Use of TNF-α-antagonists and systemic steroids is associated with attenuated imunogenicity 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

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 ≤ 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.

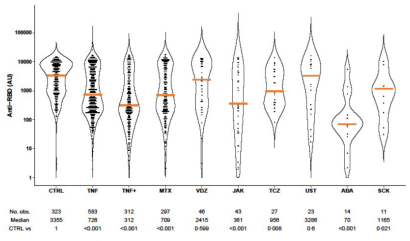

Fig 1. Anti-SARS-CoV-2 IgG antibodies following standard two dose SARS-CoV-2 vaccination according to medication group, compared to healthy controls. Violin plot showing the probability density of the data at different values, smoothed by a kernel density estimator. Each data point is a participant, and the solid orange line show the group median. The last row (CTRL vs) shows p-values for a comparison (Mann-Whitney U test) of anti-SARS-COV 2 antibodies between medication groups and healthy controls. ACE=Angiotensin converting enzyme, FL=full length, CTRL=Controls, TNF=Tumor necrosis factor inhibitor, TNF+= Tumor necrosis factor inhibitor combination therapy, MTX=methotrexate, VDZ=vedolizumab, JAK=Janus kinase inhibitor, TCZ=tocilizumab, UST=ustekinumab, ABA=abatacept, SCK=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. Bourgonje[1], P.P. Horinga[1], H.H. van der Meulen[1], C.C. van Leer-Buter[2], G. Dijkstra[1], M.C. Visschedijk[1]

[1]University Medical Center Groningen, Gastroenterology & Hepatology, Groningen, The Netherlands, [2]University 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. Vavricka[2], A. Armuzzi[3], M.C. Dubinsky[4], A.I. Sharara[5], I. Modesto[6], M. Fellmann[7], G. Liguori[8], N. Lawendy[9], M.J. Cadatal[10], G.R. Lichtenstein[11]

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