

Reference	Condition	Treatment	Design	Outcome	Results	Adverse effects	Quality score
Sørensen et al, 1997 Sørensen et al, 1998	Relapsing/remitting, relapsing/progressive MS Patients aged 20-50 years, within 10 years of diagnosis, two or more exacerbations in previous year, EDSS 2-7, at least five cerebral lesions, no corticosteroids or immunosuppressive treatment	IVIG 1g/kg daily for 2 days every four weeks for 24 weeks, or placebo	Randomised, double blind, placebo (human albumin), crossover with three month wash out. ITT and per-protocol analysis	Primary outcome was new lesions on serial MRI performed every four weeks. A number of secondary outcomes were used	Of 25 randomised (mean EDSS 3.5) 17 completed the crossover. Median of half a new lesion fewer in IVIG (ITT, p=0.002). 15/21 patients were exacerbation free with IVIG and 7/21 with placebo. There were 3 severe exacerbations with IVIG and 7 with placebo.	Eczema, urticaria and headache appeared to be more common with IVIG. One patient developed hepatitis C infection with IVIG. Severe eczema was most common cause of withdrawal from study, and affected palms of hands, arms, legs and face. Four withdrawals were on IVIG and four on placebo. 21 completing at least one month of second arm made up ITT population.	R = 1 DB=1 WD=1 Total=3/5
Fazekas et al, 1997	Relapsing/remitting, EDSS 1-6, two clearly defined relapses in previous two years. Age 15-64 with first manifestation below 60 years. No immunosuppressive therapy with three months.	IVIG 0.15-0.2 g/kg every month for two years, or saline placebo.	Randomised, double blind, parallel, placebo controlled. Intention to treat and per protocol analysis, two years duration	Primary outcome was absolute change in EDSS, and improved, stable or worse clinical disability (change of at least 1 point on EDSS) by end of study.	148 patients participated, well matched at baseline. Mean change in EDSS was -0.23 for IVIG and + 0.12 for placebo. Improvement of EDSS of 1 or more in 23/75 with EDSS (31%) and 10/73 (14%) with placebo. Deterioration occurred in 12/75 (23%) with IVIG and 17/73 (23%) with placebo. With IVIG 40/75 (53%) were relapse free compared with 26/73 (36%) with placebo.	Adverse event withdrawal occurred in 11/75 (15%) with IVIG and 17/73 (23%) with placebo, more often because of lack of efficacy.	R = 2 DB=1 WD=1 Total=4/5
Achiron et al, 1998	Relapsing/remitting MS, confirmed by MRI, age 18-60 years, EDSS 0 to 6, 0.5 to 3 exacerbations per year in prior period	IVIG 0.4 g/kg per day for five days and once every two months for 2 years, or saline placebo	Randomised, double blind, parallel, placebo controlled. Intention to treat and per protocol analysis, two years duration	Primary outcome was yearly exacerbation rate. Relapse clearly defined	40 patients were included. Significantly lower exacerbation rates with IVIG than placebo (39% reduction in relapses). 6/20 IVIG were relapse free, 0/20 with placebo. EDSS decreased by 0.3 with IVIG and rose by 0.15 with placebo.	Side effects associated with 19/630 infusions. Two discontinuations, one in each group, after one year	R = 2 DB=2 WD=1 Total=5/6

Stangel et al, 2000	Relapsing/remitting MS with EDSS 2.0-4.5, no clinical relapse within three months, no beta-interferon or immunosuppressives.	IVIG 0.4 g/kg on five consecutive days. Placebo was identical except IVIG.	Double-blind, non-randomised, with placebo treatment followed by IVIG, six weeks each treatment	Electrophysiologic al studies, neurological assessment	No major changes	Headache in 6/10 with IVIG and 3/10 with placebo	Not appropriate
Poehlau et al, 2000	Primary and secondary chronic progressive MS	IVIG 0.4 g/kg every four weeks, or placebo	Randomised, double blind,. Placebo controlled	Not given. Early report on safety	Not given	In 600 IVIG infusions in 131 patients there were 25 severe adverse events in 25 patients. None of these was considered to be drug-related, and included worsening (9), relapse (5), UTI (3), Seizure (2, both with epilepsy), pneumonia, appendectomy, dyspnoea, dysaesthesia and tremor (1 each)	Not appropriate
Noseworthy et al, 2000	Relapsing/remitting or secondary progressive MS between ages 18 and 60, with apparent irreversible motor deficit (weakness of at least one limb with more than 25% loss of power).	IVIG 0.4 g/day for five days and every two weeks thereafter for three months, with 11 infusions in total	Randomised, double blind, placebo controlled, six months duration, ITT analysis	Primary outcome was six month change in affected muscle strength	No effect of IVIG on muscle strength, or EDSS improvement at least 1 point (3/29:3/29), new MS activity, or new MS attacks, or patient global.	Rash in 8/34 IVIG and 2/33 on placebo.	R = 1 DB=2 WD=1 Total=4/5
Noseworthy et al, 2001	Patients with demyelination optic neuritis and MS, younger than 50 years, with stringent optic criteria	IVIG 0.4 g/day for five days and ever two weeks thereafter on three occasions at monthly intervals, with 8 infusions in total	Randomised, double blind, placebo controlled, six months duration, ITT analysis over 12 months	Visual function tests, clinical activity, with primary endpoint of visual acuity at 6 months	55 patients were randomised, and two groups were comparable at baseline. There was no difference in the primary outcome, or EDSS worsening of at least 1 point (3/28 placebo 4/27 IVIG), or change in EDSS or active MS, at six or 12 months	Adverse events described in detail, with rash and headache perhaps associated with IVIG	R = 1 DB=2 WD=1 Total=4/6