids is associated with attenuated immunogenicity against SARS-CoV-2 in fully vaccinated patients with Inflammatory Bowel Disease

Otten, Antonius T.; Bourgonje, Arno R.; Horinga, Petra P.; van der Meulen, Hedwig H.; van Leer-Buter, Coretta C.; Dijkstra, Gerard; Visschedijk, Marijn C.

Published in:
Journal of Crohn's and Colitis

DOI:
[10.1093/ecco-jcc/jjab232.732](https://doi.org/10.1093/ecco-jcc/jjab232.732)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Otten, A. T., Bourgonje, A. R., Horinga, P. P., van der Meulen, H. H., van Leer-Buter, C. C., Dijkstra, G., & Visschedijk, M. C. (2021). Use of TNF- α -antagonists and systemic steroids is associated with attenuated immunogenicity against SARS-CoV-2 in fully vaccinated patients with Inflammatory Bowel Disease. *Journal of Crohn's and Colitis*, 16(Suppl(1)), S538. <https://doi.org/10.1093/ecco-jcc/jjab232.732>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

of patients receiving methotrexate, tumor necrosis factor inhibitor (TNFi) monotherapy, ustekinumab, tozilizumab and vedolizumab, in 80–90% of patients receiving TNFi combination therapy and secukinumab and in $\leq 80\%$ for JAK inhibitors (78%), and abatacept (53%) (Fig 1). Lower age (OR 0.96 [95% CI 0.95–0.98]) and receiving the mRNA-1273 vaccine (OR 5.4 [95% CI 2.4–11.9]) were predictors of response. Of 153 patients with a weak response receiving a third vaccine dose, 129 (84%) became responders. After standard two dose vaccination, adverse events (AE) were reported in 50% of patients and in 78% of controls, with a comparable safety profile. Following the third dose, 44% of patients reported AEs, without new safety issues emerging. No serious AEs were reported.

Conclusion: Response rate as well as anti-RBD levels were lower in IMiD patients than healthy controls following standard vaccination. Third dose vaccination in serologically weak responders was safe and resulted in a response in most patients. Our data facilitate identification of patient groups at risk of an attenuated vaccine response eligible for post-vaccination serological monitoring. The data also support a third vaccine dose following standard SARS-CoV-2 vaccination to weak-responding IMiD-patients.

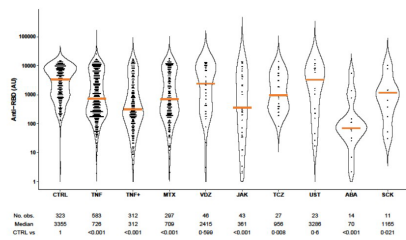


Fig 1. Anti-SARS-CoV-2 IgG antibodies following standard two-dose SARS-CoV-2 vaccination according to medication group, compared to healthy controls. Violin plot showing the probability density of the data at different values, smoothed by a kernel density estimator. Each data point is a participant, and the solid orange line shows the group median. The last row (CTLR vs) shows *p*-values for a comparison (Mann-Whitney *U* test) of anti-SARS-CoV-2 antibodies between medication groups and healthy controls. ACE2-angiotensin converting enzyme, FC=full length, CTLR=controls, TNF=tumor necrosis factor inhibitor, TNFi=tumor necrosis factor inhibitor combination therapy, MTX=methotrexate, VED=vedolizumab, JAK=janus kinase inhibitor, TCZ=tozilizumab, UST=ustekinumab, ADA=abatacept, SKC=secukinumab.

P606

Use of TNF- α -antagonists and systemic steroids is associated with attenuated immunogenicity against SARS-CoV-2 in fully vaccinated patients with Inflammatory Bowel Disease

A.T. Otten^{*1}, A.R. Bourgonje¹, P.P. Horinga¹, H.H. van der Meulen¹, C.C. van Leer-Buter², G. Dijkstra¹, M.C. Visschedijk¹

¹University Medical Center Groningen, Gastroenterology & Hepatology, Groningen, The Netherlands, ²University Medical Center Groningen, Medical Microbiology, Groningen, The Netherlands

Background: Patients with Inflammatory Bowel Disease (IBD) frequently use immunomodulating treatment, which may render them at increased risk of attenuated immunogenicity after vaccination. Immunosuppressive drugs, such as TNF- α -antagonists, have shown an attenuating effect on serological response after SARS-CoV-2 infection. Here we assessed the effects of different types of immunosuppressive medications on the serological response after vaccination against SARS-CoV-2 in patients with IBD.

Methods: This was a prospective observational cohort study in patients with IBD of whom IgG antibody titers were measured after 2–10 weeks after full vaccination against SARS-CoV-2. Patient demographics, clinical characteristics as well as a previous history of SARS-CoV-2 infection, type of vaccine (mRNA or vector), and medication use were recorded at time of sampling. The primary study outcome was the anti-SARS-CoV-2 spike (S) antibody concentrations, measured using chemiluminescence microparticle immunoassay (CMIA) after full vaccination.

Results: 312 IBD patients were included (172 Crohn's disease [CD] and 140 ulcerative colitis [UC]). Seroconversion (defined as titer of >50 AU/ml) was achieved in 98,3% of patients. Antibody concentrations were significantly lower in patients treated with TNF- α -antagonists vs. non-users of TNF- α -antagonists (geometric mean [95% confidence interval]: 2204 [1655–2935] vs. 5002 [4089–6116] AU/ml, $P<0.001$). In multivariable models, use of TNF- α -antagonists (percentage decrease -88%, $P<0.001$), age (>50 years) (-54%, $P<0.01$) and CD (vs. UC) (-39%, $P<0.05$) were independently associated with anti-SARS-CoV-2 antibody titers. In patients who received mRNA vaccines, users of systemic steroids demonstrated significantly lower antibody titers compared to patients who were steroid-free (geometric mean [95% CI]: 3410 [2233;5210] vs. 5553 [4686–6580], $P<0.05$).

Conclusion: TNF- α -antagonist use is strongly associated with an attenuated serological response after vaccination, independent of the type of vaccination (mRNA/vector), the time interval between vaccination and sampling, prior SARS-CoV-2 infection and patient age. Patients treated with systemic steroids who received mRNA vaccines demonstrated lower anti-SARS-CoV-2 antibody titers compared with patients who were steroid-free at time of serology.

P607

Efficacy and safety of tofacitinib in Ulcerative Colitis patients with extraintestinal manifestations in OCTAVE Open

D.T. Rubin^{*1}, S.R. Vavricka², A. Armuzzi³, M.C. Dubinsky⁴, A.I. Sharara⁵, I. Modesto⁶, M. Fellmann⁷, G. Liguori⁸, N. Lawendy⁹, M.J. Cadatal¹⁰, G.R. Lichtenstein¹¹

¹University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago- IL, United States, ²University Hospital Zürich, Department of Gastroenterology and Hepatology, Zürich, Switzerland, ³Fondazione Policlinico Universitario A. Gemelli IRCCS – Università Cattolica del Sacro Cuore, IBD Unit, Rome, Italy, ⁴Icahn School of Medicine at Mount Sinai, New York- NY, United States, ⁵American University of Beirut Medical Center, Division of Gastroenterology, Beirut, Lebanon, ⁶Pfizer Inc, New York- NY, United States, ⁷Pfizer Switzerland AG, Zürich, Switzerland, ⁸Pfizer Srl, Rome, Italy, ⁹Pfizer Inc, Colleagueville-PA, United States, ¹⁰Pfizer Inc, Manila, Philippines, ¹¹Perelman School of Medicine at the University of Pennsylvania, Division of Gastroenterology, Philadelphia- PA, United States

Background: Tofacitinib is an oral, small molecule JAK inhibitor for the treatment of ulcerative colitis (UC). Data from OCTAVE Induction 1&2 and OCTAVE Sustain demonstrated that a history of extraintestinal manifestations (EIMs) was shown not to influence the efficacy of tofacitinib 10 mg twice daily (BID).¹ We explored the efficacy and safety of tofacitinib in patients (pts) with and without a history of EIMs in the open-label, long-term extension study, OCTAVE Open.

Methods: Efficacy and safety (treatment-emergent serious adverse events of interest) data from OCTAVE Open (NCT01470612) were analysed by history of EIMs. Tofacitinib dose in OCTAVE Open was based on baseline remission status; pts in remission received tofacitinib 5 mg BID; all others received 10 mg BID. The frequency of pre-defined prior and active EIMs at OCTAVE Open baseline (peripheral arthritis [PA]; sacroiliitis; ankylosing spondylitis [AS]; myopathy; pyoderma gangrenosum; erythema nodosum; scleritis; episcleritis; uveitis; iritis; oral ulcer/stomatitis; and thromboembolic disorder) and new