kej oblasti, je nevyhnutné zvážiť pomer rizika a benefitu a pristupovať v tejto otázke vysoko individuálne. V tabuľke 4 je uvedená schéma odporúčaných postupov pri očkovaní živými vakcínami vo vzťahu k DMT liečbe u pacientov s RS (Ghaderi et al., 2019; Williamson et al., 2016; Lebrun et al., 2019; Zrzavy et al., 2019; Rapisarda et al., 2021; Lapucci et al., 2023; Jakimovski et al., 2020; Metze et al., 2018; Jeseňák et al., 2019; Williamson, 2016; Oreja-Guevara et al., 2014; Otero-Romero et al., 2023; www.sukl.sk).

Pri zvažovaní možnosti očkovania živými atenuovanými vakcínami je potrebné zhodnotiť parametre celulárnej imunity. U dospelých by mali byť počty CD4+ T lymfocytov ≥ 500/µl (miernejšie kritériá udávajú ≥ 200/µl) a počty CD8+ T lymfocytov ≥ 200/µl (McFarland, 1999; Papp et al., 2018; Perez et al., 2003; Principi et al., 2014).

## Záver

U pacientov s RS môže viesť imunosupresívna liečba ochorenia k lymfopénii, hypogamaglobulinémii a zvýšenému riziku výskytu a zhoršenému priebehu infekcií. Neurológ v spolupráci s imunológom využíva postupy preventívnych stratégií na minimalizáciu rizík infekcií predovšetkým očkovaním. Očkovanie je štandardnou súčasťou manažmentu pacientov s RS. V klinickej praxi je potrebné zvážiť, kedy a ktoré vakcíny podať pacientovi vzhľadom na jeho liečbu základného ochorenia preparátmi skupiny DMT, ktoré môžu ovplyvniť reakcie na vakcínu.

## LITERATÚRA

**1.** Alvarez E, Longbrake EE, Rammohan KW, et al. Secondary hypogammaglobulinemia in patients with multiple sclerosis on anti-CD20 therapy: Pathogenesis, risk of infection, and disease management. *Mult Scler Relat Disord.* 2023;17,92:105917. doi: 10.1016/j.msard.2024.105917.

**2.** Andreson D, Ali K, Blanchette V, et al. Guidelines on the use of intravenous immune globulin for hematologic conditions. *Transfus Med Rev.* 2007;21(2 Suppl 1):S9-56 doi: 10.1016/j.tmrv.2007.01.001.

**3.** Arneth BM. Impact of B cells to the pathophysiology of multiple sclerosis. *J Neuroinflammation.* 2019;25;16(1):128. doi:10.1186/s12974-019-1517-1.

**4.** Bierhansl L, Hartung HP, Aktas O, et al. Thinking outside the box: non-canonical targets in multiple sclerosis. *Nat Rev Drug Discov.* 2022;21:578-600. doi:10.1038/s41573-022-00477-5.

**5.** Casulo C, Maragulia J, Zelenetz AD, et al. Incidence of hypogammaglobulinemia in patients receiving rituximab and the use of intravenous immunoglobulin for recurrent infections. *Clin Lymphoma Myeloma Leuk.* 2013;13(2):106-11. doi: 10.1016/j.clml.2012.11.011.

**6.** De Souza KJ, Ferro RS, Prestes-Carneiro LE, at al. Infectious diseases and immunological markers associated with patients with non-Hodgkin lymphoma treated with rituximab. *Immunopharmacol Immunotoxicol.* 2018;40(1):13-17. doi: 10.1080/08923973.2017.1392562.

**7.** Du Pasquier RA, Pinschewer DD, Merkleret D, et al. Immunological mechanism of action and clinical profile of disease-modifying treatments in multiple sclerosis. *CNS Drugs.* 2014;28(6):535-58. doi:10.1007/s40263-014-0160-8.

**8.** Elgenidy A, Abdelhalim NN, Al-Mahdi Al-Kurdi M, et al. Hypogammaglobulinemia and infections in patients with multiple sclerosis treated with anti-CD20 treatments: a systematic review and meta-analysis of 19,139 multiple sclerosis patients. *Front Neurol.* 2024;18:15:1380654. doi:10.3389/fneur.2024.1380654. eCollection 2024.

**9.** Fischer S, Proschmann U, Akgün K, et al. Lymphocyte counts and multiple sclerosis therapeutics: between mechanisms of action and treatment-limiting side effects cells. *Cells.* 2021;15;10(11):3177. doi: 0.3390/cells10113177.

**10.** Fox EJ, Buckle GJ, Singer B, et al. Lymphopenia and DMTs for relapsing forms of MS: Considerations for the treating neurologist. *Neurol Clin Pract.* 2019;9(1):53-63. doi: 10.1212/CPJ.0000000000000567.

**11.** Garbo R, Lorenzut S, Del Negro I, et al. Lower lymphocyte counts and older age are associated with reduced multiple sclerosis disease activity during dimethyl fumarate treatment. *Mult Scler Relat Disord.* 2021;49:102781. doi: 0.1016/j.msard.2021.102781.

**12.** Gharibi T, Babaloo Z, Hosseini A, et al. The role of B cells in the immunopathogenesis of multiple sclerosis. *Immunology.* 2020;160(4):325-335. doi:10.1111/imm.13198.

**13.** Ghaderi S, Berg-Hansen P, Bakken IJ, et al. Hospitalization following influenza infection and pandemic vaccination in multiple sclerosis patients: a nationwide population-based registry study from Norway. *Eur J Epidemiol.* 2020;35(4):355-362. doi:10.1007/s10654-019-00595-2.

**14.** Gudesblatt M, Gerber O, Vaillancourt PD, et al. Quasi-normal cerebrospinal fluid in patients with acquired immunodeficiency syndrome and cryptococcal meningitis. *Rev Neurol (Paris).* 1987;143(4):290-3.

**15.** Gunther G and Dreger B. Post-marketing observational study on 5% intravenous immunoglobulin therapy in patients with secondary immunodeficiency and recurrent serious bacterial infections *Microbiol Immunol.* 2013;57(7):527-35. doi:10.1111/1348-0421.12060.

**16.** Hauser SL, Bar-Or A, Comi G, Giovannoni G, OPERA I and OPERA II Clinical Investigators. Ocrelizumab versus Interferon Beta-1a in Relapsing Multiple Sclerosis. *N Engl J Med.* 2017;19;376(3):221-234. doi:10.1056/NEJMoa1601277.

**17.** Chinen J, Shearer WT. Secondary immunodeficiencies, including HIV infection. *J Allergy Clin Immunol.* 2010 Feb;125(2 Suppl 2):S195-203. doi: 10.1016/j.jaci.2009.08.040.

**18.** Jakimovski D, Weinstock-Guttman B, Ramanathan M, et al. Infections, vaccines and autoimmunity: a multiple sclerosis perspective. *Vaccines (Basel).* 2020;28;8(1):50. doi: 10.3390/vaccines8010050.

**19.** Jeseňák M, Urbančíková I, et al. Očkovanie v špeciálnych situáciách. Praha: Mladá Fronta 2019. 478 ss.

**20.** Jolles S, Michallet M, Agostini C, et al. Treating secondary antibody deficiency in patients with haematological malignancy: European expert consensus. *Eur J Haematol.* 2021;106(4):439-449. doi:10.1111/ejh.13580.

**21.** 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. doi:10.1177/13524585231204121.

**22.** Lebrun Ch, Vukusic S. Immunization and multiple sclerosis: Recommendations from the French multiple sclerosis society. *Mult Scler Relat Disord.* 2019;31:173-188. doi: 10.1016/j.msard.2019.04.004.

**23.** Metze Ch, 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. doi: 10.1111/cns.13034.

**24.** Oscier D, Dearden C, Eren E, et al. Guidelines on the diagnosis, investigation and management of chronic lymphocytic leukaemia. British Committee for Standards in Haematology. *Br J Haematol.* 2012;159(5):541-64. doi:10.1111/bjh.12067.

**25.** Oreja-Guevara C, Wiendl H, Kieseier BC, et al. NeuroNet Study Group. Specific aspects of modern life for people with multiple sclerosis: considerations for the practitioner. *Ther Adv Neurol Disord.* 2014;7(2):137-49. doi:10.1177/1756285613501575.

**26.** Otero-Romero S, Lebrun-Frénay Ch, 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. *Multiple Sclerosis Journal.* 2023;29(8):904-925.

**27.** Papeix C, Mazoyer J, Maillart E, et al. Multiple sclerosis: Is there a risk of worsening after yellow fever vaccination? *Mult Scler.* 2021 Dec;27(14):2280-2283. doi: 10.1177/13524585211006372. Epub 2021 Apr 19.

**28.** Papp KA, Haraoui B, Kumar D, et al. Vaccination guidelines for patients with immune-mediated disorders on immunosuppressive therapies. *J Cutan Med Surg.* 2019;23(1):50-74. doi: 10.1177/1203475418811335.

**29.** Patel SY, Carbone J, Jolles S. The expanding field of secondary antibody deficiency: causes, diagnosis, and management. *Front Immunol.* 2019;10.33. doi. 10.3389/fimmu.2019.00033. eCollection 2019.

**30.** Perez E, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: A review of evidence. *J Allergy Clin Immunol.* 2017;139(3S):S1-46. doi: 10.1016/j.jaci.2016.09.023.

**31.** Perez E, Bokszczanin A, McDonald-McGinn D, et al. Safety of live viral vaccines in patients with chromosome 22q11.2 deletion syndrome (DiGeorge syndrome/ velocardiofacial syndrome). *Pediatrics.* 2003;112(4):e325. doi:10.1542/peds.112.4.e325.

**32.** Pikor N, Gommerman JL. B cells in MS: Why, where and how? *Mult Scler Relat Dis.* 2012;1(3):123-30. doi:10.1016/j.msard.2012.03.006.

**33.** Principi N, Esposito S. Vaccine use in primary immunodeficiency disorders. *Vaccine.* 2014;32(30):3725-31. doi:10.1016/j.vaccine.2014.05.022.

**34.** Rapisarda L, Valentino P, Barone S, et al. Varicella zoster immunity loss in multiple sclerosis patient treated with ocrelizumab. *Clin Immunol.* 2021;223:108554. doi: 10.1016/j.clim.2020.108554.

**35.** Súhrn charakteristických vlastností lieku Gilenya, Tecfidera, Lemtrada, Aubagio, Tysabri, Ocrevus, Kesimpta. Dostupné na: www.sukl.sk.

**36.** Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplant recipients: a global perspective. Preface. *Bone Marrow Transplant.* 2009;44(8):453-455. doi:10.1038/bmt.2009.254.

**37.** Tuano KS. Seth N, Chinen J. Secondary immunodeficiencies: An overview. *Ann Allergy Asthma Immunol.* 2021;127(6):617-626. doi:10.1016/j.anai.2021.08.413.

**38.** Van Langelaar J, Rijvers L, Janssen M, et al. Induction of brain-infiltrating T-bet-expressing B cells in multiple sclerosis. Ann Neurol. 2019;86(2):264-278. doi:10.1002/ana.25508.

**39.** Williamson EML, Chahin S, Berger JR. Vaccines in Multiple Sclerosis. *Curr Neurol Neurosci Rep.* 2016;16(4):36. doi:10.1007/s11910-016-0637-6.

**40.** Zrzavy T, Kollaritsch H, Rommer PS. Vaccination in Multiple Sclerosis: Friend or Foe? *Front Immunol.* 2019;10:1883. doi:10.3389/fimmu.2019.01883. eCollection 2019.