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CORRECTION

Correction to: The sequence of disease-modifying therapies in relapsing multiple sclerosis: safety and immunologic considerations

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Unfortunately, the online published article has errors in Table 2. The Peginterferon is listed as IM, when it should be SC.

The correct table (Table 2) is given in the following page.

The online version of the original article can be found under doi:10.1007/s00415-017-8594-9.

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Table 2 Mechanism of action and effects on the immune system of DMTs for RMS

DMT	Molecular mode of action	Effect on immune cells and mediators	Time taken for immune system reconstitution after DMT cessation
SC IFN beta-1b (Betaseron; Extavia) IM IFN beta-1a (Avonex) SC IFN beta-1a (Rebif) SC peginterferon beta-1a (Plegridy)	Exert autocrine and paracrine actions via activation of the IFN receptor on leucocytes	Reduces inflammatory cell migration across the blood–brain barrier, reduces the production of proinflammatory cytokines, and induces anti-inflammatory cytokines [18]	Effects on the immune system endure for five times the serum elimination half-life (i.e., 40 min to 21.5 h for SC IFN beta-1b [134], 95 h for IM IFN beta-1a [135], 345 h for SC IFN beta-1a [136], and 390 h for SC peginterferon beta-1a) [137]
Glatiramer acetate (Copaxone)	MBP mimetic; thus competes with MBP antigens to bind with MHC II [58]	Protects neurons by diverting T cell responses away from myelin in a dose-dependent manner. Increases production of anti-inflammatory cytokines and reduces the production of proinflammatory cytokines [18]	Effects on the immune system endure for five times the elimination half-life [138]
Dimethyl fumarate (Tecfidera)	Activates the nuclear factor (erythroid-derived 2)-like 2 pathway to protect against oxidative stress–induced cellular injury and loss in neurons and astrocytes [61]	Mean absolute lymphocyte count decreased by 30% during the first year then remained stable above the lower limit of normal (i.e., 0.91×10^9/L) [63] 6% of patients had lymphocyte counts $<0.5 \times 10^9$/L [67] Effective immune response to recall antigens, neoantigens, and T cell-independent antigens similarly to nonpegylated IFN therapy [143]	>4 weeks for lymphocyte counts to increase, but did not return to baseline values [67]
Teriflunomide (Aubagio)	Inhibits proliferation of activated T and B lymphocytes via mitochondrial dihydroorotate dehydrogenase inhibition [144]	Reduces neutrophils and lymphocytes by 15%, with mean counts remaining in the normal range [71] 16% and 12% of patients had neutrophil and lymphocyte counts $<1.5 \times 10^9$ and $<0.8 \times 10^9$/L with 14 mg dose, respectively [72] Effective immune response to H1N1, H3N2, and B influenza strains [145]	Unknown; reduced white blood cell counts of 15% may be related to bone marrow suppression [72]
Fingolimod (Gilenya)	Binds the sphingosine-1-phospate receptor, blocking lymphocyte egress from lymph nodes [146, 147]	Dose-dependent reduction in peripheral lymphocyte count to 20–30% of baseline values [13] Lymphopenia incidence was 7% in placebo-controlled trials [13] Attenuated response to influenza vaccine in some patients [148]	≤2 months to return to normal range [13]; average lymphocyte counts were 80% of baseline values after 3 months [149]
Daclizumab beta (Zinbryta)[a]	Humanized monoclonal antibody that selectively blocks high-affinity IL-2 receptor formation on activated T cells. Modulation of the IL-2 signal leads to selective antagonism of activated T cell responses and expansion of immunoregulatory $CD56^{bright}$ NK cells [81, 87]	Fivefold expansion in $CD56^{bright}$ NK cells at 1 year. Total lymphocyte, $CD4^+$ and $CD8^+$ T cell, and B cell counts decrease ≤10% from baseline during the first year of treatment [81, 82, 92] Effective immune responses to influenza vaccine [150]	Pharmacodynamics are related to the half-life of daclizumab beta (21 days) and are reversible [55, 81, 82] Total lymphocyte counts return to baseline levels ~8–12 weeks after the last dose [81, 82] Treg and $CD56^{bright}$ NK cell numbers return to baseline levels within 24 weeks [81, 93, 95]

Table 2 (continued)

DMT	Molecular mode of action	Effect on immune cells and mediators	Time taken for immune system reconstitution after DMT cessation
Alemtuzumab (Lemtrada)	Targets CD52 on lymphocytes and monocytes. It readily depletes B cells, T cells, monocytes, macrophages, and dendritic cells, leading to long-lasting changes in adaptive immunity, and reduces the pathogenesis of inflammatory response in MS [99]	Decrease in the level of circulating T and B lymphocytes very rapidly, with the lowest values observed within days posttreatment [99]	Lymphocytes repopulate within 8 months, but T cell populations take >1 year to fully repopulate [100, 101] T cell populations do not recover to baseline levels [101]
Natalizumab (Tysabri)	Monoclonal antibody that selectively inhibits VLA-4 (α4β1) integrins, preventing leukocyte migration across the BBB [58]	Increases the number of circulating leukocytes (including lymphocytes, monocytes, basophils, and eosinophils) [20]. Natalizumab does not affect the absolute count of circulating neutrophils [20] Effective immune responses to recall antigen (tetanus toxoid) and neoantigen (keyhole limpet hemocyanin) [151]	≤16 weeks to return to baseline levels [20]
Ocrelizumab (Ocrevus)	Targets CD20 on B cells through mechanisms that include antibody-dependent cell-mediated cytotoxicity, complement-dependent cytotoxicity, and/or the induction of apoptosis [118, 152]	$CD20^+$ targeted by ocrelizumab include pre-B cells, mature B cells, and memory B cells; lymphoid stem cells and plasma cells are unaffected [119, 152]	Median (range) time to B cell repletion to either baseline or lower limit of normal was 72 weeks (range 27–175 weeks); within 2.5 years after last infusion, B cell counts rose to either baseline or the lower limit of normal in 90% of patients [118]
Mitoxantrone (Novantrone)	Intercalates with DNA, causing strand breaks, and inhibits DNA repair via inhibition of topoisomerase II, leading to cytotoxicity [153]	Reduction of leukocytes primarily affecting neutrophils and most lymphocyte subsets except for naive and activated T lymphocytes [154]	Unknown

BBB blood–brain barrier, *DMT* disease-modifying therapy, *IFN* interferon, *IL-2* interleukin 2, *IM*, intramuscular, *MBP* myelin basic protein, *MHC II* class II major histocompatibility complex, *MS* multiple sclerosis, *NK* natural killer, *RMS* relapsing forms of multiple sclerosis, *SC*, subcutaneous, *Treg* regulatory T cell, *VLA-4* very late activation antigen 4

[a]Formerly daclizumab high-yield process (approved as ZINBRYTA®), which has a different form and structure than an earlier form of daclizumab