Relapse activity after vaccination against COVID-19 in people with multiple sclerosis: 1-year follow-up results from a nationwide longitudinal observational study

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Niklas Frahm*[1,2], Firas Fneish[1], Melanie Peters[1,3], David Ellenberger[1], Judith Haas[4], Micha Loebermann[5], Dieter Pöhlau[4], Anna-Lena Röper[1,4], Sarah Schilling[1], Alexander Stahmann[1], Herbert Temmes[4], Friedemann Paul[6], Uwe K. Zettl[2]

1: MS Forschungs- und Projektentwicklungs- gGmbH (MS Research and Project Development gGmbH), German MS Registry, Hanover, Germany
2: University Medical Center of Rostock, Department of Neurology, Neuroimmunological Section, Rostock, Germany
3: Gesellschaft für Versorgungsforschung mbH (Society for Health Care Research [GfV]), German MS Registry, Hannover, Germany
4: Deutsche Multiple Sklerose Gesellschaft, Bundesverband e.V. (German MS Society Federal Association [DMSG]), Hannover, Germany
5: University Medical Center of Rostock, Department of Tropical Medicine, Infectious Diseases and Nephrology, Rostock, Germany
6:Experimental and Clinical Research Center, Max Delbrueck Center for Molecular Medicine and Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany

Background

Several studies reported symptoms post vaccination (PV) against COVID-19. Even people with multiple sclerosis (PwMS) have concerns about disease activity PV occurring as relapses.

Objective

To analyze the timely association between COVID-19 vaccination (VACC) and subsequent occurring relapses in PwMS.

Methods

This analysis is based on a longitudinal observational study of the safety and tolerability of COVID-19 vaccines in PwMS. Socio-demographic, clinical and VACC data were acquired via longitudinal online surveys. Inclusion criteria for the present analysis were ≥18 years of age, relapsing MS diagnosis and ≥1 VACC. The proportion of PwMS reporting ≥1 relapse PV, time to relapses PV, annualized relapse rates (ARRs) and risk ratios (RRs) for the occurrence of relapses PV were calculated. Periods analyzed for the occurrence of relapse PV were from 1st to next VACC (P1), from 2nd to next VACC (P2) and from 1st booster VACC to the end of observation (P3). If there was no further VACC after the 1st or 2nd VACC, P1 and P2 were considered until the end of the observation period for the respective PwMS.

Results

	ALL (N=2332)	≥1 PV relapse (N=327)	No PV relapse (N=2005)	p-value
Gender, N (%)				0.002
Females	1860 (79.8)	284 (86.9)	1576 (78.6)	
Males	466 (20.0)	43 (13.1)	423 (21.1)	
Diverse	6 (0.3)	0 (0.0)	6 (0.3)	
Age at baseline [Years], median [Q25;Q75]	46.4 [37.5;54.4]	40.9 [33.6;50.1]	47.5 [38.5;54.8]	<0.001
Disease course, N (%)				<0.001
RRMS	1803 (77.3)	283 (86.5)	1520 (75.8)	
SPMS	431 (18.5)	33 (10.1)	398 (19.9)	
Not defined	98 (4.2)	11 (3.4)	87 (4.3)	
Disability level, N (%)				0.019
Mild: PDDS 0-1	1224 (54.2)	152 (49.4)	1072 (55.0)	
Moderate: PDDS 2-4	774 (34.3)	127 (41.2)	647 (33.2)	
Severe: PDDS ≥5	259 (11.5)	29 (9.4)	230 (11.8)	
Autoimmune comorbidities, N (%)	499 (21.4%)	89 (27.2)	410 (20.4)	0.007
DMT (Yes), N (%)	1731 (74.2)	218 (66.7)	1513 (75.5)	<0.001
≥1 Relapse within the year before 1st VACC (N=1787), N (%)	352 (19.8)	91 (35.4)	261 (17.2)	<0.001
Time from last pre-VACC relapse to 1st VACC [Years] (N=1787), median [Q25;Q75]	3.2 [1.3;6.9]	1.8 [0.6;4.4]	3.5 [1.5;7.2]	<0.001

Table 1: Characteristics of MS patients stratified by relapse activity after receiving SARS-CoV-2 vaccination. DMT – disease-modifying therapy; MS – multiple sclerosis; N – number of patients; PDDS – patient-determined disease steps; PV – post-vaccination; Q25 – 25% quantile; Q75 – 75% quantile; RRMS – relapsing remitting MS; SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2; SPMS – secondary progressive MS; VACC – SARS-CoV-2 vaccination.

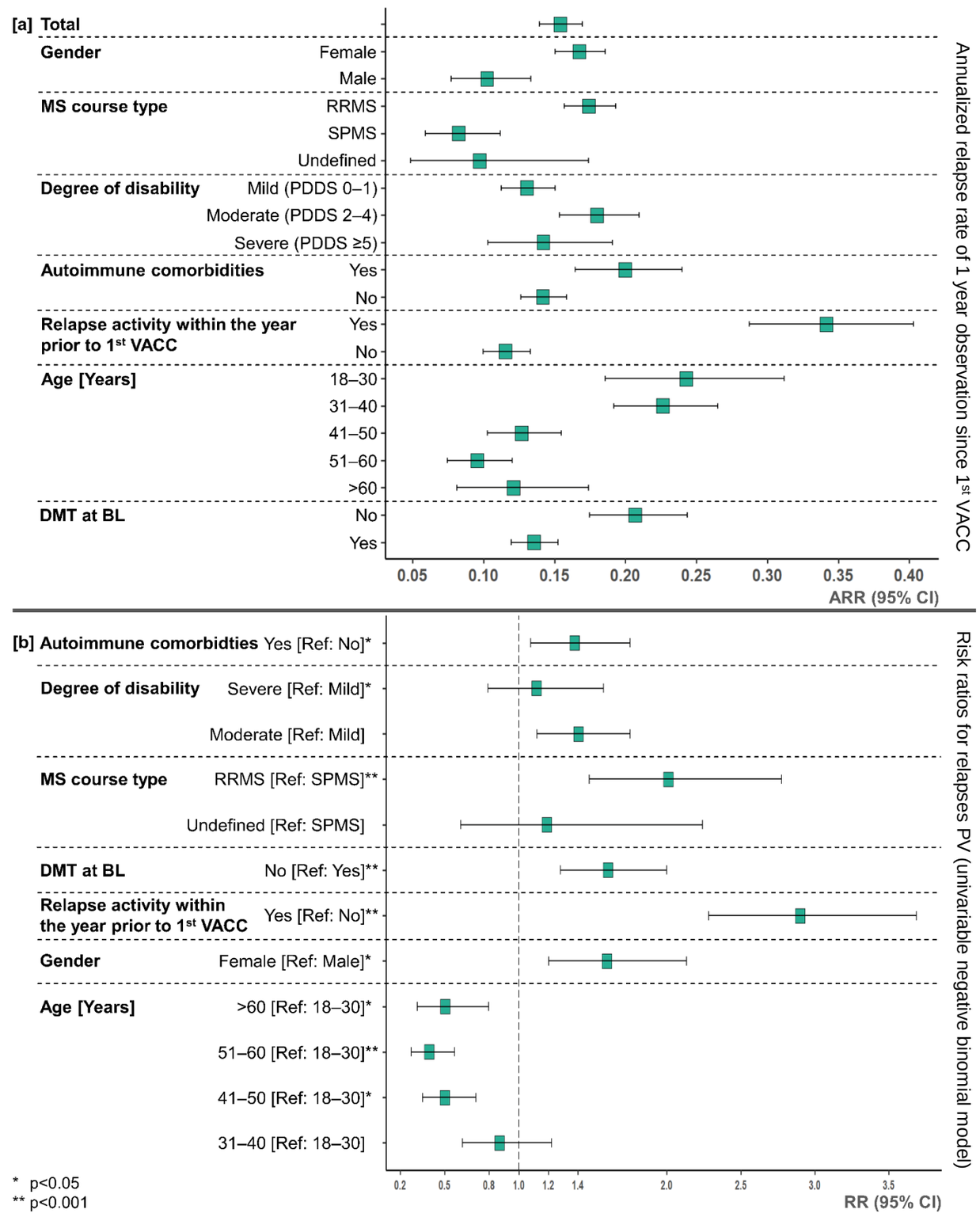

Figure 1: Frequency and risk factors of post-SARS-CoV-2-vaccination relapses in people with MS. [a] ARRs of PwMS stratified by sociodemographic and clinical variables. [b] RRs for the occurrence of relapses PV using univariable negative binomial model with observation period as an offset. ARR – annualized relapse rate; BL – baseline; CI – confidence interval; DMT – disease-modifying therapy; MS – multiple sclerosis; p – p-value; PDDS – patient-determined disease steps; PV – post vaccination; PwMS – people with MS; Ref – reference; RR – risk ratio; RRMS – relapsing-remitting MS; SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2; SPMS – secondary progressive MS; VACC – vaccination against SARS-CoV-2.

- Overall ARR of 0.154 (95% CI: 0.140–0.170) with median observation period since 1st VACC of 1.2 (Q25;Q75: 1.1;1.3)
- Risk factors for the occurrence of relapses PV:
  - Female gender (RR: 1.59 [95% CI: 1.20–2.13]; reference: male)
  - Younger age (41–50: 0.50 [0.35–0.71], 51–60: 0.39 [0.27–0.57], >60: 0.50 [0.31–0.80]; reference: 18–30)
  - Moderate degree of disability (1.40 [1.12–1.75]; reference: mild)
  - Autoimmune comorbidities (1.38 [1.08–1.75]; reference: none)
  - RRMS (2.01 [1.47–2.77]; reference: SPMS)
  - No DMT at baseline (1.60 [1.28–2.00]; reference: DMT)
  - ≥1 relapse within the year before 1st VACC (2.90 [2.28–3.69]; reference: none)
- Median time to a relapse (weeks) was shortest during P1 (4.1 [Q25;Q75: 1.8;5.5] weeks) compared to P2 (9.5 [3.9;19.7] weeks) and P3 (13.5 [6.7;20.0] weeks)
- Relapses were reported more frequently in P2 and P3 (142 and 139 patients, respectively) compared to 84 patients with relapses during P1

Conclusion

Most patients (86.0%) did not experience relapses PV. Among PwMS with relapses PV, relapses occurred most frequently after the 2nd VACC. Time to relapse PV was the shortest after 1st VACC. Gender, age, disability level, autoimmune comorbidity status, MS course type, DMT status and disease activity immediately prior to the 1st VACC appear to play determinant roles in disease activity PV.

Disclosures

Niklas Frahm is an employee of the MSFP. Moreover, he is an employee of Rostock's University Medical Center and received travel funds for research meetings from Novartis. None resulted in a conflict of interest.David Ellenberger, Firas Fneish, Sarah Schilling and Melanie Peters had no personal financial interests to disclose other than being employees of the German MS Registry.Judith Haas has no personal pecuniary interests to disclose, other than being the President of the German MS Society, federal association, which receives funding from a range of public and corporate sponsors, recently including BMG, G-BA, The German MS Trust, Biogen, (Bristol Myers Squibb, Merck Serono, Novartis, Roche, Sanofi, Viatris (former Mylan). None resulted in a conflict of interest.Micha Löbermann received speaker honoraria from Sanofi, AbbVie and Pfizer, he served as investigator in vaccine studies sponsored by Janssen, GSK and Novartis. None resulted in a conflict of interest.Friedemann Paul has received speaking fees, travel support, honoraria from advisory boards and/or financial support for research activities from Bayer, Novartis, Biogen, Bristol Myers Squibb, Teva, Sanofi-Aventis/Genzyme, Merck Serono, Alexion, Chugai, MedImmune, Shire, German Research Council, Werth Stiftung of the City of Cologne, German Ministry of Education and Research, EU FP7 Framework Program, Arthur Arnstein Foundation Berlin, Guthy Jackson Charitable Foundation and National Multiple Sclerosis of the USA. He serves as academic editor for PLoS ONE and associate editor for Neurology, Neuroimmunology and Neuroinflammation. None resulted in a conflict of interest.Dieter Pöhlau received speaking fees, travel support and financial support for research projects from: Allmirall, Bayer, Biogen-Idec, Merck-Serono, Octapharma, Novartis, Roche, Sanofi-Aventis and Teva. None resulted in a conflict of interest.Anna-Lena Röper is an employee of the MSFP and Germany MS society, which is funded by many public and corporate sponsors. She received travel funds from Novartis. None resulted in a conflict of interest.Alexander Stahmann has no personal financial interests to disclose, other than being the leader of the German MS Registry, which receives (project) funding from a range of public and corporate sponsors, recently including G-BA, The German Retirement Insurance, The German MS Trust, German MS Society, Biogen, Bristol Myers Squibb, Merck, Novartis, Roche and Sanofi. None resulted in a conflict of interest.Herbert Temmes has no personal pecuniary interests to disclose, other than being the Secretary General of the German MS Society, federal association, which receives funding from a range of public and corporate sponsors, recently including Bundesgesundheitsministerium (BMG), The German Innovation Fund (G-BA), The German MS Trust, Biogen, (Bristol Myers Squibb, Merck Serono, Novartis, Roche, Sanofi, Viatris (former Mylan). None resulted in a conflict of interest.Uwe K. Zettl has received speaking fees, travel support and /or financial support for research activities from Alexion, Almirall, Bayer, Biogen, Bristol Myers Squibb, Janssen, Merck Serono, Novartis, Octapharma, Roche, Sanofi Genzyme, Teva as well as EU, BMBF, BMWi and DFG. None resulted in a conflict of interest.AS, DE, FF, JH, SS, HT and MP have nothing to disclose.NF, ML, DP, A-LR, FP and UZ have received speaking fees, travel support, honoraria from advisory boards and/or financial support for research activities from industry sponsors. None resulted in a conflict of interest.

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