

# Comparable Efficacy of SARS-CoV-2 mRNA Vaccines (BNT162b2 and mRNA-1273) in Fingolimod-Treated Patients with Multiple Sclerosis

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## Introduction

The SARS-CoV-2 pandemic is still ongoing and will remain a major health concern and challenge for the health care systems in the upcoming years. To address this threat, our research group has been studying this issue. In addition to the vaccination behavior of Multiple Sclerosis (MS) patients, [1] difference between mRNA vaccine types and strategies were investigated in relation to vaccine efficacy in people with MS. Here, we identified that the humoral response to the mRNA vaccines BNT162b2 and mRNA-1273 did not differ in the cohort of anti-CD20 treated patients [2]. Fingolimod (FTY) is a sphingosine-1-phosphate receptor modulator and has been associated with poor COVID-19 vaccination response in preceding studies [3,4]. An association between vaccination response and extent of lymphopenia has been proposed. We aim to compare the humoral response to the two mRNA vaccines approved in Switzerland (BNT162b2 and mRNA-1273) using anti-spike IgG levels in FTY-treated MS patients.

## Methods

FTY-treated MS patients who had been vaccinated twice with either BNT162b2 or mRNA-1273 as recommended by Swiss Authorities were identified by retrospective medical chart review of

data on vaccinations of the neuroimmunological outpatient cohort. In total, 340 MS patients had an anti-spike IgG measurement during clinical routine care. 74 of these patients treated with anti-CD20 drugs are described elsewhere [2]. 33/340 patients were treated with FTY, 10/33 were vaccinated with BNT162b2 and 21/33 with mRNA-1273 (2 cases vaccine type not specified). Anti-spike IgG levels were determined using an Abbott SARS-CoV-2 IgG assay (Abbott Laboratories, Chicago, IL, USA) or Liaison SARS-CoV-2 S1/S2 IgG assay (Diasorin, Italy) or Elecys® SARS-CoV-2 Ig assay (Roche, Switzerland). We used a cut-off of  $\geq 100$  AU/mL to define a protective vaccination response (as recommended by the in-house infectious disease specialists). Continuous variables were given as a mean and a 95% confidence interval (95% CI) and categorical variables as frequencies. A Mann-Whitney test (MWU) and a Chi [2] test as well as a multivariable linear regression analysis with anti-spike IgG (AU/mL) as the dependent variable were run (SPSS Statistic 25, IBM Corp., Armonk, NY, USA). The neuroimmunological registry study at Bern University Hospital was approved by the local ethics committee (NI registry: KEK-BE no. 2017-01369, last amendment August 2020).

## Results

We identified data of vaccination response of 340 MS patients (age 45.6 years (95% confidence interval (CI) 44.2-47.1); female sex 206/340 (60.6%), anti-spike IgG serum level 100.0 AU/ml (72.8 -127.2)). Of these, 31 were treated with FTY. FTY-treated patients were in mean 44.2 years old (40.8- 47.5) and mostly female 20/31 (64.5%). No relapses were observed within 3 months after vaccination in our FTY-cohort. Time between second mRNA vaccination and anti-spike IgG assessment was 133 days (mean; 108-158) with no differences between both mRNA vaccines (MWU  $p=0.30$ ,  $n=30$ ,  $n=1$  vaccine type not given). Mean anti-spike IgG was 115.6 AU/ml (13.6 - 217.6), but with only 6/31 reaching levels  $\geq 100$  AU/ml defined as protective (BNT162b2 1/9, mRNA-1273  $n=5/21$ , not specified  $n=1$ ). No differences were found in mean levels and frequencies of reaching protective antibody levels between both vaccine types ( $\geq 100$  AU/ml BNT162b2 1/9 vs mRNA-1273 5/21  $\chi^2 p=0.64$ ; anti-spike IgG BNT162b2 114.4 AU/ml (-110.6 - 339.3),  $n=9$  vs mRNA-1273 120.0 (-9.9 - 249.8),  $n=21$  MWU  $p=0.72$ ). Multivariable linear regression analysis adjusted for age, sex and time between vaccination and titer assessment did not find a significant influence of mRNA vaccine type (BNT162b2 vs mRNA- 1273 regression coefficient 29.6 (-221.7 - 281.0),  $p=0.81$ ,  $n=30$ ).

## Conclusion

We investigated a small single center cohort of patients treated with FTY in order to detect differences in humoral responses to two mRNA vaccines labelled in Switzerland. Possibly influenced by a small cohort size, we were not able to detect a different response to either of the mRNA vaccines neither in the unadjusted analysis nor in the multivariable regression model. Only 6/31 (19%) reached protective antibody levels after two mRNA vaccinations. Further research is needed to identify strategies allowing vaccination under FTY treatment without the risk of a disease reactivation due to a prolonged drug holiday, which is known to occur in patients after stopping FTY [5]. As a limitation, the retrospective nature and small cohort size of our study have to be mentioned. This implies a non-standardized assessment of vaccination responses with respect to the time between vaccination and antibody level assessment (range 28-254 days). In order to overcome these shortcomings, we ask researchers to contact us via the corresponding author to pool vaccination data from different cohorts.

## Conflicts of Interest

H.H. received research support and travel grants within the last 5 years from Almirall, Biogen, Johnson&Johnson, Merck, Roche and Bristol Myers Squibb. C.P.K. has received honoraria for lectures as well as research support from Biogen, Novartis, Almirall, Teva, Merck, Sanofi Genzyme, Roche, Eli Lilly, Janssen, Celgene and the Swiss MS Society (SMSG).

R.H. Hoepner R received speaker/advisor honorary from Merck, Novartis, Roche, Biogen, Alexion, Sanofi, Janssen, Bristol-Myers Squibb, Teva/Mepha and Almirall. He received research support within the last 5 years from Roche, Merck, Sanofi, Biogen, Chiesi, and Bristol-Myers Squibb. He also received research grants from the Swiss MS Society and is a member of the Advisory Board of the Swiss and International MS Society. He also serves as associated editor for Journal of Central Nervous System disease. All conflicts are not related to this work.

AS received speaker honoraria and/or travel compensation for activities with Bristol Myers Squibb, CSL Behring, Novartis, and Roche, and research support by Baasch Medicus Foundation, the Medical Faculty of the University of Bern and the Swiss MS Society. She serves on the Editorial Board of Frontiers in Neurology - Multiple Sclerosis and Neuroimmunology. All not related to this work.

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