MS & VZV VACCINATION

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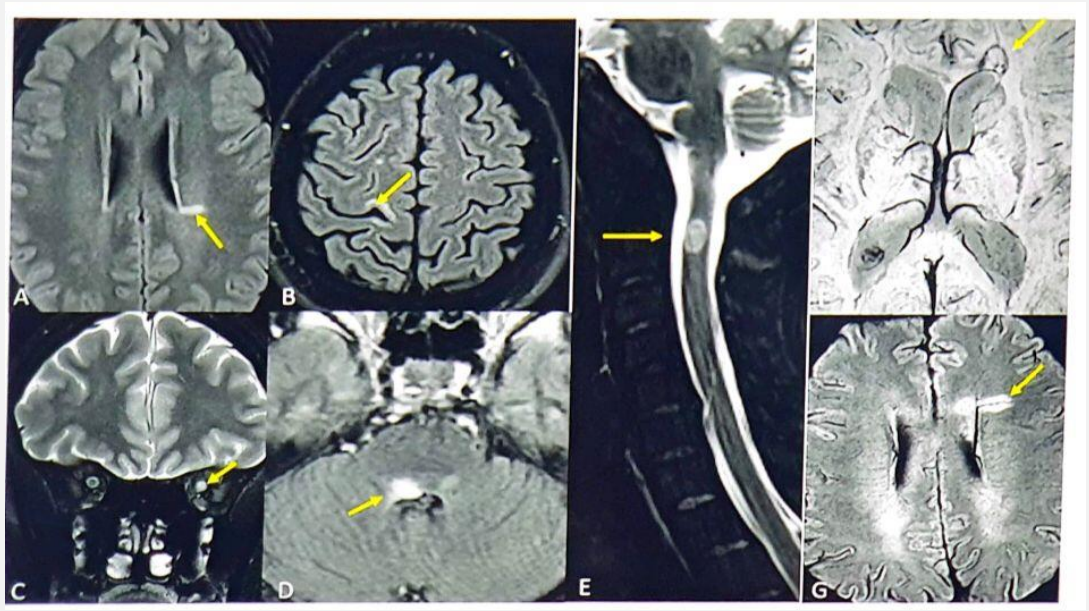
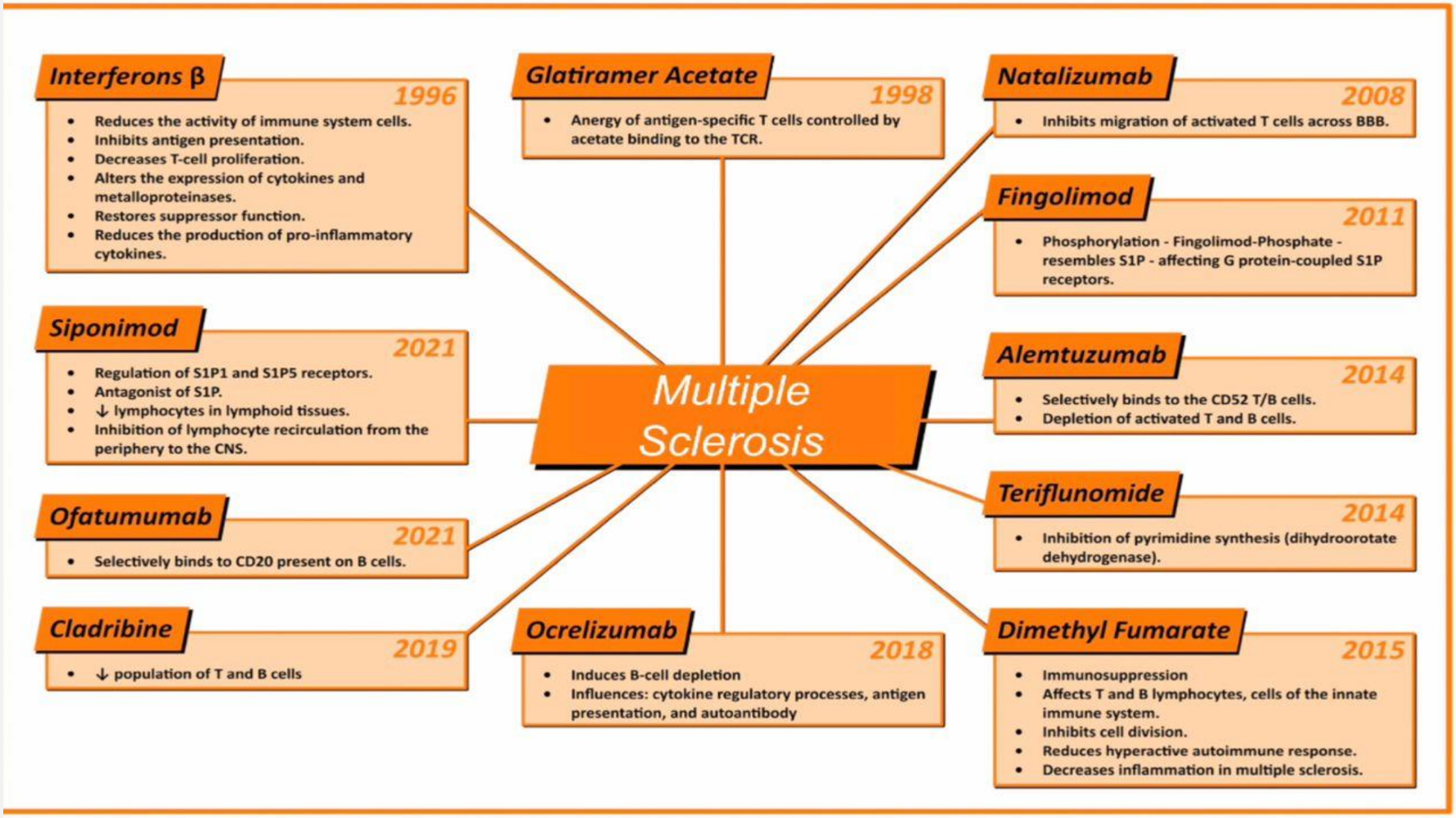
DISCLOSURES

- Have received support for scientific meetings and honorariums for Advisory Board from Cinnagen, Merck , Roche, Nano Alvand, Cobel (Dr.Abidi), Zahravi, Zist Daru Danesh, Actoverco ,MSD

Multiple Sclerosis

- **Most common *chronic inflammatory, demyelinating CNS-disease* in young adults (age of onset 20-40y).**
- **Etiology unclear:** Multifactorial, immune-mediated disease influenced by genetic and environmental factors.
- **Pathologic hallmark: focal plaques:** areas of demyelination typically around postcapillary venules




Multiple Sclerosis
Interferons β
1996
Reduces the activity of immune system cells.
Inhibits antigen presentation.
Decreases T-cell proliferation.
Alters the expression of cytokines and metalloproteinases.
Restores suppressor function.
Reduces the production of pro-inflammatory cytokines.
Glatiramer Acetate
1998
Anergy of antigen-specific T cells controlled by acetate binding to the TCR.
Natalizumab
2008
Inhibits migration of activated T cells across BBB.
Fingolimod
2011
Phosphorylation - Fingolimod-Phosphate - resembles S1P - affecting G protein-coupled S1P receptors.
Siponimod
2021
Regulation of S1P1 and S1P5 receptors.
Antagonist of S1P.
↓ lymphocytes in lymphoid tissues.
Inhibition of lymphocyte recirculation from the periphery to the CNS.
Alemtuzumab
2014
Selectively binds to the CD52 T/B cells.
Depletion of activated T and B cells.
Ofatumumab
2021
Selectively binds to CD20 present on B cells.
Teriflunomide
2014
Inhibition of pyrimidine synthesis (dihydroorotate dehydrogenase).
Cladribine
2019
↓ population of T and B cells
Ocrelizumab
2018
Induces B-cell depletion
Influences: cytokine regulatory processes, antigen presentation, and autoantibody
Dimethyl Fumarate
2015
Immunosuppression
Affects T and B lymphocytes, cells of the innate immune system.
Inhibits cell division.
Reduces hyperactive autoimmune response.
Decreases inflammation in multiple sclerosis.

MS DRUGS (DMT)

- Alemtuzumab (Lemtrada)
- Ocrelizumab (Ocrevus), Ofatumumab (Kesimpta), Ublituximab (Briumvi),Rituximab (off label)
- Fingolimod (Gilenya), Ozanimod (Zeposia), Siponimod (Mayzent),Ponesimod (Ponvory)
- Natalizumab (Tysabri)
- Cladribine (Mavenclad)
- Dimethyl fumarate (Tecfidera), Diroximel fumarate (Vumerity), Monomethyl fumarate (Bafiertam)
- Teriflunomide (Aubagio)
- Glatiramer acetate (Copaxone, Glatopa)
- Interferon beta-1a (Avonex, Rebif), Interferon beta-1b (Betaseron) ,Peginterferon beta-1a (Plegridy)
- Mitoxantrone (Novantrone)

Varivax

Live attenuated vaccine

Inactivated vaccines	Injected influenza, cholera, bubonic plague, intramuscular polio (Salk vaccine), hepatitis A, rabies
Toxoid vaccines	Tetanus, diphtheria
Subunit vaccines	Hepatitis B, human papilloma virus, influenza
Conjugate vaccines	Hemophilus influenza type B
Live attenuated vaccines	Intranasal influenza, varicella zoster virus (Zostavax and Varivax), oral polio (Sabin vaccine), yellow fever, measles, rubella, mumps, typhoid, BCG, *Yersinia pestis*

*Vaccination and the Risk of Triggering or Aggravating MS

*Vaccination Efficacy and Safety in Patients on DMTs

*Vaccines to Decrease the Risk of Zoster Reactivation in MS Patients Treated with DMTs

INDICATIONS

1. Routine childhood vaccination : between 12 and 15 months of age,
   second dose between 4 and 6 years of age.
2. Post-exposure prophylaxis within 3 to 5 days after exposure
   70%-100% effective if given within 3 days of exposure (possibly up to 5 days)

3. Catch-up vaccination for older children, adolescents, and adults who haven't had chickenpox or haven't been vaccinated: Minimum interval for children: 3 months
   Minimum interval for adults: 4 weeks

4. for susceptible individuals at high risk for varicella complications,
   such as healthcare workers and immunocompromised patients and their family members
5. 1 dose: 82% against any clinical varicella , 98% against severe disease.
   2 doses: 92% to 95% effectiveness against any clinical varicella.

VARIVAX® Recommendation for Specific Groups

Groups	Eligibility Criteria	Vaccine Timing
Solid Organ Transplantation[1]	• No evidence of immunity against varicella	At least **4 weeks** pre-transplantation
Hematopoietic Stem Cell Transplantation[2]	• No evidence of GVHD • Active bone marrow, • Platelets[4] ≥30–50 × 10^9/L • Normal immune system (lymphocytes > 1000) • After 8-11 months from the last IVIG dose	At least **24 months** after transplantation
Patients with malignancies undergoing chemotherapy or radiotherapy[2]	• In the remission phase of the disease • No evidence of immunity against varicella ➢ CD4+ T-lymphocyte ≥200 or ≥15% in >5 years old ➢ CD4+ T-lymphocyte >500 in 1-5 years old ➢ CD4+ T-lymphocyte >750 in <1 year old or ➢ Lymphocytes >1500 in <6 years old ➢ Lymphocytes >1000 in ≥6 years old	**3-6 months** after chemotherapy
Multiple sclerosis patient[2]	• No evidence of immunity against varicella	**One month** before starting medication
Patients receiving high dose systemic corticosteroids[2]	• No evidence of immunity against varicella • >20 mg/day prednisolone or equivalent and for ≥2 weeks	**2-4 weeks** before starting the medication or **One month** after stopping the medication.
Immunosuppressive drug recipients[2] including: Interleukin inhibitors TNF-alpha inhibitors Anti B-cell (Rituximab)*	• No evidence of immunity against varicella	At least **4 weeks** before starting the medication or At least **3 months** after discontinuing medication *At least **6 months** after stopping Anti B-cell
Patients with HIV infection[2,3]	• At least 6 months without severe immunodeficiency • No evidence of immunity against varicella • Children ≥12 months old with CD4+ T-lymphocyte percentages ≥15% • People >8 years old with CD4+ T-lymphocyte counts ≥200 cells/µL	2 doses separated by **3 months**
Household contacts of immunocompromised people[2]	• No evidence of immunity against varicella	As per standard vaccination schedule

IMMUNITY

Varivax triggers both humoral and cell-mediated immune responses:

- ***Humoral Response:***

Stimulates the production of IgG antibodies specific to the varicella-zoster virus, which helps neutralize the virus if the individual is exposed in the future

- ***Cell-Mediated Response:***

Activates T-lymphocytes (both CD4+ T-helper and CD8+ cytotoxic T-cells), which play a crucial role in recognizing and eliminating infected cells

VACCINES AND MULTIPLE SCLEROSIS: A PRACTICAL GUIDE I

- **Screening for past exposure and antibody titers against VZV** are recommended prior to initiation of treatment with immunosuppressive agents
- In those who **have no history of prior chickenpox and are VZV antibody negative, Varivax is recommended** to be administered by two doses at least 4 weeks apart specially before starting S1P receptor modulator drugs ,alemtuzumab ,mavenclad ,and anti CD 20 drugs.
- Vaccines to **decrease the Risk of Zoster Reactivation** in MS Patients Treated with DMTs.

- Administer all immunizations according to immunization guidelines at least 4 weeks prior to initiation of **Ocrevus , Kesimpta,or other anti CD20 drugs** and also before starting S1P receptor modulator drugs (**Gilenya, Zeposia , Mayzent)**
- Administer live-attenuated vaccines at least 4 to 6 weeks prior to starting **Mavenclad** because of a risk of active vaccine infection.
- Required vaccinations should be given 6 weeks before initiating **alemtuzumab** to ensure an adequate immunological response before lymphocyte depletion.
- **Live attenuated vaccines** should be consider at least **6 months** following therapy with **anti-B cell antibodies**.

DMT	Mechanism of Action	Vaccines That Are Avoided	Recommended Vaccines Prior to Drug Initiation	Wait Period from Recommended Vaccine Administration
Alemtuzumab	Recombinant humanized monoclonal antibody to CD52	Live attenuated, including live SARS-CoV-2 vaccine during depletion phase	VZV (necessary); HPV (optional)	At least 6 weeks
Cladribine	Deoxyadenosine purine analogue	Live attenuated, including live SARS-CoV-2 vaccine during depletion phase	VZV (necessary)	4–6 weeks
Dimethyl fumarate	Activation of Nrf2 transcriptional pathways	Live attenuated	-	-
Fingolimod	Sphingosine 1-phosphate receptor modulator	Live attenuated, including live SARS-CoV-2 vaccine during depletion phase	VZV (necessary); HPV (optional)	4 weeks after vaccination for VZV
Glatiramer acetate	Immunomodulator, analogue of MBP	-	-	-
Interferons	Immunomodulator, antiviral and immunoregulatory activities	-	-	-
Natalizumab	Recombinant humanized monoclonal antibody to integrin VLA-4	Live attenuated	-	-
Ocrelizumab	Recombinant humanized monoclonal antibody against CD20	Live attenuated, including live SARS-CoV-2 vaccine during depletion phase	-	-
Teriflunomide	Inhibition of DHODH (de novo pyrimidine synthesis)	Live attenuated	-	-

VACCINES AND MULTIPLE SCLEROSIS: A PRACTICAL GUIDE 2

- Vaccination with live attenuated vaccines is generally not recommended in patients with MS (PwMS) treated with natalizumab.

  A total of 89 MS patients participated in this study , received two doses of the live-attenuated VZV vaccine with an interval of at least one month.
  None of the patients developed serious adverse events. In addition, over a mean follow-up of 1.63 ± 0.43 years, no evidence of disease activity or progression was observed.

  Conclusion: Our preliminary findings suggest the safety of live-attenuated VZV vaccine in highly selective PwMS treated with natalizumab highlighting an individualized approach in particular circumstances.

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Is it time to consider the live attenuated varicella-zoster virus (VZV) vaccination safe in patients with multiple sclerosis treated with natalizumab? An extension study of the first Iranian experience

Sepideh Paybast et al. Mult Scler Relat Disord. 2025 Mar.

Recommended vaccines for those on corticosteroid therapy

- ≥1 month after completion of high dose (≥2 mg/kg or ≥20 mg daily) oral corticosteroid therapy ≥14 days duration.
- Initiating immunosuppressive therapy or DMTs , providers should wait 4 weeks after a live vaccine and 2 weeks after a non-live vaccine.
- **Not a contraindication**: short term (i.e., <14 days); a low to moderate dose (i.e., <20 mg of prednisone or equivalent per day ,long-term, alternate-day treatment with short-acting preparations; maintenance physiologic doses (replacement therapy); topical (skin or eyes), inhaled, or by intra-articular, bursal, or tendon injection.

SHINGLES VACCINES

- *Currently there are two types of **shingles vaccines** in the US that are recommended*
- *for adults aged 60 and above, regardless of previous infection:* ***live-attenuated (Zostavax; licensed at 2006, given as a single subcutaneous injection) and non-live recombinant (Shingrix; licensed at 2017, given as intramuscular injections, 2 doses separated by 2–6 months apart) .***
- *The Advisory committee on immunization practices (ACIP) currently recommends the **Shingrix as the preferred vaccine for shingles prevention.***

- Shingles vaccination is the only way to protect yourself against this painful disease.
- Vaccination is over 90% effective at preventing shingles and postherpetic neuralgia in adults 50 years and older with healthy immune systems.
- Adults 19 years and older who have weakened immune systems are at higher risk of complications and should also vaccinated.