THERAPEUTIC ADVANCES in
Neurological Disorders

Original Research

Cellular and humoral vaccination response under immunotherapies—German consensus on vaccination strategies in neurological autoimmune diseases

Ther Adv Neurol Disord

2025, Vol. 18: 1–40

DOI: 10.1177/17562864251396006

Muriel Schraad, Mathias Mäurer, Anke Salmen, Tobias Ruck, Timo Uphaus, Vinzenz Fleischer, Felix Luessi, Maria Protopapa, Falk Steffen, Nicholas Hanuscheck, Katrin Pape, Tobias Brummer, Josef Shin, Thomas Korn, Luisa Klotz, Jan D. Lünemann, Marc Pawlitzki, Martin S. Weber, Antonios Bayas, Brigitte Wildemann, Hans-Peter Hartung, Florian Then Bergh, Clemens Warnke, Uwe K. Zettl, Achim Berthele, Aiden Haghikia, Ralf Linker, Hayrettin Tumani, Sven G. Meuth, Bernhard Hemmer, Heinz Wiendl, Tania Kümpfel, Ralf Gold, Stefan Bittner and Frauke Zipp

Correspondence to:
Muriel Schraad
Department of Neurology, Research Center for Immunotherapy (FZI) and Focus Program Translational Neuroscience (FTN), Rhine-Main Neuroscience Network (rmn2), University Medical Center of the Johannes Gutenberg University Mainz, 55131 Mainz, Germany
muriel.schraad@unimedizin-mainz.de

Mathias Mäurer
Clinic for Neurology, Juliusspital, Klinikum Würzburg Mitte, Würzburg, Germany

Anke Salmen
Ralf Gold
Department of Neurology, St. Josef Hospital, Ruhr University Bochum, Bochum, Germany

Tobias Ruck
Marc Pawlitzki
Sven G. Meuth
Department of Neurology, University Hospital Düsseldorf, Heinrich Heine University, Düsseldorf, Germany

Timo Uphaus
Vinzenz Fleischer
Felix Luessi
Maria Protopapa
Falk Steffen
Nicholas Hanuscheck
Katrin Pape
Tobias Brummer
Josef Shin
Stefan Bittner
Frauke Zipp
Department of Neurology, Research Center for Immunotherapy (FZI) and Focus Program Translational Neuroscience (FTN), Rhine-Main Neuroscience Network (rmn2), University Medical Center of the Johannes Gutenberg University Mainz, Mainz, Germany

Abstract

Background: With the development of highly effective disease-modifying treatments, vaccinations are becoming increasingly important in people with neurological autoimmune diseases. However, questions regarding the safety and efficacy of vaccinations under immunotherapy remain.

Objective: To provide recommendations on types and timing of vaccinations for people with neuroimmunological diseases under different immunotherapies.

Design: Our study presents a German evidence-based expert consensus on vaccination under immunotherapies in neurological autoimmune diseases.

Methods: Based on literature research, a consortium of experts evaluated the quality of evidence, integrated clinical experience, and responded to a questionnaire determining an agreement (>75%) on statements concerning vaccination upon immune therapies in neuroimmunological diseases.

Results: The specific humoral and cellular response to vaccination can be compromised under alemtuzumab, azathioprine, cladribine, cyclophosphamide, CD19/CD20 antibodies (inebilizumab, ocrelizumab, ofatumumab, rituximab, ublituximab), dimethyl fumarate/diroximel fumarate, FcRn inhibitors (efgartigimod, rozanolixizumab), complement C5 inhibitors (eculizumab, ravulizumab, zilucoplan), interleukin-6 receptor antibodies (tocilizumab, satralizumab), intravenous immunoglobulins, long-term steroid administration, methotrexate, mitoxantrone, mycophenolate mofetil, tacrolimus, teriflunomide, tumor necrosis factor-α blockers, and sphingosine-1-phosphate receptor modulators (fingolimod, ozanimod, ponesimod, siponimod), as well as after autologous stem cell transplantation. The lymphocyte count can have an influence here. Overall, it is generally advisable to complete vaccination before starting immunotherapy. However, in the case of an active inflammatory disease course with possible irreversible neurological deficits, a delay in therapy initiation until immunization has been completed cannot be justified. The application of live vaccines is contraindicated for most therapies and is only recommended after a strict risk–benefit assessment.

Conclusion: Vaccinations are necessary for individuals on immunotherapy to reduce the risk of infections and the associated risk of worsening neurological autoimmune diseases. However,

Thomas Korn
Institute for Experimental Neuroimmunology, Medical Faculty of the Technical University of Munich, Munich, Germany
Department of Neurology, Medical Faculty of the Technical University of Munich, Munich, Germany
Munich Cluster for Systems Neurology, Munich, Germany
Luisa Klotz
Jan D. Lünemann
Department of Neurology with the Institute for Translational Neurology, Münster University Hospital, Münster, Germany
Martin S. Weber
Department of Neurology, University Medical Center of the Georg-August-University, Göttingen, Germany
Institute of Neuropathology, University Medical Center of the Georg-August-University, Göttingen, Germany
Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Göttingen, Germany
Antonios Bayas
Department of Neurology and Clinical Neurophysiology, Faculty of Medicine, University of Augsburg, Augsburg, Germany
Brigitte Wildemann
Neurological Clinic Heidelberg University Hospital, Ruprecht-Karls-University Heidelberg, Heidelberg, Germany
Hans-Peter Hartung
Department of Neurology, University Hospital Düsseldorf, Heinrich Heine University, Düsseldorf, Germany
Brain and Mind Center, Medical Faculty, University of Sydney, Sydney, NSW, Australia
Department of Neurology, Palacky University Olomouc, Olomouc, Czech Republic
Florian Then Bergh
Department of Neurology, Leipzig University Hospital, Leipzig, Germany
Clemens Warnke
Department of Neurology, Cologne University Hospital, Cologne, Germany

the humoral and cellular vaccination response may be impaired under immunotherapy necessitating close monitoring. Here, we provide applicable recommendations to optimize immunization for individuals receiving immunotherapy due to a neurological autoimmune disease.

Plain language summary

Cell- and antibody-mediated vaccination response under immunotherapies—German consensus on vaccination strategies in neurological autoimmune diseases

Aims and purpose of the research: Based on currently available literature on vaccination in people receiving treatment for a neurological autoimmune disease, a group of experts generated recommendations on how to handle vaccination in people receiving immunotherapy.

Background of the research: Medications used in treating autoimmune diseases may create a risk for patients due to reduced immune defence and impact on vaccination success. Protection against the respective pathogen may be reduced under different immunotherapies despite formally completed immunization. This may result in the need for repeated vaccination or special protective measures against infections.

Methods and research design: Based on a thorough literature search, a consortium of experts generated applicable recommendations and consented on these via a questionnaire.

Results and importance: The vaccination response is evaluated under alemtuzumab, azathioprine, cladribine, cyclophosphamide, CD19/CD20 antibodies (inebilizumab, ocrelizumab, ofatumuab, rituximab, and ublituximab), dimethyl fumarate/diroximel fumarate, FcRn inhibitors (efgartigimod and rozanolixizumab), complement C5 inhibitors (eculizumab, ravulizumab and zilucoplan), interleukin-6 receptor antibodies (tocilizumab, satralizumab), intravenous immunoglobulins, long-term steroid administration, methotrexate, mitoxantrone, mycophenolate mofetil, tacrolimus, teriflunomide, tumor necrosis factor-α blockers and sphingosine-1-phosphate receptor modulators (fingolimod, ozanimod, ponesiomd and siponimod), as well as after autologous stem cell transplantation. The white blood cell count can have an influence on the vaccination response. Overall, it is generally advisable to complete vaccination before starting immunotherapy. However, in the case of an active course of the disease with possible irreversible neurological deficits, a delay in the start of therapy until immunization has been completed cannot be justified. The application of live vaccines is contraindicated for most therapies and is only recommended after a strict risk-benefit assessment.

Conclusion: Vaccinations are necessary for individuals receiving immunotherapy to reduce the risk of infections and the associated risk of worsening neurological autoimmune diseases. However, the antibody- and cell-mediated vaccination response may be impaired under immunotherapy, thus necessitating close monitoring.

Keywords: immunotherapies, neuroimmunological diseases, neurological autoimmune diseases, vaccination

Received: 27 March 2025; revised manuscript accepted: 9 October 2025.

Introduction

Immunotherapies (specifically considered in this work: alemtuzumab, azathioprine, cladribine, cyclophosphamide, CD19/CD20 antibodies (inebilizumab, ocrelizumab, ofatumumab, rituximab, and ublituximab), dimethyl fumarate/diroximel fumarate, FcRn inhibitors (efgartigimod and rozanolixizumab), complement C5 inhibitors (eculizumab, ravulizumab, and zilucoplan), interleukin-6 (IL-6) receptor antibodies (tocilizumab, satralizumab), intravenous immunoglobulins (IVIG), long-term steroid administration, methotrexate (MTX), mitoxantrone, mycophenolate mofetil (MMF), tacrolimus, teriflunomide, tumor necrosis factor-α (TNF-α) blockers, and sphingosine-1-phosphate (S1P) receptor modulators (fingolimod, ozanimod, ponesimod, and siponimod), and autologous stem cell transplantation) applied in neurological autoimmune diseases (i.e., multiple sclerosis (MS), neuromyelitis optica spectrum disorders (NMOSD), myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), autoimmune encephalitis, myasthenia gravis, vasculitis of the central nervous system (CNS), neurosarcoidosis, and immune neuropathies) influence parts of the process leading to immunity after vaccination. Thus, protection against the respective pathogen may be reduced under different immunotherapies despite formally completed immunization. This may result in the need for repeated vaccination or special protective measures against infections.

A vaccination response requires a complex interaction of antigen-presenting cells, cytotoxic and memory T cells and B cells. For some vaccine types (polysaccharide vaccines), there is evidence that an intact complement system is important for the formation of antibodies after vaccination. Most of the studies on vaccinations in people receiving immunotherapy refer to antibody concentrations and compare these either with previously defined criteria for seroprotection or with control groups. Even though immunity through most vaccines could be shown to correlate with antibody levels, antibody levels are only surrogates for the actual protection provided by vaccination.[1–8] Correlates of protection vary between pathogens and large-scale studies on true protection against infection in people with autoimmune diseases are lacking. Cell-mediated (especially CD8 T cells) immune response is also necessary and measurable for certain germs.[9]

Overall, for the scope of this work, we have chosen to use antibody levels and vaccine-specific T cell responses as approximates for the effectiveness of vaccinations.

Modes of vaccines

Various modes of action of vaccines have been established to date. A distinction must be made between live vaccines and inactivated vaccines. Live vaccines contain viruses or bacteria capable of reproduction in an attenuated form.[10,11] This is brought about by growing the virus in nonhuman cell culture, which leads to a reduced ability to multiply in human cells.[11] After application, specific immunity is triggered without causing disease.[10,11] Live vaccines include the combined mumps-measles-rubella vaccine as well as yellow fever, rotavirus, and some varicella vaccines. By binding the structural pathogen components to antigen-presenting cells, the antigen is presented to T cell receptors.[10,11] This generates antigen-specific CD4+ or CD8+ effector cells as well as long-lived memory T lymphocytes.[10,11] At the same time, the natural adjuvant of the pathogen components induces the release of T cell-attracting and -stimulating chemokines and cytokines.[10,11] With the help of T helper cells, memory B cells and plasma cells are activated and expanded, which release antigen-specific antibodies.[10,11]

Inactivated vaccines contain inactivated pathogens or components of the pathogen. These include inactivated whole particle vaccines (e.g., polio, hepatitis A, rabies, tick-borne encephalitis (TBE), influenza, SARS-CoV-2, cholera, and some varicella vaccines). They induce an immune response with CD4+ T effector and memory T cells, as well as memory B cells and antibody-producing B cells.[10,11] Protein vaccines contain inactivated toxins (diphtheria toxoid, pertussis toxoid, tetanus toxoid) or immunogenic proteins (hemagglutinin from *Bordetella pertussis*, spike protein from SARS-CoV-2), which act as antigens on antigen-presenting cells to trigger a vaccine-specific T cell response and antibody production.[10,11] As these cannot trigger an immune response on their own, they are enriched with immunogenicity-enhancing components (adjuvants).[10,11] Some bacteria (*Neisseria meningitidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*) have an outer capsule of polysaccharides. In polysaccharide vaccines (e.g., PPSV23 against *S. pneumoniae*),

Uwe K. Zettl
Department of Neurology, Rostock University Medical Center, Rostock, Germany

Achim Berthele
Bernhard Hemmer
Institute for Experimental Neuroimmunology, Medical Faculty of the Technical University of Munich, Munich, Germany

Aiden Haghikia
Department of Neurology, Hannover Medical School, Hannover, Germany

Ralf Linker
Clinic for Neurology, University Clinic at the Regensburg District Hospital, Regensburg, Germany

Hayrettin Tumani
Clinic and Polyclinic for Neurology, Rehabilitation and University Clinics Ulm—RKU, Ulm, Germany

Heinz Wiendl
Department of Neurology and Neurophysiology, Freiburg University Medical Center, Freiburg, Germany

Tania Kümpfel
Institute for Clinical Neuroimmunology, Ludwig-Maximilians-University Hospital Munich, Munich, Germany

direct stimulation of B lymphocytes is induced by human leukocyte antigen-independent mediated antigen presentation, namely via B cell receptors or C3-binding type 2 complement receptors.[10,11] By coupling with carrier proteins (e.g., tetanus toxoid or diphtheria toxoid (cross-reacting material 197)), additional activation of bystander T cells (against the carrier protein, not against the polysaccharide) can enhance the B cell immune response against the polysaccharide. This can increase the affinity and longevity of the antibodies and memory B cells.[10,11] These so-called "conjugate vaccines" include, for example, the pneumococcal conjugate vaccine (PCV) against serotype 7, 10, or 13 (PCV-7, PCV-10, PCV-13); and meningococcal vaccines against serogroups C (Men C) and ACWY (Men ACWY).[12]

Messenger RNA (mRNA) vaccines (e.g., for SARS-CoV-2), a type of inactivated vaccine, have another mechanism of action. These contain mRNA, often packaged in liposomal fat envelopes, which cause translation of the antigen after cellular uptake by antigen-presenting cells, among others.[12,13] These then lead to a T and B cell-mediated immune response with CD4+ and CD8+ effector cells, as well as T and B memory cells and antibody production by plasma cells. Finally, vector vaccines use a modified viral vector (adenovirus) as a carrier of viral DNA, which is transcribed into mRNA after cellular uptake, resulting in antigen production and a subsequent immune response.[14] Protection against the Ebola virus is derived from a vector vaccine, while a vector vaccine developed for SARS-CoV-2 is no longer available.

Vaccinations and disease activity

Although it is improving, vaccination hesitancy is still an issue in people with neurological autoimmune diseases, especially in people with MS (pwMS), and depends greatly on the vaccination education of patients.[15–19] For many years, there has been concern that in autoimmune diseases such as MS, stimulation of the immune system, for example, through vaccination, could be accompanied by an activation of the disease (flare-ups). However, the available evidence clearly speaks against a connection between vaccinations and the initial manifestation of MS.[20–26] Furthermore, several studies have not found a significantly increased relapse rate 8–12 weeks after vaccination in general and specifically for vaccination against hepatitis B, tetanus, influenza, tuberculosis, TBE, rabies, SARS-CoV-2, influenza, yellow fever, diphtheria, or pneumococcus.[22,26–45] Overall, the suspicion that there was a connection between vaccination and MS, as suggested in individual case reports, could not be substantiated by larger studies.[46]

In the case of NMOSD or MOGAD, individual case reports observed relapses after vaccination, particularly in patients without immunotherapy.[47–58] A recent study describes the occurrence of NMOSD relapses after vaccination against meningococcal disease before starting therapy with eculizumab in 9 out of 45 people with aquaporin-4 (AQP-4) antibody-positive NMOSD.[59] As this disease is highly active prior to therapy, it is not possible to estimate with certainty the proportion of relapses actually related to meningococcal vaccination prior to the start of therapy. In this case, overlapping low-dose antibiotic prophylaxis could be used to postpone vaccination until the immunotherapy is fully effective.

Apart from individual case reports, no increased disease activity or triggering of myasthenia gravis is described after vaccination against influenza, hepatitis B, human papillomavirus (HPV), Japanese encephalitis and tuberculosis, diphtheria, tetanus, pneumococci, meningococcal disease, or SARS-CoV-2.[60,61] A yellow fever vaccination is contraindicated in case of thymus dysfunction (myasthenia and/or presence of a thymoma or condition after thymectomy) due to the association with the increased risk of yellow fever vaccine-associated visceral disease.[62–66]

With regard to autoimmune encephalitis, there are also only individual case reports that suggest a connection between vaccination against SARS-CoV-2 (whole particle vaccine against SARS-CoV-2), Japanese encephalitis, tetanus/diphtheria/pertussis/poliomyelitis, yellow fever and HPV, and the first manifestation of anti-N-methyl-d-aspartate (NMDA) receptor or anti-metabolic glutamate receptor 5 (mGluR5) encephalitis.[67–69] In large observational studies, these cases were very rare making any impact negligible.[67–69] In an observation of 121 people with autoimmune encephalitis (86 anti-NMDAR, 15 anti-GABAbR, 15 anti-LG1/Caspr2, 3 anti-AMPAR, 1 anti-mGluR5, and 2 anti-GFAP), 1 person experienced disease activity within 30 days after SARS-CoV-2 vaccination and 3 people

within 120 days after vaccination, 2 of whom were untreated.[70]

Although the incidence of Guillain–Barré syndrome (GBS) is slightly increased after SARS-CoV-2, herpes zoster[71,72] and influenza vaccination (but still significantly less frequent than after either infection),[73–83] there is no direct correlation between vaccination and increased disease activity or incidence of other chronic immune neuropathies. In a large study of 1.8 million vaccinations against HPV, there was no increased incidence of GBS or chronic inflammatory demyelinating polyneuropathy (CIDP).[84] In three studies of people with CIDP, 1.5% of 411, 1% of 268, and 5 of 24 patients developed GBS after influenza vaccination (timing not specified).[85–87]

In regards to an effect of vaccination on disease activity, 4% of 311 GBS patients and 8% of 65 CIDP patients experienced an exacerbation of the disease after vaccination (the specific vaccination was not reported). About 0% of 162 GBS patients, 3% of 188 CIDP patients, and 4% of 53 patients with multifocal motor neuropathy (MMN), as well as 5% (13 CIDP and 3 MMN patients) of 307 patients (260 CIDP, 47 MMN) experienced an exacerbation of the disease after vaccination against SARS-COV-2 (mRNA and vector).[88,89]

Very few reports of CNS vasculitis after vaccination were found in three international spontaneous reporting systems (<1% of vasculitis reports), of which 40% were reported in association with immunization against HPV.[90] CNS vasculitis was reported in 1 out of 158 cases of vasculitis after application of SARS-CoV-2 mRNA vaccine.[91] To date, no causal connection between vaccination (specifically against influenza, hepatitis B, tuberculosis, meningococcal C, hepatitis A, HPV, rotavirus, diphtheria, pertussis, tetanus, typhoid, yellow fever, anthrax, mumps/measles/rubella (MMR)) and vasculitis could be established.[92,93] To our knowledge, other potential consequences of vaccination have not yet been investigated with sufficient power.

Overall, for most neurological autoimmune diseases (MS, myasthenia gravis, autoimmune encephalitides, immune neuropathies, NMOSD, MOGAD) clear evidence of increased disease activity after infections is reported.[58,85,86,94–102] There are indications that immunotherapy can positively influence infection-triggered disease activity.[96] The least amount of data can be found on neurosarcoidosis and CNS vasculitis. However, vaccinations in sarcoidosis are generally considered safe.[103]

Vaccination under immunosuppression

In addition to questions concerning the stimulation of the immune system by vaccination and the extent of the humoral and cellular vaccination response under immunotherapy, the safety of live vaccines remains relevant. Vaccination with a live vaccine under immunotherapy is associated with a risk of triggering the respective infection.[104–107] The extent and quality of immunosuppression depend on the medication administered. This article assesses the available evidence regarding the safety of live vaccine application under different immunotherapies.

As described above, a humoral and cellular vaccination response requires a complex interplay of various cells and messengers. Disease-modulating therapies in MS and other neurological autoimmune diseases influence parts of this process, so that the measurable vaccination response may be reduced under different immunotherapies despite completed immunization, which may be associated with reduced protection against the respective infection. This may necessitate repeated vaccinations or special protection against infections. In the following, the current evidence on the cellular and humoral vaccination response under the various disease-modifying drugs (alemtuzumab; azathioprine; cladribine; cyclophosphamide; the CD19/CD20 antibodies inebilizumab, ocrelizumab, ofatumumab, rituximab, and ublituximab; dimethyl fumarate/diroximel fumarate; the FcRn inhibitors efgartigimod and rozanolixizumab; the complement C5 inhibitors eculizumab, ravulizumab, and zilucoplan; MTX; mitoxantrone; MMF; tacrolimus; teriflunomide; the TNF-α blockers infliximab, etanercept, dalimumab, and the S1P modulators fingolimod, ozanimod, ponesimod, and siponimod), as well as after autologous stem cell transplantation will be summarized and consensus recommendations defined; an overview is shown in Figure 1. This work aims to provide recommendations for physicians involved in the treatment of people with neuroimmunological illnesses under immunotherapies. Cooperation of these physicians, mainly involving general practitioners performing

Figure 1. Influence of respective therapy on vaccination response after inactivated vaccinations in relation to time since last therapy administration. Dark green: normal titer; light green: reduced but sufficient vaccination response; orange: anticipated slightly reduced vaccination response, check titer after complete vaccination if necessary based on an individual risk analysis; purple: anticipated reduced vaccination response (vaccination should be sought 4–6 weeks before initiating therapy).
aHSCT, autologous hematopoietic stem cell transplantation; CBC, complete blood count; FcRn, neonatal Fc receptor; IVaCD20, intravenously administered CD20 antibodies; IVIG, intravenous immunoglobulins.

the vaccination and a neurologist evaluating the patient's specific risk and benefit of the vaccination, is key for safe, patient-centered care.

Methods

In this original study, a German evidence-based expert consensus on vaccination under immunotherapies in neurological autoimmune diseases is established. First, a literature search was conducted (by author M.S.) up to June 2024 on studies in PubMed, the national guidelines of Germany's Robert Koch Institute (RKI) and the Standing Committee on Vaccination (STIKO), as well as the respective technical information (summary of product characteristics) and international and national vaccination recommendations of the professional associations the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), and the European Academy of Neurology (EAN) and the disease-related German Competence Network Multiple Sclerosis. The therapies were selected according to their use in the following neuroimmunological diseases: MS, NMOSD, MOGAD, autoimmune encephalitides, myasthenia gravis, CNS vasculitides, neurosarcoidosis, and immune neuropathies. The search included combinations of the disease name (and/or acronym), therapy (using the active ingredient, agent name, and common abbreviation as search terms), and the term "vaccination" or "vaccine." Where results were lacking for neuroimmnunological diseases research on rheumatic, malignant (for autologous hematopoietic stem cell transplantation (aHSCT)), and other autoimmune diseases was analyzed, preferably consulting national or international guidelines and professional associations on these diseases. Results in German or English were considered. An overview of the selected reports and the screening process can be found in the Supplemental Figure 1 and Supplemental Table 1. After the initial compilation, the group of authors, all of whom are specialized in the treatment of neuroimmunological diseases, assessed the quality of the evidence separately and independently. On this basis and based on clinical experience, the individual recommendations were agreed upon by means of an online questionnaire (originally conducted in German using www.empirio.de; a translation is provided as Supplemental Methods). The percentage of agreement is stated after the respective recommendation. A recommendation was accepted as consensus if approval had reached >75%; a summary of all treatment-specific recommendations can be found in Supplemental Table 2.

Results of the literature review and recommendations

Vaccinations can reduce the risk of infections and the associated possible progression of neuroimmunological diseases; an up-to-date, complete vaccination status in accordance with the guidelines of the STIKO is recommended.

Overall, the induction of disease activity after vaccination in people with neurological autoimmune diseases cannot be completely ruled out due to the lack of large studies and the availability of mainly only individual case reports. With clear evidence of the triggering of relapse events and disease activity after infection and the risk of the infection itself in all of these diseases (MS, NMOSD, MOGAD, autoimmune encephalitides, myasthenia gravis, CNS vasculitides, neurosarcoidosis, and immune neuropathies), the protection provided by vaccination certainly outweighs the risks.

Therefore, from a safety perspective, vaccinations with inactivated vaccines can generally be recommended for people with a neurological autoimmune disease, regardless of the therapy. Overall, our consensus-based recommendations are inclined toward recently published consensus recommendation of the EAN and ECTRIMS for pwMS.[40]

Diverging recommendations can be found for yellow fever vaccination in MS. An expert consensus of the RKI advises against vaccination in pwMS undergoing treatment with glatiramer acetate or interferons despite the absence of contraindications to live vaccinations.[106] A current consensus recommendation of the EAN and ECTRIMS does not describe a clear risk of relapse activity after yellow fever vaccination based on the studies also cited above.[31,36,40,42,106] The application of yellow fever vaccination in pwMS should therefore always be decided on a case-by-case basis after a strict benefit–risk assessment.

Under immunosuppressive therapy, vaccination with a live vaccine can trigger the corresponding infectious disease due to attenuated but replicable viruses.[104–107] For this reason, vaccination with a

live vaccine is still contraindicated under immunosuppressive therapy. Due to this precautionary measure, the number of vaccinated people is likely to remain too low to ever be able to make statistically justified reliable statements as to whether activation of the underlying disease is to be feared. Under immunotherapy, vaccination with a live vaccine can be considered in individual cases if there is sufficient cellular immunity and after a strict risk–benefit assessment (including the situational risk of infection).[10,106] Completion of immunization with live vaccines before starting immunosuppressive therapy is generally recommended. The extent and quality of immunosuppression depends on the medication and dosage administered. A graphical representation of the recommended intervals between therapy and vaccination with a live vaccine can be found in Figure 2 and is described further in the course of the text.

Immunization with inactivated vaccines, on the other hand, can also take place during the administration of immunotherapy. For people with neurological autoimmune diseases and especially those undergoing treatment with immunosuppressants, a recommendation should be made for seasonal influenza vaccination, pneumococcal and herpes zoster vaccination and other vaccinations.[108] The general vaccination recommendations applicable in each case should be followed. To optimize the humoral and cellular vaccination response, the immunization should be completed 4–6 weeks before the start of immunotherapy. However, if there is high disease activity (multiple relapses in a very short time, rapid progression of symptoms, and/or high paraclinical activity) and a clinically urgent indication to start immunotherapy promptly, a delayed start of therapy to complete the recommended immunization cannot be justified and the start of therapy should precede completion of the vaccination series.

If immunity is not yet present, a live vaccination against varicella zoster virus (VZV) is recommended before treatment with fingolimod, siponimod, ponesimod, cladribine, ozanimod, alemtuzumab, or CD19/CD20 antibodies.[106,109–117] The STIKO recommends this even before any immunotherapy if the VZV titer is negative.[118] In 99% of people who grew up in Germany before the VZV vaccine introduction in 2004, contact to VZV is presumed and thus titer control is not deemed necessary.[108] In an immunosuppressed state, immunisation against VZV can be performed with the inactivated vaccine, licensed to prevent herpes zoster (Shingrix®; Glaxo Smith Kline GmBH & Co. KG), as an off-label application.[108,119,120] In this case, titer control should be performed.[108] Vaccination to prevent herpes zoster through administration of an inactivated vaccine (Shingrix®; Glaxo Smith Kline GmBH & Co. KG) is recommended by the STIKO for people adults under immunosuppression.[108]

In the event of a lack of vaccination protection, measured by vaccination titers, despite a sufficient number of vaccination doses or in the case of clear contraindications against attempting vaccination, risk reduction should take place, for example, vaccination of close relatives. However, the measurable titers can also remain negative, especially with CD20 antibodies, but protection against infections can also be provided by T cell responses.[121] Administration of a higher number of vaccinations than normal is not recommended. In addition, we recommend increased vigilance for symptoms under any immunosuppression so that if necessary, early antiviral or antibiotic treatment can be initiated in the event of an infection.

Specifics of neuromyelitis optica spectrum diseases, MOG-associated disease

NMOSD and MOGAD should be considered in a more differentiated way in some cases, since relapses after vaccination are described in case reports, particularly without immunotherapy, but controlled studies are insufficient.[47–58] In the context of the SARS-CoV-2 pandemic and vaccination with the vector vaccine, cases of an initial manifestation of MOGAD after vaccination have been reported.[58] Complement activation is an essential component in the pathogenesis of NMOSD, but is also observed to some extent in MOGAD. The complement C5-neutralizing antibodies eculizumab and ravulizumab are approved not only for myasthenia gravis but also for AQP4 antibody-positive NMOSD. Vaccinations—in particular polysaccharide vaccinations (pneumococci and meningococci)[122,123] and possibly vector vaccinations[124,125]—can in turn induce activation of the complement system, so that a potential increased relapse rate in NMOSD/MOGAD could be explained by this.[126–130] The latter appears particularly relevant in the case of mandatory meningococcal

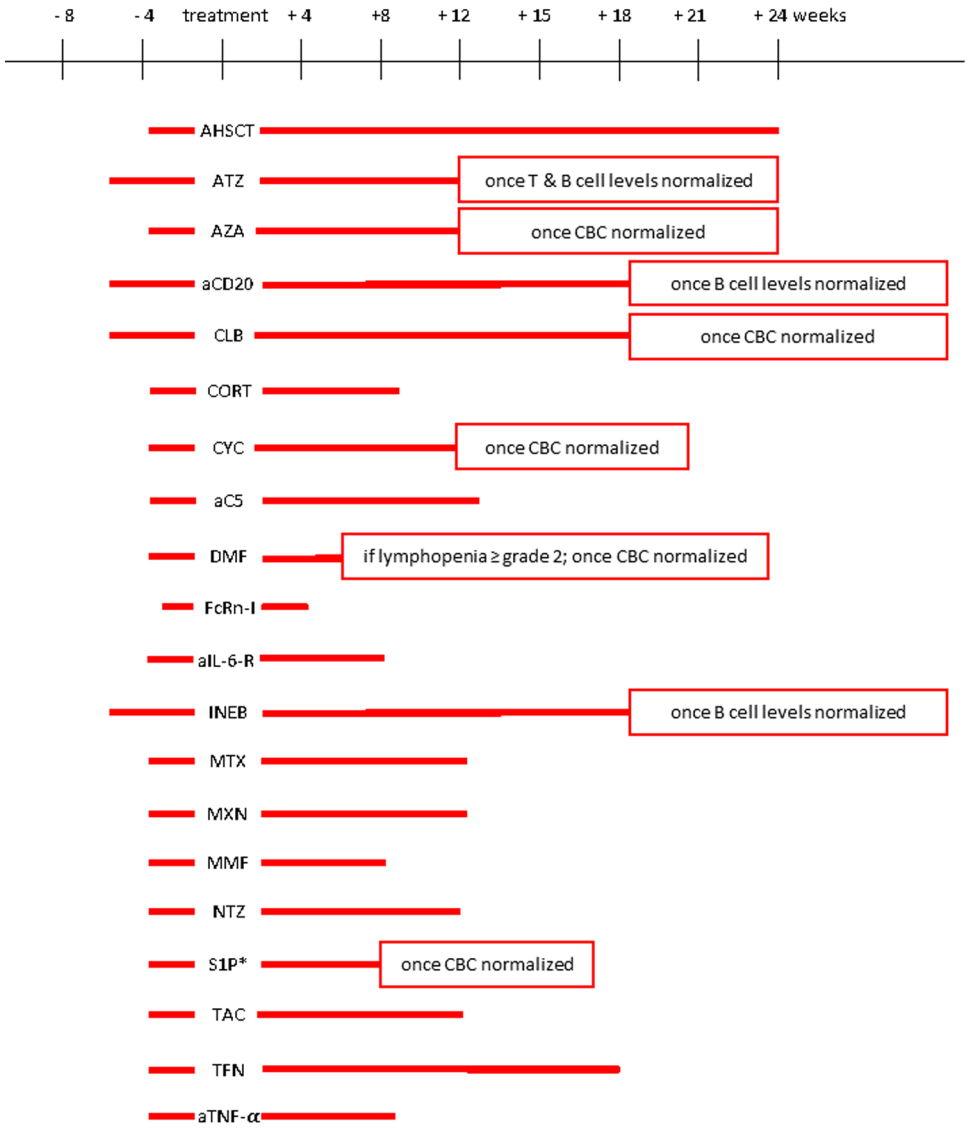

Figure 2. Recommended interval between therapy and application of a live vaccine. Administration of a live vaccine only after strict risk–benefit assessment, possibly depending on the respective dosage and cellular immunity. Red: Administration of a live vaccine contraindicated; boxes span reported repopulation, measurement of lymphocytes, and a risk–benefit analysis take precedence over absolute time as repopulation varies greatly between individuals.
*Distances between live vaccinations and different S1P modulators vary—see recommendations in the text.
aC5, anti-complement C5; aCD20, anti-CD20; aHSCT, autologous hematopoietic stem cell transplantation; aIL-6-R, anti-IL-6 receptor; aTNF-α, anti-TNF-alpha; ATZ, alemtuzumab; AZA, azathioprine; CBC, complete blood count; CLB, cladribine; CORT, glucocorticoids; CYC, cyclophosphamide; DMF, dimethyl fumarate; FcRn-I, FcRn inhibitors; INEB, inebilizumab; MMF, mycophenolate mofetil; MTX, methotrexate; MXN, mitoxantrone; NTZ, natalizumab; S1P, S1P modulators; TAC, tacrolimus; TFN, teriflunomide.

vaccination prior to therapy with eculizumab, ravulizumab, or zilucoplan and has also been described.[59] A reduction of this risk through concomitant oral glucocorticoid therapy may be useful, but must be weighed against the negative effects of steroids (and other prior therapies) on vaccination success. Another option that requires documented consultation is prophylactic antibiotic shielding until complete immunization at a time after disease stabilization under immunotherapy through complement inhibition.[47]

In NMOSD, severe relapses with incomplete remission in particular lead to relevant clinical impairments, thus prompt initiation of immunotherapy is recommended—especially in AQP4 antibody-positive NMOSD.[131–133] It is therefore recommended that immunotherapy and bridging treatment with oral steroid therapy be started immediately.[134,135] An urgent, prompt start can also influence the feasibility of other vaccinations; glucocorticoid therapy or prior immunotherapy can in turn influence seroconversion after vaccination (see below).

In NMOSD prompt complement inhibition is often needed. In such circumstance vaccination under complement inhibition and antibiotic prophylaxis is recommended. A recent German consensus recommends vaccination prior to initiation of complement inhibition in myasthenia gravis, as some antibiotics can aggravate symptoms of the underlying autoimmune disease.[136]

Consensus—general

1. The administration of inactivated vaccines is safe in most cases of neuroimmunological diseases and should follow the recommendations for nondiseased. (100%)
2. If there is an urgent indication for therapy, it must be individually considered whether waiting until complete immunization is justifiable. (97%)
3. Live vaccinations are generally contraindicated under immunotherapies. An interval should be maintained before the start of therapy and after discontinuation of therapy as shown in Figure 2. (97%)
4. Vaccination against yellow fever is contraindicated for people with myasthenia gravis. (93%)
5. A completion of the immune status (inactivated vaccines) according to STIKO should be sought before starting immunotherapy, especially with alemtuzumab, anti-CD19/CD20 antibodies, S1P receptor modulators, or cladribine, if clinically justifiable. (100%)
6. Before treatment with alemtuzumab, anti-CD19/CD20 antibodies, cladribine, or S1P modulators (obligatory before fingolimod, ponesimod, or siponimod; recommended before ozanimod), seronegative people must be fully immunized against the VZV. (100%)
7. Pre- and co-therapies can influence the humoral and cellular vaccination response. (100%)

Vaccination under specific immunotherapy

The following paragraphs list the studies that have been carried out on humoral and cellular vaccination responses in people with neuroimmunological diseases under the respective immunotherapy. From this, clinically applicable recommendations are formulated with regard to the expected vaccination response. The therapeutic agents are arranged alphabetically below and the agreed consensus is found at the end of each paragraph. An overview of the expected vaccination response in relation to the interval between therapy termination and vaccination can be found in Figure 1. If medication is administered in intervals, Figure 1 can help identify the optimal time point for a vaccination (green or orange). It also gives an overview of expected vaccination response and as such can help identify risk groups.

In addition, the humoral and cellular vaccination response after vaccination can be influenced by previous immunotherapy, in particular by long-term depletion of immune cells or a high number of previous immunotherapies. A control of vaccination titers under immunotherapy would be desirable in principle, but is not always possible and feasible for all vaccines and is often not financed. A patient-specific risk analysis including past-medical history (e.g., previous infection, other risk-increasing chronic illnesses), exposure to certain germs (e.g., through occupation or geographic prevalence), or specificities of immunotherapy (e.g., complement-inhibitors) should be applied to evaluate value of titer measurement.

Autologous hematopoietic stem cell transplantation

In aHSCT, high-dose chemotherapy leads to an ablation of existing immune cells, including memory cells. Subsequent transplantation of previously acquired hematopoietic stem cells leads to a repopulation of immune cells.

According to current data, a partial or complete loss of previously existing vaccination protection due to aHSCT can be assumed, measured by the frequency of the seroreversion.[137–140] A study of 58 individuals with hematologic malignancies

found seroconversion in 67% of individuals vaccinated after transplantation, with titers increasing with increasing time between vaccination and transplantation. Interestingly, seroconversion persisted in all 24 individuals vaccinated against SARS-CoV-2 (mRNA vaccines) prior to aHSCT.[140] Another study also found higher antibody titers with increasing intervals between mRNA vaccination against SARS-CoV-2 and aHSCT in 192 people with hematologic malignancies.[141] Another study described a seroconversion in 89.2% of 65 people with hematologic malignancies after aHSCT, with significantly lower titers than healthy controls.[142] Furthermore, an influence of CD19+ B cell and immunoglobulin G (IgG) levels was mentioned here. The interval between vaccination and transplantation had an influence on titer levels after allogeneic hematopoietic stem cell transplantation, but not after aHSCT.[142] In a separate study, 61 people were randomized to receive either a vaccination against pneumococci (heptavalent conjugate vaccine PCV7) or placebo prior to aHSCT. After transplantation, all subjects were vaccinated again after 3 and 6 months. A higher titer was detected in the subjects who had been vaccinated before aHSCT; after triple vaccination, seroprotection (concentration $\geqslant$0.35 µg/mL against all seven vaccine serotypes) was achieved in >60% of patients regardless of their previous vaccination status.[143] The following recommendations are based on the guidelines of the German Society for Hematology and Medical Oncology and the recommendations of the STIKO working group on immunodeficiency.[144,145]

Consensus—aHSCT

1. Partial or complete loss of previously existing vaccination protection due to aHSCT is likely. (96,67%)
2. Re-immunization after transplantation is recommended. Seroconversion appears to increase with increasing time between vaccination and aHCST. To optimize the effectiveness of the vaccination, a certain repopulation of immune cells should already exist: (100%)
   (a) An interval of 3 months after aHSCT should be maintained for tetravalent influenza vaccinations, pneumococcal vaccination (PPSV23), VZV vaccination (Shingrix, inactivated vaccine), and SARS-CoV-2 vaccinations. (97%)
   (b) An interval of 6 months after aHSCT should be maintained for inactivated vaccines against tetanus, diphtheria, pertussis, poliomyelitis (inactivated polio vaccine. Salk), *H. influenzae* type B (conjugate vaccine), meningococcus (meningococcus ACWY and B), and hepatitis B. (97%)
   (c) An interval of 24 months must be upheld for live vaccines (measles/mumps/rubella).[146] (93%)

Alemtuzumab

By binding to CD52, which is expressed on both T and B cells, alemtuzumab leads to cell death, and thus a reduction in the number of lymphocytes. Repopulation of B cells takes place within 4–6 months, while repopulation of T cells takes several years.[147]

The evidence regarding seroconversion after vaccination under alemtuzumab is limited. One study (n=20) described a preserved seroprotection compared to previously published data in healthy controls after vaccination against diphtheria, tetanus, poliomyelitis, *H. influenzae* type B, meningococcus C, and pneumococcus (PPSV23) with a median interval of 18 months (1.5–86 months) since the last alemtuzumab administration.[148] Another study (n=12) showed a regular development of antibody-mediated and cell-mediated immunity against SARS-CoV-2 after vaccination with an mRNA vaccine compared to untreated controls.[149] An analysis of the influence of the interval between alemtuzumab administration and vaccination response was not carried out. Nevertheless, the interval was also extended with a mean of 16 months since last application.[149] Another small study described a preserved vaccination response (antibody levels compared to untreated individuals) in 15 individuals with MS treated with alemtuzumab after vaccination with an mRNA vaccine, but without more detailed subanalyses.[150] In another small cohort (n=8), a dependence of seroconversion on the time since the last administration of alemtuzumab was described.[151]

Consensus—Alemtuzumab

1. A reduced humoral and cellular vaccination response under therapy with alemtuzumab

as well as a dependence on the lymphocyte count and repopulation of immune cells is to be expected. (100%)
2. Completion of immunizations as per recommendations of the STIKO is therefore advised 6 weeks prior to the start of therapy; SARS-CoV-2 immunization up to 4 weeks before the start of therapy. If there is an urgent indication for therapy, starting therapy before completing immunizations should be considered. (97%)
3. The VZV status should be checked before therapy. In the absence of an immune response against VZV, vaccination against VZV should be carried out before administration of alemtuzumab and seroconversion should be verified. (97%)
4. Live vaccinations have not been sufficiently studied and vaccination under alemtuzumab therapy is not recommended until the complete blood count normalizes after therapy; in any case, a strict individualized benefit–risk assessment should be applied. (93%)

Azathioprine

Azathioprine is a purine analog that inhibits RNA/DNA synthesis and thereby reduces the proliferation of immune cells. The evidence regarding vaccination under azathioprine therapy is very limited. In 13 individuals with systemic lupus erythematosus (SLE), reduced seroconversion (31% against H1N1, 8% against H3N2, and 23% against influenza B compared to 58% for influenza A and B in untreated individuals), and reduced seroprotection (hemagglutination inhibition titer (HI) ⩾40; 69% vs 92% against H1N1, 62% vs 100% against H3N2, 62% vs 92% against B/Hong Kong) compared to untreated individuals with SLE has been described.[152] A study of six people with NMOSD treated with azathioprine (2 mg/kg/d) showed seroprotection (HI ⩾40) after H1N1 influenza vaccination.[153] A study of five people with NMOSD showed seroconversion (without a more detailed description of the antibody levels) after SARS-CoV-2 vaccination (mRNA or vector vaccine) or infection under azathioprine.[154]

Consensus—Azathioprine

1. Overall, it can be assumed that the vaccination response under azathioprine therapy is at least slightly reduced until a complete repopulation of the immune cells is achieved after discontinuation. (97%)
2. Live vaccination is contraindicated until the lymphocytes normalize. (93%)

CD19/CD20 antibodies

Inebilizumab

By binding to CD19, inebilizumab leads to a broad depletion within the B cell lineage, including pro-B cells and plasmablasts, which are spared by CD20 antibodies. There is very little data on seroconversion or vaccine-specific T cell response with inebilizumab, which was recently approved against AQP4 antibody-positive NMOSD. A single study reports seroconversion in one of four people under inebilizumab after SARS-CoV-2 infection, but not after vaccination.[154] Whether previously existing immunity could also be lost due to depletion of the plasmablasts as a result of the therapy remains to be investigated in respect to the various vaccinations.

Ocrelizumab

The humanized CD20 antibody ocrelizumab causes the complete peripheral depletion of CD20-positive B cells, with repopulation after termination of therapy with a median of 62 weeks (range 27–175 weeks).[155] Reduced seroconversion has been described with ocrelizumab. One study showed that antibody levels against tetanus toxoid in pwMS treated with ocrelizumab ($n = 68$) were reduced by half (54.5% vs 23.9%) compared to those not treated or treated with interferon-beta ($n = 34$), by two-thirds (100% vs 71.6%) against pneumococci (PPSV23), and by 20% (75%–97% vs 55.6%–80%) against influenza vaccines (5 strains).[156] Similarly, the humoral response against keyhole limpet hemocyanin (KLH) as a nonspecific immunostimulant for testing immunocompetence was reduced by half.[156] It should be noted that in this study, the interval between ocrelizumab infusion and vaccination was at least 12 weeks.[156]

With regard to SARS-CoV-2 (mRNA vaccines), there was overall evidence of a greatly reduced antibody-mediated vaccination response (30%–60% seropositivity; $n = 20$ and $n = 22$) compared to healthy controls and untreated individuals with MS, which was also seen in relation to the time

since vaccination and associated B cell count.[150,157] However, some studies showed a comparable to slightly increased specific T cell-mediated vaccination response in anti-CD20-treated individuals compared to healthy controls.[157–160]

Data to date indicate persistent vaccination protection with ocrelizumab when vaccinated before starting therapy.[161–163]

Ofatumumab

The subcutaneously administered CD20 antibody ofatumumab has only been approved for the treatment of relapsing MS since 2020 in the USA (2021 in Europe) and also leads to a depletion of CD20-positive B cells. Recovery of B cells is achieved at a median of 24 weeks.[113] The data available on seroconversion after vaccination with ofatumumab are limited and restricted to the vaccination response to SARS-CoV-2 vaccinations. A seropositivity of 60% (defined by the respective assay used) and a preserved T cell response against SARS-CoV-2 after vaccination in pwMS treated with ofatumumab was detected; absolute antibody levels were significantly lower than in untreated persons or in pwMS receiving ofatumumab who had already received the vaccinations before starting therapy ($n=5$, $n=10$, $n=26$, respectively).[164–166] A recently published study showed a seroprotection (HI $\geqslant$40) in pwMS vaccinated against several influenza A and B strains under ofatumumab comparable to a cohort treated with glatiramer acetate and interferon as well as patients vaccinated $\geqslant$2 weeks prior to ofatumumab initiation. Seroprotection against influenza B Washington strain was lower in those vaccinated under ofatumumab.[167] The rate of seroconversion (here defined as a fourfold increase in HI titer after vaccination if the prevaccination HI titers were $\geqslant$10, or postvaccination HI titers $\geqslant$40 with prevaccination HI titers $<$10) and HI titer change trended to be lower in those vaccinated under ofatumumab but did not reach significance in the limited number of cases ($<$20).[167] To our knowledge, there is no evidence regarding the effect of ofatumumab therapy on the success of other vaccinations.

Rituximab

Rituximab, the first available anti-CD20 antibody, also induces CD20-positive B cell depletion, with a variable repopulation of naïve B cells taking between 12 and 15 months, while memory B cells do not return to baseline levels until more than 25 months.[168] There are only a few studies on the efficacy of vaccinations under therapy with rituximab in people with neurological autoimmune diseases. On the other hand, there are some studies on patients with malignant diseases and rheumatoid arthritis (RA) who were treated with rituximab. Here, a meta-analysis of 38 studies with 905 people under anti-CD20 therapies rituximab or ocrelizumab showed a seroconversion of 44% after pandemic influenza (13 studies with 222 patients), 17% after seasonal influenza (12 studies with 252 patients), 31%–69% after tetanus, diphtheria, and pertussis (12 studies with 309 patients), 73%–77% after *H. influenzae* B (3 studies with 52 patients), 56% after hepatitis B (3 studies with 61 patients), 0–67% after hepatitis A (2 studies with 57 patients), and 0–20% after PPSV23 vaccination (7 studies with 217 patients).[169] A relative risk compared to healthy controls was calculated with a relative risk of 0.22 for lower antibody levels with vaccination within 3 months, 0.44 within 6 months, 0.77 within 6–12 months, and 1.1 at $>$12 months since last rituximab infusion in relation to influenza vaccination. Increased levels tended to be described with longer intervals since the last infusion.[169] The latter observation related to vaccinations against influenza, tetanus, hepatitis A and B, *H. influenzae* B, pertussis, and diphtheria.[169]

A study of 16 people with NMOSD taking rituximab showed seroprotection (HI $\geqslant$40) in 18.8% after vaccination against influenza (H1N1) compared with 100% in healthy controls.[153]

Another study described significantly lower antibody levels against influenza A and B and pneumococci after vaccination in 16 pwMS under rituximab compared to pwMS who were untreated or treated with interferon-beta. In this study, the titer did not correlate with the interval since the last infusion.[170]

After vaccination against SARS-CoV-2 (mRNA vaccine), absolute antibody levels were 20-fold lower in pwMS under rituximab compared to untreated pwMS ($n=25$); seroconversion was exhibited in only 25% of the 19 people with NMOSD or 21 pwMS under rituximab compared to healthy controls.[150,171] Another study described seroconversion in 11% under rituximab ($n=10$) and in 100% without therapy in

people with neuroimmunological diseases (MS, NMOSD, clinically isolated syndrome, autoimmune encephalitis).[172]

In contrast, the SARS-COV-2-specific T cell response was detectable in 100% of individuals with MS or NMOSD receiving the vaccination under rituximab.[171] A similar result with a reduced antibody response (23.8% vs 100% in healthy controls) and equivalent SARS-CoV-2-specific T cell response was shown in another study investigating anti-CD20 treated individuals ($n=16$ rituximab and $n=27$ ocrelizumab) compared to healthy controls.[173]

Ublituximab

The intravenous monoclonal antibody against CD20 ublituximab, approved for the treatment of MS in the USA in late 2022 and in Europe in 2023, also causes a complete depletion of CD20-positive B cells. Repopulation is reported after 70 weeks.[174] No studies have been reported as of yet on seroconversion following vaccination under ublituximab.

Consensus—anti-CD19/CD20

1. A significantly reduced humoral vaccination response is to be expected under anti-CD19/CD20 therapy. (93%)
2. Vaccinations recommended by the STIKO should be completed up to 4 weeks prior to the start of therapy. In the case of a highly active course, starting therapy before complete immunization should also be considered. (100%)
3. Basic immunization against VZV in the absence of antibody detection is recommended before therapy. (80%)
4. Live vaccination is contraindicated 4 weeks before, during therapy, and until B cell repopulation. (97%)

Cladribine

Treatment with cladribine induces apoptosis of T and B cells, in particular a long-lasting elimination of CD27+ memory B cells.[175] Repopulation of B cells takes around 30 weeks after the last dose of cladribine each treatment year, while CD4 T cells require around 43 weeks; CD8 T cells do not seem to drop below the lower normal limit.[176] Recent data collected during the SARS-CoV-2 pandemic showed antibody levels comparable to healthy controls and untreated pwMS when treated with cladribine ($n=48$).[177] Another study in 38 pwMS undergoing cladribine therapy described a seroconversion of 100% against SARS-CoV-2. An influence of the time between last cladribine dose and vaccination was rejected; however the variance was large and only nine people had been vaccinated within 4 months of cladribine administration. Titers were not compared to a control group in this study.[178] A seroconversion of 94% was described in 34 pwMS under cladribine after vaccination against SARS-CoV-2, again without correlation to the interval between cladribine administration and vaccination, but with only two subjects who had been vaccinated within 3 months of the last cladribine administration.[179] A seroconversion of 100% was also described in another study including 32 pwMS treated with cladribine in comparison to healthy controls ($n=30$). Similarly, there was no correlation between treatment interval and antibody levels, again with only two subjects vaccinated approximately 4 months after cladribine treatment.[180] SARS-CoV-2 titers equivalent to those in pwMS under glatiramer acetate or interferons were also described in 25 pwMS under cladribine, without specifying the interval between vaccination and the last cladribine dose.

Another small study showed that influenza ($n=12$) and VZV vaccinations (Shingrix, $n=14$) under cladribine therapy also induced a sufficient vaccination titer regardless of the time of vaccination or lymphocyte count.[181] Only two patients were vaccinated within 6 months of cladribine administration and still lymphopenic.[181]

A recent study investigated the vaccination response against influenza A and B in 90 patients under cladribine and showed a discretely reduced seroprotection rate (HI ≥ 40) against influenza B, but not against influenza A.[182] This study also showed no correlation with duration of treatment, interval between last administration of cladribine or with the lymphocyte count or number of B cells.[182] The rapid reconstitution of naïve B cells is suggested as an explanation.[183,184]

Consensus—Cladribine

1. Overall, there is relatively little data available for cladribine regarding vaccinations at short intervals after each cycle. To optimize seroconversion, a 3–4 month interval after

the cladribine therapy cycle or approximately 1–2 months after reaching the lymphocyte nadir appears to be sensible. (90%)
2. A completed basic immunization according to the STIKO recommendation should be sought before starting therapy with cladribine (4–6 weeks). (97%)
3. A basic immunization against VZV in case of seronegativity 4–6 weeks before starting cladribine therapy is indicated.[117] (83%)
4. Live vaccinations should only be given after a strict risk–benefit assessment and normalization of the leukocytes/lymphocytes. A subsequent treatment with cladribine should only be given at least 4–6 weeks after vaccination.[111] (93%)

Cyclophosphamide

Cyclophosphamide is a cytostatic drug that prevents the proliferation of lymphocytes; recovery is stated to take 1–2 months for CD8 T cells, 2–4 months for B cells, and more than 4 months for CD4 T cells.[185] There are hardly any studies on cyclophosphamide as a stand-alone therapy, but mainly in combination with other chemotherapeutic agents. None of these studies were conducted in people with neuroimmunological diseases. One study describes reduced antibody levels against SARS-CoV-2 after vaccination in a treatment group receiving cyclophosphamide or rituximab compared to those treated with sulfasalazine; it is not possible to determine with certainty how many of the nine patients with RA received rituximab or cyclophosphamide.[186] Seroconversion after vaccination against HPV 18 under cyclophosphamide in 10 children (9–20 years) with SLE was reduced by 50% compared to healthy controls, with preserved seroconversion against HPV16.[187] In three children with juvenile autoimmune rheumatic disease treated with cyclophosphamide, there was no effect on seroconversion or seroprotection after H1N1 vaccination (HI $\geqslant$40) compared to untreated children.[188]

Consensus—Cyclophosphamide

1. A reduced seroconversion until normalization of lymphocyte levels can be expected under therapy with cyclophosphamide. (97%)
2. Vaccination with a live vaccine is contraindicated 4 weeks before, during and for at least 3 months after treatment with cyclophosphamide and until the differential blood count has normalized.[106] (93%)

Dimethyl fumarate/diroximel fumarate

Dimethyl fumarate and diroximel fumarate lead to a reduction in pro-inflammatory and cytotoxic T cells and an increase in regulatory T cells. In addition, the substances have an antioxidative effect within the CNS. Recovery of lymphopenia, if present, can take a median of 3.4 months after termination of treatment.[189] One study on the vaccination response under dimethyl fumarate therapy described maintained antibody-mediated and T cell-dependent vaccination responses against tetanus/diphtheria, pneumococcal (serotype 3 and 8), and meningococcal C vaccinations in comparison to persons treated with interferons ($n=38$).[190] Another study ($n=20$) showed an adequate antibody response against influenza after vaccination (seroprotection HI $\geqslant$40 and seroconversion) compared to healthy controls.[191] The vaccination response against SARS-CoV-2 under dimethyl fumarate was also described as equivalent to healthy controls (three independent studies with $n=114$, $n=74$, and $n=5$).[150,158,192] To date, there are no studies with a sufficient number of pwMS who have been vaccinated under diroximel fumarate. However, given the bioequivalence of both substances, a preserved vaccination response can also be assumed here.

Consensus—Dimethyl fumarate/diroximel fumarate

1. According to current data, a preserved vaccination response can be assumed under dimethyl fumarate/diroximel fumarate. (100%)
2. Vaccination with live vaccines should only be carried out after a strict risk–benefit assessment and is contraindicated in cases of severe lymphopenia (common terminology criteria for adverse events grade 2 or higher $<$800/µl).[193,194] (93%)

Complement inhibitors: Eculizumab/ravulizumab/zilucoplan

Eculizumab and ravulizumab are monoclonal antibodies that bind the complement C5 and thus inhibit its cleavage/activation preventing the

formation of the terminal membrane attack complex (MAC). Zilucoplan, on the other hand, is a macrocyclic peptide that binds both C5 and C5b, ultimately also preventing the formation of the MAC. During therapy, an increased risk of infections has been described, particularly from encapsulated bacteria (e.g., *Neisseria meningitides*, *Neisseria gonorrhoeae*, *S. pneumoniae*, and *H. influenzae* type B). Serious meningococcal infections can occur under complement inhibition and other infections such as Aspergillus have also been described. In this regard, vaccination against meningococci (serogroups A, C, Y, W135, B) is recommended at least 2 weeks prior to initial administration. Otherwise, prophylactic bridging with antibiotics (e.g., ceftriaxone, penicillin, azithromycin, rifampicin or other antibiotics effective against *N. meningitidis*) is recommended up to 2 weeks after vaccination if treatment is urgently indicated.[117,135,195]

A study in people with cold agglutinin disease (autoimmune hemolytic anemia, $n=9$) who received vaccinations against meningococcal ACWY (Menveo®; Glaxo Smith Kline GmBH & Co. KG) under eculizumab described seroprotection (defined by rabbit serum bactericidal assay ⩾1: 128; over 50% of bacterial growth is prevented) in 75% of patients against serogroup Y, 62.5% against serogroup W, 37.5% against serogroup C, and 25% against serogroup A, compared to the described seroprotection (here, however, human serum ⩾1: 8) of 88% (Y), 94% (W), 90% (C), and 87% (A) in healthy controls.[196] There was evidence that prior therapies play a relevant role for seroconversion after meningococcal vaccination before or during eculizumab therapy.[196,197]

In a study of 52 people with paroxysmal nocturnal hemoglobinuria under eculizumab or ravulizumab, a preserved formation of SARS-CoV-2 antibodies was described under therapy after vaccination with a vector vaccine or infection, but without comparison of the absolute values to a control group.[198] Corresponding data on zilucoplan is not yet available. It therefore remains unclear whether the additional binding of C5b has a comparable or different effect on vaccination success.

Consensus—Complement inhibitors

1. With very little evidence on the efficacy of vaccination under complement inhibitors, reduced seroconversion after vaccination is likely, possible effects of pre-/co-therapies should be taken into account. (90%)
2. Due to the immunosuppression induced by complement inhibition, an update of the vaccination status including vaccination against pneumococci and Haemophilus influenza B is indicated and obligatory against meningococci. (83%)
   (a) If there is an increased risk of relapse in NMOSD, treatment with steroids may be necessary until the start of therapy, especially in the context of highly active NMOSD, or bridging antibiotic treatment may be necessary until vaccination is completed.[47] (97%)
   (b) Seroconversion after vaccination may be reduced under long-term oral steroid therapy and therapy with other immunosuppressants. Monitoring the success of vaccination by means of antibody determination appears to be useful with regard to these vaccinations. (87%)
3. With regard to the application of live vaccines, there is no reliable evidence; we recommend an interval of 4 weeks before the start of therapy and up to 3 months after therapy and in any case a strict benefit-risk assessment. (97%)

FcRn inhibitors: Efgartigimod alfa, rozanolixizumab

Efgartigimod alfa is a fragment of the human IgG1 antibody with increased affinity for the neonatal Fc receptor (FcRn), while rozanolixizumab is a monoclonal antibody that binds to the FcRn directly. Both substances prevent the recycling of IgG antibodies including pathogenic myasthenia gravis-causing autoantibodies. This reduces serum IgG levels to approximately 40%; IgA and IgM are not affected.[195] FcRn inhibitors are currently only approved for neurological indications in seropositive myasthenia gravis.

One investigation of the humoral vaccination response after vaccination as part of the open-label study Extension ADAPT+ in 17 people with myasthenia treated with efgartigimod is available.[199] An increase in titers after mRNA vaccination against SARS-CoV-2 compared to before mRNA vaccination, as well as

seroconversion, was described in three people with myasthenia gravis treated with efgartigimod alone.[199] Reduced antibody levels after influenza vaccination (H1N1, H3N2, Victoria, and Yamagata) were detected in nine people with myasthenia gravis treated with efgartigimod compared to placebo-treated patients, with preserved seroprotection (HI ⩾40).[199] In this context, an increase in titers after discontinuation of the medication to the same extent as the increase in total IgG levels was described.[199]

Only one person with myasthenia gravis under efgartigimod after vaccination with PCV13 and one after PPSV23 were described, in each case without comparison to a control. Both showed antibody levels borderline to below the defined protective level of 350 ng/ml.[199]

No comparable data are available for rozanolixizumab. However, similar effects are likely with a similarly pronounced reduction in serum IgG levels during therapy.

Consensus—FcRn inhibitors

1. With very little data available, a moderately reduced seroconversion is to be expected when vaccinated under FcRn inhibitors according to the mechanism of action and initial data. A temporary reduction in titer is to be expected to the same extent as the reduction in total IgG. (100%)
2. Live vaccinations are contraindicated up to 4 weeks before and 2 weeks after therapy.[200] (93%)

Glatirameroids

Glatiramer acetate has an immunomodulatory effect without quantitatively influencing adaptive immunity. Overall, in two studies ($n = 23$ and $n = 26$), no reduced influenza antibody levels were detectable after vaccination of pwMS under glatiramer acetate compared to healthy controls.[201,202] However, another study reported a halved antibody titer (21.6% vs 43.5%) in the hemagglutination inhibition test after H1N1 vaccination ($n = 37$).[203] An additional study showed no change in the T cell response to a tetanus toxoid in vitro.[204] Vaccination titers against SARS-CoV-2 were also found to be comparable to healthy controls.[150,192]

Live vaccination is not listed as a contraindication in the product information of glatiramer acetate. There are also no reports of infection as a result of live vaccination under glatiramer acetate therapy.[106,205] A special note on yellow fever vaccination according to the expert consensus of the RKI recommends against the administration of this vaccine.[106]

Consensus—Glatirameroids

1. The vaccination response under glatiramer acetate therapy is maintained. (100%)

Glucocorticoids

Glucocorticoids act by inhibiting pro-inflammatory protein synthesis, inhibiting the pro-inflammatory signaling cascade NF-κB, and activating lipocortins. A study in a cohort of patients with chronic inflammatory diseases (including inflammatory bowel disease, RA, spondyloarthritis, SLE, MS ($n = 9$), NMOSD ($n = 1$), and vasculitis ($n = 5$)) showed a reduced immune response after vaccination against SARS-CoV-2 under continuous glucocorticoid therapy ($n = 17$), although the study does not clearly describe how many MS, NMOSD, and vasculitis patients were treated with glucocorticoids.[206] A study in people with SLE, MS, autoimmune CNS disease, vasculitis, myositis, sarcoidosis, and other immunologically mediated diseases ($n = 11$) showed a reduced (odds ratio 8.38) T cell-mediated and humoral vaccination response against SARS-CoV-2 (mRNA and vector vaccines) under glucocorticoids alone (⩾10 mg/day prednisone) compared to healthy controls.[207] Another study in individuals with RA, SLE, vasculitis, other rheumatic diseases, other inflammatory bowel diseases, MS, inflammatory neuro- and myopathies, or myasthenia gravis ($n = 51$) under oral glucocorticoid therapy (median 7.5 mg/day) showed equally high SARS-CoV-2 antibody levels compared to healthy controls.[208]

A seroconversion of 93% after hepatitis A vaccination was described in people with ulcerative colitis or Crohn's disease under glucocorticoids (⩾20 mg prednisolone equivalent over ⩾2 weeks, $n = 30$)—comparable to healthy controls.[209]

Another study described reduced seroconversion after vaccination against pneumococci (PPSV23)

in a cohort of 16 people with immune-mediated inflammatory disease under high-dose glucocorticoid therapy (⩾20 mg/day) with a rate of 22% seropositivity.[210]

In addition, another study described an association between lower seroconversion rates and antibody levels compared to healthy controls in children with juvenile autoimmune rheumatic disease under add-on (to azathioprine, MMF, MTX, cyclosporine, leflunomide, cyclophosphamide) or singular glucocorticoid therapy after influenza vaccination (H1N1), correlating with the dose of glucocorticoid therapy (mean 17.4 mg/day).[188]

Consensus—Glucocorticoids

1. In case of short-term high-dose therapy, vaccination under high-dose glucocorticoids is not advisable, if clinically justifiable, as the efficiency of the immune response may be reduced. (100%)
2. In patients undergoing short-term steroid therapy, a regular vaccination response can be expected after about 4 weeks. (97%)
3. In case of long-term steroid administration (⩾10 mg/day prednisolone equivalent over ⩾2 weeks), reduced seroconversion can be assumed until up to 3 months after the end of therapy. (97%)
4. During long-term high-dose steroid therapy (⩾10 mg/day prednisolone equivalent for ⩾2 weeks), vaccination with a live vaccine is contraindicated and an interval of 2–4 weeks before and at least 2 months after therapy should be observed.[106] (97%)

Interferon-beta preparations

Interferons influence a variety of transcription and translation programs of cells and thus have a broad immunomodulatory effect. Previous studies on SARS-CoV-2 and influenza have shown no limited seroconversion under therapy with interferons.[150,192,201,211]

Consensus—interferon-beta preparations

1. Preserved seroconversion is to be expected under interferons. (100%)

Intravenous immunoglobulins

IVIG are concentrates of homologous (human) IgG antibodies. A study in children with Kawasaki disease showed reduced seroconversion after live vaccination against measles, mumps, rubella, and varicella within 6 months, with an increase in seroconversion after booster vaccination 12 months after administration of IVIG.[212] A single study described slightly increased vaccination titers against SARS-CoV-2 in people with idiopathic inflammatory myopathies under IVIG therapy depending on the dosage. As such, vaccination titers could also be increased from healthy convalescents in the donor pool.[213] Product information describes a possibly reduced vaccination response for up to 3 months after IVIG. After application of live vaccinations against mumps, rubella, and measles, the vaccination response could be decreased even up to 1 year; the RKI even recommends an interval of the MMR vaccination of 3 weeks before and up to 8 months after IVIG, as the replication of the vaccine virus could be influenced by the antibodies of the blood product.[145,214] The mechanistic reason given here is that in contrast to activated vaccines, antigens contained in inactivated vaccines could continue to be presented and therefore IVIG administration would evoke no influence on the immune response after vaccination.[145]

Since it is difficult to assess whether the antibodies originate from the donor pool or the recipient, it only makes sense to check the antibody status after the therapy has been completed.[214]

Consensus—IVIG

1. Seroconversion after vaccination may be reduced during treatment with IVIG. (93.33%)
2. Live vaccines should only be administered during therapy after a strict risk–benefit assessment. (93%)

Methotrexate

MTX is a folic acid antagonist that inhibits the enzyme dihydrofolate reductase and thereby RNA/DNA synthesis and thus the proliferation of lymphocytes. Recovery of lymphopenia is stated to be <12 weeks.[215] Evidence on seroconversion rates after vaccination under MTX is mainly

limited to people with rheumatic disease. Here, compared to healthy controls and untreated individuals with RA, antibody levels against SARS-CoV-2 were found to be reduced after vaccination under MTX ($n=23$) with a direct correlation between dose and antibody response.[216] No significantly reduced vaccination response was described at low doses below 10 mg/week.[217–221] In contrast, a study of 50 people with RA taking 7.5–25 mg MTX/week described moderately reduced absolute antibody levels after pneumococcal (PPSV23) vaccination compared to healthy controls.[222] Another study described the possibly improved vaccination success (fourfold increase in antibodies compared to before vaccination) after a short break in MTX therapy for 2 weeks before and up to 2 weeks after vaccination.[223]

Consensus—MTX

1. Maintained to moderately reduced absolute antibody levels are to be expected after vaccination under MTX, which can be increased by taking a short break from therapy. However, the latter should only be done after a strict benefit–risk analysis. (93%)
2. Application of live vaccines should be avoided and are contraindicated, especially under high-dose therapy (>20 mg/week). Under low-dose MTX therapy (⩽20 mg/week), immunizations with vaccines against mumps, measles, rubella, or varicella can be considered after an individual benefit–risk assessment.[106,217,220] (83%)

Mitoxantrone

Mitoxantrone leads to an inhibition of topoisomerase II and DNA intercalation. This prevents T cell activation and proliferation of B and T cells. In a study of 11 pwMS treated with mitoxantrone, no protective seroconversion (HI ⩾40) against influenza was achieved.[203] Furthermore, to our knowledge, no studies on seroconversion after vaccination under mitoxantrone have been published. Due to increased cardiotoxic side effects and the development of secondary lymphomas, mitoxantrone has disappeared from neurological therapy.

Consensus—Mitoxantrone

1. It can be assumed that vaccination success is reduced under therapy with mitoxantrone and only increases again after discontinuation of therapy and repopulation of lymphocytes. (97%)
2. Application of a live vaccine is contraindicated during therapy, 4 weeks before the start of therapy and up to 3 months after therapy.[106] (97%)

Mycophenolate mofetil

MMF is a reversible inhibitor of inosine monophosphate dehydrogenase, thus interfering with the synthesis of guanosine and reducing cell growth. The vaccination response under therapy with MMF was primarily investigated in rheumatic diseases. Studies have shown that there is a dose dependency with regard to antibody levels after HPV ($n=9$) and SARS-CoV-2 ($n=100$) vaccination.[224,225] In patients with renal disease ($n=130$), MMF therapy (dose 500–1000 mg) was described as a negative predictor of lower antibody levels after SARS-CoV-2 vaccination (vector and mRNA).[226] Another small study on three patients with NMOSD under MMF reported that all patients developed antibodies after vaccination or infection with SARS-CoV-2; the dose of therapy is not stated in this article.[154]

Furthermore, a study on people with NMOSD ($n=5$) receiving MMF (2 g/d) described seroconversion in only 40% of people after vaccination against influenza A (H1N1).[153] The higher dose compared to the studies described above should be noted here in particular.

Consensus—MMF

1. A dose-dependent reduced vaccination response is to be expected under therapy with MMF. (100%)
2. Application of a live vaccine should be avoided during therapy with MMF. Under low-dose MMF therapy (⩽1.2 g/m^2 body surface area), immunization with the vaccines against mumps, measles, rubella, or varicella can be considered after individual benefit–risk assessment.[106,217,220] (90%)

Natalizumab

Natalizumab prevents immune cells from crossing the blood–brain barrier by binding the adhesion molecule α-4 integrin. Data on seroconversion after vaccination with natalizumab therapy is controversial. Three studies describe reduced seroprotection (HI ⩾40; $n=12$, 11%–30% vs 58%–69% in healthy controls against H3N2 and 72.7%–75% vs 94%–94.5% against H1N1; $n=17$, 23.5% vs 43.5% in healthy controls against H1N1; $n=14$, 14.3% vs 73% in interferon-treated against H1N1, H3N2, and B combined).[201–203] In contrast to these stands one study ($n=17$) describing equivalent antibody levels compared to healthy controls after vaccination against influenza.[227] Immune responses against tetanus toxoid and KLH were comparable to untreated controls in another study ($n=30$).[228] The latter is a large protein complex (obtained from the hemolymph of the large Californian keyhole snail of the slit snail family) that induces a strong humoral and cellular immune response. This can therefore be used as an immunostimulator to assess immunocompetence. The antibody response against SARS-CoV-2 was also similar to those of healthy controls ($n=100$ and $n=41$).[150,192] A recent study showed a 93% seroprotection against hepatitis A, hepatitis B, and SARS-CoV-2 vaccinations under natalizumab therapy in a cohort of 60 pwMS.[229]

With regard to live vaccination under natalizumab, two case reports describe a live vaccination against VZV under natalizumab therapy without side effects, in particular without evidence of triggered relapse activity or infection.[230,231] In contrast, there is a case report of vaccine-associated measles infection following MMR vaccination under natalizumab.[105] There is also a described case of VZV meningoencephalitis under natalizumab therapy.[232] The balance between the risk of infection and benefit of vaccination is difficult to assess; with currently only case reports available, this can only be decided on a case-by-case basis.

Consensus—Natalizumab

1. Overall, a slightly reduced but sufficiently efficient vaccination response after immunization under natalizumab is likely. (97%)
2. Vaccination with a live vaccine is contraindicated and should only be carried out after a strict risk-benefit analysis and, if necessary, in consultation with infectious disease specialists. (90%)

Plasmapheresis and immunoadsorption

Plasmapheresis is the exchange of plasma, while immunoadsorption extracts antibodies from the blood.

A single study ($n=8$) even showed an increased titer of pneumococcal antibodies (against 12 antigens) in patients with myasthenia gravis 28 days after plasmapheresis under co-therapy with prednisolone compared to myasthenia patients without therapy, but not to healthy controls.[233] This effect was eliminated by therapy with azathioprine and is explained in the study by a rebound effect after antibody removal by plasmapheresis.[233] A study on 10 people with myasthenia gravis described no achievement of normal IgG levels in up to 5 weeks, but rising levels after completion of plasmapheresis. Normal immunoglobulin A and M levels were sustained.[234] Antibody levels against VZV and Epstein–Barr virus, diphtheria, and tetanus toxoid were also still detectable at reduced levels within 4 weeks after plasmapheresis compared to previous values with an upward trend.[234]

Another study examined the antibody levels in 14 people with myasthenia gravis, Waldenström's disease, or other autoimmune diseases who received plasmapheresis at regular intervals (every 3.5 weeks on average) and were also vaccinated against SARS-CoV-2 with mRNA ($n=13$) or vector ($n=1$) vaccine.[235] A drop in SARS-CoV-2 titers by 60.7% was observed after plasmapheresis in comparison to before the intervention. Right before the next intervention a proportion of 32.7% of the original titer was detected.[235] It should be noted that 64.3% of the subjects were co-treated with other immunotherapies (primarily glucocorticoid, followed by azathioprine and MMF). According to the study, this had no significant influence on the antibody levels.[235] Similar results with a transient drop in SARS-CoV-2 titers after immunoadsorption and a subsequent rise within 12 weeks were found in a study of six people with an autoimmune disease (four with myasthenia gravis) who had been vaccinated during therapy.[236]

Overall, studies indicate a transient reduction in antibodies after plasmapheresis or immunoadsorption; vaccination within the first 4 weeks after

intervention may possibly result in a reduced vaccination success. However, other studies support the hypothesis that cellular immune responses and antibody levels are normalized again within days and therefore no restriction in the vaccination response is to be expected.[107,234–236] With time, previously existing titers also rise again, so a sufficient immune response after previous vaccination is likely.

Consensus—Plasmapheresis and immunoadsorption

1. During and up to 1 month after plasmapheresis/immunoadsorption, seroconversion after vaccination may be reduced. (100%)
2. Live vaccinations should only be considered after a strict risk–benefit analysis and only after the acute phase of a relapse. (90%)

S1P receptor modulators

S1P receptor modulators functionally antagonize S1P receptors selectively, for example, ponesimod (receptor 1) or siponimod and ozanimod (receptors 1 and 5) or nonselectively, that is, fingolimod (receptors 1, 3, 4, and 5), thereby preventing lymphocyte egress from lymph nodes. Although lymphocyte levels are reported to normalize around 3 months after fingolimod cessation, recovery to pretreatment levels might take more than 12 months.[237] The cellular and antibody-mediated vaccination response against influenza A and B in individuals treated with the S1P modulator fingolimod compared to healthy controls was the same in one study ($n = 14$).[238] The binding strength of anti-influenza antibodies as a sign of qualitative function in pwMS treated with fingolimod ($n = 10$) was described as lower compared to healthy controls and pwMS treated with interferon-beta.[239] Other studies ($n = 95$ and $n = 15$) showed reduced seroconversion (54% vs 85% in placebo-treated individuals with MS) and seroprotection (HI $\geq$40; 40% vs 90.6% in healthy controls) after influenza vaccination.[201,240] Similarly, another study in 24 healthy individuals treated with fingolimod showed a vaccination response with mild to moderately reduced antibody levels after KLH exposure and pneumococcal vaccination (PPSV23) with equivalent cellular response against recall antigens (KLH, tetanus toxoid, and candida albicans).[241] In this study, as well as in another previously described study in pwMS taking fingolimod versus placebo ($n = 93$), there was a slightly reduced antibody formation against tetanus toxoid (40% vs 61%).[240,241] Recent studies described a reduced T cell and antibody-mediated vaccination response against SARS-CoV-2 after vaccination under fingolimod ($n = 25$, 26-fold lower antibody levels compared to untreated pwMS; $n = 42$, 9.5% seroconversion vs 100% in untreated pwMS, 0% vs 56.7% SARS-CoV-2 specific memory T-cells; $n = 28$, seroconversion 86% vs 100% in untreated pwMS with significantly reduced antibody levels).[150,177,192]

Recent evidence suggests a better vaccination response with higher absolute antibody levels and seroconversion with selective S1P modulators, such as ozanimod, ponesimod, and siponimod, compared to the nonselective S1P modulator fingolimod, after SARS-CoV-2 vaccination (fingolimod: $n = 20$, selective S1P: $n = 13$; fingolimod: $n = 143$, siponimod: $n = 31$, ozanimod: $n = 41$).[192,242] After vaccination against influenza, there was an equivalent proportion of seroprotection (HI $\geq$40) with reduced antibody titers and after vaccination against pneumococci (PPSV23) equally high antibody levels under siponimod compared to placebo-treated healthy individuals ($n = 90$).[243]

Consensus—S1P receptor modulators

1. A preserved, but quantitatively and/or qualitatively reduced vaccination response can be assumed under S1P receptor modulators, in particular under fingolimod, possibly less pronounced under siponimod/ozanimod/ponesimod. (93%)
2. Vaccination against VZV is mandatory for seronegative pwMS before starting treatment with fingolimod, ponesimod, or siponimod, and recommended before ozanimod. (90%)
3. Vaccinations with live vaccines are contraindicated during therapy and up to 4 weeks before and 4 weeks after siponimod, 4 weeks before and 3 months after ozanimod, 1 week before and 4 weeks after ponesimod, as well as 8 weeks after therapy with fingolimod and until the differential blood count normalizes.[106] (97%)

Satralizumab/tocilizumab

Satralizumab and tocilizumab block membrane-bound and soluble IL-6 receptors, thereby preventing the interleukin's pro-inflammatory effect. One study on 13 people with NMOSD or MOGAD regarding the vaccination response against SARS-COV-2 under IL-6 receptor antibodies showed a 100% seroconversion, albeit moderately reduced absolute antibody levels in comparison to healthy controls.[244] In seven subjects with RA, vasculitis, or adult-onset Still's syndrome, tocilizumab resulted in 83.3% seroconversion after SARS-CoV-2 vaccination.[245] In 10 individuals with RA, vasculitis, idiopathic inflammatory myositis, SLE, systemic sclerosis, or variable immunodeficiency syndrome, seroconversion was preserved with slightly reduced absolute antibody levels and preserved T cell response to SARS-CoV-2 after vaccination compared to healthy controls.[246] However, 60% of these were co-treated with low-dose steroids, 30% with MTX, 10% with leflunomide, 10% with cyclosporine, and 10% with MMF.[246]

A study on 50 people with RA treated with tocilizumab showed the same increase in titers against pneumococcal serotypes 6B and 23F after vaccination with PPV23 as in untreated people with RA.[247] In another cohort of 38 people with RA or Castleman's disease treated with tocilizumab, seroprotection against influenza (H1N1, H3N2; defined here as a 40-fold increase in titer) and pneumococci (PPSV23; doubling of titer in 9 of the 12 serotypes) was described in 88%–100% of patients, but without a control group.[248] In a further study of 13 people with NMOSD/MOGAD under IL-6 receptor therapy (4 under satralizumab, 9 under tocilizumab), preserved seroconversion was described with lower antibody levels compared to controls, equivalent compared to oral immunotherapies ($n=9$; azathioprine, MMF) and higher than anti-CD20-treated patients ($n=17$) after mRNA or vector vaccination against SARS-COV-2.[244]

Consensus—Satralizumab/tocilizumab

1. Under therapy with satralizumab or tocilizumab, a reduced humoral vaccination response with most likely preserved T cell-mediated vaccination response is to be expected. (93%)
2. The application of live vaccines is contraindicated during, 4 weeks before, and up to 2 months after therapy.[106] (97%)

Tacrolimus

By forming a complex with FKBP-12, calcium, calmodulin, and calcineurin, tacrolimus acts as an inhibitor of the serine/threonine phosphatase activity of calcineurin. This blocks the dephosphorylation and translocation of NF-κB and prevents T cell activation.

A lot of evidence relates to nonneurological patients, particularly those who have undergone whole organ transplantation, usually in combination therapy with glucocorticoids and MMF.

A study on 23 people with glomerulonephritis treated with tacrolimus showed a seroconversion of 26% after the first and 67.7% after the second vaccination against SARS-COV-2 with a significantly reduced SARS-CoV-2-specific T cell response compared to other immunotherapies.[249]

Another study on 43 people with SLE showed seroconversion after two mRNA vaccinations against SARS-CoV-2 in 65%—however, it should be noted that people with nephritis received co-therapy with MMF, although it is not clear how many this affected in the study.[250] Another study showed a correlation between T cell immunity after SARS-CoV-2 vaccination and the concentration of tacrolimus in the blood, but again in combination with MMF and prednisolone in 40 people after kidney transplantation.[251]

Reduced antibody levels were also reported after vaccination against pneumococci (PPSV23) in 18 people under tacrolimus after kidney transplantation (most of whom had been additionally treated with glucocorticoids ($n=11$), 6 patients were additionally treated with azathioprine and 2 with MMF) compared to those who had been treated with cyclosporine without further control.[252] In 29 people with RA under tacrolimus, pneumococcal vaccination (PPSV23) resulted in equivalent antibody concentration and functionality, as assessed by a multiplex opsonophagocytic killing assay, compared to healthy controls.[253]

Another study on 32 people with rheumatic and musculoskeletal diseases (RA, SLE, Sjögren's,

spondyloarthritis, etc.) after SARS-CoV-2 mRNA vaccination showed significantly but moderately reduced antibody levels compared to healthy controls (antibody titers median 374.4 U/ml (interquartile range 43.7–823.2) compared to median 741.6 U/ml (interquartile range 509.2–1103.0)). Of those, 21 were without and 11 with co-therapy with MTX, through which no significant influence on the antibody level was observed.[254] The cumulative dose of tacrolimus received was higher in women with SLE ($n = 50$) who had negative antibody detection 5 years after initial seroconversion following HPV vaccination (seroreversion, $n = 7$).[255]

Consensus—Tacrolimus

1. With little data available and, to our knowledge, no studies in people with myasthenia, moderately reduced antibody levels can be assumed under therapy with tacrolimus, as well as a moderately reduced vaccine-specific T cell response. (97%)
2. A live vaccination should only be considered after a strict risk–benefit assessment. (90%)

Teriflunomide

Teriflunomide blocks the mitochondrial enzyme dihydroorotate dehydrogenase, resulting in reduced pyrimidine synthesis. This leads to reduced proliferation of activated immune cells. A previous study described a preserved seroprotection (titer >0.5 IU/ml) with discretely reduced antibody levels against rabies in 23 pwMS compared to placebo-treated individuals.[256] The delayed hypersensitivity reaction as a mediator of the cellular response against recall antigens (candidin, trichophytin, and tuberculin) was also investigated in this context and no difference was found compared to the placebo group.[256] After influenza vaccination in pwMS treated with teriflunomide, preserved seroprotection (HI ⩾40) was described in 97% against H1N1 and B strains and in 77% against H3N2.[257] Recent studies also showed equally high antibody levels after SARS-CoV-2 vaccination under teriflunomide compared to healthy controls and untreated pwMS ($n = 48$ and $n = 15$).[150,192]

Consensus—Teriflunomide

1. Based on current evidence, no relevant restriction of seroconversion after vaccination with teriflunomide can be assumed. (97%)
2. Vaccination with a live vaccine is contraindicated 4 weeks before, during and up to 6 months after therapy with teriflunomide.[106,258] (97%)

TNF-alpha blockers (infliximab, etanercept, adalimumab)

TNF-alpha blockers inhibit the effect of the pro-inflammatory cytokine TNF-alpha.

Infliximab

Reduced seroprotection (HI ⩾40; 45% against H3N2 and 66% against H1N1) against influenza was described in two separate cohorts of people with inflammatory bowel disease ($n = 23$ and $n = 137$) treated with infliximab.[259,260] In 96 people with inflammatory bowel disease, there was also reduced seroconversion after vaccination against pneumococcal pneumonia (PPSV23; 57.6%) compared to those treated with mesalazine (88.6%).[261] In 46 individuals with inflammatory bowel disease, antibody levels after vaccination against SARS-CoV-2 were described to be lower than in healthy controls with an equivalent specific T cell response.[262] After hepatitis B vaccination, significantly reduced seroprotection (14% and 35.5%; antibodies ⩾10 IU/ml) was described in 14 and 62 individuals, respectively, with inflammatory bowel disease treated with infliximab compared to untreated individuals (67.1%).[263,264] One study interpreted reduced antibody levels against SARS-CoV-2 after vaccination under anti-TNF-alpha therapy in people with inflammatory bowel disease ($n = 19$) compared to healthy controls by the impaired plasticity of memory B cells and thus reduced long-term antibody response.[265]

One study described no influence of the interval since the last infliximab infusion on seroprotection against influenza (day 21–28 vs day 0–4).[260]

Adalimumab

Interestingly, the antibody levels after vaccination against influenza or pneumococcus (PPSV23) under adalimumab (soluble TNF receptor; $n=111$) are described as equivalent compared to placebo-treated individuals with RA.[266] After vaccination against hepatitis B, seroprotection rate (antibodies $\geqslant$10 IU/ml) was also equivalent to that of untreated subjects with inflammatory bowel disease.[264]

Etanercept

A study on 94 people with psoriatic arthritis and 17 children with juvenile idiopathic arthritis receiving etanercept (soluble TNF receptor) described comparable seroconversion after pneumococcal (PPSV23 or PCV13) vaccination compared to placebo in combination therapy with MTX.[267,268] Another study on seven people with RA taking etanercept also described equivalent antibody levels to a control group with osteoarthritis after pneumococcal vaccination (PCV13).[269] Antibody levels against influenza A and even more so against influenza B were reduced in 30 children with juvenile idiopathic arthritis under etanercept compared to healthy controls with preserved seroconversion and seroprotection (HI $\geqslant$40).[270]

Consensus—TNF-alpha blockers

1. In the absence of evidence, particularly with regard to neurosarcoidosis, a reduced vaccination response is possible under therapy with TNF-alpha antibodies. (97%)
2. Live vaccinations during therapy are contraindicated and should be given at the earliest 2 months after discontinuation of therapy with TNF-alpha blockage. (97%)

Discussion

Here, we summarize and evaluate currently available evidence on vaccinations among a variety of medications used to treat neurological autoimmune diseases. The scope of this work did not include a formal but an expert-based evaluation of the available data, which could be named as a limitation. The compilation of this data has not been without challenges as studies on vaccinations under several immunotherapies are rare, outcome measures vary greatly, real-world data is often lacking and studies are typically of a small number of cases or only focus on a specific type of vaccines. The "real protection" induced through vaccination is hardly assessable. In the future, further large-scale studies would be needed to accurately evaluate the clinical protection from infection through vaccination under immunotherapies. Furthermore, people with neuroimmunological illnesses and those involved in their care might remain hesitant toward vaccination until large controlled studies investigating disease activity after vaccination are presented.

Conclusion

This summary and consensus of the main recommendations on vaccination in people with neurological autoimmune diseases is intended to help ensure that these people receive the most adequate vaccination possible without putting them at unnecessary risk. This is important, as existing uncertainties regarding the handling of immunotherapies leads to hesitation surrounding necessary vaccinations in both doctors and patients. Establishing a close interdisciplinary construct including general practitioners and neurologists will further support a safe patient-centered vaccination and treatment regimen.

Declarations

Ethics approval and consent to participate

Since this study used available literature to develop a German evidence-based expert consensus on vaccination under immunotherapies in neurological autoimmune diseases.

Consent for publication

Not applicable.

Author contributions

Muriel Schraad: Conceptualization; Data curation; Formal analysis; Methodology; Visualization; Writing – original draft; Writing – review & editing.

Mathias Mäurer: Methodology; Writing – review & editing.

Anke Salmen: Methodology; Writing – review & editing.

Tobias Ruck: Methodology; Writing – review & editing.

Timo Uphaus: Methodology; Writing – review & editing.

Vinzenz Fleischer: Methodology; Writing – review & editing.

Felix Luessi: Methodology; Writing – review & editing.

Maria Protopapa: Methodology; Writing – review & editing.

Falk Steffen: Methodology; Writing – review & editing.

Nicholas Hanuscheck: Methodology; Writing – review & editing.

Katrin Pape: Methodology; Writing – review & editing.

Tobias Brummer: Methodology; Writing – review & editing.

Josef Shin: Methodology; Writing – review & editing.

Thomas Korn: Methodology; Writing – review & editing.

Luisa Klotz: Methodology; Writing – review & editing.

Jan D. Lünemann: Methodology; Writing – review & editing.

Marc Pawlitzki: Methodology; Writing – review & editing.

Martin S. Weber: Methodology; Writing – review & editing.

Antonios Bayas: Methodology; Writing – review & editing.

Brigitte Wildemann: Methodology; Writing – review & editing.

Hans-Peter Hartung: Methodology; Writing – review & editing.

Florian Then Bergh: Methodology; Writing – review & editing.

Clemens Warnke: Methodology; Writing – review & editing.

Uwe K. Zettl: Methodology; Writing – review & editing.

Achim Berthele: Methodology; Writing – review & editing.

Aiden Haghikia: Methodology; Writing – review & editing.

Ralf Linker: Methodology; Writing – review & editing.

Hayrettin Tumani: Methodology; Writing – review & editing.

Sven G. Meuth: Methodology; Writing – review & editing.

Bernhard Hemmer: Methodology; Writing – review & editing.

Heinz Wiendl: Methodology; Writing – review & editing.

Tania Kümpfel: Methodology; Writing – review & editing.

Ralf Gold: Methodology; Writing – review & editing.

Stefan Bittner: Methodology; Writing – review & editing.

Frauke Zipp: Conceptualization; Supervision; Writing – original draft; Writing – review & editing.

Acknowledgments

The authors thank Dr Cheryl Ernest for proof-reading and editing the manuscript.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: T.U. is supported by the Else Kröner-Fresenius-Foundation (EKFS) grant 2022_EKCS.10. S.B. is supported by the Hermann and Lilly Schilling Foundation.

Competing interests

M.M. receives compensation for lectures, consulting, and travel expenses from Almirall, Alexion, Argenx, Biogen, BMS, CSL Behring, Sanofi, GSK, Merck, Novartis, Roche, Sanofi, UCB. A.S. receives honoraria for lectures from Bristol Myers Squibb, CSL Behring, Merck, Neuraxpharm, Novartis, and research funding from the Baasch Medicus Foundation, the Medical Faculty of the University of Bern, the Swiss MS Society, and the DMSG Landesverband NRW. T.R. receives funding from the German Federal Ministry of Education and Research (BMBF), the German Federal Institute for Risk Assessment (BfR), the German Research Foundation (DFG), as well as funding and compensation from Sanofi-Aventis, Novartis, Argenx,

and Alexion, personal fees from Argenx, Biogen, Novartis, Roche, and Teva, and compensation and nonfinancial support from Merck, independent of submitted work. T.U. reports personal fees from Merck Serono and Pfizer, and grants from Else Kröner-Fresenius Stiftung. V.F. received research funding from Novartis. F.L. received honoraria from Roche and travel expenses from Teva Pharma. L.K. received compensation for serving on the Scientific Advisory Board for Alexion, Biogen, Bristol-Myers Squibb, Hexal, Horizon, Janssen, Merck Serono, Novartis, Roche, Sandoz, Sanofi, Teva, and Viatris. She has received honoraria and travel expenses from Argenx, Bayer, Biogen, Bristol-Myers Squibb, Grifols, Horizon, Merck Serono, Novartis, Roche, Sanofi, Santhera, and Teva. She has received funding from the German Research Foundation, the IZKF Münster, Biogen, Novartis, and Merck Serono. J.D.L. has received honoraria for lectures, grants, and travel expenses and/or served on advisory boards for Abbvie, Alexion, Adivo, Argenx, Biogen, CSL Behring, Merck, Moderna, Novartis, Roche, Sanofi, Takeda, and UCB Pharma. M.Pa. receives honoraria for lectures and travel expenses for participation in meetings from Argenx, Amicus Therapeutics Germany, Bayer Health Care, Biogen, Demecan, Hexal AG, Janssen Cilag, Merck Serono, Neuraxpharm, Novartis, Roche, Sanofi-Aventis, Teva, Viatris. His research is funded by the German Federal Ministry of Education and Research (BMBF), the Interdisciplinary Center for Clinical Research (IZKF) Münster, Alexion, Amgen, Argenx, Biogen, DMSG NRW, DGM e.v., Gesellschaft von Freunden und Förderern der Heinrich-Heine-Universität Düsseldorf e.V., Hexal, Merck Serono, Novartis, Roche, and Viatris. A.Ba. fees for consultancy and/or speaker activities from Merck, Biogen, Novartis, Sanofi-Aventis/Genzyme, Roche, TEVA, Celgene/Bristol Myers Squibb, Janssen, Sandoz/HEXAL, Alexion, argenx, Horizon, UCB. Congress travel support from Biogen, Sanofi-Aventis/Genzyme, TEVA, Celgene/BMS, Merck, Janssen, Novartis. B.W. received research support from the German Research Foundation, the Federal Ministry of Education and Research, the Dietmar Hopp Foundation, the Klaus Tschira Foundation, Merck, Novartis, and honoraria for lectures from Alexion, Argenx, Merck, INSTAND, Novartis, Roche. H.-P.H. received honoraria for memberships in Steering and Data Monitoring Committees of BayerHealthcare, Biogen, BMS Celgene, Merck, Novartis, Octapharma, Roche, TG Therapeutics, with the approval of the Rector of HHU. He is Editorial Board member of *Therapeutic Advances in Neurological Disorders*, therefore, the peer review process was managed by alternative members of the Board and the submitting Editor was not involved in the decision-making process. F.T.B. has received over his career: Research support and travel grants, each through the institution, from the German Research Foundation (DFG), the Federal Ministry of Education and Research (BMBF), the companies Actelion, Bayer-Schering, Diamed, Fresenius, Merck, Novartis, Pfizer, Roche, Sanofi, and Teva; personal fees for speaking or consulting activities from Actelion, Alexion, Bayer, Biogen, CSL Behring, Fresenius, Horizon, Merck, Novartis, Roche, Sanofi-Genzyme, Takeda, and Teva. C.W. received institutional honoraria or grants from Novartis, Sanofi-Genzyme, Alexion, Janssen, Merck, Biogen, Hexal, and Roche. U.K.Z. has received honoraria for lectures and/or financial support for research activities from Alexion, Almirall, Bayer, Biogen, Bristol Myers Squibb, Janssen, Merck Serono, Novartis, Octapharm, Roche, Sanofi Genzyme, Teva, as well as EU, BMBF, BMWi, and DFG. None are in conflict with the submitted work. A.Be. receives funding from the Innovation Committee of the Federal Joint Committee (G-BA; grant no. 01VSF23040) and from the Federal Ministry of Education and Research (BMBF; grant no. 01ZZ2102B). He has received honoraria as a consultant and/or speaker from Alexion/Astra Zeneca, Argenx, Biogen, Horizon/Amgen, Merck, Neuraxpharm, Novartis, Roche, and Sandoz/Hexal, and his institution receives remuneration for clinical trials from Alexion, Biogen, Merck, Novartis, Roche, and Sanofi Genzyme; all outside the present work. A.H. has received honoraria for lectures from Merck Serono, Kyverna, Sanofi, Alexion, Roche, and Novartis and has served on the advisory boards of Sanofi, Merck Serono, and Galapagos, and has received research funding from Merck Serono. R.L. has received speaking and consulting fees from Biogen, BMS Celgene, Janssen, Merck, Novartis, Roche, and Sanofi. H.T. has received speaking and AdBoard fees from BayerHealthcare, Biogen, BMS Celgene, Horizon, Janssen Cilag, Merck, Novartis, Roche, Siemens, Teva, and

Viatris. S.G.M. receives honoraria for presentations and travel expenses for participation in meetings from Academy 2, Alexion, Argenx, Almirall, Amicus Therapeutics Germany, Bayer Health Care, Biogen, BioNtech, BMS, Celgene, Datamed, Demecan, Desitin, Diamed, Diaplan, DIU Dresden, DPmed, Gen Medicine and Healthcare products, Genzyme, Hexal AG, IGES, Impulze GmbH, Janssen Cilag, KW Medipoint, MedDay Pharmaceuticals, Merck Serono, MICE, Mylan, Neuraxpharm, Neuropoint, Novartis, Novo Nordisk, ONO Pharma, Oxford PharmaGenesis, QuintilesIMS, Roche, Sanofi-Aventis, Springer Medizin Verlag, STADA, Chugai Pharma, Teva, UCB, Viatris, Wings for Life international, and Xcenda. His research is funded by the Federal Ministry of Education and Research (BMBF), the Federal Institute for Risk Assessment (BfR), the German Research Foundation (DFG), the Else-Kröner-Fresenius Foundation, the German Academic Exchange Service, the Federal Joint Committee (G-BA), the Hertie Foundation, the Interdisciplinary Center for Clinical Research (IZKF) Münster, the German Neurology Foundation and Alexion, Almirall, Amicus Therapeutics Germany, Biogen, Diamed, DGM e.v., Fresenius Medical Care, Genzyme, Gesellschaft von Freunden und Förderern der Heinrich-Heine-Universität Düsseldorf e.V., HERZ Burgdorf, Merck Serono, Novartis, ONO Pharma, Roche, and Teva. B.H. has served as a member of the scientific advisory board for Novartis, Polpharma, and Hoffman La Roche; his institution has received research grants from Hoffmann La Roche and Regeneron for MS research. He has received honoraria for consulting work (Gerson Lehrman Group). He has been a DMSC member for AllergyCare, Sandoz, Polpharma, Biocon, and TG therapeutics. He has received honoraria for educational activities from patients.today and med.today. H.W. receives honoraria for service on the Scientific Advisory Board for Alexion, Argenx, Biocryst, Bristol Myers Squibb, Cellerys, Galapagos, Janssen, Merck, Novartis, Sandoz-Hexal, uniQure biopharma B.V., and honoraria for presentations and travel expenses from Alexion, AOCN, AstraZeneca, Biogen, BGP Products Operations GmbH, Bristol Myers Squibb, CEMCAT, EPG Health/Medthority, Genzyme, Kohlhammer, Merck, MS at the Limits, Neurodiem, NMSS, Novartis, Ology, Roche, and Sanofi. T.Kü. has received honoraria for lectures and/or AdBoard participation from Novartis Pharma, Roche Pharma, Alexion/Astra Zeneca, Horizon Therapeutics/Amgen, Merck, Chugai Pharma, and Biogen. The entity for which she works received compensation for membership on the Roche Steering Committee. T.Kü. is principal investigator on several randomized clinical trials (Novartis Pharma, Roche Pharma, BMS, and Sanofi Genzyme) and on a randomized clinical trial supported by the BMBf (funding code: 01GM1908E); her institution has received compensation for clinical trials, all of which are outside the present work. R.G.: Bayer Schering, Biogen-Idec, BMS, Chugai, Eisai, ELAN, Janssen, Kyverna, Merck Serono, Nikkiso Pharma, Novartis, Roche, Sanofi-Genzyme, TEVA; Honoraria for consultancy: ZLB Behring, Baxter, Talecris Private shares of Merck, Kyverna, Novartis, and Roche. R.G. is Editor-in-Chief of *Therapeutic Advances in Neurological Disorders*, therefore, the peer review process was managed by alternative members of the Board and the submitting Editor was not involved in the decision-making process. S.B. has received honoraria from Biogen, Bristol Myers Squibb, Hexal, Merck Healthcare, Novartis, Roche, Sanofi Genzyme, and Teva. His research is funded by the German Research Foundation (DFG, SFB CRC-TR-355) and the Hermann and Lilly Schilling Foundation. F.Z. has received funding for research projects and consultations from Biogen, German Federal Ministry of Education and Research (BMBF), Bristol-Myers-Squibb, Celgene, German Research Foundation (DFG), Janssen, Max Planck Society (MPG), Merck Serono, Novartis, Progressive MS Alliance (PMSA), Roche, Sanofi Genzyme, and Sandoz. M.S., M.Pr., F.S., N.H., K.P., T.B., J.S., T.Ko., and M.S.W. have no conflicts of interest in relation to this article.

Availability of data and materials

All data are provided in the manuscript or Supplemental Material.

ORCID iDs

Anke Salmen https://orcid.org/0000-0002-4751-299X

Timo Uphaus https://orcid.org/0000-0001-5526-0510

Vinzenz Fleischer https://orcid.org/0000-0002-3293-5121

Felix Luessi https://orcid.org/0000-0003-4334-4199

Maria Protopapa https://orcid.org/0009-0000-7707-9050

Katrin Pape https://orcid.org/0000-0001-9211-5873

Tobias Brummer https://orcid.org/0000-0002-7887-7211

Luisa Klotz https://orcid.org/0000-0001-5439-9633

Jan D. Lünemann https://orcid.org/0000-0002-3007-708X

Marc Pawlitzki https://orcid.org/0000-0003-3080-2277

Antonios Bayas https://orcid.org/0000-0002-7418-9040

Hans-Peter Hartung https://orcid.org/0000-0002-0614-6989

Ralf Linker https://orcid.org/0000-0002-8740-3106

Hayrettin Tumani https://orcid.org/0000-0002-1647-6201

Bernhard Hemmer https://orcid.org/0000-0001-5985-6784

Tania Kümpfel https://orcid.org/0000-0001-7509-5268

Stefan Bittner https://orcid.org/0000-0003-2179-3655

Frauke Zipp https://orcid.org/0000-0002-1231-1928

Supplemental material

Supplemental material for this article is available online.

References

1. Khoury DS, Cromer D, Reynaldi A, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med* 2021; 27(7): 1205–1211.
2. Harder T, Remschmidt C, Falkenhorst G, et al. Background paper to the revised recommendation for hepatitis B vaccination of persons at particular risk and for hepatitis B postexposure prophylaxis in Germany. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2013; 56(11): 1565–1576.
3. Verschoor CP, Singh P, Russell ML, et al. Microneutralization assay titres correlate with protection against seasonal influenza H1N1 and H3N2 in children. *PLoS One* 2015; 10(6): e0131531.
4. Tsang TK, Cauchemez S, Perera RA, et al. Association between antibody titers and protection against influenza virus infection within households. *J Infect Dis* 2014; 210(5): 684–692.
5. Andrews N, Borrow R and Miller E. Validation of serological correlate of protection for meningococcal C conjugate vaccine by using efficacy estimates from postlicensure surveillance in England. *Clin Diagn Lab Immunol* 2003; 10(5): 780–786.
6. Habib MA, Prymula R, Carryn S, et al. Correlation of protection against varicella in a randomized phase III varicella-containing vaccine efficacy trial in healthy infants. *Vaccine* 2021; 39(25): 3445–3454.
7. Amanna IJ, Messaoudi I and Slifka MK. Protective immunity following vaccination: how is it defined?*Hum Vaccin* 2008; 4(4): 316–319.
8. Wei J, Pouwels KB, Stoesser N, et al. Antibody responses and correlates of protection in the general population after two doses of the ChAdOx1 or BNT162b2 vaccines. *Nat Med* 2022; 28(5): 1072–1082.
9. Hirai T and Yoshioka Y. Considerations of CD8(+) T cells for optimized vaccine strategies against respiratory viruses. *Front Immunol* 2022; 13: 918611.
10. Niehues T, Bogdan C, Hecht J, et al. Impfen bei immundefizienz [Vaccination in immunodeficiency]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2017; 60(6): 674–684.
11. Kenneth M.*Janeway immunologie* [Janeway's immunology]. London: Springer-Verlag, 2012.
12. Pardi N, Hogan MJ, Porter FW, et al. MRNA vaccines—a new era in vaccinology. *Nat Rev Drug Discov* 2018; 17(4): 261–279.
13. Bettini E and Locci M. SARS-CoV-2 mRNA vaccines: immunological mechanism and beyond. *Vaccines (Basel)* 2021; 9(2): 147.
14. Deng S, Liang H, Chen P, et al. Viral vector vaccine development and application during the COVID-19 pandemic. *Microorganisms* 2022; 10(7): 1450.

15. Hochmeister S, Rakusa M, Moro E, et al. Is there still hesitancy towards SARS-CoV-2 vaccination among people with neurological disease—a survey of the NeuroCOVID-19 task force of the European Academy of Neurology. *Neurol Sci* 2025; 46(4): 1467–1476.

16. Schade P, Nguyen HA, Steinle J, et al. Vaccination coverage and its determinants in patients with multiple sclerosis—a multicenter cross-sectional study. *Ther Adv Neurol Disord* 2025; 18: 17562864241309806.

17. Xu Y, Cao Y, Ma Y, et al. COVID-19 vaccination attitudes with neuromyelitis optica spectrum disorders: vaccine hesitancy and coping style. *Front Neurol* 2021; 12: 717111.

18. Yazdani A, Mirmosayyeb O, Ghaffary EM, et al. COVID-19 vaccines and patients with multiple sclerosis: willingness, unwillingness and hesitancy: a systematic review and meta-analysis. *Neurol Sci* 2022; 43(7): 4085–4094.

19. Yap SM, Al Hinai M, Gaughan M, et al. Vaccine hesitancy among people with multiple sclerosis. *Mult Scler Relat Disord* 2021; 56: 103236.

20. Zrzavy T, Kollaritsch H, Rommer PS, et al. Vaccination in multiple sclerosis: friend or foe?*Front Immunol* 2019; 10: 1883.

21. DeStefano F, Verstraeten T, Jackson LA, et al. Vaccinations and risk of central nervous system demyelinating diseases in adults. *Arch Neurol* 2003; 60(4): 504–509.

22. Confavreux C, Suissa S, Saddier P, et al.; Vaccines in Multiple Sclerosis Study Group. Vaccinations and the risk of relapse in multiple sclerosis. Vaccines in Multiple Sclerosis Study Group. *N Engl J Med* 2001; 344(5): 319–326.

23. Ascherio A, Zhang SM, Hernan MA, et al. Hepatitis B vaccination and the risk of multiple sclerosis. *N Engl J Med* 2001; 344(5): 327–332.

24. Eftekharian MM, Mousavi M, Hormoz MB, et al. Multiple sclerosis and immunological-related risk factors: results from a case-control study. *Hum Antibodies* 2014; 23(1–2): 31–36.

25. Langer-Gould A, Qian L, Tartof SY, et al. Vaccines and the risk of multiple sclerosis and other central nervous system demyelinating diseases. *JAMA Neurol* 2014; 71(12): 1506–1513.

26. Scheller NM, Svanstrom H, Pasternak B, et al. Quadrivalent HPV vaccination and risk of multiple sclerosis and other demyelinating diseases of the central nervous system. *JAMA* 2015; 313(1): 54–61.

27. Salvetti M, Pisani A, Bastianello S, et al. Clinical and MRI assessment of disease activity in patients with multiple sclerosis after influenza vaccination. *J Neurol* 1995; 242(3): 143–146.

28. Miller AE, Morgante LA, Buchwald LY, et al. A multicenter, randomized, double-blind, placebo-controlled trial of influenza immunization in multiple sclerosis. *Neurology* 1997; 48(2): 312–314.

29. Mokhtarian F, Shirazian D, Morgante L, et al. Influenza virus vaccination of patients with multiple sclerosis. *Mult Scler* 1997; 3(4): 243–247.

30. Auriel E, Gadoth A, Regev K, et al. Seasonal and H1N1v influenza vaccines in MS: safety and compliance. *J Neurol Sci* 2012; 314(1–2): 102–103.

31. Farez MF and Correale J. Yellow fever vaccination and increased relapse rate in travelers with multiple sclerosis. *Arch Neurol* 2011; 68(10): 1267–1271.

32. Farez MF, Ysrraelit MC, Fiol M, et al. H1N1 vaccination does not increase risk of relapse in multiple sclerosis: a self-controlled case-series study. *Mult Scler* 2012; 18(2): 254–256.

33. McNicholas N and Chataway J. Relapse risk in patients with multiple sclerosis after H1N1 vaccination, with or without seasonal influenza vaccination. *J Neurol* 2011; 258(8): 1545–1547.

34. Ristori G, Buzzi MG, Sabatini U, et al. Use of Bacille Calmette-Guerin (BCG) in multiple sclerosis. *Neurology* 1999; 53(7): 1588–1589.

35. Ristori G, Romano S, Cannoni S, et al. Effects of Bacille Calmette-Guerin after the first demyelinating event in the CNS. *Neurology* 2014; 82(1): 41–48.

36. Huttner A, Eperon G, Lascano AM, et al. Risk of MS relapse after yellow fever vaccination: a self-controlled case series. *Neurol Neuroimmunol Neuroinflamm* 2020; 7(4): e726.

37. Huttner A, Lascano AM, Roth S, et al. Rabies vaccination and multiple sclerosis relapse: a retrospective cohort study. *Mult Scler Relat Disord* 2021; 51: 102906.

38. Winkelmann A, Metze C, Frimmel S, et al. Tick-borne encephalitis vaccination in multiple sclerosis: a prospective, multicenter study. *Neurol Neuroimmunol Neuroinflamm* 2020; 7(2): e664.

39. Baumhackl U, Franta C, Retzl J, et al. A controlled trial of tick-borne encephalitis vaccination in patients with multiple sclerosis. *Vaccine* 2003; 21(Suppl. 1): S56–S61.

40. Otero-Romero S, Lebrun-Frenay C, Reyes S, et al. ECTRIMS/EAN consensus on vaccination in people with multiple sclerosis: improving immunization strategies in the era of highly active immunotherapeutic drugs. *Mult Scler* 2023; 29(8): 904–925.

41. Achiron A, Dolev M, Menascu S, et al. COVID-19 vaccination in patients with multiple sclerosis: what we have learnt by February 2021. *Mult Scler* 2021; 27(6): 864–870.

42. Papeix C, Mazoyer J, Maillart E, et al. Multiple sclerosis: is there a risk of worsening after yellow fever vaccination?*Mult Scler* 2021; 27(14): 2280–2283.

43. Grimaldi L, Papeix C, Hamon Y, et al. Vaccines and the risk of hospitalization for multiple sclerosis flare-ups. *JAMA Neurol* 2023; 80(10): 1098–1104.

44. Winkelmann A, Metze C, Zettl UK, et al. Side effects following vaccination in multiple sclerosis: a prospective, multi-centre cohort study. *Sci Rep* 2023; 13(1): 14480.

45. Zipp F, Weil JG and Einhaupl KM. No increase in demyelinating diseases after hepatitis B vaccination. *Nat Med* 1999; 5(9): 964–965.

46. Hapfelmeier A, Gasperi C, Donnachie E, et al. A large case-control study on vaccination as risk factor for multiple sclerosis. *Neurology* 2019; 93(9): e908–e916.

47. Mealy MA, Cook LJ, Pache F, et al. Vaccines and the association with relapses in patients with neuromyelitis optica spectrum disorder. *Mult Scler Relat Disord* 2018; 23: 78–82.

48. Esmanhotto BB, Rocha IM, Vilar CRL, et al. Neuromyelitis optica associated with yellow fever vaccination. *Acta Neurol Belg* 2021; 121(2): 567–569.

49. Menge T, Cree B, Saleh A, et al. Neuromyelitis optica following human papillomavirus vaccination. *Neurology* 2012; 79(3): 285–287.

50. Furukawa Y, Komai K and Yamada M. Neuromyelitis optica after Japanese encephalitis vaccination. *Eur J Neurol* 2011; 18(2): e26–e27.

51. Kitazawa Y, Warabi Y, Bandoh M, et al. Elderly-onset neuromyelitis optica which developed after the diagnosis of prostate adenocarcinoma and relapsed after a 23-valent pneumococcal polysaccharide vaccination. *Intern Med* 2012; 51(1): 103–107.

52. Cho JH, Park Y and Woo N. A case of neuromyelitis optica spectrum disorder following seasonal influenza vaccination. *Mult Scler Relat Disord* 2019; 30: 110–113.

53. Schöberl F, Csanadi E, Eren O, et al. NMOSD triggered by yellow fever vaccination—an unusual clinical presentation with segmental painful erythema. *Mult Scler Relat Disord* 2017; 11: 43–44.

54. Chang H, Lee HL, Yeo M, et al. Recurrent optic neuritis and neuromyelitis optica-IgG following first and second human papillomavirus vaccinations. *Clin Neurol Neurosurg* 2016; 144: 126–128.

55. Kline LB, Margulies SL and Oh SJ. Optic neuritis and myelitis following rubella vaccination. *Arch Neurol* 1982; 39(7): 443–444.

56. Jarius S, Ruprecht K, Kleiter I, et al. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 2: Epidemiology, clinical presentation, radiological and laboratory features, treatment responses, and long-term outcome. *J Neuroinflammation* 2016; 13(1): 280.

57. Harahsheh E, Callister M, Hasan S, et al. Aquaporin-4 IgG neuromyelitis optica spectrum disorder onset after Covid-19 vaccination: systematic review. *J Neuroimmunol* 2022; 373: 577994.

58. Jarius S, Bieber N, Haas J, et al. MOG encephalomyelitis after vaccination against severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2): case report and comprehensive review of the literature. *J Neurol* 2022; 269(10): 5198–5212.

59. Ringelstein M, Asseyer S, Lindenblatt G, et al. Eculizumab use in neuromyelitis optica spectrum disorders: routine clinical care data from a European cohort. *Neurology* 2024; 103(9): e209888.

60. Sansone G and Bonifati DM. Vaccines and myasthenia gravis: a comprehensive review and retrospective study of SARS-CoV-2 vaccination in a large cohort of myasthenic patients. *J Neurol* 2022; 269(8): 3965–3981.

61. Zheng W, Cao X, Luo J, et al. Safety and neutralization antibody levels of inactivated SARS-CoV-2 vaccine in adult patients with myasthenia gravis: a prospective observational cohort study. *Neurol Sci* 2024; 45(4): 1707–1717.

62. Kling K, Wichmann O and Burchard G. [Travel vaccinations for certain groups of persons]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2020; 63(1): 85–92.

63. Barwick Eidex R; Yellow Fever Vaccine Safety Working Group. History of thymoma and yellow fever vaccination. *Lancet* 2004; 364(9438): 936.

64. Marx A, Pfister F, Schalke B, et al. The different roles of the thymus in the pathogenesis of the various myasthenia gravis subtypes. *Autoimmun Rev* 2013; 12(9): 875–884.

65. Eidex RB. History of thymoma and yellow fever vaccination. *Lancet* 2004; 364(9438): 936.

66. Gnanadurai R, Campos-Matos I, Kanagarajah S, et al. National review of reported Yellow fever vaccine incidents in the UK. *Travel Med Infect Dis* 2022; 47: 102289.

67. Martin S, Azzouz B, Morel A, et al. Anti-NMDA receptor encephalitis and vaccination: a disproportionality analysis. *Front Pharmacol* 2022; 13: 940780.

68. Wang H. Anti-NMDA receptor encephalitis and vaccination. *Int J Mol Sci* 2017; 18(1): 193.

69. Zhang Y, Lian B, Yang S, et al. Metabotropic glutamate receptor 5-related autoimmune encephalitis with reversible splenial lesion syndrome following SARS-CoV-2 vaccination. *Medicine (Baltimore)* 2023; 102(7): e32971.

70. Vasilevska V, Guest PC, Szardenings M, et al. Possible temporal relationship between SARS-CoV-2 infection and anti-NMDA receptor encephalitis: a meta-analysis. *Transl Psychiatry* 2024; 14(1): 139.

71. Goud R, Lufkin B, Duffy J, et al. Risk of Guillain-Barré syndrome following recombinant zoster vaccine in medicare beneficiaries. *JAMA Intern Med* 2021; 181(12): 1623–1630.

72. Anderson TC, Leung JW, Harpaz R, et al. Risk of Guillain-Barré syndrome following herpes zoster, United States, 2010-2018. *Hum Vaccin Immunother* 2021; 17(12): 5304–5310.

73. Martín Arias LH, Sanz R, Sáinz M, et al. Guillain-Barré syndrome and influenza vaccines: a meta-analysis. *Vaccine* 2015; 33(31): 3773–3778.

74. Juurlink DN, Stukel TA, Kwong J, et al. Guillain-Barré syndrome after influenza vaccination in adults: a population-based study. *Arch Intern Med* 2006; 166(20): 2217–2221.

75. Lasky T, Terracciano GJ, Magder L, et al. The Guillain-Barré syndrome and the 1992–1993 and 1993–1994 influenza vaccines. *N Engl J Med* 1998; 339(25): 1797–1802.

76. Fiore AE, Uyeki TM, Broder K, et al. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. *MMWR Recomm Rep* 2010; 59(RR-8): 1–62.

77. Centers for Disease Control and Prevention (CDC). Preliminary results: surveillance for Guillain-Barré syndrome after receipt of influenza A (H1N1) 2009 monovalent vaccine—United States, 2009–2010. *MMWR Morb Mortal Wkly Rep* 2010; 59(21): 657–661.

78. Tokars JI, Lewis P, DeStefano F, et al. The risk of Guillain-Barré syndrome associated with influenza A (H1N1) 2009 monovalent vaccine and 2009–2010 seasonal influenza vaccines: results from self-controlled analyses. *Pharmacoepidemiol Drug Saf* 2012; 21(5): 546–552.

79. Wise ME, Viray M, Sejvar JJ, et al. Guillain-Barre syndrome during the 2009–2010 H1N1 influenza vaccination campaign: population-based surveillance among 45 million Americans. *Am J Epidemiol* 2012; 175(11): 1110–1119.

80. Abolmaali M, Rezania F, Behnagh AK, et al. Guillain-Barré syndrome in association with COVID-19 vaccination: a systematic review. *Immunol Res* 2022; 70(6): 752–764.

81. Taga A and Lauria G. COVID-19 and the peripheral nervous system. A 2-year review from the pandemic to the vaccine era. *J Peripher Nerv Syst* 2022; 27(1): 4–30.

82. Jaffry M, Mostafa F, Mandava K, et al. No significant increase in Guillain-Barré syndrome after COVID-19 vaccination in adults: a vaccine adverse event reporting system study. *Vaccine* 2022; 40(40): 5791–5797.

83. Willison AG, Pawlitzki M, Lunn MP, et al. SARS-CoV-2 vaccination and neuroimmunological disease: a review. *JAMA Neurol* 2024; 81(2): 179–186.

84. Sundaram ME, Kieke BA, Hanson KE, et al. Extended surveillance to assess safety of 9-valent human papillomavirus vaccine. *Hum Vaccin Immunother* 2022; 18(7): 2159215.

85. Doneddu PE, Bianchi E, Cocito D, et al. Risk factors for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP): antecedent events, lifestyle and dietary habits. Data from the Italian CIDP Database. *Eur J Neurol* 2020; 27(1): 136–143.

86. Rajabally YA, Peric S, Bozovic I, et al. Antecedent infections and vaccinations in chronic inflammatory demyelinating polyneuropathy: a European collaborative study. *Muscle Nerve* 2021; 64(6): 657–661.

87. Kuitwaard K, Bos-Eyssen ME, Blomkwist-Markens PH, et al. Recurrences, vaccinations and long-term symptoms in GBS and CIDP. *J Peripher Nerv Syst* 2009; 14(4): 310–315.

88. Baars AE, Kuitwaard K, de Koning LC, et al. SARS-CoV-2 vaccination safety in Guillain-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, and multifocal motor neuropathy. *Neurology* 2023; 100(2): e182–e191.

89. Doneddu PE, Briani C, Cocito D, et al. Risk of disease relapse, safety and tolerability of SARS-CoV-2 vaccination in patients with chronic inflammatory neuropathies. *Eur J Neurol* 2023; 30(7): 1907–1918.

90. Felicetti P, Trotta F, Bonetto C, et al. Spontaneous reports of vasculitis as an adverse event following immunization: a descriptive analysis across three international databases. *Vaccine* 2016; 34(51): 6634–6640.

91. Abuhammad A, Albandak M, Ayyad M, et al. COVID-19 vaccine-associated vasculitis: a systematic review. *SAGE Open Med* 2024; 12: 20503121241261165.

92. Stassen PM, Sanders JS, Kallenberg CG, et al. Influenza vaccination does not result in an increase in relapses in patients with ANCA-associated vasculitis. *Nephrol Dial Transplant* 2008; 23(2): 654–658.

93. Bonetto C, Trotta F, Felicetti P, et al. Vasculitis as an adverse event following immunization—systematic literature review. *Vaccine* 2016; 34(51): 6641–6651.

94. Steelman AJ.Infection as an environmental trigger of multiple sclerosis disease exacerbation. *Front Immunol* 2015; 6: 520.

95. Correale J, Fiol M and Gilmore W. The risk of relapses in multiple sclerosis during systemic infections. *Neurology* 2006; 67(4): 652–659.

96. Miele G, Cepparulo S, Abbadessa G, et al. Clinically manifest infections do not increase the relapse risk in people with multiple sclerosis treated with disease-modifying therapies: a prospective study. *J Clin Med* 2023; 12(3): 1023.

97. Zhong X, Zhou Y, Lu T, et al. Infections in neuromyelitis optica spectrum disorder. *J Clin Neurosci* 2018; 47: 14–19.

98. Loos J, Pfeuffer S, Pape K, et al. MOG encephalomyelitis: distinct clinical, MRI and CSF features in patients with longitudinal extensive transverse myelitis as first clinical presentation. *J Neurol* 2020; 267(6): 1632–1642.

99. Ramanathan S, Mohammad S, Tantsis E, et al. Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination. *J Neurol Neurosurg Psychiatry* 2018; 89(2): 127–137.

100. Jarius S, Ruprecht K, Kleiter I, et al. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 1: frequency, syndrome specificity, influence of disease activity, long-term course, association with AQP4-IgG, and origin. *J Neuroinflammation* 2016; 13(1): 279.

101. Vellozzi C, Iqbal S and Broder K. Guillain-Barre syndrome, influenza, and influenza vaccination: the epidemiologic evidence. *Clin Infect Dis* 2014; 58(8): 1149–1155.

102. Hu Y, Frisell T, Alping P, et al. Hospital-treated infections and risk of disability worsening in multiple sclerosis. *Ann Neurol* 2024; 96(4): 694–703.

103. Rondaan C, Furer V, Heijstek MW, et al. Efficacy, immunogenicity and safety of vaccination in adult patients with autoimmune inflammatory rheumatic diseases: a systematic literature review for the 2019 update of EULAR recommendations. *RMD Open* 2019; 5(2): e001035.

104. Weirauch T, Burger G, Cadar D, et al. Vaccine-derived yellow fever in an immunocompromised patient on anti-CD20-antibody therapy and its treatment with sofosbuvir. *Int J Infect Dis* 2024; 143: 107017.

105. Miauton A, Tan R, Pantazou V, et al. Vaccine-associated measles in a patient treated with natalizumab: a case report. *BMC Infect Dis* 2020; 20(1): 753.

106. Wagner N, Assmus F, Arendt G, et al. Impfen bei immundefizienz [vaccination in immunodeficiency]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2019; 62(4): 494–515.

107. Winkelmann A, Loebermann M, Barnett M, et al. Vaccination and immunotherapies in neuroimmunological diseases. *Nat Rev Neurol* 2022; 18(5): 289–306.

108. Seedat J and Winkler M. Epidemiologisches bulletin, extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.rki.de/DE/Aktuelles/Publikationen/Epidemiologisches-Bulletin/2025/04_25.pdf?__blob=publicationFile&v=7 (2025, accessed 13 November 2025).

109. Europharm Limited Novartis. Gilenya 0.25 mg hard capsules Gilenya 0.5 mg hard capsules, summary of product characteristics, https://

www.ema.europa.eu/en/documents/product-information/gilenya-epar-product-information_en.pdf (2020, accessed 12 June 2024).

110. Pharma EEIG Bristol-Myers-Squibb. Zeposia 0.23 mg hard capsules Zeposia 0.46 mg hard capsules Zeposia 0.92 mg hard capsules, summary of product characteristics, https://www.ema.europa.eu/en/documents/product-information/zeposia-epar-product-information_en.pdf (2020, accessed 12 June 2024).

111. Europe B.V. Merck. MAVENCLAD 10 mg tablets, summary of product characteristics, https://www.ema.europa.eu/en/documents/product-information/mavenclad-epar-product-information_en.pdf (2024, 30 April 2024).

112. Europharm Limited Novartis. Mayzent 0.25 mg film-coated tablets Mayzent 1 mg film-coated tablets Mayzent 2 mg film-coated tablets, summary of product characteristics, https://www.ema.europa.eu/en/documents/product-information/mayzent-epar-product-information_en.pdf (2020, accessed 12 June 2024).

113. Ireland Limited Novartis. Kesimpta 20 mg solution for injection in pre-filled syringe Kesimpta 20 mg solution for injection in pre-filled pen, summary of product characteristics, https://www.ema.europa.eu/en/documents/product-information/kesimpta-epar-product-information_en.pdf (2021, accessed 12 June 2024).

114. Registration GmbH Roche. Ocrevus 300 mg concentrate for solution for infusion, summary of product characteristics, https://www.ema.europa.eu/en/documents/product-information/ocrevus-epar-product-information_en.pdf (2022, 12 June 2024).

115. Pharma AG Roche. MabThera 100 mg concentrate for solution for infusion. *MabThera 500 mg concentrate for solution for infusion, summary of product characteristics*, https://www.ema.europa.eu/en/documents/product-information/mabthera-epar-product-information_en.pdf (2008, accessed 12 June 2024).

116. Belgium Sanofi. LEMTRADA 12 mg concentrate for solution for infusion, summary of product characteristics, https://www.ema.europa.eu/en/documents/product-information/lemtrada-epar-product-information_en.pdf (2018, 12 June 2024).

117. Krankheitsbezogenes Kompetenznetz MultipleSklerose (KKNMS). Qualitätshandbuch MS, NMOSD, MOGAD https://ms-qualitaetshandbuch.de/erstdiagnose-sop/ (2012, accessed 12 June 2024).

118. Seedat J and Winkler M. Epidemiologisches Bulletin 20/21, exhttps://www.rki.de/DE/Aktuelles/Publikationen/Epidemiologisches-Bulletin/2024/20-21_24.pdf?__blob=publicationFile&v=5 (2024, accessed 12 June 2024).

119. Wessely A, Zwazl I and Poturica M. Recombinant herpes zoster vaccine (Shingrix((R))) in VZV seronegative immunocompromised adults. Vaccines (Basel) 2025; 13(7).

120. WHO position paper on herpes zoster vaccines - July 2025. Weekly Epidemiological Record, No 27/28. 2025.

121. Apostolidis SA, Kakara M, Painter MM, et al. Cellularand humoral immune responses following SARS-CoV-2 mRNA vaccination in patients with multiple sclerosis on anti-CD20 therapy. *Nat Med* 2021; 27(11): 1990–2001.

122. Hazlewood MA, Kumararatne DS, Webster AD, et al. An association between homozygous C3 deficiency and low levels of anti-pneumococcal capsular polysaccharide antibodies. *Clin Exp Immunol* 1992; 87(3): 404–409.

123. Peset Llopis MJ, Harms G, Hardonk MJ, et al. Human immune response to pneumococcal polysaccharides: complement-mediated localization preferentially on CD21-positive splenic marginal zone B cells and follicular dendritic cells. *J Allergy Clin Immunol* 1996; 97(4): 1015–1024.

124. Mellors J, Tipton T, Longet S, et al. Viral evasion of the complement system and its importance for vaccines and therapeutics. *Front Immunol* 2020; 11: 1450.

125. Zaiss AK, Cotter MJ, White LR, et al. Complement is an essential component of the immune response to adeno-associated virus vectors. *J Virol* 2008; 82(6): 2727–2740.

126. Miyamoto K, Minamino M, Kuwahara M, et al. Complement biomarkers reflect the pathological status of neuromyelitis optica spectrum disorders. *Front Immunol* 2023; 14: 1090548.

127. Asavapanumas N, Tradtrantip L and Verkman AS. Targeting the complement system in neuromyelitis optica spectrum disorder. *Expert Opin Biol Ther* 2021; 21(8): 1073–1086.

128. Pache F, Ringelstein M, Aktas O, et al. C3 and C4 complement levels in AQP4-IgG-positive NMOSD and in MOGAD. *J Neuroimmunol* 2021; 360: 577699.

129. Pittock SJ, Berthele A, Fujihara K, et al. Eculizumab in aquaporin-4-positive neuromyelitis optica spectrum disorder. *N Engl J Med* 2019; 381(7): 614–625.

130. Nishiyama S, Seok JM, Wright AE, et al. Anti-aquaporin-4 immune complex stimulates complement-dependent Th17 cytokine release in neuromyelitis optica spectrum disorders. *Sci Rep* 2024; 14(1): 3146.

131. Khalilidehkordi E, Clarke L, Arnett S, et al. Relapse patterns in NMOSD: evidence for earlier occurrence of optic neuritis and possible seasonal variation. *Front Neurol* 2020; 11: 537.

132. Jarius S, Ruprecht K, Wildemann B, et al. Contrasting disease patterns in seropositive and seronegative neuromyelitis optica: a multicentre study of 175 patients. *J Neuroinflammation* 2012; 9: 14.

133. Du Q, Shi Z, Chen H, et al. Comparison of clinical characteristics and prognoses in patients with different AQP4-Ab and MOG-Ab serostatus with neuromyelitis optica spectrum disorders. *J Neuroimmunol* 2021; 353: 577494.

134. Mealy MA, Mossburg SE, Kim SH, et al. Long-term disability in neuromyelitis optica spectrum disorder with a history of myelitis is associated with age at onset, delay in diagnosis/preventive treatment, MRI lesion length and presence of symptomatic brain lesions. *Mult Scler Relat Disord* 2019; 28: 64–68.

135. Kumpfel T, Giglhuber K, Aktas O, et al. Update on the diagnosis and treatment of neuromyelitis optica spectrum disorders (NMOSD)—revised recommendations of the Neuromyelitis Optica Study Group (NEMOS). Part II: Attack therapy and long-term management. *J Neurol* 2024; 271(1): 141–176.

136. Berthele A, Aktas O, Ayzenberg I, et al. Expertenkonsensus: Meningokokkenprophylaxe in der Therapie neurologischer Erkrankungen mit Komplementinhibitoren. *DGNeurologie* 2025; 8(5): 398–407.

137. Engelhard D, Handsher R, Naparstek E, et al. Immune response to polio vaccination in bone marrow transplant recipients. *Bone Marrow Transplant* 1991; 8(4): 295–300.

138. Pauksen K, Duraj V, Ljungman P, et al. Immunity to and immunization against measles, rubella and mumps in patients after autologous bone marrow transplantation. *Bone Marrow Transplant* 1992; 9(6): 427–432.

139. Colton H, Greenfield DM, Snowden JA, et al. Long-term survivors following autologous haematopoetic stem cell transplantation have significant defects in their humoral immunity against vaccine preventable diseases, years on from transplant. *Vaccine* 2021; 39(34): 4778–4783.

140. Autore F, Stirparo L, Innocenti I, et al. Immunogenicity of SARS-CoV-2 vaccination in patients undergoing autologous stem cell transplantation. A multicentric experience. *Front Oncol* 2022; 12: 897937.

141. Maneikis K, Sablauskas K, Ringeleviciute U, et al. Immunogenicity of the BNT162b2 COVID-19 mRNA vaccine and early clinical outcomes in patients with haematological malignancies in Lithuania: a national prospective cohort study. *Lancet Haematol* 2021; 8(8): e583–e592.

142. Tsushima T, Terao T, Narita K, et al. Antibody response to COVID-19 vaccine in 130 recipients of hematopoietic stem cell transplantation. *Int J Hematol* 2022; 115(5): 611–615.

143. Antin JH, Guinan EC, Avigan D, et al. Protective antibody responses to pneumococcal conjugate vaccine after autologous hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant* 2005; 11(3): 213–222.

144. Rieger C, Liss B, Mellinghoff S, et al. Impfungen bei tumorpatienten—leitlinie, https://www.onkopedia.com/de/onkopedia/guidelines/impfungen-bei-tumorpatienten/@@guideline/html/index.html (2019, accessed 30 April 2024).

145. Laws HJ, Baumann U, Bogdan C, et al. Impfen bei immundefizienz [vaccination in immunodeficiency]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2020; 63(5): 588–644.

146. Task Force aHSCTdes KKNMS inZusammenarbeit mit DGN BDN BVDN DMSG DAG-HSZT. Empfehlungsposition zum Einsatz der autologen hämatopoetischen Stammzelltransplantation (aHSCT) bei Multipler Sklerose in Deutschland, https://www.zns-news-neurologen-psychiater-nervenaerzte.de/wp-content/uploads/2022/12/KKN_2211_WEB_empfehlung_aHSCT-1.pdf. (2022, accessed 30 April 2024).

147. Rolla S, Maglione A, De Mercanti SF, et al. The meaning of immune reconstitution after alemtuzumab therapy in multiple sclerosis. *Cells* 2020; 9(6): 1396.

148. McCarthy CL, Tuohy O, Compston DA, et al. Immune competence after alemtuzumab treatment of multiple sclerosis. *Neurology* 2013; 81(10): 872–876.

149. Achiron A, Mandel M, Dreyer-Alster S, et al. In-depth characterization of long-term humoral and cellular immune responses to COVID-19m-RNA vaccination in multiple sclerosis patients treated with teriflunomide or alemtuzumab. *Mult Scler Relat Disord* 2023; 72: 104616.

150. Sormani MP, Inglese M, Schiavetti I, et al. Effect of SARS-CoV-2 mRNA vaccination in MS patients treated with disease modifying therapies. *EBioMedicine* 2021; 72: 103581.

151. Bsteh G, Hegen H, Traxler G, et al. Comparing humoral immune response to SARS-CoV2 vaccines in people with multiple sclerosis and healthy controls: an Austrian prospective multicenter cohort study. *Eur J Neurol* 2022; 29(5): 1538–1544.

152. Holvast A, Huckriede A, Wilschut J, et al. Safety and efficacy of influenza vaccination in systemic lupus erythematosus patients with quiescent disease. *Ann Rheum Dis* 2006; 65(7): 913–918.

153. Kim W, Kim SH, Huh SY, et al. Reduced antibody formation after influenza vaccination in patients with neuromyelitis optica spectrum disorder treated with rituximab. *Eur J Neurol* 2013; 20(6): 975–980.

154. Jovicevic V, Ivanovic J, Momcilovic N, et al. Humoral response to SARS-CoV-2 infection and vaccines against COVID-19 in patients with neuromyelitis optica spectrum disorders: impact of immunosuppressive treatment. *Mult Scler Relat Disord* 2022; 62: 103794.

155. Baker D, Pryce G, James LK, et al. The ocrelizumab phase II extension trial suggests the potential to improve the risk: benefit balance in multiple sclerosis. *Mult Scler Relat Disord* 2020; 44: 102279.

156. Bar-Or A, Calkwood JC, Chognot C, et al. Effect of ocrelizumab on vaccine responses in patients with multiple sclerosis: the VELOCE study. *Neurology* 2020; 95(14): e1999–e2008.

157. Apostolidis SA, Kakara M, Painter MM, et al. Cellular and humoral immune responses following SARS-CoV-2 mRNA vaccination in patients with multiple sclerosis on anti-CD20 therapy. *Nat Med* 2021; 27(11): 1990–2001.

158. Sabatino JJ Jr, Mittl K, Rowles WM, et al. Multiple sclerosis therapies differentially affect SARS-CoV-2 vaccine-induced antibody and T cell immunity and function. *JCI Insight* 2022; 7(4): e156978.

159. Tan AT, Linster M, Tan CW, et al. Early induction of functional SARS-CoV-2-specific T cells associates with rapid viral clearance and mild disease in COVID-19 patients. *Cell Rep* 2021; 34(6): 108728.

160. Rauber S, Korsen M, Huntemann N, et al. Immune response to SARS-CoV-2 vaccination in relation to peripheral immune cell profiles among patients with multiple sclerosis receiving ocrelizumab. *J Neurol Neurosurg Psychiatry* 2022; 93(9): 978–985.

161. Schraad M, Runkel S, Hitzler W, et al. Long-term observation of SARS-CoV-2 vaccination response upon high efficacy treatment in multiple sclerosis—a real-world scenario. *Vaccines (Basel)* 2024; 12(3): 296.

162. DiLillo DJ, Hamaguchi Y, Ueda Y, et al. Maintenance of long-lived plasma cells and serological memory despite mature and memory B cell depletion during CD20 immunotherapy in mice. *J Immunol* 2008; 180(1): 361–371.

163. Lu L, Chan CY, Lim YY, et al. SARS-CoV-2 humoral immunity persists following rituximab therapy. *Vaccines (Basel)* 2023; 11(12): 1864.

164. Ziemssen T, Groth M, Ettle B, et al. Immune response to SARS-CoV-2 mRNA vaccines in an open-label multicenter study in participants with relapsing multiple sclerosis treated with ofatumumab. *Vaccines (Basel)* 2022; 10(12): 2167.

165. Sabatino JJ Jr, Mittl K, Rowles W, et al. Longitudinal adaptive immune responses following sequential SARS-CoV-2 vaccinations in MS patients on anti-CD20 therapies and sphingosine-1-phosphate receptor modulators. *Mult Scler Relat Disord* 2023; 70: 104484.

166. Bar-Or A, Aburashed R, Chinea AR, et al. Humoral immune response to COVID-19 mRNA vaccines in patients with relapsing multiple sclerosis treated with ofatumumab. *Mult Scler Relat Disord* 2023; 79: 104967.

167. Steingo B, Subei A, Riser E, et al. Immune response to influenza vaccine in patients with relapsing multiple sclerosis treated with ofatumumab: results from an open-label, multicenter, phase 4 study. *Mult Scler Relat Disord* 2025; 97: 106382.

168. Cotchett KR, Dittel BN and Obeidat AZ. Comparison of the efficacy and safety of anti-CD20 B cells depleting drugs in multiple sclerosis. *Mult Scler Relat Disord* 2021; 49: 102787.

169. Vijenthira A, Gong I, Betschel SD, et al. Vaccine response following anti-CD20 therapy: a systematic review and meta-analysis of 905 patients. *Blood Adv* 2021; 5(12): 2624–2643.

170. Marantos T, Kyriazopoulou E, Angelakis E, et al. Immunogenicity of a seasonal influenza and a pneumococcal polysaccharide vaccine in multiple sclerosis patients under disease modifying therapies: a single-center prospective study. *Vaccine* 2024; 42(22): 126001.

171. Nytrova P, Stastna D, Tesar A, et al. Immunity following SARS-CoV-2 vaccination in autoimmune neurological disorders treated with rituximab or ocrelizumab. *Front Immunol* 2023; 14: 1149629.

172. Levit E, Longbrake EE and Stoll SS. Seroconversion after COVID-19 vaccination for multiple sclerosis patients on high efficacy disease modifying medications. *Mult Scler Relat Disord* 2022; 60: 103719.

173. Alfonso-Dunn R, Lin J, Kirschner V, et al. Strong T-cell activation in response to COVID-19 vaccination in multiple sclerosis patients receiving B-cell depleting therapies. *Front Immunol* 2022; 13: 926318.

174. Neuraxpharm P.Briumvi 150 mg concentrate for solution for infusion, summary of product characteristics, https://www.ema.europa.eu/en/documents/product-information/briumvi-epar-product-information_en.pdf (2023, accessed 3 June 2024).

175. Teschner VE, Fleck AK, Walter C, et al. Single-cell profiling reveals preferential reduction of memory B cell subsets in cladribine patients that correlates with treatment response. *Ther Adv Neurol Disord* 2023; 16: 17562864231211077.

176. Comi G, Cook S, Giovannoni G, et al. Effect of cladribine tablets on lymphocyte reduction and repopulation dynamics in patients with relapsing multiple sclerosis. *Mult Scler Relat Disord* 2019; 29: 168–174.

177. Achiron A, Mandel M, Dreyer-Alster S, et al. Humoral immune response in multiple sclerosis patients following PfizerBNT162b2 COVID19 vaccination: up to 6 months cross-sectional study. *J Neuroimmunol* 2021; 361: 577746.

178. Grothe C, Steffen F and Bittner S. Humoral immune response and lymphocyte levels after complete vaccination against COVID-19 in a cohort of multiple sclerosis patients treated with cladribine tablets. *J Cent Nerv Syst Dis* 2021; 13: 11795735211060118.

179. Mimpen M, Kreiter D, Kempkens T, et al. Humoral immune response after SARS-CoV-2 vaccination in cladribine-treated multiple sclerosis patients. *Vaccine X* 2024; 16: 100445.

180. Brill L, Rechtman A, Zveik O, et al. Effect of cladribine on COVID-19 serology responses following two doses of the BNT162b2 mRNA vaccine in patients with multiple sclerosis. *Mult Scler Relat Disord* 2022; 57: 103343.

181. Schmierer K, Wiendl H, Oreja-Guevara C, et al. Varicella zoster virus and influenza vaccine antibody titres in patients from MAGNIFY-MS who were treated with cladribine tablets for highly active relapsing multiple sclerosis. *Mult Scler* 2022; 28(13): 2151–2153.

182. Rolfes L, Pfeuffer S, Skuljec J, et al. Immune response to seasonal influenza vaccination in multiple sclerosis patients receiving cladribine. *Cells* 2023; 12(9): 1243.

183. Rolfes L, Pfeuffer S, Huntemann N, et al. Immunological consequences of cladribine treatment in multiple sclerosis: a real-world study. *Mult Scler Relat Disord* 2022; 64: 103931.

184. Carlini F, Lusi V, Rizzi C, et al. Cladribine tablets mode of action, learning from the pandemic: a narrative review. *Neurol Ther* 2023; 12(5): 1477–1490.

185. Moody DJ, Fahey JL, Grable E, et al. Administration of monthly pulses of cyclophosphamide in multiple sclerosis patients. Delayed recovery of several immune parameters following discontinuation of long-term cyclophosphamide treatment. *J Neuroimmunol* 1987; 14(2): 175–182.

186. Kashiwado Y, Kimoto Y, Sawabe T, et al. Antibody response to SARS-CoV-2 mRNA vaccines in patients with rheumatic diseases in Japan: interim analysis of a multicentre cohort study. *Mod Rheumatol* 2023; 33(2): 367–372.

187. Rotstein Grein IH, Pinto NF, Lobo A, et al. Safety and immunogenicity of the quadrivalent human papillomavirus vaccine in patients with childhood systemic lupus erythematosus: a real-world interventional multi-centre study. *Lupus* 2020; 29(8): 934–942.

188. Aikawa NE, Campos LM, Silva CA, et al. Glucocorticoid: major factor for reduced immunogenicity of 2009 influenza A (H1N1) vaccine in patients with juvenile autoimmune rheumatic disease. *J Rheumatol* 2012; 39(1): 167–173.

189. Lucchini M, Prosperini L, Buscarinu MC, et al. Predictors of lymphocyte count recovery after dimethyl fumarate-induced lymphopenia in people with multiple sclerosis. *J Neurol* 2021; 268(6): 2238–2245.

190. von Hehn C, Howard J, Liu S, et al. Immune response to vaccines is maintained in patients treated with dimethyl fumarate. *Neurol Neuroimmunol Neuroinflamm* 2018; 5(1): e409.

191. Moser T, Seiberl M, Feige J, et al. Tetravalent influenza vaccine is not associated with neuroaxonal damage in multiple sclerosis patients. *Front Immunol* 2021; 12: 718895.

192. Schraad M, Uphaus T, Runkel S, et al. Predictors for insufficient SARS-CoV-2 vaccination response upon treatment in multiple sclerosis. *EBioMedicine* 2023; 87: 104411.

193. Netherlands B.V. Biogen. Tecfidera 120 mg gastro-resistant hard capsules Tecfidera 240 mg gastro-resistant hard capsules, summary of product characteristic, https://www.ema.europa.eu/en/documents/product-information/tecfidera-epar-product-information_en.pdf (2024, accessed 12 May 2024).

194. Netherlands B.V. Biogen. Vumerity 231 mg gastro-resistant hard capsules, https://www.ema.europa.eu/en/documents/product-information/vumerity-epar-product-information_en.pdf (2024, accessed 12 May 2024).

195. Nair SS and Jacob S. Novel immunotherapies for myasthenia gravis. *Immunotargets Ther* 2023; 12: 25–45.

196. Alashkar F, Vance C, Herich-Terhurne D, et al. Serologic response to meningococcal vaccination in patients with cold agglutinin disease (CAD) in the novel era of complement inhibition. *Vaccine* 2019; 37(44): 6682–6687.

197. Gackler A, Kaulfuss M, Rohn H, et al. Failure of first meningococcal vaccination in patients with atypical haemolytic uraemic syndrome treated with eculizumab. *Nephrol Dial Transplant* 2020; 35(2): 298–303.

198. Ptushkin V, Arshanskaya E, Vinogradova O, et al. The features of COVID-19's course and the efficacy of the Gam-COVID-Vac vaccine in patients with paroxysmal nocturnal hemoglobinuria. *Hematol Rep* 2023; 15(3): 503–512.

199. Guptill JT, Sleasman JW, Steeland S, et al. Effect of FcRn antagonism on protective antibodies and to vaccines in IgG-mediated autoimmune diseases pemphigus and generalised myasthenia gravis. *Autoimmunity* 2022; 55(8): 620–631.

200. BV Argenx. Vyvgart 20 mg/mL concentrate for solution for infusion, summary of product characteristics, https://www.ema.europa.eu/en/documents/product-information/vyvgart-epar-product-information_en.pdf (2022, accessed 3 June 2024).

201. Olberg HK, Eide GE, Cox RJ, et al. Antibody response to seasonal influenza vaccination in patients with multiple sclerosis receiving immunomodulatory therapy. *Eur J Neurol* 2018; 25(3): 527–534.

202. Metze C, Winkelmann A, Loebermann M, et al. Immunogenicity and predictors of response to a single dose trivalent seasonal influenza vaccine in multiple sclerosis patients receiving disease-modifying therapies. *CNS Neurosci Ther* 2019; 25(2): 245–254.

203. Olberg HK, Cox RJ, Nostbakken JK, et al. Immunotherapies influence the influenza vaccination response in multiple sclerosis patients: an explorative study. *Mult Scler* 2014; 20(8): 1074–1080.

204. Duda PW, Schmied MC, Cook SL, et al. Glatiramer acetate (Copaxone) induces degenerate, Th2-polarized immune responses in patients with multiple sclerosis. *J Clin Invest* 2000; 105(7): 967–976.

205. Pharma AbZ. Glatirameracetat AbZ 20 mg/ml injektionslösung in einer Fertigspritze. *Fachinformationen*, https://www.fachinfo.de/pdf/022864 (2024, accessed 17 May 2024).

206. Deepak P, Kim W, Paley MA, et al. Effect of immunosuppression on the immunogenicity of mRNA vaccines to SARS-CoV-2: a prospective cohort study. *Ann Intern Med* 2021; 174(11): 1572–1585.

207. Renaudineau Y, Sailler L, Abravanel F, et al. Glucocorticoid use as a cause of non-cellular immune response to SARS-Cov2 spike in patients with immune system diseases. *J Autoimmun* 2022; 133: 102912.

208. Wieske L, van Dam KPJ, Steenhuis M, et al. Humoral responses after second and third SARS-CoV-2 vaccination in patients with immune-mediated inflammatory disorders on immunosuppressants: a cohort study. *Lancet Rheumatol* 2022; 4(5): e338–e350.

209. Park SH, Yang SK, Park SK, et al. Efficacy of hepatitis A vaccination and factors impacting on seroconversion in patients with inflammatory bowel disease. *Inflamm Bowel Dis* 2014; 20(1): 69–74.

210. Fischer L, Gerstel PF, Poncet A, et al. Pneumococcal polysaccharide vaccination in adults undergoing immunosuppressive treatment for inflammatory diseases—a longitudinal study. *Arthritis Res Ther* 2015; 17(1): 151.

211. Schwid SR, Decker MD and Lopez-Bresnahan M; Rebif-Influenza Vaccine Study Investigators. Immune response to influenza vaccine is maintained in patients with multiple sclerosis receiving interferon beta-1a. *Neurology* 2005; 65(12): 1964–1966.

212. Morikawa Y, Sakakibara H, Kimiya T, et al.; Tokyo Pediatric Clinical Research Network. Live attenuated vaccine efficacy six months after intravenous immunoglobulin therapy for Kawasaki disease. *Vaccine* 2021; 39(39): 5680–5687.

213. Bae SS, Faure-Kumar E, Ferbas K, et al. Assessment of antibody levels to SARS-CoV-2 in patients with idiopathic inflammatory myopathies receiving treatment with intravenous immunoglobulin. *Rheumatol Int* 2023; 43(9): 1629–1636.

214. Committee for Medicinal Products for Human Use (CHMP). Guideline on core SmPC for human normal immunoglobulin for intravenous administration (IVIg), https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-core-smpc-human-normal-immunoglobulin-intravenous-administration-ivig-rev-6_en.pdf (2021, accessed 30 April 2024).

215. Inui Y, Matsuoka H, Yakushijin K, et al. Methotrexate-associated lymphoproliferative disorders: management by watchful waiting and observation of early lymphocyte recovery after methotrexate withdrawal. *Leuk Lymphoma* 2015; 56(11): 3045–3051.

216. Shirata M, Ito I, Tanaka M, et al. Impact of methotrexate on humoral and cellular immune responses to SARS-CoV-2 mRNA vaccine in patients with rheumatoid arthritis. *Clin Exp Med* 2023; 23(8): 4707–4720.

217. Van Assen S, Agmon-Levin N, Elkayam O, et al. EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. *Ann Rheum Dis* 2011; 70(3): 414–422.

218. Wiedermann U, Sitte HH, Burgmann H, et al. [Guidelines for vaccination of immunocompromised individuals]. *Wien Klin Wochenschr* 2016; 128(Suppl. 4): 337–376.

219. Buhler S, Eperon G, Ribi C, et al. Vaccination recommendations for adult patients with autoimmune inflammatory rheumatic diseases. *Swiss Med Wkly* 2015; 145: w14159.

220. Heijstek MW, Ott de, Bruin LM, Bijl M, et al. EULAR recommendations for vaccination in paediatric patients with rheumatic diseases. *Ann Rheum Dis* 2011; 70(10): 1704–1712.

221. Kapetanovic MC, Saxne T, Nilsson JA, et al. Influenza vaccination as model for testing immune modulation induced by anti-TNF and methotrexate therapy in rheumatoid arthritis patients. *Rheumatology (Oxford)* 2007; 46(4): 608–611.

222. Kapetanovic MC, Saxne T, Sjoholm A, et al. Influence of methotrexate, TNF blockers and prednisolone on antibody responses to pneumococcal polysaccharide vaccine in patients with rheumatoid arthritis. *Rheumatology (Oxford)* 2006; 45(1): 106–111.

223. Park JK, Lee MA, Lee EY, et al. Effect of methotrexate discontinuation on efficacy of seasonal influenza vaccination in patients with rheumatoid arthritis: a randomised clinical trial. *Ann Rheum Dis* 2017; 76(9): 1559–1565.

224. Wallwork R, Connolly CM, Shneyderman M, et al. Effect of mycophenolate mofetil dose on antibody response following initial SARS-CoV-2 vaccination in patients with systemic sclerosis. *Lancet Rheumatol* 2022; 4(7): e462–e464.

225. Mok CC, Ho LY, Fong LS, et al. Immunogenicity and safety of a quadrivalent human papillomavirus vaccine in patients with systemic lupus erythematosus: a case-control study. *Ann Rheum Dis* 2013; 72(5): 659–664.

226. Smith RM, Cooper DJ, Doffinger R, et al. SARS-COV-2 vaccine responses in renal patient populations. *BMC Nephrol* 2022; 23(1): 199.

227. Vagberg M, Kumlin U and Svenningsson A. Humoral immune response to influenza vaccine in natalizumab-treated MS patients. *Neurol Res* 2012; 34(7): 730–733.

228. Kaufman M, Pardo G, Rossman H, et al. Natalizumab treatment shows no clinically meaningful effects on immunization responses in patients with relapsing-remitting multiple sclerosis. *J Neurol Sci* 2014; 341(1–2): 22–27.

229. Carvajal R, Zabalza A, Carbonell-Mirabent P, et al. Vaccine safety and immunogenicity in patients with multiple sclerosis treated with natalizumab. *JAMA Netw Open* 2024; 7(4): e246345.

230. Paybast S, Sahraian MA, Nahayati MA, et al. Investigation of the safety of live attenuated varicella-zoster virus vaccination in patients with relapse-remitting multiple sclerosis treated with natalizumab: a case series and review of the literature. *Mult Scler Relat Disord* 2023; 77: 104793.

231. Lapucci C, Boccia VD, Sirito T, et al. Safety of anti-varicella zoster virus vaccination in patients

with multiple sclerosis treated with natalizumab: a case series. *Mult Scler* 2023; 29(11–12): 1514–1517.

232. Mulero P, Auger C, Parolin L, et al. Varicella-zoster meningovasculitis in a multiple sclerosis patient treated with natalizumab. *Mult Scler* 2018; 24(3): 358–360.

233. Nasca TJ, Muder RR, Thomas DB, et al. Antibody response to pneumococcal polysaccharide vaccine in myasthenia gravis: effect of therapeutic plasmapheresis. *J Clin Apher* 1990; 5(3): 133–139.

234. Guptill JT, Juel VC, Massey JM, et al. Effect of therapeutic plasma exchange on immunoglobulins in myasthenia gravis. *Autoimmunity* 2016; 49(7): 472–479.

235. Lambert C, Scohy A, Yombi JC, et al. Impact of therapeutic plasma exchange on acquired vaccinal anti-SARS-CoV-2 antibodies. *Eur J Intern Med* 2022; 100: 140–142.

236. Gaggl M, Aschauer C, Aigner C, et al. SARS-CoV-2 IgG spike protein antibody response in mRNA-1273 Moderna® vaccinated patients on maintenance immunoapheresis—a cohort study. *Front Immunol* 2022; 13: 969193.

237. Nagy S, Kuhle J and Derfuss T. Lymphocyte recovery after fingolimod discontinuation in patients with MS. *Neurol Neuroimmunol Neuroinflamm* 2020; 7(6): e874.

238. Mehling M, Hilbert P, Fritz S, et al. Antigen-specific adaptive immune responses in fingolimod-treated multiple sclerosis patients. *Ann Neurol* 2011; 69(2): 408–413.

239. Mehling M, Eichin D, Hafner P, et al. Avidity of vaccine-induced influenza IgG fails to increase in fingolimod-treated patients with MS. *Neurol Neuroimmunol Neuroinflamm* 2014; 1(3): e28.

240. Kappos L, Mehling M, Arroyo R, et al. Randomized trial of vaccination in fingolimod-treated patients with multiple sclerosis. *Neurology* 2015; 84(9): 872–879.

241. Boulton C, Meiser K, David OJ, et al. Pharmacodynamic effects of steady-state fingolimod on antibody response in healthy volunteers: a 4-week, randomized, placebo-controlled, parallel-group, multiple-dose study. *J Clin Pharmacol* 2012; 52(12): 1879–1890.

242. Proschmann U, Mueller-Enz M, Woopen C, et al. Differential effects of selective versus unselective sphingosine 1-phosphate receptor modulators on T- and B-cell response to SARS-CoV-2 vaccination. *Mult Scler* 2023; 29(14): 1849–1859.

243. Ufer M, Shakeri-Nejad K, Gardin A, et al. Impact of siponimod on vaccination response in a randomized, placebo-controlled study. *Neurol Neuroimmunol Neuroinflamm* 2017; 4(6): e398.

244. Schwake C, Pakeerathan T, Kleiter I, et al. Humoral COVID-19 vaccine response in patients with NMOSD/MOGAD during anti-IL-6 receptor therapy compared to other immunotherapies. *Mult Scler* 2023; 29(6): 757–761.

245. Krasselt M, Wagner U, Nguyen P, et al. Humoral and cellular response to COVID-19 vaccination in patients with autoimmune inflammatory rheumatic diseases under real-life conditions. *Rheumatology (Oxford)* 2022; 61(SI2): SI180–SI188.

246. Filippini F, Giacomelli M, Bazzani C, et al. Efficacy of COVID-19 mRNA vaccination in patients with autoimmune disorders: humoral and cellular immune response. *BMC Med* 2023; 21(1): 210.

247. Mori S, Ueki Y, Akeda Y, et al. Pneumococcal polysaccharide vaccination in rheumatoid arthritis patients receiving tocilizumab therapy. *Ann Rheum Dis* 2013; 72(8): 1362–1366.

248. Tsuru T, Terao K, Murakami M, et al. Immune response to influenza vaccine and pneumococcal polysaccharide vaccine under IL-6 signal inhibition therapy with tocilizumab. *Mod Rheumatol* 2014; 24(3): 511–516.

249. Prendecki M, Clarke C, Edwards H, et al. Humoral and T-cell responses to SARS-CoV-2 vaccination in patients receiving immunosuppression. *Ann Rheum Dis* 2021; 80(10): 1322–1329.

250. Petri M, Joyce D, Haag K, et al. Effect of systemic lupus erythematosus and immunosuppressive agents on COVID-19 vaccination antibody response. *Arthritis Care Res (Hoboken)* 2023; 75(9): 1878–1885.

251. Zhang L, Yang J, Deng M, et al. Blood unconjugated bilirubin and tacrolimus are negative predictors of specific cellular immunity in kidney transplant recipients after SAR-CoV-2 inactivated vaccination. *Sci Rep* 2023; 13(1): 7263.

252. Lindemann M, Heinemann FM, Horn PA, et al. Long-term response to vaccination against pneumococcal antigens in kidney transplant recipients. *Transplantation* 2012; 94(1): 50–56.

253. Migita K, Akeda Y, Akazawa M, et al. Pneumococcal polysaccharide vaccination

in rheumatoid arthritis patients receiving tacrolimus. *Arthritis Res Ther* 2015; 17(1): 149.

254. Sugihara K, Wakiya R, Kameda T, et al. Humoral immune response against BNT162b2 mRNA COVID-19 vaccine in patients with rheumatic disease undergoing immunosuppressive therapy: a Japanese monocentric study. *Medicine (Baltimore)* 2022; 101(42): e31288.

255. Mok CC, Ho LY and To CH. Long-term immunogenicity of a quadrivalent human papillomavirus vaccine in systemic lupus erythematosus. *Vaccine* 2018; 36(23): 3301–3307.

256. Bar-Or A, Wiendl H, Miller B, et al. Randomized study of teriflunomide effects on immune responses to neoantigen and recall antigens. *Neurol Neuroimmunol Neuroinflamm* 2015; 2(2): e70.

257. Bar-Or A, Freedman MS, Kremenchutzky M, et al. Teriflunomide effect on immune response to influenza vaccine in patients with multiple sclerosis. *Neurology* 2013; 81(6): 552–558.

258. Winthrop Industrie Sanofi. AUBAGIO 7 mg film-coated tablets AUBAGIO 14 mg film-coated tablets, summary of product characteristics, https://www.ema.europa.eu/en/documents/product-information/aubagio-epar-product-information_en.pdf (2023, acessed 12 June 2024).

259. Hagihara Y, Ohfuji S, Watanabe K, et al. Infliximab and/or immunomodulators inhibit immune responses to trivalent influenza vaccination in adults with inflammatory bowel disease. *J Crohns Colitis* 2014; 8(3): 223–233.

260. deBruyn J, Fonseca K, Ghosh S, et al. Immunogenicity of influenza vaccine for patients with inflammatory bowel disease on maintenance infliximab therapy: a randomized trial. *Inflamm Bowel Dis* 2016; 22(3): 638–647.

261. Fiorino G, Peyrin-Biroulet L, Naccarato P, et al. Effects of immunosuppression on immune response to pneumococcal vaccine in inflammatory bowel disease: a prospective study. *Inflamm Bowel Dis* 2012; 18(6): 1042–1047.

262. Alexander JL, Liu Z, Munoz Sandoval D, et al. COVID-19 vaccine-induced antibody and T-cell responses in immunosuppressed patients with inflammatory bowel disease after the third vaccine dose (VIP): a multicentre, prospective, case-control study. *Lancet Gastroenterol Hepatol* 2022; 7(11): 1005–1015.

263. Andrade P, Santos-Antunes J, Rodrigues S, et al. Treatment with infliximab or azathioprine negatively impact the efficacy of hepatitis B vaccine in inflammatory bowel disease patients. *J Gastroenterol Hepatol* 2015; 30(11): 1591–1595.

264. Pratt PK Jr, David N, Weber HC, et al. Antibody response to hepatitis B virus vaccine is impaired in patients with inflammatory bowel disease on infliximab therapy. *Inflamm Bowel Dis* 2018; 24(2): 380–386.

265. Garner-Spitzer E, Wagner A, Gudipati V, et al. Lower magnitude and faster waning of antibody responses to SARS-CoV-2 vaccination in anti-TNF-alpha-treated IBD patients are linked to lack of activation and expansion of cTfh1 cells and impaired B memory cell formation. *EBioMedicine* 2023; 96: 104788.

266. Kaine JL, Kivitz AJ, Birbara C, et al. Immune responses following administration of influenza and pneumococcal vaccines to patients with rheumatoid arthritis receiving adalimumab. *J Rheumatol* 2007; 34(2): 272–279.

267. Mease PJ, Ritchlin CT, Martin RW, et al. Pneumococcal vaccine response in psoriatic arthritis patients during treatment with etanercept. *J Rheumatol* 2004; 31(7): 1356–1361.

268. Aikawa NE, Franca IL, Ribeiro AC, et al. Short and long-term immunogenicity and safety following the 23-valent polysaccharide pneumococcal vaccine in juvenile idiopathic arthritis patients under conventional DMARDs with or without anti-TNF therapy. *Vaccine* 2015; 33(5): 604–609.

269. Rakoczi E, Perge B, Vegh E, et al. Evaluation of the immunogenicity of the 13-valent conjugated pneumococcal vaccine in rheumatoid arthritis patients treated with etanercept. *Joint Bone Spine* 2016; 83(6): 675–679.

270. Dell'Era L, Corona F, Daleno C, et al. Immunogenicity, safety and tolerability of MF59-adjuvanted seasonal influenza vaccine in children with juvenile idiopathic arthritis. *Vaccine* 2012; 30(5): 936–940.