

Supplementary Table 1. Embase® and MEDLINE® searches using Embase.com platform (searched on 08 December 2016)

No.	Search terms	Facet
#1	'multiple sclerosis'/exp OR 'multiple sclerosis' OR rrms OR rms OR 'chariot disease' OR 'disseminated sclerosis' OR 'insular sclerosis' OR 'multiple sclerosis, relapsing-remitting' OR 'relapsing remitting multiple sclerosis' OR 'relapsing-remitting multiple sclerosis' OR 'sclerosis multiplex' OR 'sclerosis, disseminated' OR 'sclerosis, insular' OR 'sclerosis, multiple' OR 'optic neuritis'	Disease: Relapsing- remitting multiple sclerosis
#2	drug AND holiday*	Outcomes
#3	drug NEAR/2 holiday*	
#4	discontinuu*	
#5	halt*	
#6	cessat*	
#7	interrupt*	
#8	stop*	
#9	quit*	
#10	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9	
#11	'beta interferon'/exp OR 'beta1 interferon'/exp OR 'beta1a interferon'/exp OR 'interferon beta serine'/exp OR 'recombinant beta interferon'/exp OR interferon NEAR/2 beta OR avonex OR belerofon OR ifn NEAR/2 beta OR ifn?beta OR beta1* NEAR/2 interferon OR betaferon OR rebif OR betaseron OR extavia	Interventions
#12	'glatiramer'/exp OR glatiramer OR copaxone OR co*polymer*1 OR 'copolymer 1' OR 'co polymer 1' OR 'cop 1'	
#13	'natalizumab'/de OR natalizumab OR tysabri OR antegren OR 'anti vla4' OR 'anti-vla 4' OR 'anti alpha4 integrin' OR an100226 OR 'an 100226'	
#14	'fingolimod'/exp OR fingolimod OR fty720 OR 'fty 720' OR gilen?a	
#15	'alemtuzumab'/exp OR alemtuzumab OR campath OR mabcampath OR 'ldp 103' OR ldp103 OR lemtrada	
#16	'fumaric acid dimethyl ester'/exp OR 'bg 00012' OR bg00012 OR 'bg 12' OR 'brn 0774590' OR tecfidera	
#17	'teriflunomide'/exp OR teriflunomide OR 'a 771726' OR 'a77 1726' OR a771726 OR 'hmr 1726' OR hmr1726 OR 'rs 61980' OR rs61980 OR 'su 0020' OR su0020 OR 'aubagio'	
#18	'peginterferon beta1a'/exp OR 'beta 1a peginterferon' OR 'beta1a peginterferon' OR 'biib 017' OR 'biib017' OR 'peginterferon beta 1a' OR 'peginterferon beta-1a' OR 'pegylated human interferon beta 1a' OR 'pegylated interferon beta 1a' OR 'pegylated interferon beta-1a' OR 'pegylated interferon beta1a' OR plegridy	
#19	'Cladribine'/exp OR biodribin OR Cladribine OR 'deoxyadenosine, 2 chloro' OR 'intoce' OR 'leustat' OR 'leustatin' OR 'leustatine' OR 'litak' OR 'litax' OR 'movectro' OR 'mylinax' OR 'rwj 26251' OR 'rwj26251'	
#20	'Ocrelizumab'/exp OR 'monoclonal antibody 2H7' OR 'monoclonal antibody PRO 70769' OR 'monoclonal antibody PRO70769' OR 'pro 70769' OR 'pro70769' OR 'rhumab 2H7'	
#21	'daclizumab'/exp OR dacliximab OR dacluzimab OR zenapax	
#22	'laquinimod'/exp OR 'nerventra' OR 'abr 215062' OR abr215062 OR 'SAIK MS' OR 'tv 5600' OR tv5600	

#23	'mitoxantrone'/syn OR 'cl 232, 315' OR 'cl 232315' OR 'cl232, 315' OR cl232315 OR dhad OR dhaq OR domitrone OR elsep OR formyxan OR misostol OR mitoxanthrone OR mitoxantron* OR mitoxgen OR mitozantrone OR mitroxantrone OR mitroxone OR neotalem OR norexan OR novanthron OR novantron OR novantrone OR 'now 85 34' OR 'now 8534' OR now8534 OR 'nsc 279836' OR 'nsc 301739' OR 'nsc 301739d' OR nsc279836 OR nsc301739 OR nsc301739d OR oncotron OR onkotrone	
#24	'rituximab'/syn OR 'idec c2b8' OR mabthera OR reditux OR rituxan OR rituxin	
#25	#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24	
#26	#1 AND #10 AND #25	Final combination

Supplementary Table 2. Summary of criteria for systematic literature review data extraction

Categories	Relevant criteria
Study details	<ul style="list-style-type: none"> • Study design • Study objective • Study setting • Study methods • Study phase • Study population • Inclusion/exclusion criteria • Primary/secondary endpoints • Concomitant medications • Study duration • Statistical methods • Author's conclusion and comments
Treatment details	<ul style="list-style-type: none"> • Treatment arms • Treatment dosing details (including average dose received and route of administration) • Number of patients (per treatment arm)
Information to extract	<ul style="list-style-type: none"> • Relevant patient characteristics of patients who discontinued (age, sex, EDSS score etc.) • Proportion of patients discontinuing DMT <ul style="list-style-type: none"> ○ Proportion discontinuing due to any cause ○ Proportion discontinuing due to adverse events ○ Proportion discontinuing due to lack of efficacy • Reasons for discontinuing primary DMT • Patient characteristics who discontinued the primary DMT • Proportion of patients switching to alternate DMT • Type of alternate DMT • Time to treatment failure • Time to switch • Time to treatment discontinuation • Treatment satisfaction questionnaire • Disease characteristics after drug discontinuation

DMT = disease-modifying treatment; EDSS = Expanded Disability Status Scale