

E-REFERENCES

- e1. Group IMSS. Interferon beta-1b is effective in relapsing-remitting multiple sclerosis. I. Clinical results of a multicenter, randomized, double-blind, placebo-controlled trial. The IFNB Multiple Sclerosis Study Group. *Neurology* 1993;43:655–661.
- e2. Currier R, Haerer AR, Meydrecht EF. Low dose oral methotrexate treatment of multiple sclerosis: a pilot study. *J Neurol Neurosurg Psychiatry* 1993;56:1217–1218.
- e3. Rudick R, Stuart WH, Calabresi PA, et al.; for the SENTINEL Investigators. Natalizumab plus interferon beta-1a for relapsing multiple sclerosis. *N Engl J Med* 2006;354:911–923.
- e4. Goodman A, Rossman H, Bar-Or A, et al.; or the GLANCE Investigators. GLANCE: results of a phase 2, randomized, double-blind, placebo-controlled study. *Neurology* 2009;72:806–812.
- e5. Kappos L. Placebo-controlled multicentre randomised trial of interferon β -1b in treatment of secondary progressive multiple sclerosis. *Lancet* 1998;352:1486–1487.
- e6. Panitch H, Miller A, Paty D, Weinshenker B; for the North American Study Group on Interferon beta-1b in Secondary Progressive MS. Interferon beta-1b in secondary progressive MS. Results from a 3-year controlled study. *Neurology* 2004;63:1788–1795.
- e7. Cohen J, Cutter GR, Fischer JS, et al.; for the IMPACT Investigators. Benefit of interferon beta-1a on MSFC progression in secondary progressive MS. *Neurology* 2002;59:679–687.
- e8. Hartung H, Gonsette R, Konig N, et al.; for the Mitoxantrone in Multiple Sclerosis Study Group (MIMS). Mitoxantrone in progressive multiple sclerosis: a placebo-controlled, double-blind, randomised, multicentre trial *Lancet* 2002;360:2018–2025.
- e9. Hommes O, Sorensen PS, Fazekas F, et al.; for the INFORMS study investigators. Intravenous immunoglobulin in secondary progressive multiple sclerosis: randomised placebo-controlled trial. *Lancet* 2004;364:1149–1156.
- e10. Pohlau D, Przuntek H, Sailer M, et al. Intravenous immunoglobulin in primary and secondary chronic progressive multiple sclerosis: a randomized placebo controlled multicentre study. *Mult Scler* 2007;13:1107–1117.
- e11. Goodkin D, Rudick RA, Medendorp SV, et al. Low-dose (7.5 mg) oral methotrexate reduces the rate of progression in chronic progressive multiple sclerosis. *Ann Neurol* 1995;37:30–40.
- e12. Goodkin DE, Kinkel RP, Weinstock-Guttman B, et al. A phase II study of IV methylprednisolone in secondary-progressive multiple sclerosis. *Neurology* 1999;52:896–897.
- e13. Hartung H, Gonsette R, Konig N, et al. Mitoxantrone in progressive multiple sclerosis: a placebo-controlled, double-blind, randomised, multicentre trial *Lancet* 2002;360:2018–2025.
- e14. Montalban X, Hauser SL, Kappos L, et al.; or the ORATORIO Clinical Investigators. Ocrelizumab versus placebo in primary progressive multiple sclerosis. *N Engl J Med* 2017;376:209–220.
- e15. Rice G, Filippi M, Comi G. Cladribine and progressive MS clinical and MRI outcomes of a multicenter controlled trial. Cladribine MRI Study Group. *Neurology* 2000;54:1145–1155.
- e16. Lublin F, Miller DH, Freedman MS, et al.; for the INFORMS study investigators. Oral fingolimod in primary progressive multiple sclerosis (INFORMS): a phase 3, randomised, double-blind, placebo-controlled trial. *Lancet* 2016;387:1075–1084.
- e17. Bornstein M, Miller A, Slagle S, et al. A placebo-controlled, double-blind, randomized, two-center, pilot trial of Cop 1 in chronic progressive multiple sclerosis. *Neurology* 1991;41:533–539.

- e18. Wolinsky JS, Narayana PA, O'Connor P, et al.; for the PROMiSe Trial Group. Glatiramer acetate in primary progressive multiple sclerosis: results of a multinational, multicenter, double-blind, placebo-controlled trial. *Ann Neurol* 2007;61:14–24.
- e19. Leary S, Miller D, Stevenson VL, et al.; Brex PA, Chard DT, Thompson AJ. Interferon β -1a in primary progressive MS: an exploratory, randomized, controlled trial. *Neurology* 2003;60:144–151.
- e20. SPECTRIMS Study Group. Randomized controlled trial of interferon- beta-1a in secondary progressive MS: clinical results. *Neurology* 2001;56:1496–1504.
- e21. Montalban X, Sastre-Garriga J, Tintore M, et al. A single-center, randomized, double-blind, placebo-controlled study of interferon beta-1b on primary progressive and transitional multiple sclerosis. *Mult Scler* 2009;15:1195–1205.
- e22. Hawker K, O'Connor P, Freedman MS, et al.; for the OLYMPUS trial group. Rituximab in patients with primary progressive multiple sclerosis: results of a randomized double-blind placebo-controlled multicenter trial. *Ann Neurol* 2009;66:460–471.
- e23. Rahimdel A, Zeinali A, Mellat A. Evaluating the role of corticosteroid pulse therapy in patients with secondary progressive multiple sclerosis receiving mitoxantrone: a double blind randomized controlled clinical trial. *Iran Red Crescent Med J* 2015;17:e30618.
- e24. The Canadian Cooperative Multiple Sclerosis Study Group. The Canadian cooperative trial of cyclophosphamide and plasma exchange in progressive multiple sclerosis. *Lancet* 1991;337:441–446.
- e25. Likosky W, Fireman B, Elmore R, et al. Intense immunosuppression in chronic progressive multiple sclerosis: The Kaiser study. *J Neurol Neurosurg Psychiatry* 1991;54:1055–1060.
- e26. Goodkin DE, Kinkel RP, Weinstock-Guttman B, et al. A phase II study of IV methylprednisolone in secondary-progressive multiple sclerosis. *Neurology* 1998;51:239–245.
- e27. Comi G, Martinelli V, Rodegher M, et al.; PreCISe study group. Effect of glatiramer acetate on conversion to clinically definite multiple sclerosis in patients with clinically isolated syndrome (PreCISe study): a randomised, double-blind, placebo-controlled trial.[Erratum appears in *Lancet*. 2010 Apr 24;375(9724):1436]. *Lancet* 2009;374:1503–1511.
- e28. Comi G, Filippi M, Barkhof F, et al.; Early Treatment of Multiple Sclerosis Study Group. Effect of early interferon treatment on conversion to definite multiple sclerosis: a randomised study. *Lancet* 2001;357:1576–1582.
- e29. Leist T, Comi G, Cree BAC, et al.; on behalf of the Oral Cladibrine for Early MS Study Group. Effect of oral cladribine on time to conversion to clinically definite multiple sclerosis in patients with a first demyelinating event (ORACLE MS): a phase 3 randomised trial. *Lancet Neurol* 2014;13:257–267.
- e30. Achiron A, Kishner I, Sarova-Pinhas I, et al. Intravenous immunoglobulin treatment following the first demyelinating event suggestive of multiple sclerosis: A randomized, double-blind, placebo-controlled trial. *Arch Neurol* 2004;61:1515–1520.
- e31. Jacobs LD, Beck RW, Simon JH, et al. Intramuscular interferon beta-1a therapy initiated during a first demyelinating event in multiple sclerosis. CHAMPS Study Group. *N Engl J Med* 2000;343:898–904.
- e32. Kappos L, Polman CH, Freedman MS, et al. Treatment with interferon beta-1b delays conversion to clinically definite and McDonald MS in patients with clinically isolated syndromes. *Neurology* 2006;67:1242–1249.

- e33. Miller A, Wolinsky JS, Kappos L, et al.; TOPIC Study Group. Oral teriflunomide for patients with a first clinical episode suggestive of multiple sclerosis (TOPIC): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Neurol* 2014;13:977–986.
- e34. Romine JS, Sipe JC, Koziol JA, Zyroff J, Beutler E. A double-blind, placebo-controlled, randomized trial of cladribine in relapsing-remitting multiple sclerosis. *Proc Assoc Am Physicians* 1999;111:35–44.
- e35. Etemadifar M, Janghorbani M, Shaygannejad V. Comparison of interferon beta products and azathioprine in the treatment of relapsing-remitting multiple sclerosis. *J Neurol* 2007;254:1723–1728.
- e36. Saida T, Kikuchi S, Itoyama Y, et al. A randomized, controlled trial of fingolimod (FTY720) in Japanese patients with multiple sclerosis. *Mult Scler* 2012;18:1269–1277.
- e37. Khan O, Rieckmann P, Boyke A, et al.; Selmaj K, Zivadinov R; on behalf of the GALA Study Group. Three times weekly glatiramer acetate in relapsing–remitting multiple sclerosis. *Ann Neurol* 2013;73:705–713.
- e38. O’Connor P, Li D, Freedman MS, Bar-Or A, et al.; for the University of British Columbia MS/MRI Research Group. A phase II study of the safety and efficacy of teriflunomide in multiple sclerosis with relapses. *Neurology* 2006;66:894–900.
- e39. Confavreux C, O’Connor, P, Comi, G, et al.; for the TOWER Trial Group. Oral teriflunomide for patients with relapsing multiple sclerosis (TOWER): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Neurol* 2014;13:247–256.
- e40. Goodkin D, Bailly RC, Teetzen ML, et al. The efficacy of azathioprine in relapsing-remitting multiple sclerosis. *Neurology* 1991;41:20–25.
- e41. Sorensen PS, Mellgren SI, Svenningsson A, et al. NORdic trial of oral Methylprednisolone as add-on therapy to Interferon beta-1a for treatment of relapsing-remitting Multiple Sclerosis (NORMIMS study): a randomised, placebo-controlled trial. *Lancet Neurol* 2009;8:519–529.
- e42. Killian JM, Bressler RB, Armstrong RM, Huston DP. Controlled pilot trial of monthly intravenous cyclophosphamide in multiple sclerosis. *Arch Neurol* 1988;45:27–30.
- e43. Etemadifar M, Kazemi M, Chitsaz A, et al. Mycophenolate mofetil in combination with interferon beta-1a in the treatment of relapsing-remitting multiple sclerosis: a preliminary study. *J Res Med Sci* 2010;16:1–5.
- e44. Cohen J, Belova A, Selmaj K, et al. Equivalence of generic glatiramer acetate in multiple sclerosis: a randomized clinical trial. *JAMA Neurol* 2015;72:1433–1441.
- e45. Mikol D, Barkhof F, Chang P, et al.; on behalf of the REGARD study group. Comparison of subcutaneous interferon beta-1a with glatiramer acetate in patients with relapsing multiple sclerosis (the REbif vs Glatiramer Acetate in Relapsing MS Disease [REGARD] study): a multicentre, randomised, parallel, open-label trial. *Lancet Neurol* 2008;7:903–914.
- e46. Cavadid D, Wolanski LJ, Skurnick J, et al. Efficacy of treatment of MS with IFN β -1b or glatiramer acetate by monthly brain MRI in the BECOME study. *Neurology* 2009;72:1976–1983.
- e47. O’Connor P, Filippi M, Arnason B, et al. 250 μ g or 500 μ g interferon beta-1b versus 20 mg glatiramer acetate in relapsing-remitting multiple sclerosis: a prospective, randomised, multicentre study. *Lancet Neurol* 2009;8:889–897.
- e48. Fazekas F, Lublin FD, Li D, et al.; on behalf of the PRIVIG Study Group and the UBC MS/MRI Research Group. Intravenous immunoglobulin in relapsing remitting multiple sclerosis A dose-finding trial. *Neurology* 2008;71:265–271.

e49. Lewanska M, Siger-Zajdel M, Selmaj K. No difference in efficacy of two different doses of intravenous immunoglobulins in MS: clinical and MRI assessment. *Eur J Neurol* 2002;9:565–572.