

Supplementary Information

Title: Comparative Efficacy and Safety of Tolebrutinib Versus Biologic Agents in Relapsing Multiple Sclerosis: A Systematic Review and Network Meta-Analysis

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Figure S1. Flowchart of the Data Screening Process

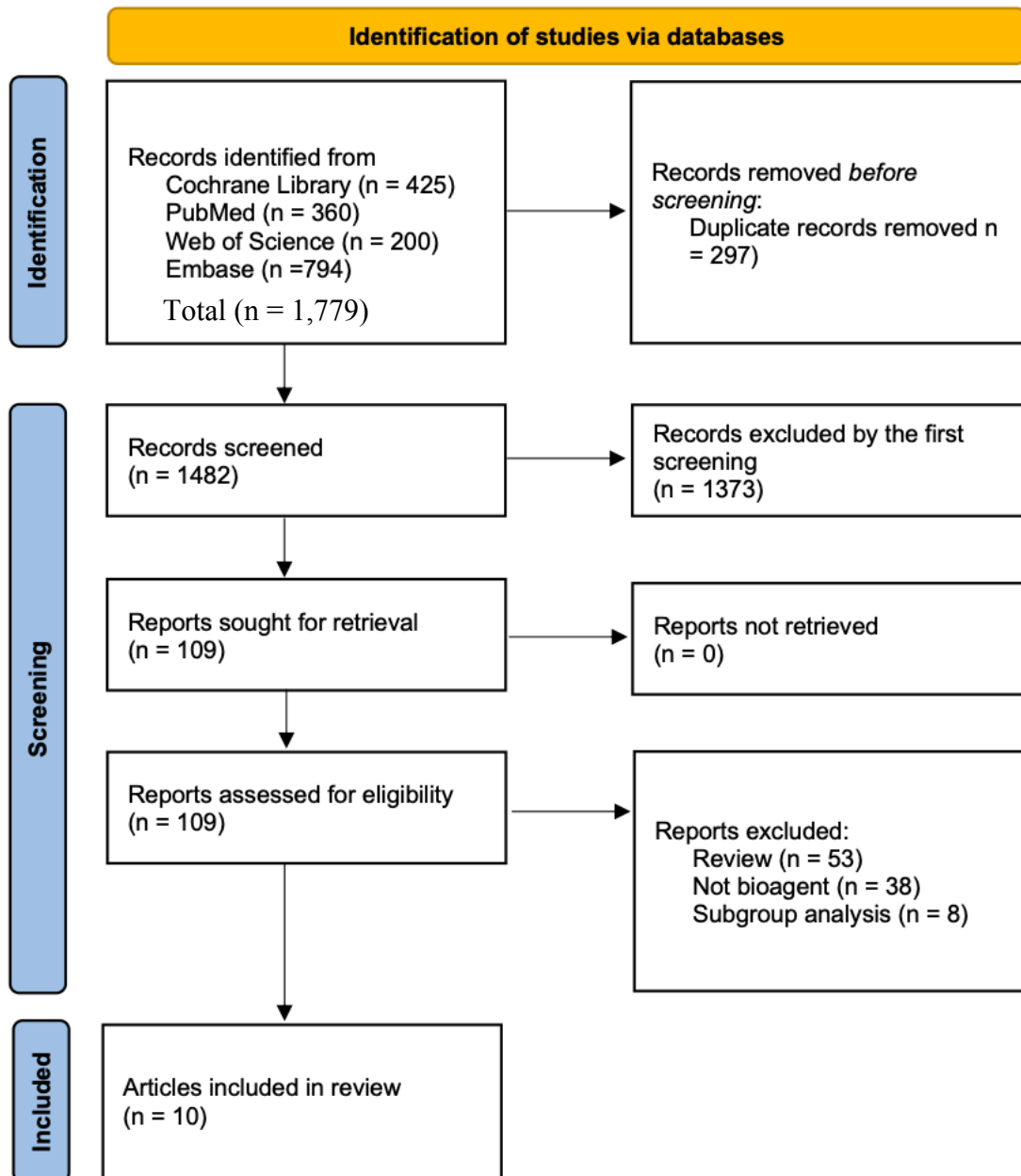


Figure S2. The network graph of the included studies evaluating ARR

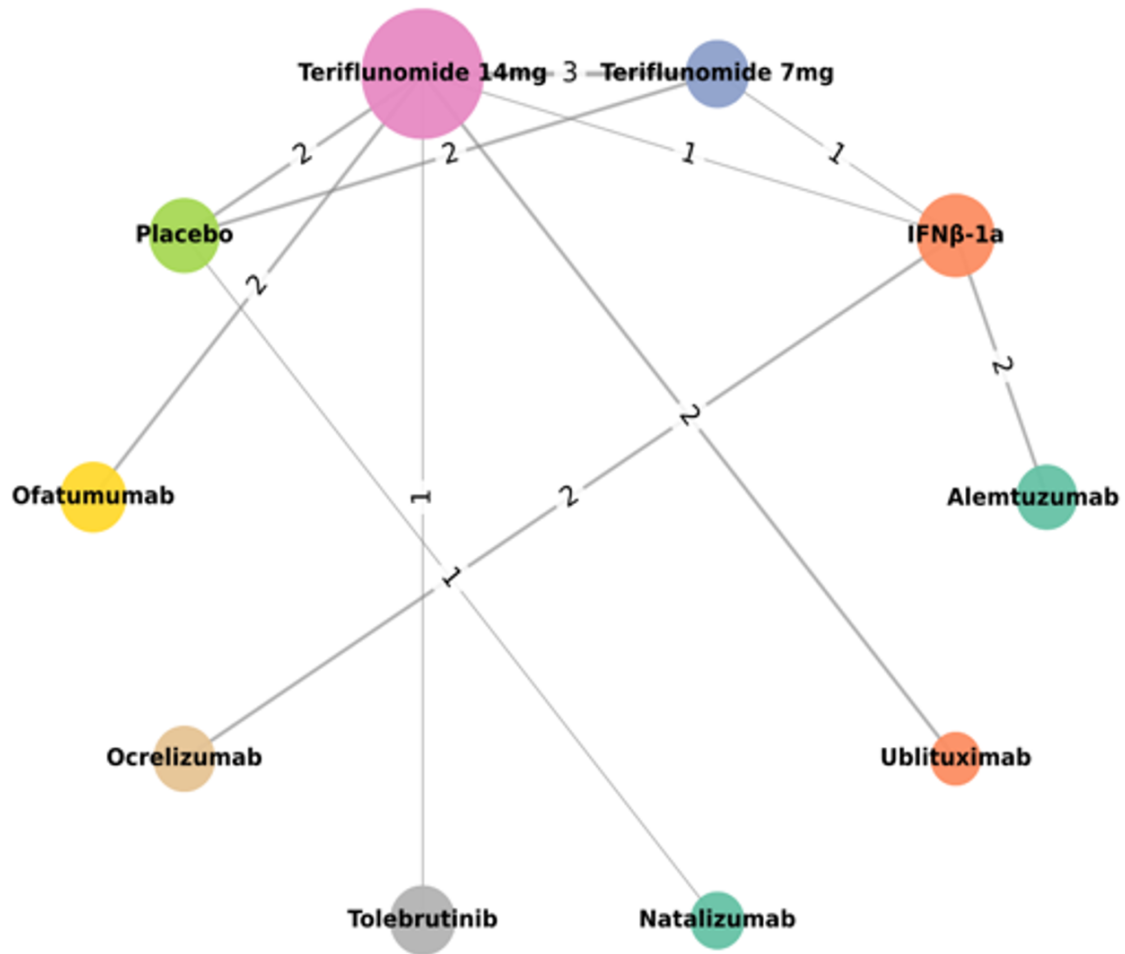


Figure S3. SUCRA ranking of ARR

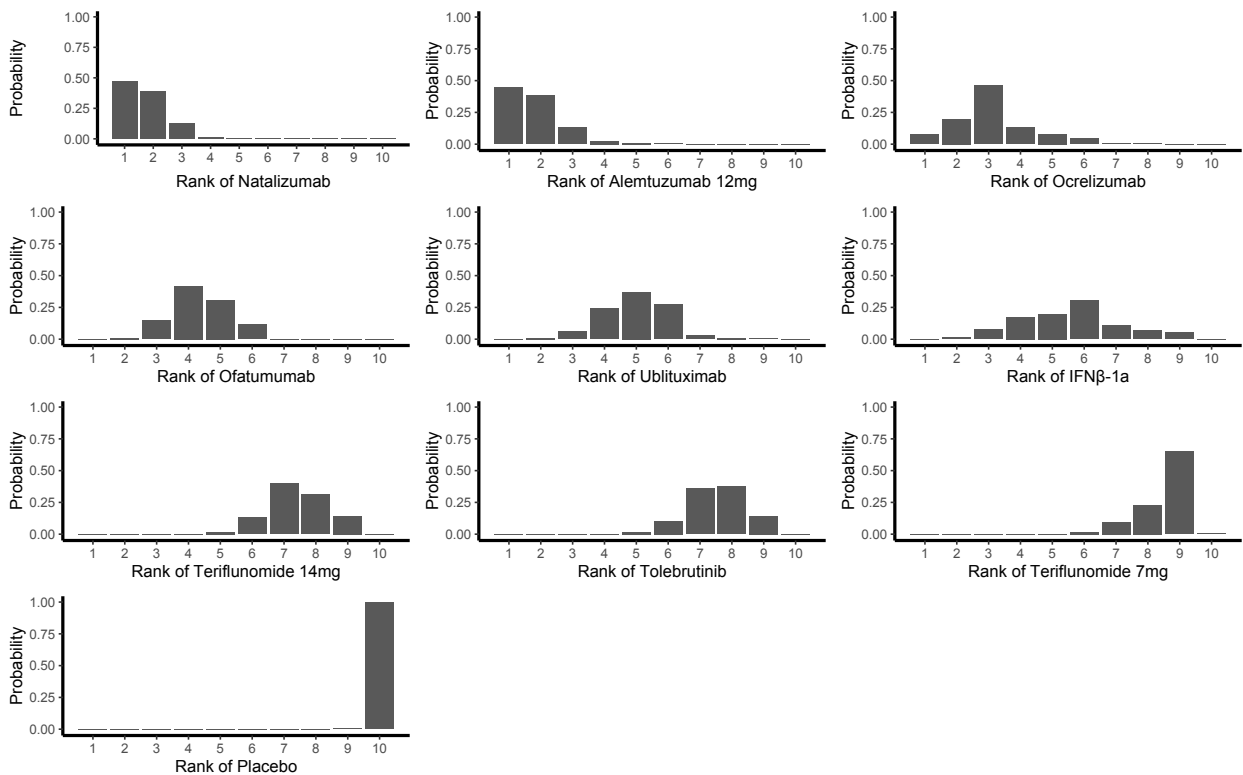


Figure S4. The network graph of the included studies evaluating CDP

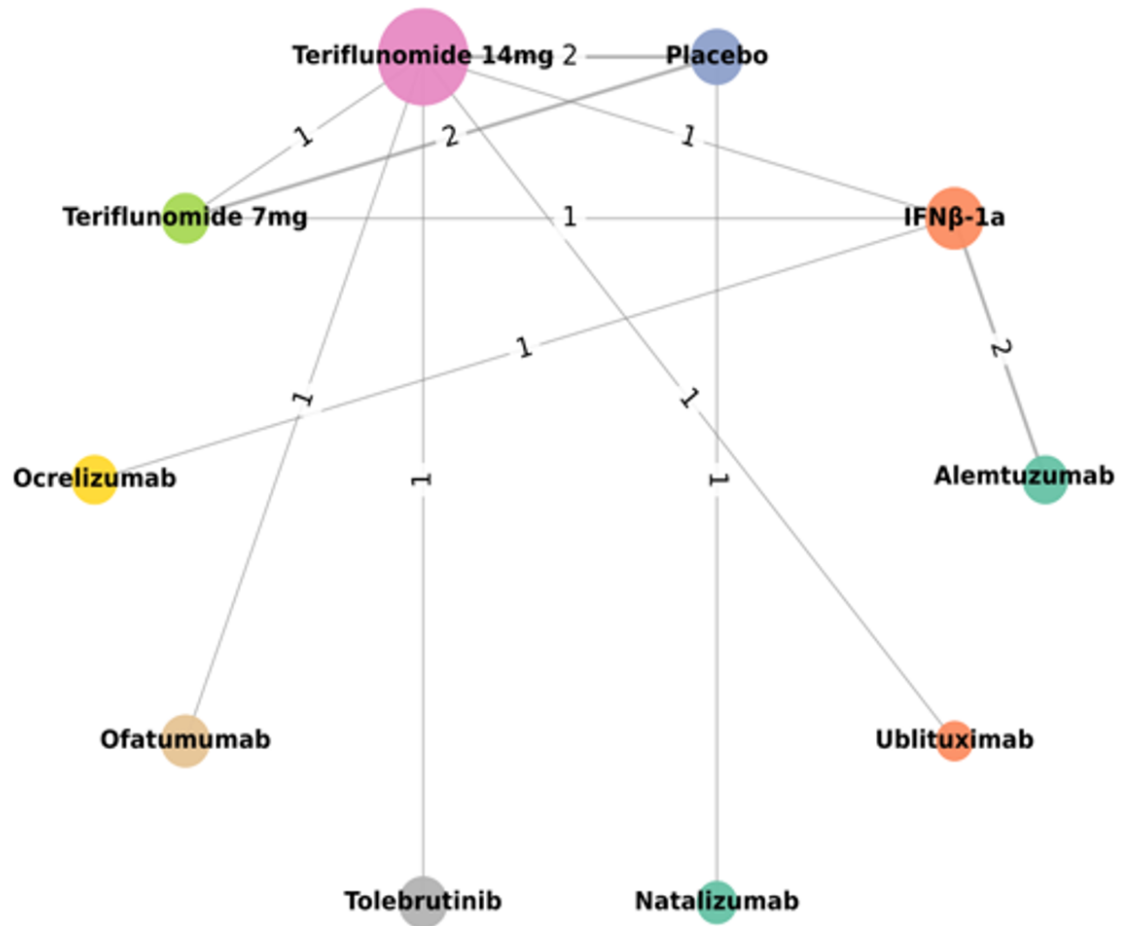


Figure S5. SUCRA ranking of CDP

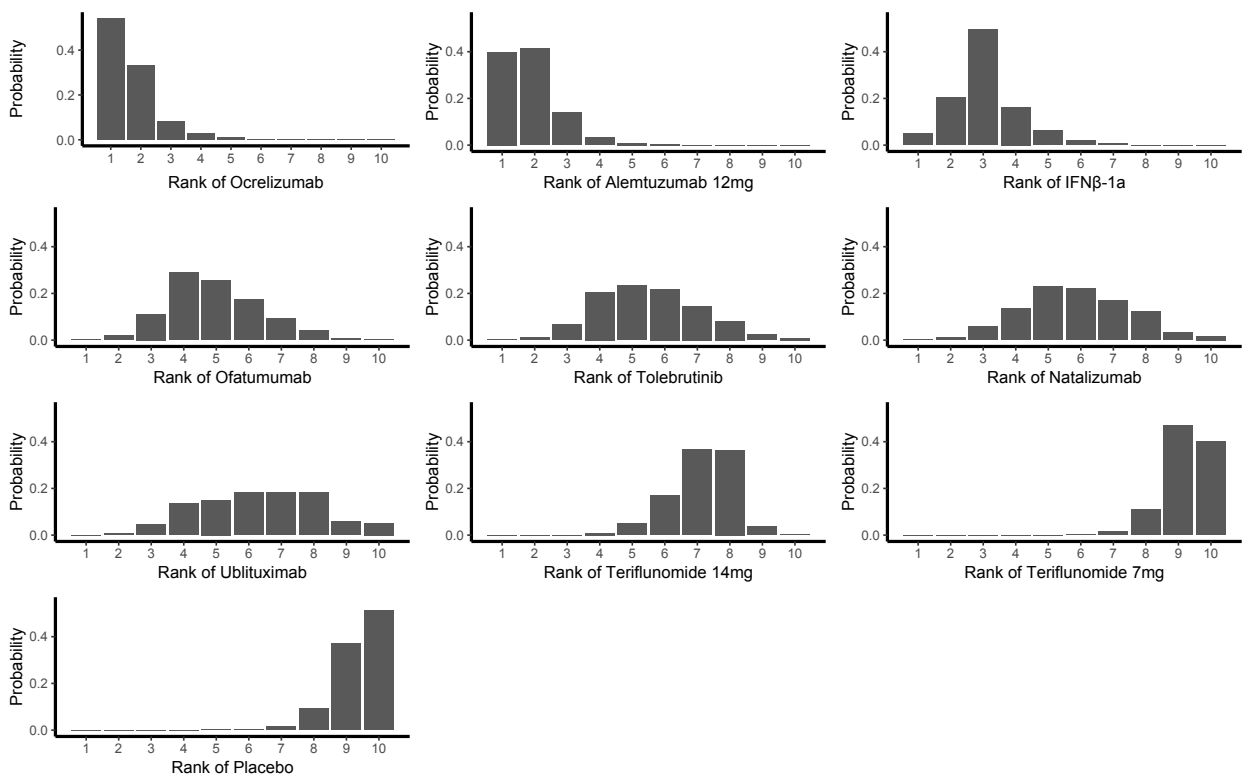


Figure S6. The network graph of the included studies evaluating SAEs

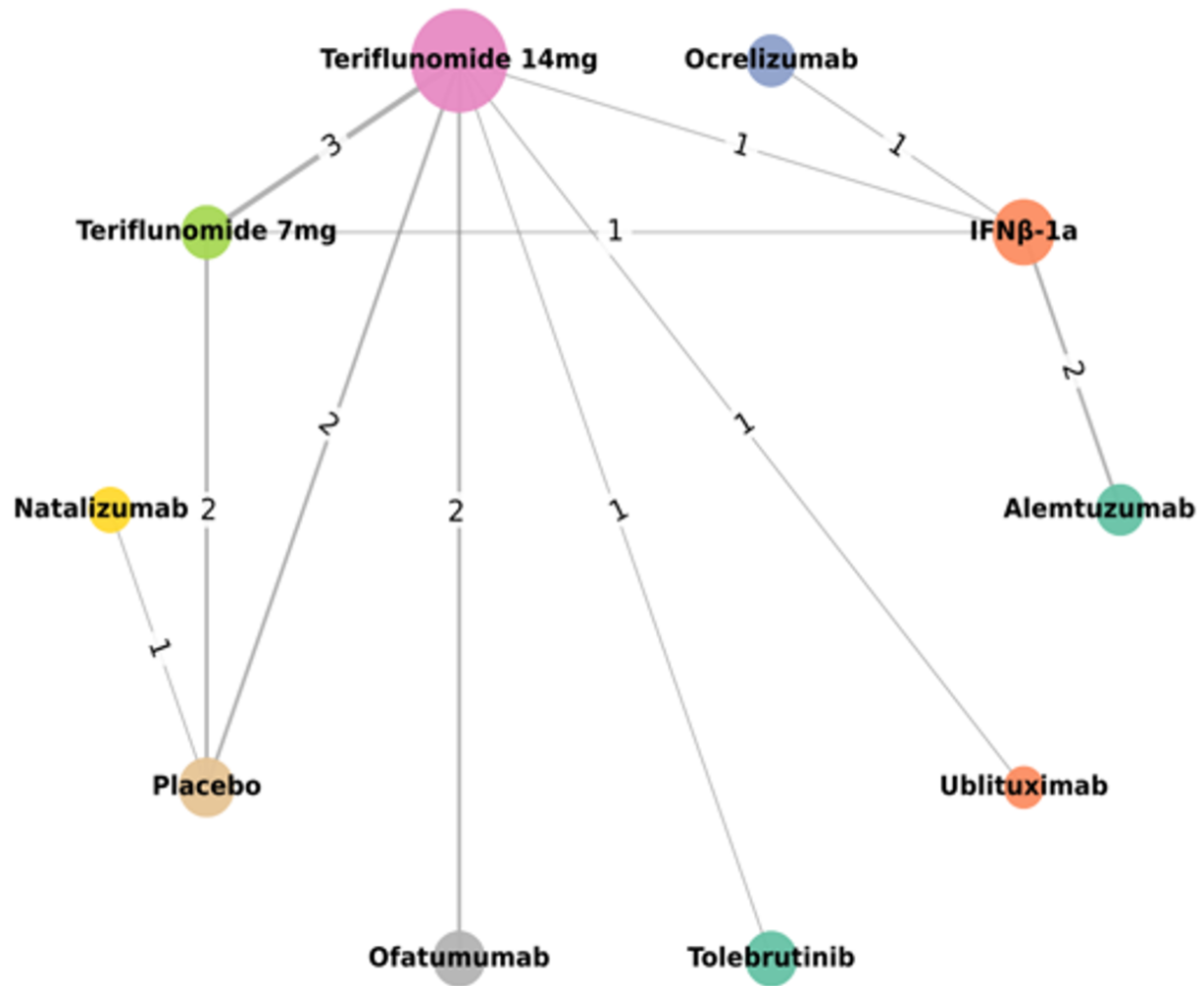
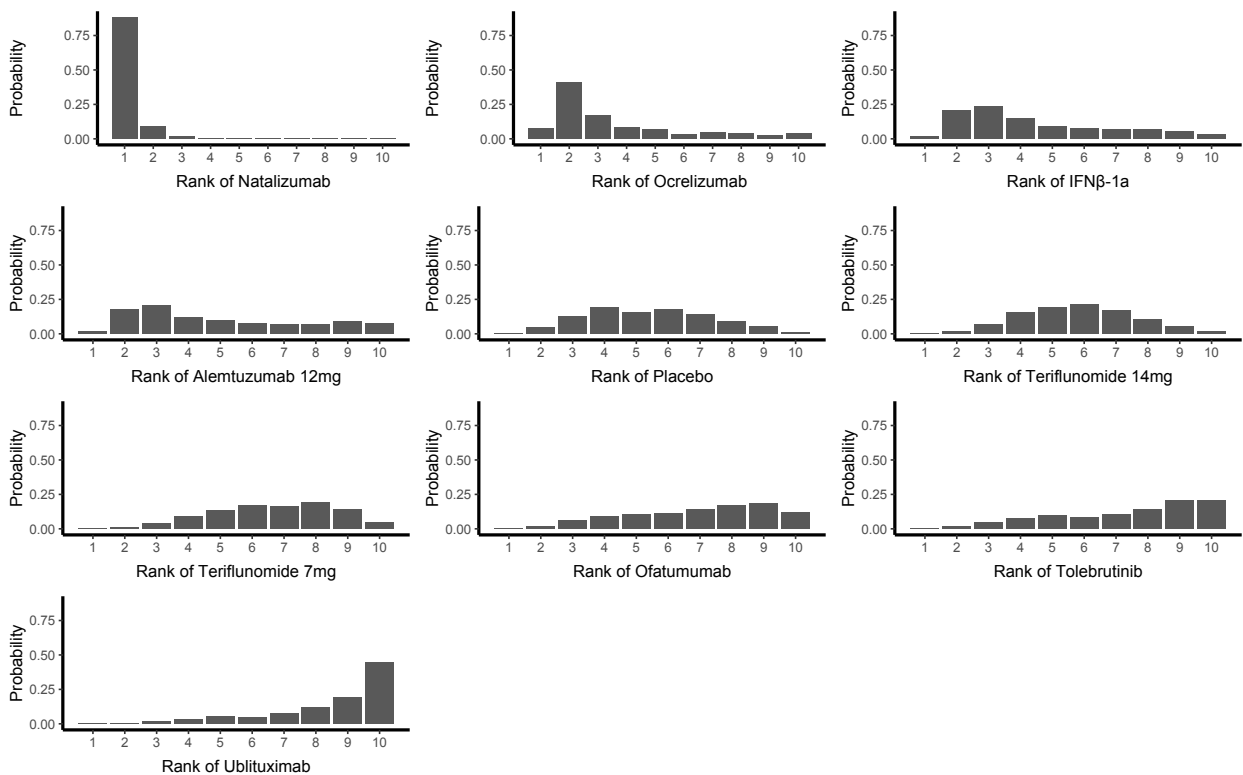


Figure S7. SUCRA ranking of SAEs



Study

Domains:

D2: Bias due to deviations from intended intervention.

D4: Bias in measurement of the outcome.

D5: Bias in selection of the reported result.

Judgement

- Some concerns

+ Low

Table S1. Network meta-analysis of all comparisons in ARR

Alemtuzumab									
0.00 [-0.26; 0.26]	Natalizumab								
-0.10 [-0.21; 0.01]	-0.11 [-0.36; 0.14]	Ocrelizumab							
-0.19 [-0.41; 0.03]	-0.19 [-0.34; -0.04]	-0.08 [-0.29; 0.12]	Ofatumumab						
-0.21 [-0.44; 0.01]	-0.22 [-0.38; -0.05]	-0.11 [-0.32; 0.10]	-0.03 [-0.11; 0.05]	Ublituximab					
-0.23 [-0.33; -0.14]	-0.24 [-0.48; 0.00]	-0.13 [-0.18; -0.08]	-0.05 [-0.24; 0.15]	-0.02 [-0.23; 0.19]	IFN β -1a				
-0.31 [-0.53; -0.10]	-0.32 [-0.47; -0.17]	-0.21 [-0.41; -0.01]	-0.13 [-0.16; -0.09]	-0.10 [-0.17; -0.03]	-0.08 [-0.28; 0.11]	Teriflunomide 14mg			
-0.31 [-0.53; -0.10]	-0.32 [-0.47; -0.17]	-0.21 [-0.41; -0.01]	-0.13 [-0.17; -0.09]	-0.10 [-0.18; -0.03]	-0.08 [-0.28; 0.11]	0.00 [-0.02; 0.02]	Tolebrutinib		
-0.36 [-0.57; -0.14]	-0.36 [-0.51; -0.21]	-0.25 [-0.46; -0.05]	-0.17 [-0.24; -0.10]	-0.14 [-0.24; -0.05]	-0.12 [-0.32; 0.07]	-0.04 [-0.10; 0.02]	-0.04 [-0.10; 0.02]	Teriflunomide 7mg	
-0.50 [-0.72; -0.27]	-0.50 [-0.63; -0.37]	-0.39 [-0.60; -0.18]	-0.31 [-0.39; -0.23]	-0.28 [-0.38; -0.18]	-0.26 [-0.46; -0.06]	-0.18 [-0.25; -0.11]	-0.18 [-0.25; -0.11]	-0.14 [-0.21; -0.07]	Placebo

Table S2. Network meta-analysis of all comparisons in CDP

Ocrelizumab									
0.89 [0.43; 1.85]	Alemtuzumab								
0.57 [0.33; 0.99]	0.64 [0.40; 1.04]	IFN β -1a							
0.37 [0.13; 1.08]	0.42 [0.15; 1.17]	0.65 [0.26; 1.62]	Ofatumumab						
0.34 [0.12; 1.00]	0.38 [0.14; 1.09]	0.60 [0.24; 1.51]	0.92 [0.43; 1.98]	Tolebrutinib					
0.32 [0.10; 0.97]	0.36 [0.12; 1.06]	0.55 [0.21; 1.47]	0.86 [0.36; 2.03]	0.93 [0.39; 2.22]	Natalizumab				
0.28 [0.09; 0.89]	0.32 [0.10; 0.97]	0.49 [0.18; 1.36]	0.76 [0.32; 1.82]	0.82 [0.34; 1.98]	0.89 [0.34; 2.33]	Ublituximab			
0.25 [0.10; 0.62]	0.28 [0.11; 0.67]	0.43 [0.20; 0.91]	0.66 [0.39; 1.13]	0.72 [0.42; 1.24]	0.77 [0.39; 1.53]	0.87 [0.44; 1.74]	Teriflunomide 14mg		
0.17 [0.07; 0.41]	0.18 [0.08; 0.45]	0.29 [0.14; 0.60]	0.45 [0.23; 0.85]	0.48 [0.25; 0.93]	0.52 [0.26; 1.02]	0.59 [0.27; 1.28]	0.67 [0.47; 0.96]	Teriflunomide 7mg	
0.16 [0.06; 0.42]	0.18 [0.07; 0.46]	0.28 [0.13; 0.63]	0.43 [0.22; 0.84]	0.47 [0.24; 0.92]	0.51 [0.29; 0.88]	0.57 [0.26; 1.26]	0.65 [0.44; 0.97]	0.97 [0.66; 1.44]	Placebo

Table S3. Network meta-analysis of all comparisons in SAEs

Natalizumab									
0.35 [0.07; 1.82]	Ocrelizumab								
0.27 [0.06; 1.26]	0.78 [0.42; 1.44]	IFN β -1a							
0.22 [0.07; 0.67]	0.65 [0.19; 2.27]	0.84 [0.28; 2.48]	Placebo						
0.25 [0.05; 1.23]	0.71 [0.33; 1.52]	0.91 [0.58; 1.43]	1.09 [0.34; 3.54]	Alemtuzumab					
0.21 [0.06; 0.69]	0.61 [0.18; 2.06]	0.79 [0.28; 2.23]	0.94 [0.60; 1.49]	0.86 [0.28; 2.68]	Teriflunomide 14mg				
0.19 [0.06; 0.63]	0.56 [0.17; 1.83]	0.71 [0.26; 1.98]	0.85 [0.54; 1.35]	0.78 [0.26; 2.38]	0.91 [0.59; 1.39]	Teriflunomide 7mg			
0.18 [0.05; 0.66]	0.53 [0.14; 1.94]	0.68 [0.22; 2.14]	0.81 [0.42; 1.57]	0.74 [0.22; 2.54]	0.86 [0.53; 1.39]	0.95 [0.50; 1.81]	Ofatumumab		
0.17 [0.05; 0.66]	0.51 [0.13; 1.95]	0.65 [0.20; 2.15]	0.78 [0.37; 1.64]	0.71 [0.20; 2.56]	0.83 [0.46; 1.49]	0.91 [0.44; 1.89]	0.96 [0.45; 2.05]	Tolebrutinib	
0.14 [0.04; 0.53]	0.40 [0.10; 1.57]	0.51 [0.15; 1.75]	0.61 [0.28; 1.35]	0.56 [0.15; 2.07]	0.65 [0.34; 1.25]	0.72 [0.33; 1.56]	0.75 [0.34; 1.69]	0.79 [0.33; 1.89]	Ublituximab