



CORRECTION

Correction to: Vaccine Considerations for Multiple Sclerosis in the COVID-19 Era

Patricia K. Coyle · Anne Gocke · Megan Vignos  · Scott D. Newsome

Published online: November 18, 2021
© Springer Healthcare Ltd., part of Springer Nature 2021

Correction to: Adv Ther (2021) 38:3550–3588
<https://doi.org/10.1007/s12325-021-01761-3>

The original article was published with an error regarding response to vaccination with

ozanimod on page 3561 and in Table 4. The correct sentence and Table 4 are given below

The few data available for other S1P receptor modulators suggest there can be some negative impact on vaccine response (145).

The original article can be found online at <https://doi.org/10.1007/s12325-021-01761-3>.

P. K. Coyle
Department of Neurology, Stony Brook University
Medical Center, Stony Brook, NY, USA

A. Gocke · M. Vignos
Biogen, Cambridge, MA, USA

S. D. Newsome
Johns Hopkins University School of Medicine,
Baltimore, MD, USA

M. Vignos (✉)
US Medical MS Franchise and Interferons, Biogen,
133 Boston Post Rd, Weston, MA 20493, USA
e-mail: megan.vignos@biogen.com

Table 4 Studies on effect of DMTs on response to vaccination

DMT	Study groups ^a	Vaccine
IFN	IFN beta-1b (Betascron [®])	2011/2012 influenza
	IFN beta-1b (Extavia [®])	2010/2011 and 2011/2012 influenza
	IFN beta-1a SC (Rebif [®])	2008/2009 and 2009/2010 influenza
	IFN beta-1a IM (Avonex [®])	2002/2003 influenza
	PegIFN beta-1a (Plegridy [®])	2009 swine flu (H1N1)
		2010 influenza
		2012/2013 influenza
		TT-containing
		Pneumococcal polysaccharide
		Meningococcal
		Tick-borne encephalitis
		TT
		Influenza
		Recombinant vaccinia viruses followed by fowlpox virus recombinants at 2-week intervals

Table 4 continued

DMT	Study groups ^a	Vaccine
Glatiramer acetates		
Copaxone®	Glatiramer acetate, <i>n</i> = 37 HCs, <i>n</i> = 216	2009 swine flu (H1N1)
	Glatiramer acetate, <i>n</i> = 12 HCs, <i>n</i> = 73	2010 influenza
	Glatiramer acetate, <i>n</i> = 23 HCs, <i>n</i> = 53	2012/2013 influenza
	Glatiramer acetate, <i>n</i> = 26 Glatiramer acetate, <i>n</i> = 5	2010/2011 and 2011/2012 influenza Tick-borne encephalitis
DHODH inhibitor		
Teriflunomide	Teriflunomide, 7 mg, <i>n</i> = 41 14 mg, <i>n</i> = 41	2011/2012 influenza
	Teriflunomide, <i>n</i> = 23 HCs placebo, <i>n</i> = 23	Rabies

Table 4 continued

DMT	Study groups ^a	Vaccine
SIP receptor modulators	Fingolimod	2008/2009 and 2009/2010 influenza
	Fingolimod, <i>n</i> = 14	
	HCs, <i>n</i> = 18	
	Fingolimod, <i>n</i> = 95	2010/2011 influenza
	Placebo, <i>n</i> = 43	TT booster (recall antigen)
	Fingolimod, <i>n</i> = 10	Influenza
	IFN beta, <i>n</i> = 10	
	HCs, <i>n</i> = 15	
	Fingolimod, <i>n</i> = 6	2010/2011 and 2011/2012 influenza
	Fingolimod, <i>n</i> = 15	2012/2013 influenza
	HCs, <i>n</i> = 53	
	Fingolimod, <i>n</i> = 11	VZV
	Fingolimod, <i>n</i> = 2	Tick-borne encephalitis
	Fingolimod, <i>n</i> = 48	KLH
HCs placebo, <i>n</i> = 24	Pneumococcal polysaccharide (PPV-23)	
	TT	
	Fingolimod, 1 patient with MS and childhood history of chicken pox [case report]	VZV
	Fingolimod, 1 patient with MS and chicken pox as a child [case report]	VZV (shingles vaccine 6 months before initiating fingolimod)
	Fingolimod	BCG
	Mouse model	
	Fingolimod	Ovalbumin plus CpG oligodeoxynucleotide adjuvant; priming via nasal route
	Mouse model	
	Fingolimod	Influenza A
	Mouse model	Treated with fingolimod before and during <i>M. tuberculosis</i> challenge
Siponimod	Siponimod, <i>n</i> = 90 across 3 groups of HCs	Pneumococcal polysaccharide (PPV-23)
	Placebo, <i>n</i> = 30	Influenza

Table 4 continued

DMT	Study groups ^a	Vaccine
Fumarates		
Dimethyl fumarate (DMF)	DMF, <i>n</i> = 38	TT-containing
	Nonpegylated IFN, <i>n</i> = 33	Pneumococcal polysaccharide Meningococcal
High-efficacy DMTs		
Anti-VLA4		
Natalizumab	Natalizumab, <i>n</i> = 30	TT
	Natalizumab, <i>n</i> = 17	Neoantigen (KLH)
	HCs, <i>n</i> = 10	Influenza A H1N1/A-H3N2/B)
	Natalizumab, <i>n</i> = 17	
	HCs, <i>n</i> = 216	2009 swine flu (H1N1)
	Natalizumab, <i>n</i> = 8	2010 influenza (including H1N1, H3N2, and B strains)
	HCs, <i>n</i> = 73	
	Natalizumab, <i>n</i> = 12	2012/2013 influenza
	HCs, <i>n</i> = 53	
	Natalizumab, <i>n</i> = 14	2010/2011 and 2011/2012 influenza
Anti-CD20		
Ocrelizumab	Ocrelizumab, <i>n</i> = 68 [patients with MS]	TT
	HCs, <i>n</i> = 34	Pneumococcal KLH Influenza VZV
	Patient with MS who received VZV vaccine 4 months before first dose of ocrelizumab [case report], <i>n</i> = 1	
Anti-CD52		
Alemtuzumab	Alemtuzumab, <i>n</i> = 24	Pneumococcal polysaccharide Diphtheria, TT, and poliomyelitis HiB and meningococcal group C

Table 4 continued

Study groups ^a		Vaccine
DNA synthesis disrupter		
Mitoxantrone	Mitoxantrone, <i>n</i> = 11 HCs, <i>n</i> = 216	2009 swine flu
Mitoxantrone	Mitoxantrone, <i>n</i> = 4 HCs, <i>n</i> = 73	2010 influenza
DMT	Outcome	AEs
IFN		
IFN beta-1b (Betaseron [®])	> 90% achieved antibody titers \geq 40 for all strains [86]	Injection site pain (<i>n</i> = 3)
IFN beta-1b (Extavia [®])	> 84% seroprotection rate [87]	Flu-like symptoms (<i>n</i> = 4); headache (<i>n</i> = 1); feeling weak (<i>n</i> = 1)
IFN beta-1a SC (Rebif [®])	Comparable frequencies of influenza-specific T cells and concentrations of anti-influenza A and B IgM and IgG [88]	Not studied
IFN beta-1a IM (Avonex [®])	No difference in antibody titer response [89]	Not studied
PegIFN beta-1a (Plegridy [®])	Similar protection rates [90]	7.9% and 7.8% MS exacerbations with 2009 and 2010 vaccine
	Comparable protection rates against H1N1 at 3, 6, and 12 months [130]	Not studied
	Similar antibody responses [85]	Vaccination-emergent AEs in 55%, nonpegylated IFN; 42%, DMF
	Increased antibody titers in 9 [131]	Local side effects (pain, induration) but DMT not specified
	Reduced IFN-gamma and IL-4 responses to TT; no change in TT-induced CD4 + T-cell proliferation [91]	Not studied
	Th1 type of immune response and protection against virus challenge [132]	Not applicable
	Robust anti-HA CD8 + T-cell response [133]	Not applicable
Glatiramer acetates		
Copaxone [®]	Reduced response in glatiramer acetate group (21.6% vs 43.5%) [90]	Not studied
	Reduced response in glatiramer acetate group (58.3% vs 71.2% H1N1; 41.7% vs 79.5% H3N2) [90]	Not studied
	Similar protection rates against H1N1 at 3, 6, and 12 months [130]	Not studied
	> 73.1% seroprotection rate to 3 different strains [87]	Flu-like symptoms (<i>n</i> = 3); temperature increase (<i>n</i> = 2); nightly sweating (<i>n</i> = 1)
	3 had protective titers before vaccination and developed 2- to 9.6-fold increases in antibody titers [131]	Local side effects (pain, induration); DMT not specified

Table 4 continued

DMT	Outcome	AEs
DHODH inhibitor		
Teriflunomide	> 70% achieved antibody titers ≥ 40 for all strains; seroprotection to H3N2 was lower with 14 mg dose [86] Lower antibody titers in teriflunomide group; no adverse impact on recall antigen response [134]	Injection site pain, $n = 1$ in each group Treatment-emergent AEs: teriflunomide, 17.4%; placebo, 30.4%
S1P receptor modulators		
Fingolimod	Cellular and humoral immune responses similar to controls [135] Fingolimod group had lower immune responses [136] Fingolimod group had no increases in avidity (binding) of influenza-specific IgG vs IFN beta or control [137] Low protective antibody titers to H3N2 [87] Lower protection rates were seen in fingolimod group at 3, 6, and 12 months [130] 7/11 patients had lower IgG-VZV antibody titers 2.4 years after starting fingolimod [138] Lowest increase in antibody titer compared with other DMTs [131] Mild to moderate decreases in anti-KLH and anti-PPV-23 IgG and IgM levels, indicating mild to moderate decrease in humoral and cellular immune responses to neoantigens; no effect on recall antigen (TT) response [139] Response to vaccination diminished [140] Developed VZV encephalitis after 6 months of fingolimod and 5 days of high-dose systemic corticosteroids [141] Reduced protection against TB infection; administration during infectious challenge did not. Suggests memory T lymphocytes that migrate to the lung following vaccination are sufficient for protection [142] Greater buildup of more extensively divided T cells within draining lymph nodes; in distal lymph nodes percentage of divided transgenic cells was mostly reduced [143] Protected against TB by CD4 + memory T cells [144]	Not studied No new safety or tolerability signals Comparable tolerability across groups Exanthema, $n = 2$ Not studied 3/7 patients stopped treatment due to an AE Local side effects (pain, induration) but DMT not specified Most common AEs: headache, injection site pain, and dizziness, which occurred across all treatment groups Patient infected daughter with chicken pox and had 2 bouts of shingles Not applicable Not applicable Not applicable Not applicable Not applicable Similar incidence of AEs between siponimod and placebo
Siponimod	No effect on PPV-23 antibody response. Response criteria were also met for influenza, but lower titers at time of vaccination [145]	

Table 4 continued

DMT	Outcome	AEs
Fumarates		
Dimethyl fumarate (DMF)	Concomitant exposure to DMF did not diminish antibody responses versus antibody responses in patients treated with nonpegylated IFN [85]	Vaccination-emergent AEs occurred in 42% with DMF and in 55% with nonpegylated IFN
High-efficacy DMTs		
Anti-VLA4		
Natalizumab	Protective levels of anti-TT IgG antibodies achieved and demonstrated primary immunization responses to a neoantigen [147]	No unexpected events observed
	Significant increases in anti-influenza B IgG following influenza A and B vaccination; humoral response was comparable to HCs [148]	Not studied
	Reduced (23.5%) response compared with HCs (43.5%) [90]	Not studied
	H1N1 protection: natalizumab, 75.0%; controls, 71.2%	Not studied
	H3N2 protection: natalizumab, 50.0%; controls, 79.5% [90]	
	Note: limited sample size and no adjustment for disease factors	
	Reduced response at 3 and 6 months post vaccination; comparable response to HCs at 12 months [130]	Not studied
	Low response rates (14.3% seroprotection, all strains) [87]	Not studied
	Note: small sample size is a limitation of this study	
Anti-CD20		
Ocrelizumab	Reduced response compared with controls [149]	No new safety signals
	VZV IgG negative 5 months later; remained VZV IgG negative despite additional varicella vaccination [150]	Not applicable
Anti-CD52		
Alemtuzumab	Humoral response was normal, but when vaccination occurred \leq 6 months after treatment, smaller proportions responded (2/5 vs 12/15 vaccinated $>$ 6 months after alemtuzumab) [151]	Not studied
DNA synthesis disrupter		

Table 4 continued

DMT	Outcome	AEs
Mitoxantrone	Those treated with mitoxantrone failed to respond (unprotected) [90]; 1 patient treated with mitoxantrone was protected against H1N1 and 1 against H3N2 [90]	Not studied

AE adverse event, *BCG* Bacillus Calmette–Guérin, *DHODH* dihydroorotate dehydrogenase, *DMF* dimethyl fumarate, *DMT* disease-modifying therapy, *HA*-hemagglutinin, *HC* healthy control, *H5B* *Haemophilus influenzae* type b, *HPIV* human papillomavirus, *IFN* interferon, *Ig* immunoglobulin, *IM* intramuscular; *KLH* keyhole limpet hemocyanin, *MS* multiple sclerosis, *PPV* pneumococcal polysaccharide vaccine, *SIP* sphingosine-1-phosphate, *SC* subcutaneous, *TB* tuberculous, *TT* tetanus toxoid, *VZV* varicella zoster virus

^a Unless indicated otherwise, all study groups are people with MS