NYU Langone Health

Abstract # 2697

Humoral and Cellular Responses to SARS-CoV-2 Vaccines in MS Patients on Ocrelizumab and Other Disease-Modifying Therapies: A Prospective Study From NYU Multiple Sclerosis Care Center

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Disclosures

- **Ilya Kister** served on the scientific advisory board for Biogen Idec, Genentech, Alexion, EMDSerono; received consulting fees from Roche; and received research support from Guthy-Jackson Charitable Foundation, National Multiple Sclerosis Society, Biogen Idec, Serono, Genzyme, and Genentech/Roche; he receives royalties from Wolters Kluwer for “Top 100 Diagnosis in Neurology” (co-written with Jose Biller)
- **Jinglan Pei** and **Ryan C. Winger** are employees and shareholders of Genentech, Inc
- **Mark J. Mulligan** had laboratory research and shareholder of F. Hoffmann-La Roche Ltd; clinical trials contracts for vaccines or MAB vs SARS-CoV-2 with Lilly, Pfizer, and Sanofi; personal fees for Scientific Advisory Board service from Merck, Meissa Vaccines, and Pfizer; contract funding from USG/HHS/BARDA for research specimen characterization and repository; research grant funding from USG/HHS/NIH for SARS-CoV-2 vaccine and MAB clinical trials
- **Lana Zhovtis Ryerson** served on the scientific advisory board for Biogen, Genentech, Celgene, and Novartis and received research support from Consortium of Multiple Sclerosis Centers, Biogen, and Genentech
- **Catarina Raposo** is an employee and shareholder of F. Hoffmann-La Roche
- **Jessica Priest** is an employee of Genentech, Inc. and shareholder of F. Hoffmann-La Roche
- **Michelle Krogsgaard** is on the scientific advisory board for NexImmune and Genentech and received research support from Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Genentech, the Mark Foundation, NIH-NIGMS, and NIH-NCI
- **Gregg J. Silverman** received honoraria from BMS, Eli Lilly and Genentech, and research support from BMS, Genentech, Lupus Research Alliance, NIHNIAMS, NIH-NIAID, and NIH-NILB
- **Yury Patskovsky, Ryan Curtin, Iryna Voloshyna, Katherine Perdomo, Zoe Rimler, Nicole Ferstler, Yogambigai Velmurugu, Samantha Nyovanie, Joseph Kim, Ethan Tardio, Tamar Bacon, Marie Samanovic-Golden,** and **Amber Cornelius** have nothing to disclose

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Background

- Multiple sclerosis (MS) is treated with disease-modifying therapies (DMTs) some of which may attenuate immune responses to COVID-19 vaccination
- Understanding the impact of DMTs on the immune response to SARS-CoV-2 vaccination is critical for determining whether a patient who had COVID-19 vaccination on a particular DMT is likely to derive a similar degree of protective immunity as untreated individuals.
- Whether immune responses to COVID-19 vaccines in MS patients receiving different DMTs depend on prior COVID-19 infection or specific vaccine is poorly understood

Objectives:

- **To compare humoral and cellular responses to COVID-19 vaccines in MS patients who were on B-cell depleting ocrelizumab (OCR) and other DMTs (non-OCR) at the time of vaccination**
- **To compare humoral and cellular responses to COVID-19 vaccines in MS patients with prior COVID-19 infection and those without prior infection**
- **To compare humoral and cellular responses to different COVID-19 vaccines in MS patients in OCR and non-OCR**

DMT, disease-modifying therapy; MS, multiple sclerosis; OCR, ocrelizumab.

Methods

Study population

- Consecutive MS patients from NYU MS Care Center who completed COVID-19 vaccination were invited to participate

Inclusion criteria

- Clinician-diagnosed MS
- Age 18–60 years
- EDSS 0–7
- Fully vaccinated with COVID-19 vaccine ≥6 weeks prior to sample collection

Exclusion criteria

- Use of anti-CD20 drugs other than OCR
- High-dose steroids, IVIG, PLEX, plasma or antibody treatments within 3 months of vaccination
- Comorbidity that may suppress immune system
- Booster doses of vaccines

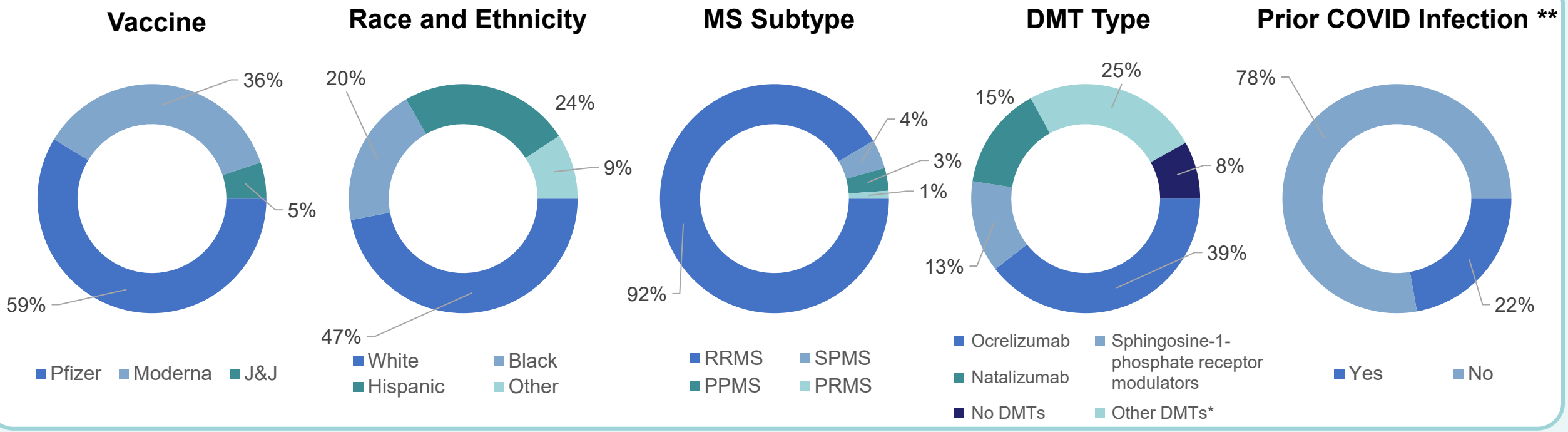
Study assessments

- Immune testing included:
  - Anti-nucleocapsid and anti-Spike RBD antibody (Elecsys Anti-SARS-CoV-2) (Roche Diagnostics)
  - Multi-epitope bead-based immunoassays (MBI) of antibody responses to SARS-CoV-2 Spike proteins
  - Live virus immunofluorescence-based microneutralization assay (neutralizing antibodies)
  - T-cell responses to SARS-CoV-2 Spike protein using whole blood TruCulture (Myriad RBM) assay
  - T-cell responses to SARS-CoV-2 Spike protein using IFNγ enzyme-linked immune-absorbent spot (ELISpot, Invitrogen)

CD20, cluster of differentiation 20; EDSS, Expanded Disability Status Scale; IFNγ, interferon gamma; IVIG, intravenous immune globulin; MS, multiple sclerosis; OCR, ocrelizumab; PLEX, plasma exchange; RBD, receptor binding domain.

Demographics and clinical characteristics of MS patients (n=370)

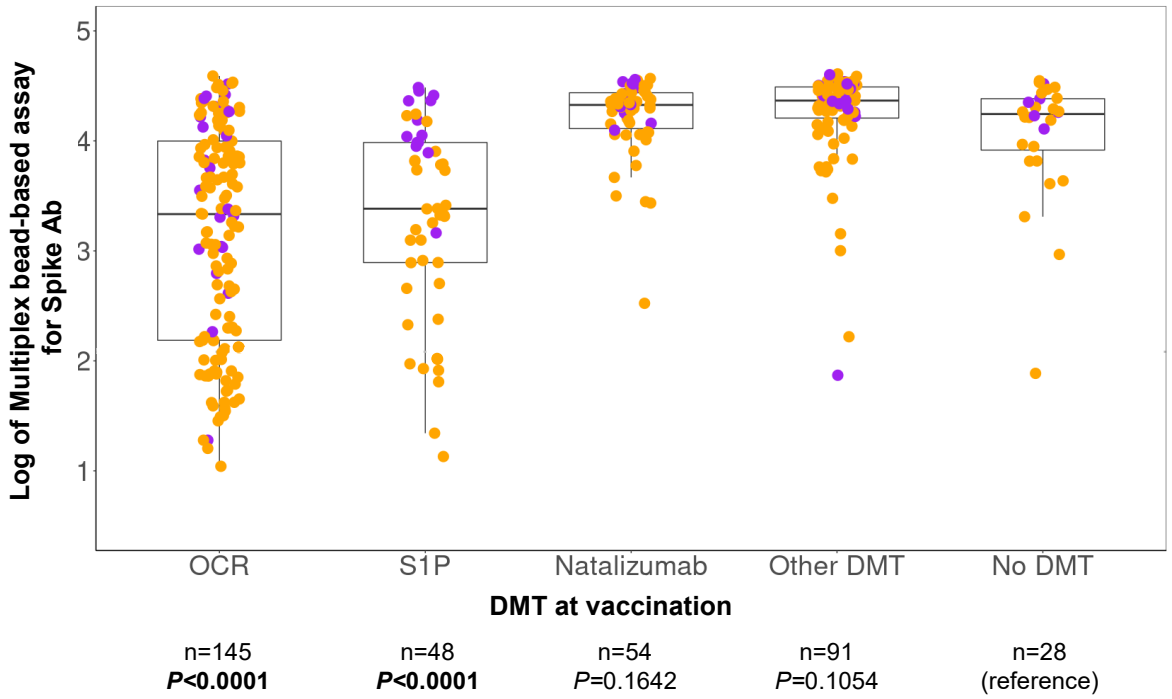
Female, 75.9%, Age (median [IQR]), 41.0 (32.0–49.0) years
MS duration (median [IQR]), 9.6 (4.8–17.7) years
Time from last vaccine to sample collection (mean [SD]), 18.7 (7.7) weeks

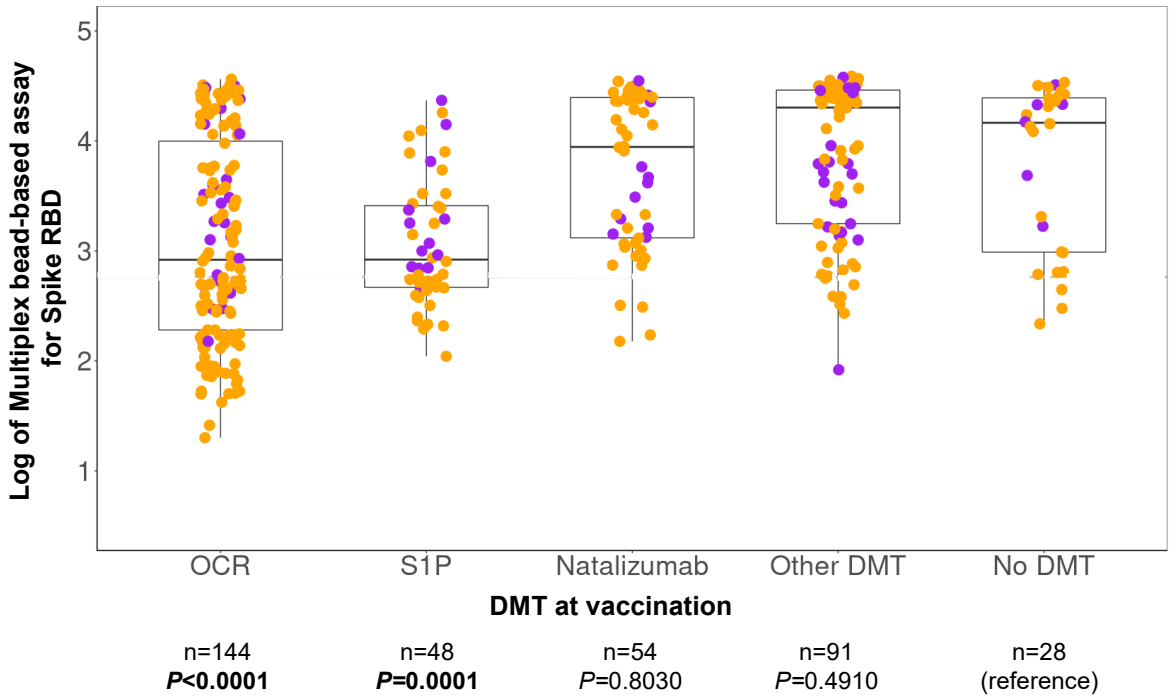


DMT, disease-modifying therapy; IQR, interquartile range; MS, multiple sclerosis; PPMS, primary progressive multiple sclerosis; PRMS, primary relapsing multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.
* Other DMTs include IFNβ, glatiramer acetate, teriflunomide, and fumarates. ** All infections were lab confirmed (either PCR or positive Anti-SARS CoV-2 serologic responses prior to vaccination)

Antibody responses by MBI were ↓ in patients receiving OCR and S1P *vs* patients on no DMT. Antibody responses were ↑ in patients with prior COVID-19 across all DMTs

Post-vaccination antibody responses by DMT – MBI Spike (left) and MBI RBD (right)



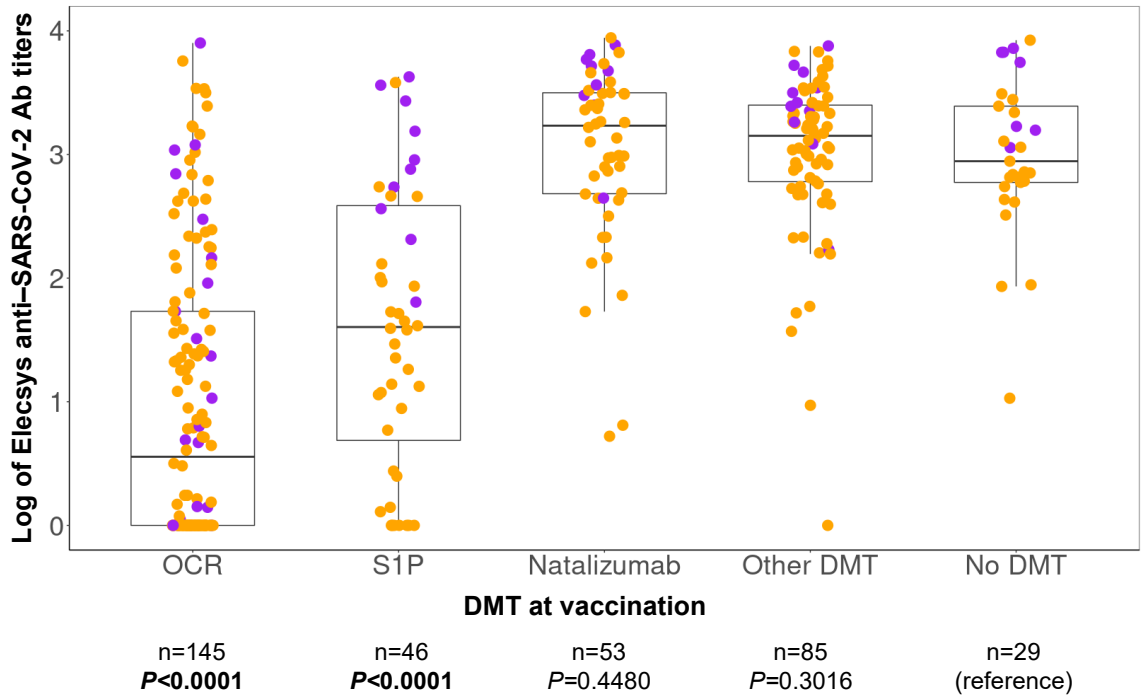


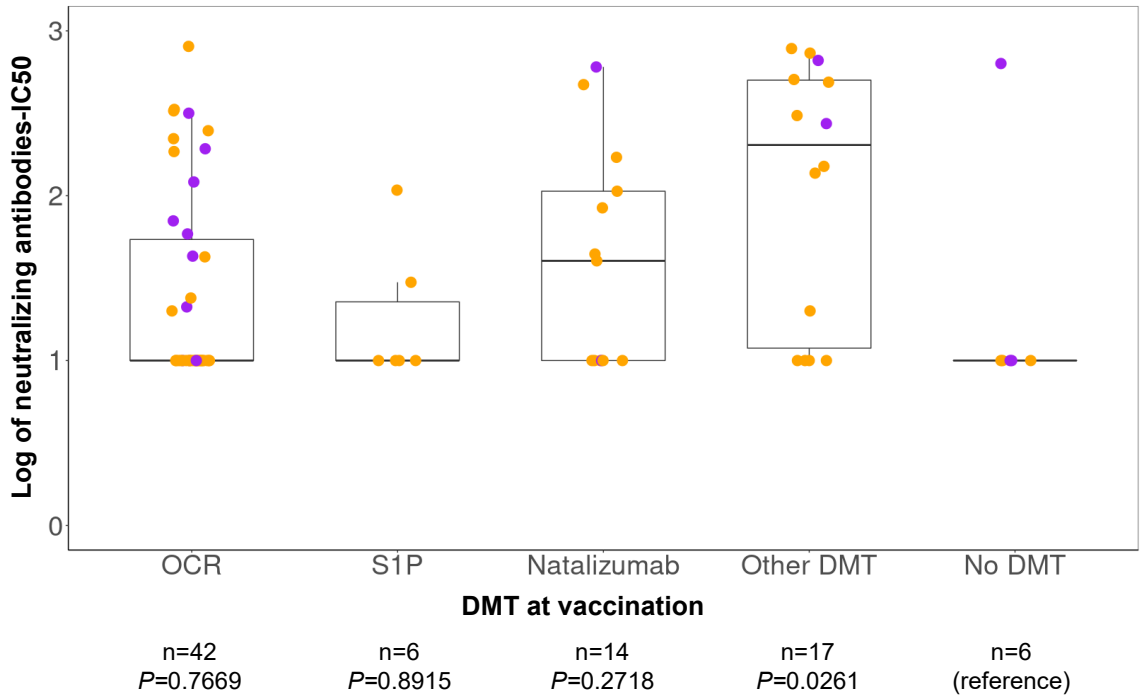
Prior COVID-19 infection No prior COVID-19 infection

DMT, disease-modifying therapy; OCR, ocrelizumab; S1P, sphingosine-1-phosphate receptor modulators.

Antibody response by Elecsys were ↓ in patients on OCR and S1P *vs* those on no DMT. Neutralizing antibodies were tested in a subset of 85 patients: compared to patients on no DMT, Nabs levels were similar in OCR, S1P, NTZ, and higher in the 'other DMT' group.

Post-vaccination Ab responses by DMT class – Elecsys (left), microneutralization (right) assays



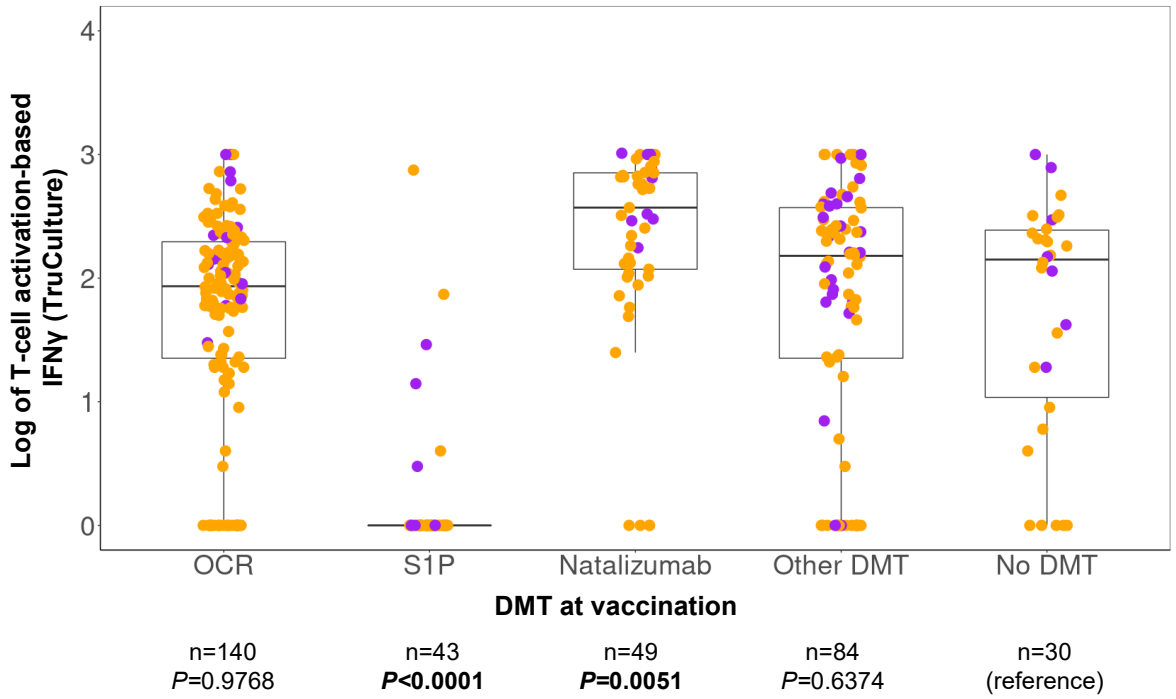


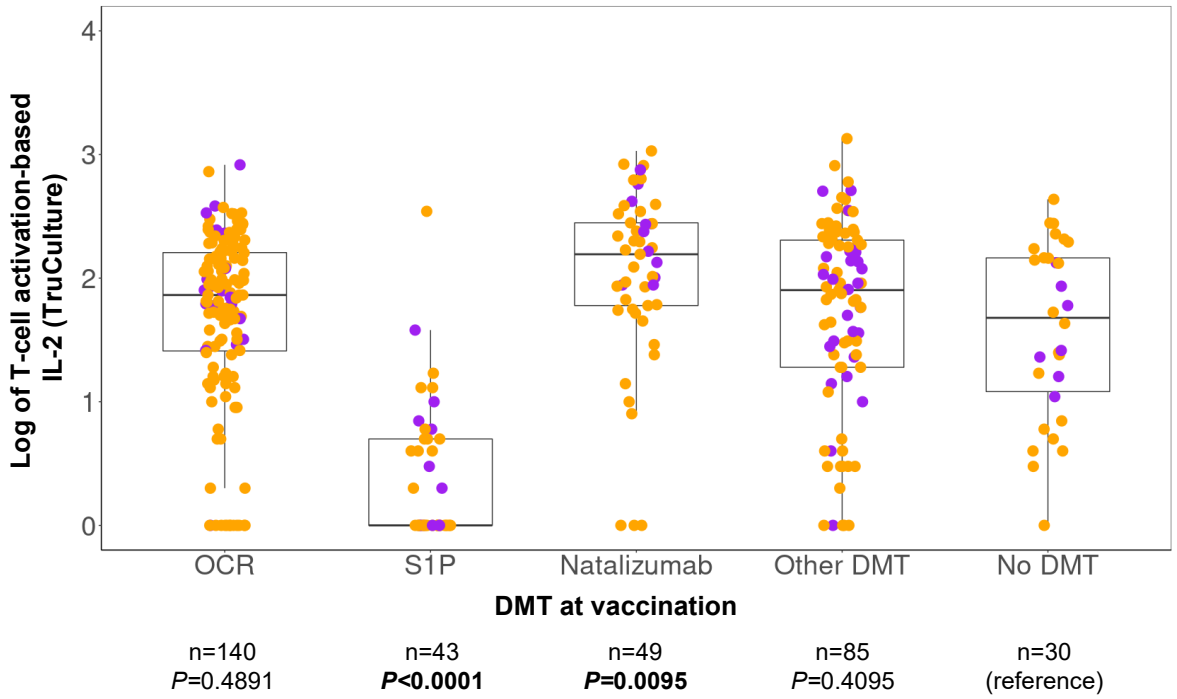
Prior COVID-19 infection No prior COVID-19 infection

DMT, disease-modifying therapy; OCR, ocrelizumab; S1P, sphingosine-1-phosphate receptor modulators.

T-cell responses assessed by TruCulture assay were ↓ in patients on S1P, and ↑ in patients on natalizumab compared to patients on no DMT

Post-vaccination T-cell activation by DMT – TruCulture IFNγ (left) and TruCulture IL-2 (right)



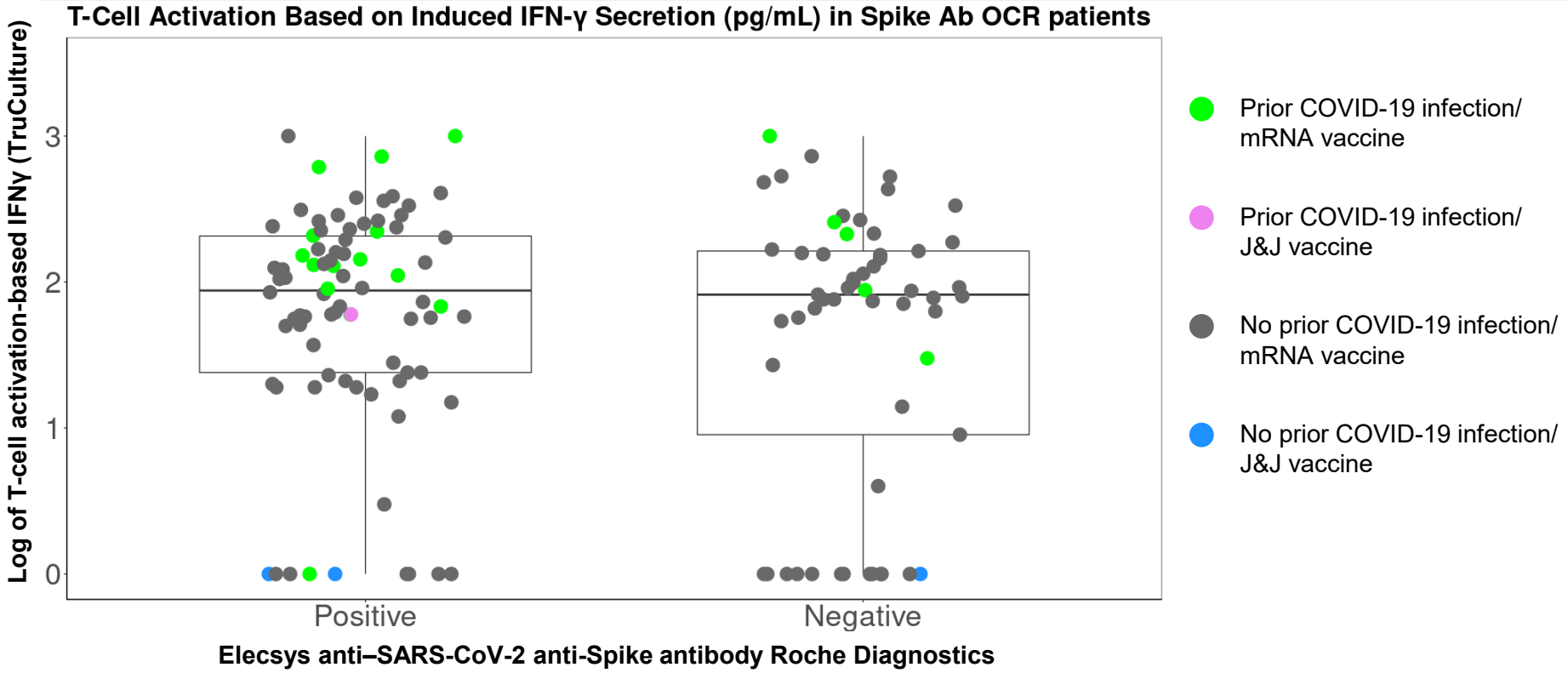


Prior COVID-19 infection No prior COVID-19 infection

DMT, disease-modifying therapy; OCR, ocrelizumab; S1P, sphingosine-1-phosphate receptor modulators.

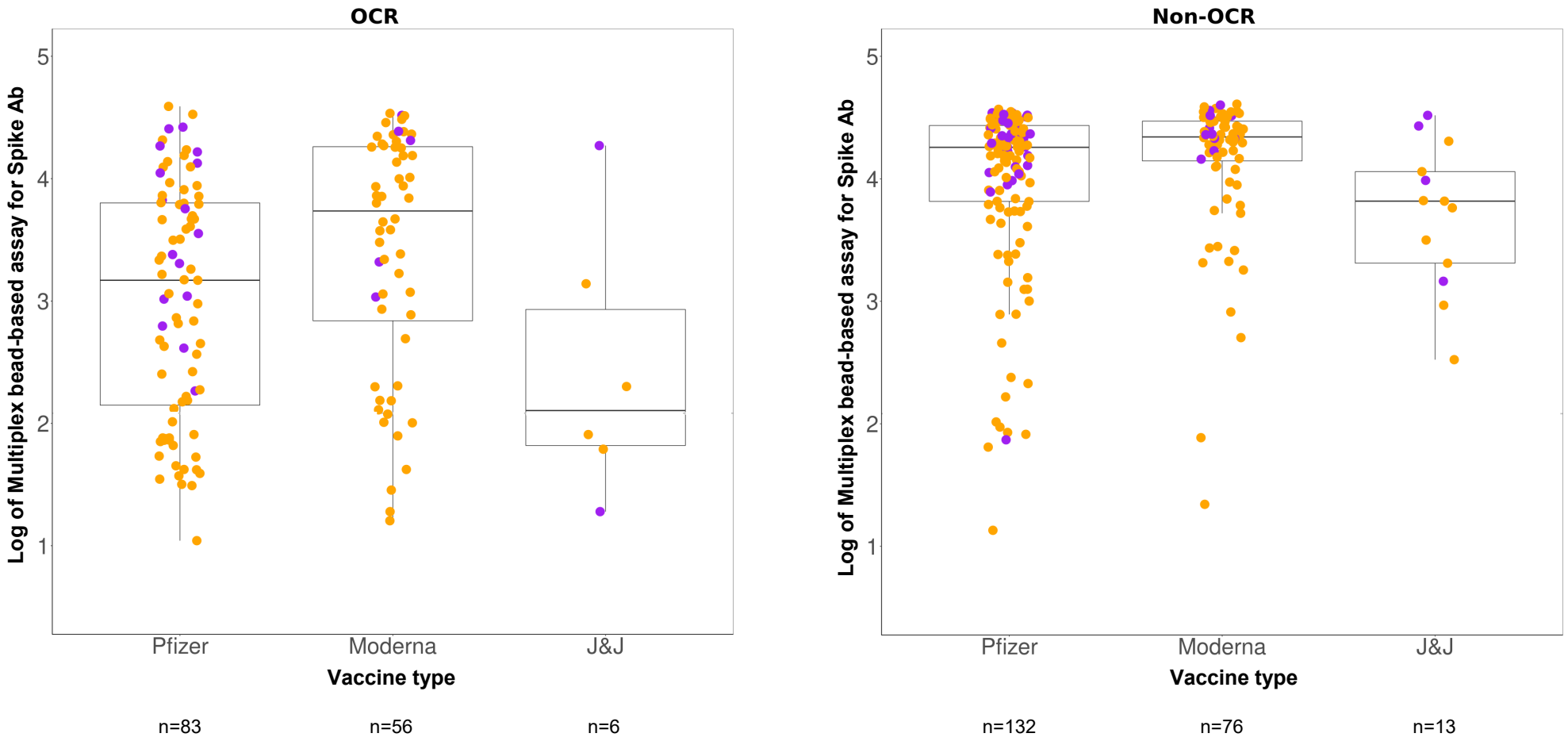
T-cell activation did not significantly differ between patients with positive (detected) or absent (undetected) Elecsys antibody response in OCR-treated patients

Comparing post-vaccination T-cell activation in OCR patients with detectable and undetectable anti-Spike antibody response (assessed with Elecsys)



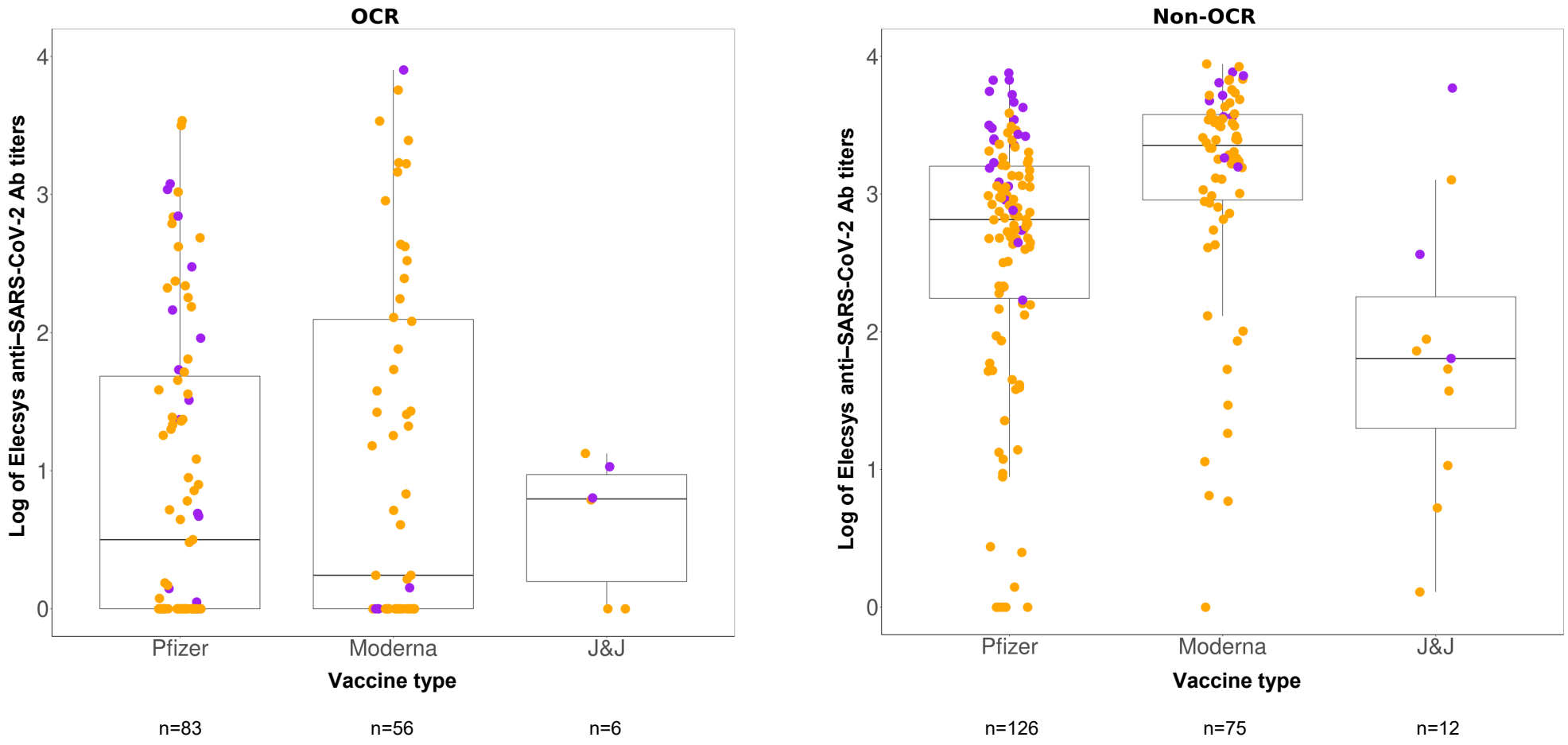
IFN, interferon; OCR, ocrelizumab.

Post-vaccination antibody responses by vaccine type in OCR and non-OCR patients assessed with MBI Spike



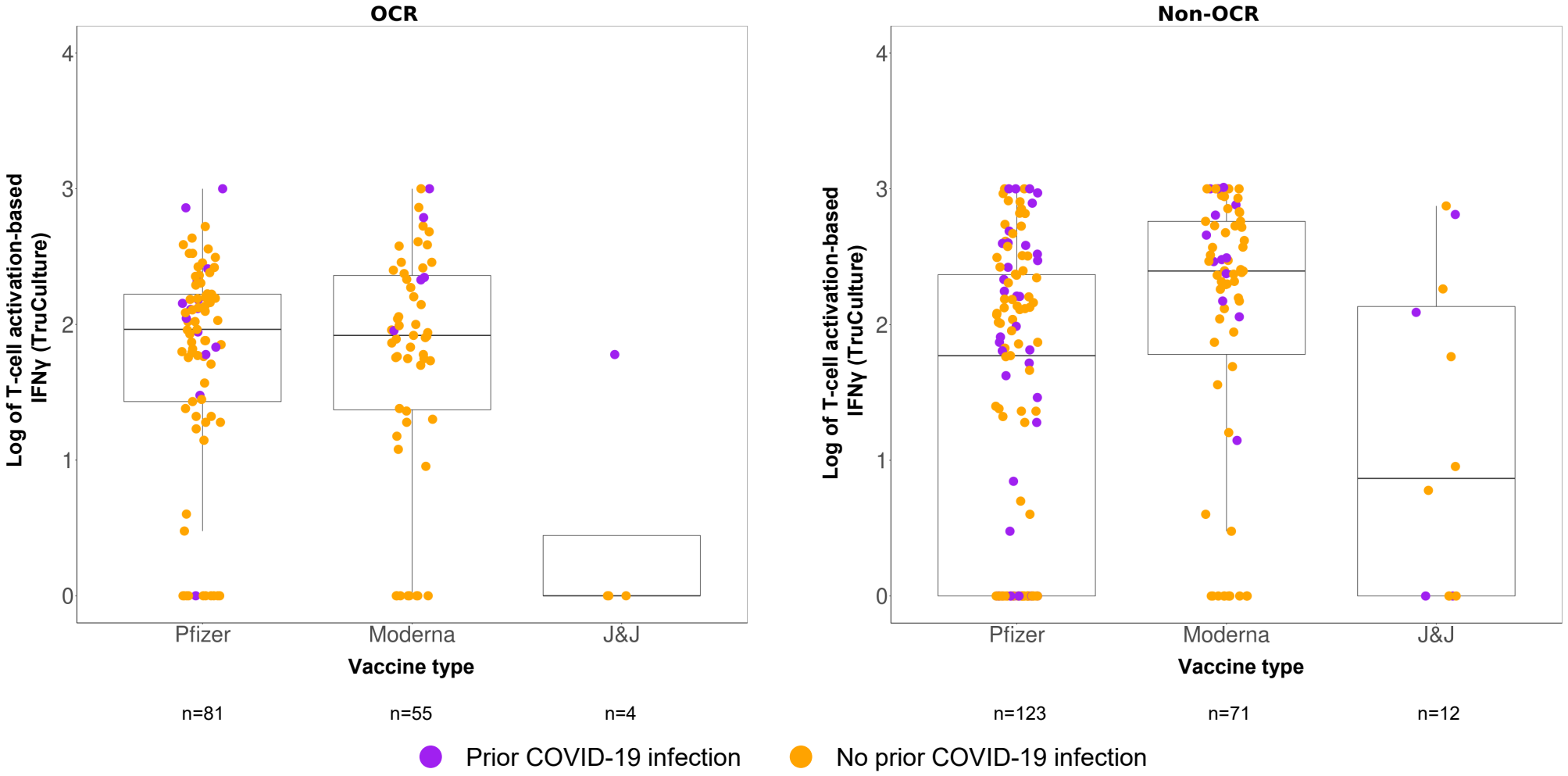
OCR, ocrelizumab.

Post-vaccination antibody responses by vaccine type in OCR and non-OCR patients assessed with Elecsys Spike RBD



OCR, ocrelizumab.

Post-vaccination T-cell activation by vaccine type in OCR and non-OCR patients assessed with TruCulture IFNγ assay



OCR, ocrelizumab.

In multivariate analyses*, predictors of **higher** post-vaccination Ab responses on both Elecsys and MBI were: **non-OCR group, prior COVID infection and vaccine**

Elecsys anti–SARS-CoV-2 Ab titers (log transformed)

	OCR (N=146)	Non-OCR (N=224)
n	145	213
Adjusted mean (SE)	1.04 (0.121)	2.84 (0.105)
95% CI for adjusted mean	0.80, 1.28	2.63, 3.04
Difference in adjusted mean (SE)	−1.80 (0.110)	
95% CI for difference in adjusted mean	−2.011, −1.580	
P value	**< 0.0001**	

Multiplex bead-based assay Spike Ab (log transformed)

	OCR (N=146)	Non-OCR (N=224)
n	145	221
Adjusted mean (SE)	3.12 (0.091)	4.02 (0.078)
95% CI for adjusted mean	2.94, 3.30	3.87, 4.17
Difference in adjusted mean (SE)	−0.90 (0.084)	
95% CI for difference in adjusted mean	−1.063, −0.733	
P value	**< 0.0001**	

Model: *P* value of fixed effects

	P value
Age (in years)	**0.0021**
Sex (female vs male)	0.5180
Prior COVID infection	**< 0.0001**
Vaccine to collection (weeks)	0.6438
Vaccine type (Pfizer vs Moderna vs J&J)	**< 0.0001**
DMT at vaccination (OCR vs non-OCR)	**< 0.0001**

Model: *P* value of fixed effects

	P value
Age (in years)	0.0545
Sex (female vs male)	0.3871
Prior COVID infection	**< 0.0001**
Vaccine to collection (weeks)	**0.0123**
Vaccine type (Pfizer vs Moderna vs J&J)	**< 0.0001**
DMT at vaccination (OCR vs non-OCR)	**< 0.0001**

CI, confidence interval; DMT, disease-modifying therapy; OCR, ocrelizumab; SE, standard error.
* Mixed-effect model: log of Elecsys or Multiplex bead-based assay for Spike Ab = DMT group at COVID infection (OCR vs non-OCR) + age + sex (female vs male) + vaccine type (Pfizer vs Moderna vs J&J) + vaccine to collection (week)

In multivariate analyses*, predictors of **higher** T-cell activation (TruCulture IFNγ assay) were: **prior COVID infection, vaccine and shorter time from vaccine**. Post vaccination T-cell reactivation was similar in patients on OCR vs non OCR-treated groups

T-cell activation-based IFNγ (TruCulture)

	OCR (N=146)	Non-OCR (N=224)
n	140	206
Adjusted mean (SE)	1.58 (0.127)	1.50 (0.107)
95% CI for adjusted mean	1.33, 1.84	1.29, 1.71
Difference in adjusted mean (SE)	0.08 (0.114)	
95% CI for difference in adjusted mean	−0.144, 0.304	
P value	0.4817	

Model: *P* value of fixed effects

	P value
Age (in years)	0.1393
Sex (female vs male)	0.6103
Prior COVID infection	**0.0093**
Vaccine to collection (weeks)	**0.0415**
Vaccine type (Pfizer vs Moderna vs J&J)	**< 0.0001**
DMT at vaccination (OCR vs non-OCR)	0.4817

CI, confidence interval; DMT, disease-modifying therapy; IFN, interferon; OCR, ocrelizumab; SE, standard error.
* Mixed-effect model: log of T-cell activation based IFNγ (TruCulture) = DMT group at COVID infection (OCR vs non-OCR) + age + sex (female vs male) + vaccine type (Pfizer vs Moderna vs J&J) + vaccine to collection (week)

Conclusions

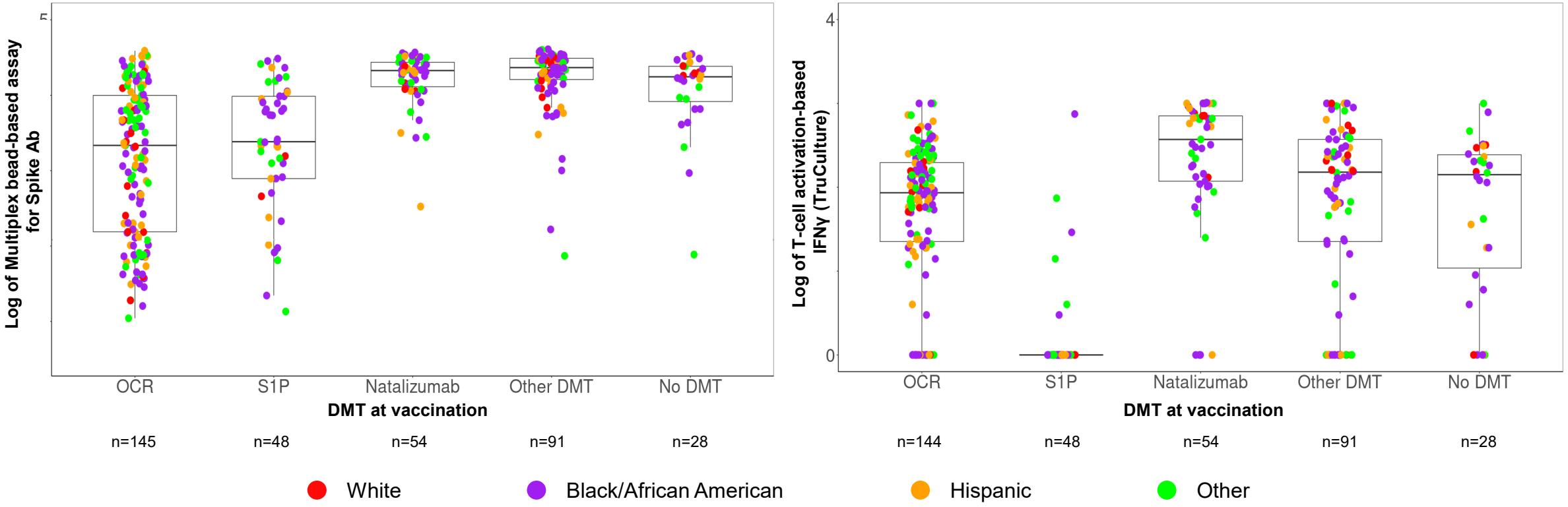
- After a mean of 18.7 (±7.7) weeks post-vaccine, Spike-specific Ab responses were attenuated in patients on OCR and S1P compared to patients on no DMT
- Compared to patients on no DMT, T-cell response post vaccine were depressed in patients on S1P, elevated in patients on Natalizumab. T-cell responses were very similar between patients on OCR group and on no DMT.
- Ab and T-cell responses to COVID-19 vaccine were elevated in patients with prior COVID-19 infection, including in patients on OCR and S1P
- Vaccine was a predictor of Ab and T-cell responses. Additional study is needed to understand whether specific vaccine may be preferred for subsets of patients.

DMT, disease-modifying therapy; OCR, ocrelizumab; S1P, sphingosine-1-phosphate receptor modulators.

Supplement

Immune responses did not differ by race/ethnicity in this cohort, which was comprised of 53% minorities

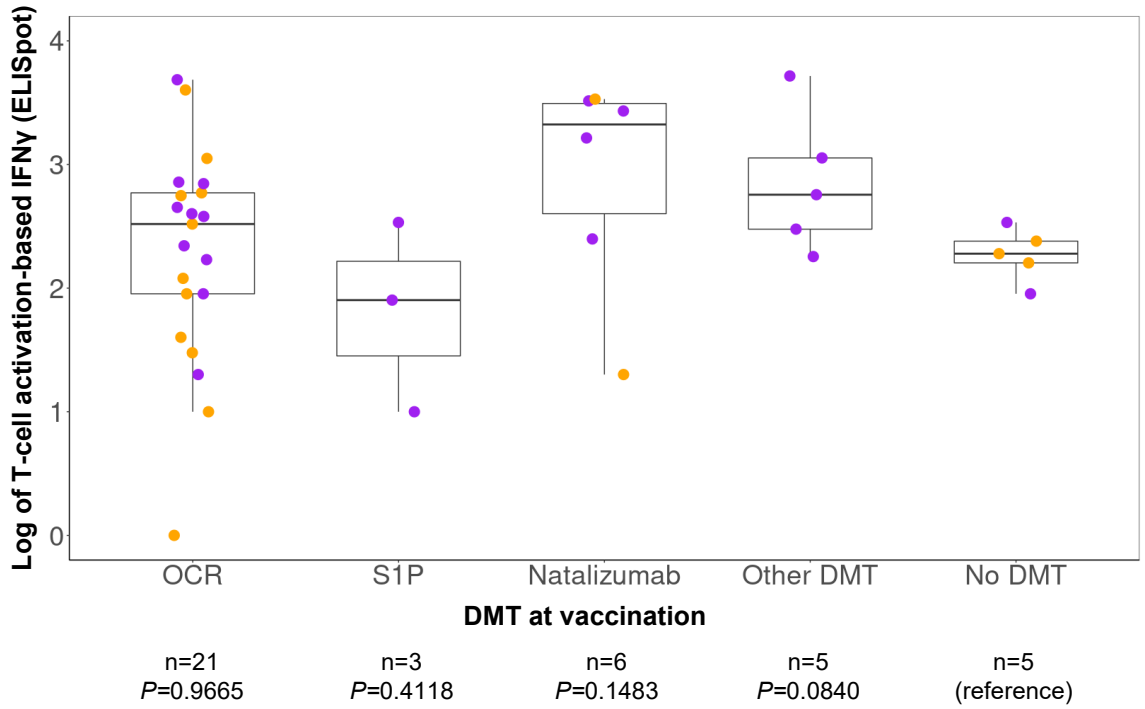
Antibody responses (MBI) and T-cell activation (Truculture) post-vaccination by race and COVID-19 status

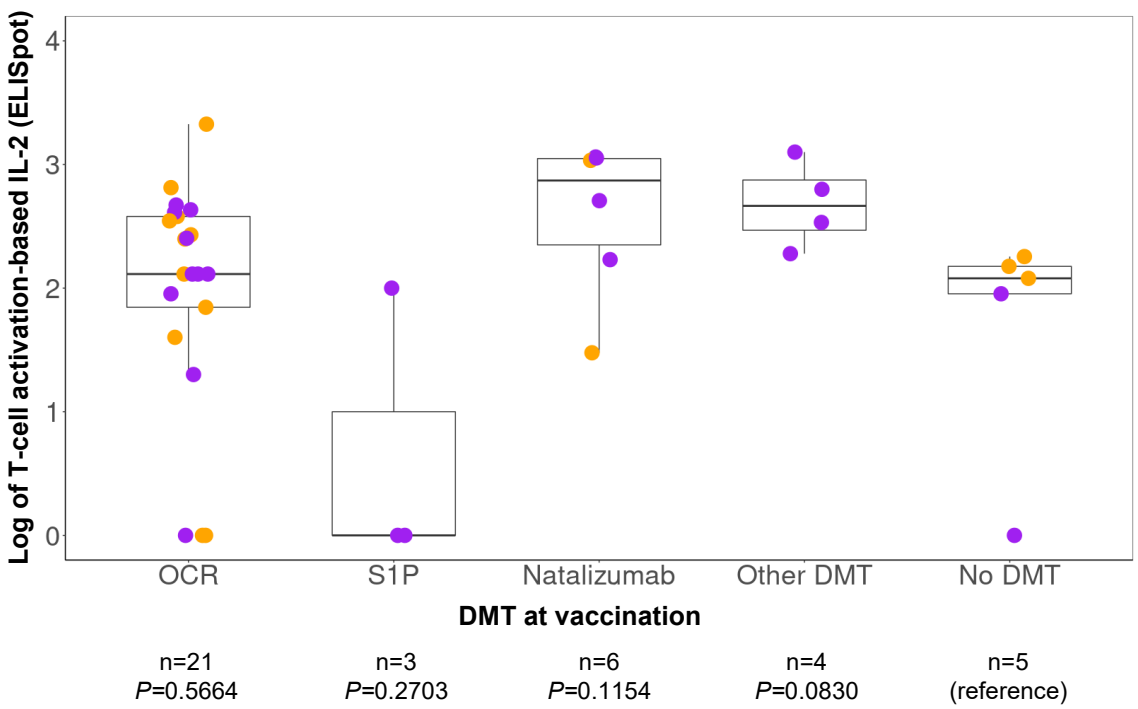


OCR, ocrelizumab.

Similar trends for T-cell activation were observed using ELISpot and TruCulture assays

Post-vaccination T-cell activation by DMT - ELISpot IFNγ (left) and ELISpot IL-2 (right) in a subset of patients (n=40)





Prior COVID-19 infection No prior COVID-19 infection

DMT, disease-modifying therapy; IFN, interferon; OCR, ocrelizumab; S1P, sphingosine-1-phosphate receptor modulators.