Omicron breakthrough disease activity in the Swiss Multiple Sclerosis Cohort Study

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CONCLUSIONS

- SARS-CoV-2-S antibody levels are highly dependent on disease modifying treatment at time of vaccination.
- Higher SARS-CoV-2-S antibody levels after 2nd vaccination are associated with a lower hazard of Omicron breakthrough infection in patients with Multiple Sclerosis.
- A third vaccination reduces the risk of breakthrough infection in patients with Multiple Sclerosis.

INTRODUCTION

- Specific disease modifying treatments (DMTs) reduce humoral immune response to SARS-CoV-2 vaccines in patients with Multiple Sclerosis (pwMS).[1-3]
- Limited information on Omicron breakthrough infections in pwMS treated with different DMTs is available.[4]

OBJECTIVE

- To determine the rate and severity of breakthrough infections with the Omicron variant of SARS-CoV-2 in the Swiss MS Cohort Study (SMSC).
- To estimate the impact of SARS-CoV-2-S antibody levels and third vaccination on breakthrough infection risk.

METHODS

- Data on SARS-CoV-2 infections (positive PCR- or antigen self-test), severity of COVID-19 according to the WHO scale[5] and SARS-CoV-2 vaccines were collected by questionnaires 6 or 12 monthly.
- For this subgroup analysis pwMS fulfilling the following criteria were included:
  - At least two doses of SARS-CoV-2 vaccines before Omicron became the dominant variant in Switzerland on Dec-15, 2021 (= Omicron start).
  - Available SARS-CoV-2-S antibody level after second vaccine dose (determined by ECLIA, Elecsys, Anti-SARS-CoV-2, Roche Diagnostics)
  - At least one follow-up after Dec-15, 2021
  - Stable DMT at time of vaccination, antibody measurement and Omicron start.

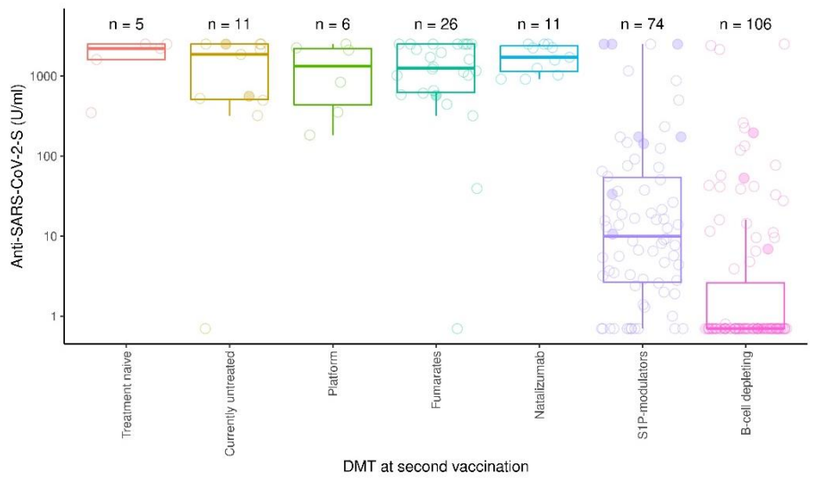
RESULTS STUDY POPULATION AND ANTIBODY LEVELS

- 281 pwMS were included. Median follow-up after Dec-15, 2021 was 138 days [IQR 110-184]. 31 (11%) pwMS had a previous SARS-CoV-2-infection (Table 1).
- SARS-CoV-2-S antibody levels were measured median 84 days [IQR 41-157] after second vaccine dose and median 117 days [IQR 50-188] before Omicron start. Antibody levels in different DMT groups are shown in Figure 1.

Table 1: Demographics and MS characteristics (n = 281)

Age, median [IQR], years	49.4 [40.4-58.8]
Female, No (%)	190 (67.6)
BMI, median [IQR], kg/m2	23.9 [21.6-27.1]
Disease subtype	
RMS, No (%)	234 (83.2)
PPMS, No (%)	19 (6.8)
SPMS, No (%)	28 (10.0)
Disease duration, median [IQR], years	14.8 [8.5-23.5]
EDSS, median [IQR]	2.5 [1.5-4.0]
Disease modifying therapy	
Treatment naive, No (%)	5 (1.8)
Currently untreated, No (%)	11 (3.9)
Platform, No (%)	9 (3.2)
Fumarates, No (%)	32 (11.4)
Natalizumab, No (%)	13 (4.6)
S1P-modulators, No (%)	88 (31.3)
B-cell depleting therapies, No (%)	116 (41.3)
Other, No (%)	7 (2.5)
Treatment duration, median [IQR], years	3.8 [2.7-7.1]
Vaccinations at Omicron-Start	
2, No (%)	105 (37.4)
3, No (%)	173 (61.5)
4, No (%)	3 (1.1)

Figure 1: Antibody levels after second vaccination



PwMS with a third vaccination prior to measurement (n = 37) or treated with other DMTs (n = 5) are not shown. Filled dots represent pwMS with previous SARS-CoV-2-infection.

RESULTS CASES

- 92 breakthrough infections were reported between Dec-15 2021 and Aug-15 2022.
- Severity of breakthrough disease on WHO scale ranged from 1-10. Characteristics of cases are shown in table 2.

Table 2: Characteristics of cases with breakthrough disease (n = 92)

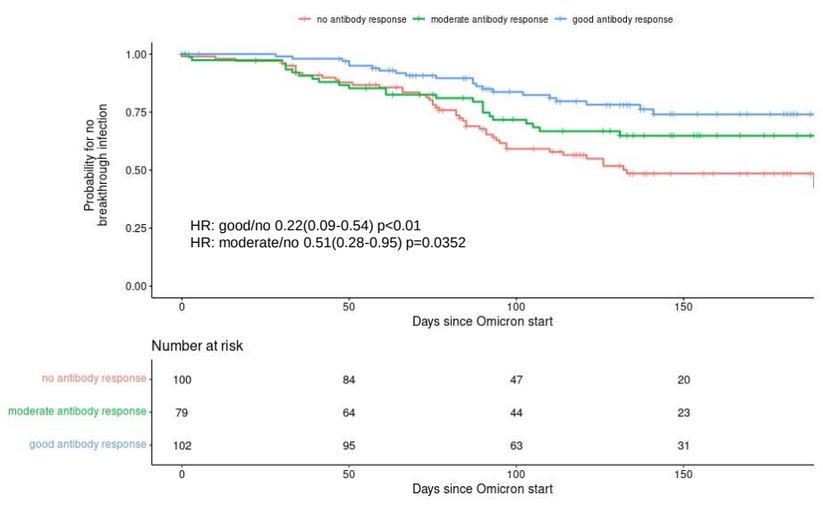
	Ambulatory mild disease (Score# 1 to 3) n = 81	Hospitalized: moderate disease (Score# 4 to 5) n = 10	Hospitalized: severe disease (Score# 6 to 9) n = 0	Dead (Score# 10) n = 1
Age*, median [range], years	44.6 [24.2-77.3]	48.2 [25.8-71.6]		56.9
Female, No (%)	57 (70.4)	6 (60.0)		0 (0.0)
EDSS** [range]	2.0 [0.0-6.5]	4.8 [0.0-7.5]		4.0
Disease subtype**				
RMS, No (%)	73 (90.1)	6 (60.0)		1
PPMS, No (%)	3 (3.7)	2 (20.0)		0
SPMS, No (%)	5 (6.2)	2 (20.0)		0
Disease duration* [range], years	14.0 [1.4-44.8]	20 [1.8-37.0]		41.7
Disease modifying therapy*, No				
Treatment naive	2 (2.5)	1 (10.0)		0
Currently untreated	2 (2.5)	0		0
Plafform	2 (2.5)	0		0
Fumarates	8 (9.9)	0		0
Natalizumab	5 (6.1)	0		0
S1P-modulators	27 (33.3)	0		0
B-cell depleting therapies	34 (42.0)	9 (90.0)		1
Other	1 (1.2)	0		0
Treatment duration*, median [IQR], years	3.9 [2.8-7.8]	3.7 [3.4-4.1]		4.2
SARS-CoV-2-S antibody level***, median [range], U/ml	3.7 [0.7-2500]	0.7 [0.7-1604]		9.6

* At date with positive COVID-19 test result; ** At SMSC visit before positive SARS-CoV-2 test result; *** after second vaccination; #WHO clinical progression scale

RESULTS ANTIBODY LEVEL

- Good antibody response (>150U/ml) was associated with a 78% lower risk of breakthrough infection during follow up (HR = 0.22, 95%CI = 0.09-0.54, p<0.01, Cox regression model, adjusted for age and DMT) compared to no antibody response (<0.7U/ml).
- Moderate antibody response (0.71-150U/ml) was associated with a 49% lower risk of breakthrough infection during follow up (HR = 0.51, 95%CI = 0.28-0.95, p=0.0352, Cox regression model, adjusted for age and DMT) compared to no antibody response (Figure 2).

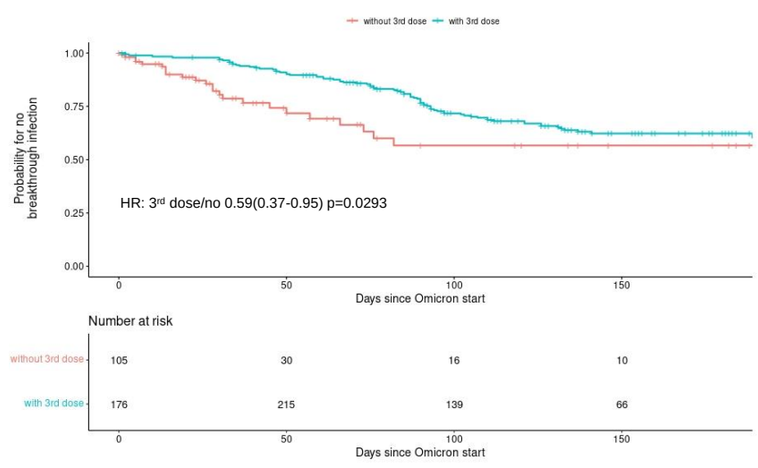
Figure 2: Infection rate in groups with different antibody levels



RESULTS THIRD VACCINATION

- PwMS who received a third vaccination had a 41% lower hazard of breakthrough infection during follow up (HR = 0.59, 95%CI = 0.37-0.95, p=0.0293, Cox regression model adjusted for age) compared to those who did not receive a third vaccine dose (Figure 3).

Figure 3: Infection rate in pwMS with a third vaccine dose



OUTLOOK

- Completion of antibody-measurements in remaining samples of a total of 1020 pwMS within the Swiss MS Cohort is under way.
- This will allow to analyze the effect of additional vaccine doses on serology and infection rates in a large real world cohort of pwMS.

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