# Incidence of COVID-19 in patients with multiple sclerosis who received SARS-CoV-2 vaccines and are under treatment with high-efficacy therapies in Argentina

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## SUMMARY

- The effectiveness of SARS-CoV-2 vaccines in PwMS is focused on mRNA vaccines (the type of vaccines not widely implemented in Argentina),
- It is difficult to extrapolate results from international research studies into Argentina's context
- We found an incidence density of breakthrough SARS_CoV-2 infection of 3.5 per 10,000 patients/day (95%CI 2.3-6.7) after vaccination in Argentina mainly with Sputnik or Astra Zeneca vaccines.
- We described the incidence rate after vaccination for every HET used, it being significantly higher for ocrelizumab compared with other HETs.
- We also observed a decrease in the frequency of COVID-19 infection between pre- and post-vaccination in the included HET patients.

## INTRODUCTION

- Different vaccines are being used to achieve immunization against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) worldwide.
- As data generated regarding the effectiveness of SARS-CoV-2 vaccines in PwMS is focused on mRNA vaccines (the type of vaccines not widely implemented in Argentina), it is difficult to extrapolate results from international research studies into Argentina context and the need of local data is urgent and necessary.

## OBJECTIVE

- We aimed to evaluate the incidence of SARS-CoV-2 breakthrough infection and the side effects of SARS-CoV-2 vaccines in people with MS (PwMS) on high-efficacy disease-modifying therapies (DMTs) (HET) included in the national MS registry in Argentina (RelevarEM).

## METHODS

- Non-interventional, retrospective cohort study that collected information directly from RelevarEM (clinical trials registry number NCTNCT03375177). Adult PwMS who had been treated for at least 6 months with a HET (ocrelizumab, natalizumab, alemtuzumab, cladribine) who had received at least 2 doses of SARS-CoV-2 vaccines available in Argentina were included. A full course of vaccination was considered after the second dose of the corresponding vaccines. A positive COVID-19 case was defined according to the definition established by the Ministry of Health in Argentina.
- The primary outcome was to assess the incidence of SARS-CoV-2 breakthrough infection in PwMS on HET vaccinated for COVID-19. Clinical activity after the first dose and up to 6 months after full course vaccine was also collected. Cumulative incidence of SARS-CoV-2 infection was reported for the whole cohort by Kaplan Meier survival curves (which is expressed in percentage) as well as incidence density (which is expressed per 10.000 patient/days with 95%CI).

## RESULTS

- 228 PwMS were included. Most frequent first and second dose received was Astra-Zeneca vaccine, followed by Sputnik vaccine. Most frequent HETs used in included patients were cladribine in 79 (34.8%), as shown in **Table 1**.
- A total of 15 positive COVID-19 cases were observed for a total exposure time of 43,180 patient/days and 4 cases of hospitalization due to severe SARS-CoV-2 infection). We found an incidence density of breakthrough COVID-19 infection of 3.5 x 10.000 patients/day (95%CI 2.3-6.7) after vaccination in Argentina. We described the incidence rate after vaccination for every HET used, it being significantly higher for ocrelizumab compared with other HETs (p=0.005). Only 5 patients presented a relapse during the follow-up period with no differences regarding the pre-vaccination period.

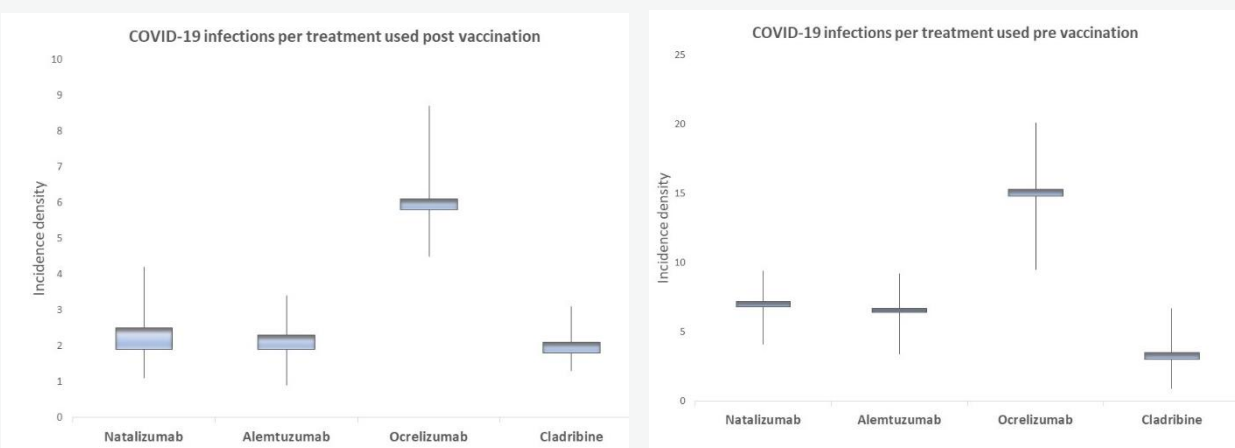**Figure 1.** Incidence density of COVID-19 infections post- and pre-vaccination



**Figure 2.** Pre- and post-vaccination comparison of incidence density infection with COVID 19 in included patients.
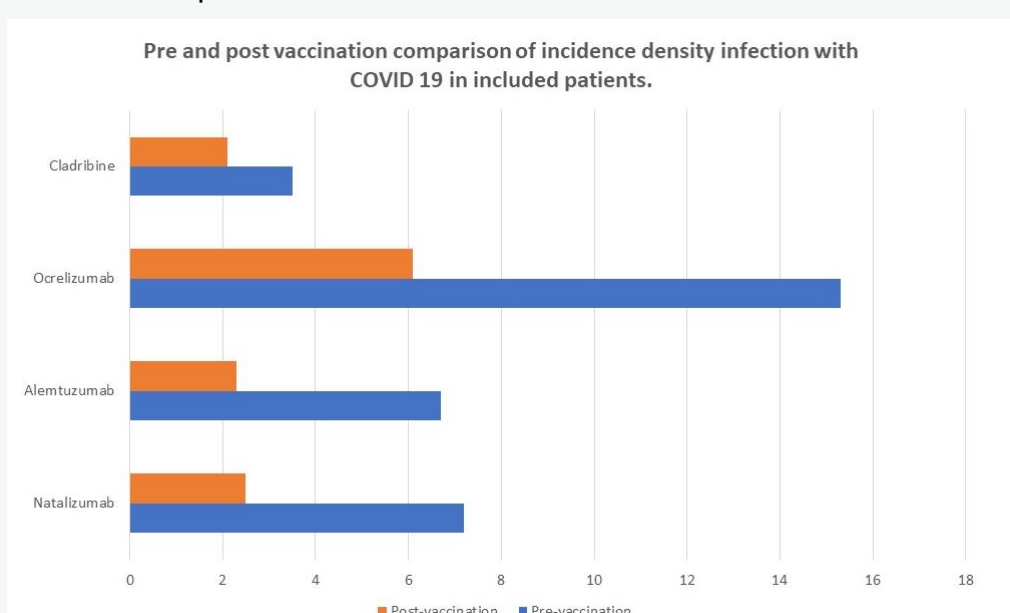


**Table 1.** Baseline characteristics, follow-up time, and vaccines received

| | N = 228 |
|---|---|
| Mean age at study entry, years (SD) | 38.7± 8.5 |
| Mean disease duration, years (SD) | 7.6± 5.5 |
| RRMS, n (%) | 196 (86) |
| SPMS, n (%) | 32 (14) |
| Female gender, n (%) | 166 (72.8) |
| Median EDSS at Study entry, (IQR)(Range) | 3 (2.0) (1-7) |
| ARR in the 6 months previous first dose of vaccine | 0.32 ± 0.18 |
| Disease modifying treatment (DMT)* | |
| Natalizumab, n (%) | 65 (28.5) |
| Alemtuzumab, n (%) | 23 (10) |
| Ocrelizumab, n (%) | 61 (26.7) |
| Cladribine, n (%) | 79(34.8) |
| Median Charlson score of comorbidities, (IQR) | 0.31 (0.41) |
| Median follow up time after second dose, days (IQR) | 190±12 |
| Mean follow up time after second dose, days, SD, Range | 191.3±16(174-245) |
| Number of patients infected with SARS-CoV-2 breakthrough treated with a HET in the pre vaccinated period | 42 (18.4) |
| First dose of SARS-CoV-2 vaccine received. | |
| Sputnik V, n (%) | 65 (28.5) |
| Astra Zeneca, n (%) | 115 (50.5) |
| Sinopharm | 48 (21) |
| Second dose of SARS-CoV-2 vaccine received. | |
| Sputnik V, n (%) | 47 (20.6) |
| Astra Zeneca, n (%) | 126 (55.3) |
| Sinopharm | 34 (14.9) |
| Moderna | 11 (4.8) |
| Pfizer | 10 (4.4) |
| Median time between first and second vaccine dose, (SD) days, | 61 ±19 |
| Homologous vaccine scheme, n (%) | 194 (85) |

* From first dose of the SARS-CoV-2 vaccine up to 6 months after the full course of the vaccine
RRMS= relapsing remitting multiple sclerosis; SPMS= secondary progressive multiple sclerosis; PPMS= primary progressive multiple sclerosis; EDSS= expanded disability status scale; SD= standard deviation IQR (interquartile range)

## CONCLUSIONS

- We found an incidence density of breakthrough SARS_CoV-2 infection of 3.5 per 10,000 patients/day (95%CI 2.3-6.7) after vaccination in Argentina mainly with Sputnik or Astra Zeneca vaccines.
- We described the incidence rate after vaccination for every HET used, it being significantly higher for ocrelizumab compared with other HETs. We also observed a decrease in the frequency of COVID-19 infection between pre- and post-vaccination in the included HET patients.

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