Trade name	Reduction in ARR[1]	Mechanism of Action	Dosing	Side effects	REMS[2]
Natalizumab (Tysabri)	67%	Natalizumab is a monoclonal antibody that binds to alpha4-integrin which is on all WBC (except neutrophils) and prevents transmigration of leukocytes from the blood into the CNS.	300mg intravenously every 28 days	Herpes encephalitis, meningitis, hepatotoxicity, hypersensitivity, antibody formation, immunosuppression, PML	Check JCV antibody titer every 6 months; if JCV positive, risk for PML goes up from 1:1000 to 1:100 after being on the drug > 2 years; check CBC/CMP every 6 months
dimethyl fumarate (Tecfidera)	53% cf. placebo	DMF and the metabolite, monomethyl fumarate (MMF), have been shown to activate the Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway *in vitro* and *in vivo* in animals and humans. The Nrf2 pathway is involved in the cellular response to oxidative stress.	Titrate up from 120mg po every day to 240mg po twice daily over the course of a month	Anaphylaxis, angioedema, PML, lymphopenia, flushing, gastrointestinal discomfort	Check JCV antibody titer every 6 months, follow lymphocyte count every 3 months for the first year; stop medication if count drops continuously over 1st year or stays below 650 for over 9 months, check CBC/CMP every 6 months
fingolimod (Gilenya)	52% cf. Rebif	Fingolimod is metabolized by sphingosine kinase to the active metabolite, fingolimod-phosphate, which blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood.	0.5mg po every day	Bradyarrhythmia, atrioventricular blocks, HSV, VZV, PML, cryptococci, atypical mycobacteria, HHV-8 (Kaposi's sarcoma) PML, macular edema, PRES, basal cell carcinoma, increased blood pressure	Before starting check JCV antibody titer, VZV antibody titer (immunize if negative), ophthalmologist evaluation for macular edema

Trade name	Reduction in ARR[1]	Mechanism of Action	Dosing	Side effects	REMS[2]
daclizumab (Zinbryta)	49% cf. Rebif	An antibody that binds the alpha chain of the interleukin-2 receptor which decreases the activation of lymphocytes.	150mg/ml prefilled syringe every month; indicated for use after failing two other medications	Auto-immune hepatitis, skin reactions, lymphadenopathy, colitis and others	Baseline LFTs; check LFTs every month; stop if AST/ALT>5x ULN or Total bilirubin >2x ULN or AST/ALT > 3xULN & total bilirubin > 1.5 but <2x ULN
alemtuzumab (Lemtrada)	49% cf. Rebif	Binds to CD52, a cell surface antigen present on T and B lymphocytes, and on natural killer cells, monocytes, and macrophages. Following binding to T and B lymphocytes, alemtuzumab results in antibody-dependent cellular cytolysis and complement-mediated lysis	12 mg/day on 5 consecutive days (60 mg total dose) then 12 mg/day on 3 consecutive days (36 mg total dose) administered 12 months after the first treatment course; indicated for use after failing two other medications	Immune thrombocytopenia and anti-glomerular basement membrane disease, life-threatening infusion reactions, risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams	Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine cell counts at periodic intervals for 48 months after the last dose; monitor patients for two hours after each infusion; Make patients aware that serious infusion reactions can also occur after the 2-hour monitoring period; perform baseline and yearly skin exams
teriflunomide (Aubagio)	33%	Inhibits dihydroorotate dehydrogenase, a mitochondrial enzyme involved in de novo pyrimidine synthesis leading to a decreased number of activated lymphocytes in the CNS.	7mg or 14mg po every day	Hepatotoxicity, birth defects, peripheral neuropathy, renal failure, hyperkalemia, skin reactions, elevated blood pressure, interstitial lung disease	Screen patients for latent tuberculosis infection with a tuberculin skin test; check LFTs before starting and every month for 6 months and then every 6 months

Trade name	Reduction in ARR[1]	Mechanism of Action	Dosing	Side effects	REMS[2]
pegylated B-interferon 1a (Plegridy)	36% cf. placebo	Interferon beta balances the expression of pro- and anti-inflammatory agents in the brain, and reduces the number of inflammatory cells that cross the blood brain barrier. Overall, therapy with interferon beta leads to a reduction of neuron inflammation. Moreover, it is also thought to increase the production of nerve growth factor and consequently improve neuronal survival. In vitro, interferon beta reduces production of Th17 cells which are a subset of T lymphocytes believed to have a role in the pathophysiology of MS.	125 mcg single dose prefilled syringe, subcutaneously every 14 days	Injection site erythema, influenza-like illness, pyrexia, headache, myalgia, chills, injection site pain, asthenia, injection site pruritus, and arthralgia, elevated liver function tests.	Dose should be titrated up, starting with 63 micrograms on day 1, 94 micrograms on day 15, and 125 micrograms (full dose) on day 29
B-interferon 1a (Rebif)	32% cf. placebo		22 or 44 µgm subcutaneously three times per week		Follow complete blood count and comprehensive metabolic profile every 6 months
B-interferon 1a (Avonex)	32% cf. placebo		30 µgm IM every week		
B-interferon 1b (Betaseron/ Extavia)			0.0625mg subcutaneously, every other day x 2 weeks titrated up by 0.065mg every two weeks to 0.25mg.		

Trade name	Reduction in ARR[1]	Mechanism of Action	Dosing	Side effects	REMS[2]
glatiramer acetate (Copaxone/ Glatopa)	30% cf. placebo	Glatiramer acetate-specific suppressor T-cells are induced and activated in the periphery to decrease the immune attack on CNS myelin.	40mg subcutaneously three times per week	Injection site erythema, influenza-like illness, pyrexia, headache, myalgia, chills, injection site pain, asthenia, injection site pruritus, and arthralgia, elevated liver function tests, skin breakdown	Follow complete blood count and comprehensive metabolic profile every 6 months; monitor for skin breakdown

1. Annualized relapse rate
2. Risk Evaluation and Mitigation Strategy

- The medications that have a black box around them have a BLACK BOX WARNING in their package insert.