Clinical Trials in Multiple Sclerosis 2007: Planned, In Progress, Recently Completed

This listing is prepared on behalf of the National Multiple Sclerosis Society’s Advisory Committee on Trials of New Drugs in MS from materials provided by principal investigators and from information gathered from published literature and public presentations. While we strive for accuracy and completeness, there are surely additional trials that are not included. Because clinical trials are dynamic studies, there may be inaccuracies due to changes in protocol for selected studies.

Index Information: The list is arranged in alphabetical order, largely by commercial name. Two indexes (one by generic name or product description, and one by type of MS/type of patient) and a key to abbreviations are included.

Trial Information: Where information was not provided to us or has not been reported, we have indicated that this information is “Not available.” Trials that have been completed or terminated are marked as such. These studies will be removed after two years. We maintain an archive of older lists, in case of an inquiry, and published studies can be found on PubMed [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed].

ClinicalTrials.gov: Where available, we have provided the link to the study listing on the ClinicalTrials.gov Web site [http://www.clinicaltrials.gov/]. A statement from the International Committee of Medical Journal Editors released in September 2004 required investigators to register clinical trials, except studies designed to study pharmacokinetics or major toxicity, such as phase 1 trials (The New England Journal of Medicine 2004 Sep 16;351(12):1250-1). For studies not registered at the time this list was compiled, this information is cited as “Not available.”

A list of trials recruiting people with MS is available at: [http://www.nationalmssociety.org/Research-trialsrecruiting.asp]
This list is indexed by State and includes international studies.

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Research & Clinical Programs
National Multiple Sclerosis Society
733 Third Avenue, New York, NY 10017
Tel: (212) 476-0411; Fax: (212) 986-7981
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**Professional Resource Center of the National MS Society**

[http://www.nationalmssociety.org/prc.asp](http://www.nationalmssociety.org/prc.asp)

The Society's Professional Resource Center (PRC), which houses the most comprehensive library of MS information in the world, provides a variety of information and consultation services. Our goal is to partner with healthcare professionals to enhance quality of care and increase access to care for people with MS.

**PRC Services**
- Get free PRC Publications
- Keep current with Clinical Bulletins, Clinical Updates, and Research Bulletins
- Request a free Literature Search
- Read about Fellowships and Training Opportunities
- Learn the latest on Pediatric MS
- See our Professional Education Offerings
- Access Resources for MS Clinicians
- Access Resources for MS Researchers
- Find National MS Society Affiliated Clinical Facilities
Measures for Use in Clinical Studies of MS
http://www.nationalmssociety.org/ClinicalStudyMeasures.asp

This section provides information on the following measures used in MS clinical studies. Where possible, the forms needed to use the measure are provided.

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Agent: 3-4 diaminopyridine
Purpose of study: To improve fatigue and quality of life
Possible mechanism: Blocks potassium channels on axons, permitting demyelinated axon to transmit impulses
Study description: Double blinded, placebo controlled, dose escalation
Dose/route: 30-60 mg/d po vs. PBO po
Outcome parameters: Fatigue Impact Scale, Visual Analogic Scale, quality of life
Type of MS: All types
Number of Subjects: 126
Start date: February 2005
Observation period: 8 weeks
Investigators: G. Edan and others
Sites: CHU de Rennes, and others, France
Results/Publications: Not available
Funding: French Health Ministry
ClinicalTrials.gov Identifier: NCT00190268 Last update: 2007

Agent: ABT-874
Purpose of study: To determine safety and effectiveness in reducing disease activity
Possible mechanism: Inhibits the role of cytokine IL-12 in immune attack
Study description: Double blinded, placebo controlled, parallel groups
Dose/route: 200 mg/wk sc vs. 200 mg every other week (alternating with PBO) sc vs. PBO every other week sc
Outcome parameters: Frequency of relapse, scoring technique, MRI
Type of MS: RR, SP
Number of Subjects: 195
Start date: May 2004
Observation period: 24 weeks, with 24-week double-blinded active extension phase
Investigators: Multiple
Sites: Multicenter, United States
Results/Publications: Clinical trial met primary endpoint, but no longer under development for MS (Cambridge Antibody Technology product summary, March 2007)
Funding: Abbott Laboratories
ClinicalTrials.gov Identifier: NCT00086671 Last update: 2007

***************************************************************************
Agent: Actos® (pioglitazone, Takeda Pharmaceuticals North America, Inc.)
Purpose of study: To test safety and tolerability
Possible mechanism: Reduces proinflammatory gene expression and T cell activation
Study description: Pilot, double blinded
Dose/route: 30 mg/d po vs. PBO po
Outcome parameters: Frequency of relapse, MSFC, EDSS, MRI, liver function
Type of MS: RR
Number of Subjects: 15
Start date: April 2004
Observation period: 2 years
Investigators: D. Skias and others
Sites: University of Illinois at Chicago
Results/Publications: 22 patients completed the trial; no indications of liver toxicity, edema, or increased Gd+ lesions; EDSS did not change over 1 year; average MSFC score showed similar improvement in both groups; after 1 year FLAIR lesion volume increased in PBO group but decreased in Actos group; grey matter atrophy significantly reduced by Actos (Abstract #S02.006, AAN 2007)
Funding: Takeda Pharmaceuticals North America, Inc.
ClinicalTrials.gov Identifier: NCT00242177
Last update: 2007

Agent: AndroGel® (testosterone gel, Solvay Pharmaceuticals, Inc.)  
Purpose of study: To test safety and detect impact on disease activity
Possible mechanism: Anti-inflammatory
Study description: 6-month run-in observation, 12-month treatment phase
Dose/route: 100 mg/d sc
Outcome parameters: Frequency of relapse, EDSS, MSFC, MRI
Type of MS: RR, Male
Number of Subjects: 10
Start date: April 2002
Observation period: 18 months
Investigators: R. Voskuhl and others
Sites: University of California, Los Angeles
Results/Publications: Well tolerated; improvements in PASAT and spatial memory tasks; brain-derived neurotrophic factor increased more than twofold; brain atrophy slowed by 67% during last 9 mos of treatment (Abstract #P01.070, AAN 2006; Archives of Neurology 2007;64:683-688)
Funding: National MS Society
ClinicalTrials.gov Identifier: NCT00405353
Last update: 2006
Agent: Aricept® (donepezil, Eisai Co.)
Purpose of study: To improve memory, also known as AIMS study
Possible mechanism: Cholinesterase inhibitor
Study description: Randomized, double blinded, placebo controlled
Dose/route: Aricept 5 mg/d po for 4 wks, then 10 mg/d for 20 wks vs. PBO po
Outcome parameters: Selective Reminding Test
Type of MS: All types
Number of Subjects: 144
Start date: Spring 2005
Observation period: 24 weeks
Investigators: L. Krupp and others
Sites: SUNY Stony Book, NY, and others, New York and Rhode Island
Results/Publications: Not available
Funding: NIH
ClinicalTrials.gov Identifier: NCT00062972 Last update: 2006

********************************************************************************

Agent: Aspirin
Purpose of study: To improve fatigue
Possible mechanism: Inhibits prostaglandins
Study description: Double blinded, placebo controlled
Dose/route: Aspirin 81 mg bid po vs. aspirin 650 mg bid po vs. PBO po
Outcome parameters: Modified Fatigue Impact Scale, Visual Analog Scale, cognitive fatigue measure, motor fatigue measure
Type of MS: RR, SP
Number of Subjects: 135
Start date: March 2007
Observation period: 8 weeks
Investigators: D. Wingerchuk and others
Sites: Mayo Clinic and Mayo Foundation, Scottsdale, AZ, Jacksonville, FL, Rochester, MN
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: NCT00467584 Last update: 2007
********************************************************************************
Agent: ATL1102
Purpose of study: To determine the pharmacokinetic profile
Possible mechanism: Synthetic, second generation antisense oligonucleotide which acts as an inhibitor of VLA-4 mediated cell adhesion; targets alpha 4 integrin at the mRNA level, inhibiting protein translation and hence downregulation of VLA-4 surface expression
Study description: Randomized, double blinded, placebo controlled
Dose/route: ATL1102 200 mg biw sc vs. PBO sc
Outcome parameters: MRI
Type of MS: RR
Number of Subjects: 80
Start date: 2006
Observation period: 16 weeks
Investigators: V. Limmroth and others
Sites: Multicenter, Central/Eastern Europe
Results/Publications: Not available
Funding: Antisense Therapeutics
ClinicalTrials.gov Identifier: Not available  Last update: 2006

Agent: Avandia® (rosiglitazone maleate, Glaxo SmithKline)  COMPLETED
Purpose of study: To investigate safety
Possible mechanism: Agonist for peroxisome proliferator-activated receptor-gamma, member of a hormone receptor family known to affect immune response
Study description: Double blinded, placebo controlled
Dose/route: 8 mg/d po vs. PBO po
Outcome parameters: Safety
Type of MS: RR
Number of Subjects: 51
Start date: August 2003
Observation period: 44 weeks
Investigators: M. Carrithers and others
Sites: Yale Center for MS Treatment and Research, New Haven, CT
Results/Publications: No statistically significant differences observed for any endpoints (Abstract #P620, ECTRIMS 2005)
Funding: GlaxoSmithKline
ClinicalTrials.gov Identifier: Not available  Last update: 2006

************************************************************************************
**Agent:** Avonex® (interferon beta-1a, Biogen Idec)

**Purpose of study:** To follow patients longitudinally who had been part of the CHAMPS study, also known as CHAMPIONS study

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells

**Study description:** Open label, ongoing neurological surveillance study

**Dose/route:** 30 mcg/wk im

**Outcome parameters:** Development of clinically definite MS; subsequent course

**Type of MS:** Individuals in CHAMPS study (RR, first clinical demyelinating event suggestive of MS)

**Number of Subjects:** 203

**Start date:** November 2000

**Observation period:** 10 years

**Investigators:** R. Kinkel and others

**Sites:** Cleveland Clinic Foundation and others, United States and Canada

**Results/Publications:** At 5 yrs, cumulative probability of development of MS was significantly lower in immediate treatment group compared with delayed group; few patients in either group developed major disability within 5 yrs (Neurology 2006 Jan 25; [Epub ahead of print])

**Funding:** Biogen Idec, Inc.

**ClinicalTrials.gov Identifier:** NCT00179478

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**Agent:** Avonex® (interferon beta-1a, Biogen Idec) + CellCept® (mycophenolate mofetil, Roche Laboratories, Inc.)

**Purpose of study:** To test safety and tolerability

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)/Inhibits proliferation of T and B cells, suppresses antibody formation (CellCept)

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** Avonex 30 mcg/wk im + CellCept 250-1000 mg bid po vs. Avonex + PBO po

**Outcome parameters:** MRI, EDSS, quality of life, frequency of relapse, pharmacogenomics

**Type of MS:** RR

**Number of Subjects:** 24

**Start date:** July 2004

**Observation period:** 12 months

**Investigators:** E. Frohman

**Sites:** University of Texas Southwestern Medical Center at Dallas

**Results/Publications:** Not available

**Funding:** Biogen Idec, Inc.

**ClinicalTrials.gov Identifier:** NCT00223301

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Agent: Avonex® (interferon beta-1a, Biogen Idec) + CellCept® (mycophenolate mofetil, Roche Laboratories, Inc.)

Purpose of study: To test safety and tolerability

Possible mechanism: Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)/Inhibits proliferation of T and B cells, suppresses antibody formation (CellCept)

Study description: Randomized, open label, parallel group

Dose/route: Avonex 30 mcg/wk im + PBO po vs. CellCept 500-1000 mg bid po + PBO im for 6 mos; then Avonex 30 mcg/wk im + CellCept 500-1000 mg bid po for 6 mos

Outcome parameters: EDSS, MSFC, frequency of relapse, MRI

Type of MS: RR

Number of Subjects: 60

Start date: 2006

Observation period: 3 years

Investigators: E. Frohman and others

Sites: University of Texas Southwestern Medical Center at Dallas, and others, United States

Results/Publications: Not available

Funding: Biogen Idec, Inc.

ClinicalTrials.gov Identifier: NCT00324506

Last update: 2007

************************************************************************************

Agent: Avonex® (interferon beta-1a, Biogen Idec) + Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.)

Purpose of study: To test combination therapy on brain lesion load and underlying disease course, also known as CombiRx Study

Possible mechanism: Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)

Study description: Double blinded, placebo controlled

Dose/route: Avonex 30 mcg/wk im + Copaxone 20 mg/d sc vs. Avonex + PBO sc vs. Copaxone + PBO im

Outcome parameters: Annualized relapse rate, EDSS, MSFC, MSQOLI, MRI

Type of MS: RR

Number of Subjects: 1000

Start date: Summer 2004

Observation period: 36 months

Investigators: F. Lublin and others

Sites: Mount Sinai Medical Center, New York, and others, North America

Results/Publications: Not available

Funding: NINDS, agents provided by Biogen Idec, Inc. and Teva Neuroscience

ClinicalTrials.gov Identifier: NCT00211887

Last update: 2006

*******************************************************************************
Agent: Avonex® (interferon beta-1a, Biogen Idec) + doxycycline

Purpose of study: To test safety and control disease activity

Possible mechanism: Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)/synthetic tetracycline derivative that inhibits matrix metalloproteinases (doxycycline)

Study description: Open label

Dose/route: Avonex 30 mcg/wk im + doxycycline 100 mg/d po

Outcome parameters: Frequency of relapse, MRI, other

Type of MS: RR

Number of Subjects: 15

Start date: Not available

Observation period: 6 months

Investigators: A. Minagar

Sites: LSU-HSC Shreveport, LA

Results/Publications: Interim analysis of 11 patients; significant decrease in Gd+ lesions and EDSS; one patient had transiently elevated hepatic enzymes on combination therapy (Abstract #P01.087, AAN 2006)

Funding: Biogen Idec, Inc.

ClinicalTrials.gov Identifier: NCT00246324 Last update: 2006

Agent: Avonex® (interferon beta-1a, Biogen Idec) + COMPLETED

EMLA (lidocaine + prilocaine, Abraxis Biosciences, Inc.) anesthetic cream

Purpose of study: To reduce injection side effects

Possible mechanism: Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)/Provides dermal analgesia (EMLA)

Study description: Crossover, placebo controlled

Dose/route: Avonex 30 mcg/wk im + EMLA 2 hrs before injection every 4 wks vs. Avonex + PBO

Outcome parameters: Decreased fear of injection, decreased pain after injection

Type of MS: RR, SP

Number of Subjects: 18

Start date: January 2002

Observation period: 8 weeks

Investigators: M. Buhse

Sites: North Shore University Hospital, Manhasset, NY

Results/Publications: With the application of EMLA cream, the mean pain-of-injection score was found to be significantly lower than the mean fear-of-injection score; 18 patients who completed the study experienced a statistically significant decrease in both scores (Journal of Neuroscience Nursing 2006;38(4):222-6)

Funding: Biogen Idec, Inc.

ClinicalTrials.gov Identifier: Not available Last update: 2007

************************************************************************************
Agent: Avonex® (interferon beta-1a, Biogen Idec) + azathioprine + prednisone

**Purpose of study:** To reduce relapses

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)/Releases 6-MP, inhibits nucleic acid biosynthesis, preventing proliferation of proinflammatory cells (azathioprine)/Closes damaged blood-brain barrier and reduces inflammation in CNS (prednisone)

**Study description:** Double blinded, randomized, placebo controlled

**Dose/route:** Avonex 30 mcg/wk im + prednisone 10 mg/qod po + PBO po vs. Avonex 30 mcg/wk im + azathioprine 50 mg/d po + PBO po vs. Avonex 30 mcg/wk im + azathioprine 50 mg/d po + prednisone 10 mg/qod po

**Outcome parameters:** EDSS, frequency of relapse, MRI

**Type of MS:** RR

**Number of Subjects:** 181

**Start date:** 1999

**Observation period:** 5 years

**Investigators:** E. Havrdova and others

**Sites:** Charles University, Prague, Czech Republic and others, worldwide

**Results/Publications:** No statistically significant differences (Abstracts #61,P701, ECTRIMS 2006, Abstract #P06.089, AAN 2007)

**Funding:** Biogen Idec, Inc.

**ClinicalTrials.gov Identifier:** Not available

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Agent: Avonex® (interferon beta-1a, Biogen Idec) + methotrexate + methylprednisolone

**Purpose of study:** To control breakthrough disease, also known as ACT study

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across, and inducing suppressive T cells (Avonex)/Diminishes leukocyte accumulation (methotrexate)/Closes damaged BBB, reducing inflammation in CNS (methylprednisolone)

**Study description:** Multicenter, randomized, blinded, parallel-group study

**Dose/route:** Avonex 30 mcg/wk im + PBO po weekly vs. Avonex + methotrexate 20 mg/wk po vs. Avonex + PBO + methylprednisolone 1000 mg/d iv for 3 days every 2 mo vs. Avonex + methotrexate + methylprednisolone

**Outcome parameters:** Relapse rate, brain atrophy progression, MSFC, EDSS, MRI

**Type of MS:** RR with breakthrough disease

**Number of Subjects:** 313

**Start date:** June 2003

**Observation period:** 1 year

**Investigators:** J. Cohen and others

**Sites:** Cleveland Clinic Foundation and others, United States

**Results/Publications:** Favorable nonsignificant trends in clinical/MRI outcomes; further analyses ongoing (Abstract #P01.081, AAN 2006; Abstract #S12.005, AAN 2007)

**Funding:** Biogen Idec, Inc.

**ClinicalTrials.gov Identifier:** NCT00112034

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Last update: 2007
**Agent:** Avonex® (interferon beta-1a, Biogen Idec) + Novantrone® (mitoxantrone for injection concentrate, EMD Serono, Inc.)

**Purpose of study:** To evaluate safety and effect on disease course

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)/Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion (Novantrone)

**Study description:** Pilot, open label

**Dose/route:** Avonex 30 mcg/wk im + Novantrone 20 mg/mo iv for 6 months

**Outcome parameters:** Safety, MRI, disease progression, time to and frequency of relapse

**Type of MS:** Worsening RR

**Number of Subjects:** 10

**Start date:** March 2002

**Observation period:** 18 months

**Investigators:** N. Kachuck

**Sites:** USC Keck School of Medicine, Los Angeles

**Results/Publications:** Not available

**Funding:** Investigator sponsored

**ClinicalTrials.gov Identifier:** Not available  
**Last update:** 2006

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**Agent:** Avonex® (interferon beta-1a, Biogen Idec) + Zocor® (simvastatin, Merck & Co., Inc.)

**Purpose of study:** To delay time to definite MS in patients with clinically isolated syndrome

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)/Promotes anti-inflammatory Th2 response (Zocor)

**Study description:** Randomized, double-blinded, placebo-controlled

**Dose/route:** Avonex 30 mcg/wk im + Zocor 80 mg/d po vs. Avonex 30 mcg/wk im + PBO po

**Outcome parameters:** Frequency of relapse, EDSS, MRI

**Type of MS:** First clinical demyelinating event suggestive of MS

**Number of Subjects:** 30

**Start date:** 2005

**Observation period:** 12 months

**Investigators:** S. Markovic-Plese

**Sites:** University of North Carolina, Chapel Hill

**Results/Publications:** Not available

**Funding:** Biogen Idec, Inc.

**ClinicalTrials.gov Identifier:** NCT00146068  
**Last update:** 2007

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Agent: Avonex® (interferon beta-1a, Biogen Idec) vs. Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.) vs. Betaseron® (interferon beta-1b, Bayer HealthCare Pharm-aaceuticals, Inc.) vs. Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.)

Purpose of study: To evaluate impact in patients < 16, also known as ITEMS study

Possible mechanism: Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex, Betaseron, Rebif)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)

Study description: Prospective data collection study, open label

Dose/route: Avonex 30 mcg/wk im vs. Rebif 22 mg tiw sc vs. Betaseron 250 mcg qod sc vs. Copaxone 20 mg/d sc

Outcome parameters: Demographic and clinical data

Type of MS: Clinically definite MS, below age 16

Number of Subjects: 81

Start date: Not available

Observation period: Mean duration, 2 years

Investigators: A. Ghezzi and others

Sites: Ospedale di Gallarate, Gallarate, and others, Italy

Results/Publications: Relapse rate decreased from 2.4 to 0.4 (Avonex), 3.2 to 0.8 (Rebif-Betaseron), 2.8 to 0.25 (Copaxone); EDSS unchanged; interferon side effects recorded in 46; in Copaxone group, side effects in 3 (Multiple Sclerosis 2005;11(4):420-4; Neurological Sciences 2005;26 Suppl 4:s183-6)

Funding: Not available

ClinicalTrials.gov Identifier: Not available

Last update: 2006
Agent: Avonex® (interferon beta-1a, Biogen Idec) vs. Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.)

**Purpose of study:** To determine impact of NAbs on clinical/MRI outcomes, also known as PROOF Study

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation/movement across blood-brain barrier, inducing suppressive T cells (Avonex, Rebif)

**Study description:** Prospective, retrospective, observational

**Dose/route:** Avonex 30 mcg/wk im vs. Rebif 44 mcg tiw sc for 12-24 mos

**Outcome parameters:** Brain parenchymal fraction, EDSS, relapse rates, EDSS, MRI

**Type of MS:** RR

**Number of Subjects:** 374

**Start date:** August 2002

**Observation period:** 3 years

**Investigators:** T. J. Murray and others

**Sites:** Multicenter, United States and Canada

**Results/Publications:** Discontinued due to insufficient recruitment; data analysis showed that EDSS to month 6 increased significantly more in NAb+ compared with NAb- patients (communication with principal investigator; Abstract #P705, ECTRIMS 2006)

**Funding:** Biogen Idec, Inc.

ClinicalTrials.gov Identifier: Not available

Last update: 2007

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Agent: Betaseron® (interferon beta-1b, Bayer HealthCare Pharmaceuticals, Inc.)

**Purpose of study:** To delay time to definite MS in patients with clinically isolated syndrome, also known as BENEFIT study

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells

**Study description:** Double blinded, placebo controlled

**Dose/route:** 250 mcg qod sc vs. PBO sc

**Outcome parameters:** Time to definite MS, frequency of relapse, EDSS, MSFC, MRI

**Type of MS:** First clinical demyelinating event suggestive of MS

**Number of Subjects:** 487

**Start date:** January 2002

**Observation period:** 24 months

**Investigators:** Multiple

**Sites:** Multicenter, Europe, Canada, Israel

**Results/Publications:** 28% of Betaseron group developed definite MS compared with 45% of PBO group; development of MS delayed by 363 days in Betaseron group compared to PBO group; in 1st year of 5-yr follow-up study, group that had early treatment with Betaseron had reduced risk of EDSS progression by 40% over delayed treatment group (Abstracts #P50, #P583, ECTRIMS 2005; Abstracts #P01.073, #S02.001, #S02.002, AAN 2006; Abstract #S02.004, AAN 2007)

**Funding:** Schering AG

ClinicalTrials.gov Identifier: Not available

Last update: 2007

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Agent: Betaseron® (interferon beta-1b, Bayer HealthCare Pharmaceuticals, Inc.)

Purpose of study: To investigate long-term effects, also known as BEST study

Possible mechanism: Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells

Study description: Observational study of over 3500 case reports

Dose/route: 250 mcg qod sc

Outcome parameters: Clinical parameters, MSFC, EuroQoL 5-Dimensions

Type of MS: RR

Number of Subjects: Over 3500

Start date: 2003

Observation period: 5 years

Investigators: L. Kappos and others

Sites: University Hospitals, Basel, Switzerland, and others, worldwide

Results/Publications: Interim analysis: 27.4% dropped out in the 2-year cohort and 46.4% in the 3-year cohort; of remaining patients, after 2 years 82.6% were progression-free, 52.4% were relapse-free, and 46.5% were progression- and relapse-free; after 3 years, 77.8% were progression-free, 44.8% relapse-free and 39.7% progression- and relapse-free (Abstract #P595, ECTRIMS 2004; Abstract #P694, ECTRIMS 2006)

Funding: Schering AG

ClinicalTrials.gov Identifier: Not available

Last update: 2007

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Agent: Betaseron® (interferon beta-1b, Bayer HealthCare Pharmaceuticals, Inc.)

Purpose of study: Follow-up of patients in original Betaseron trial

Possible mechanism: Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells

Study description: Observational study

Dose/route: 250 mcg qod sc

Outcome parameters: Frequency of relapse, EDSS, MSFC, MRI

Type of MS: RR, SP

Number of Subjects: 329

Start date: January 2005

Observation period: 16 years

Investigators: G. Ebers and others

Sites: University of Oxford, Oxford, United Kingdom

Results/Publications: Results divided into “never” users of IFNB-1b (<=10% of the time), “ever” users (>10–80%), and “always” users (>80%); wheelchair use required by 44.2% of “never” group and 29.4% of “always”; median time to EDSS 6 was 6 yrs later for “always” than for “never”; annualised relapse rates lower in “always” than “never”; no significant differences on MRI; self-reported QOL better in “always” group (Abstract #P01.079, AAN 2006, Abstracts #P664,P665,P666, ECTRIMS 2006; Abstract #P06.089, AAN 2007)

Funding: Schering AG, Berlex Laboratories

ClinicalTrials.gov Identifier: NCT00206635

Last update: 2007

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Agent: Betaseron® (interferon beta-1b, Bayer HealthCare Pharmaceuticals, Inc.) + azathioprine

**Purpose of study:** To determine safety and impact on disease course and brain lesions

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Betaseron)/Releases 6-MP, inhibits nucleic acid biosynthesis, preventing proliferation of proinflammatory cells (azathioprine)

**Study description:** Open label, add-on study

**Dose/route:** Betaseron 250 mcg qod sc (3 mos), Betaseron + azathioprine 2 mg/kg/d po (6 mos)

**Outcome parameters:** Safety tolerability, Gd-MRI, EDSS, MSFC, labs

**Type of MS:** RR, SP

**Number of Subjects:** 18

**Start date:** October 1999

**Observation period:** 9 months

**Investigators:** P. Calabresi

**Sites:** Brown University, Providence; University of Maryland, College Park

**Results/Publications:** No serious adverse events; gastrointestinal side effects and leukopenia most common; 65% reduction in Gd+ lesions with combination therapy; total white blood cell count of less than 4800/mm3 was best predictor of MRI response (Abstract # P06.089, AAN 2004; Multiple Sclerosis 2005;11(2):169-74)

**Funding:** Berlex Laboratories, Inc.

**ClinicalTrials.gov Identifier:** Not available

*Last update: 2006*


Agent: Betaseron® (interferon beta-1b, Bayer HealthCare Pharmaceuticals, Inc.) vs. Avonex® (interferon beta-1a, Biogen Idec)

**Purpose of study:** To compare interferon treatments in impact on immune function and disease course, also known as ABOVE Study

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Betaseron, Avonex)

**Study description:** Examining MD blind

**Dose/route:** Betaseron 250 mcg qod sc vs. Avonex 30 mcg/wk im

**Outcome parameters:** Frequency of relapse, scoring technique, MRI

**Type of MS:** RR

**Number of Subjects:** 400

**Start date:** March 2003

**Observation period:** 2 years

**Investigators:** Multiple

**Sites:** Multicenter, United States and Canada

**Results/Publications:** Terminated (communication with Berlex, inc.)

**Funding:** Berlex, Inc.

**ClinicalTrials.gov Identifier:** NCT00206648

*Last update: 2006*
Agent: Betaseron® (interferon beta-1b, Bayer HealthCare Pharmaceuticals, Inc., two doses) vs. Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.)

Purpose of study: To determine impact on disease course, also known as BEYOND study

Possible mechanism: Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Betaseron)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)

Study description: Examining MD blind

Dose/route: Betaseron 250 mcg qod sc vs. 500 mcg qod sc vs. Copaxone 20 mg/d sc

Outcome parameters: Frequency of relapse, scoring technique, MRI

Type of MS: RR

Number of Subjects: 2000

Start date: December 2003

Observation period: 2 years

Investigators: Multiple

Sites: Multicenter, worldwide

Results/Publications: In pilot phase, active lesions decreased by 90% on 500 mcg and by 70% on 250 mcg; enrollment completed (Abstract #P182, ECTRIMS 2003; Abstract #P06.086, AAN 2004; Betaseron MS Information Center)

Funding: Bayer HealthCare Pharmaceuticals, Inc.

ClinicalTrials.gov Identifier: NCT00099502

Last update: 2007

Agent: Betaseron® (interferon beta-1b, Bayer HealthCare Pharmaceuticals, COMPLETED Inc.) vs. Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.)

Purpose of study: To determine impact on disease course, also known as BECOME

Possible mechanism: Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Betaseron)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)

Study description: Randomized, rater-blinded

Dose/route: Betaseron 250 mcg qod sc vs. Copaxone 20 mg/d sc

Outcome parameters: Relapses, EDSS, MSFC, cognitive stability, 3-Tesla Gd-MRI

Type of MS: RR

Number of Subjects: 110

Start date: January 2003

Observation period: 1 year

Investigators: D. Cadavid, L. Wolansky

Sites: UMDNJ; Holy Name Hospital, Teaneck, NJ

Results/Publications: Both groups showed disease activity on MRI either continuously (33%) or intermittently (44-50%) (Abstract #P236, ECTRIMS 2005; Abstract #324, American Society of Neuroradiology, 2005; Journal of Neuroimaging 2005;15(3):289-90; Abstract, CMSC 2007)

Funding: Berlex Laboratories, Inc.

ClinicalTrials.gov Identifier: NCT00176592

Last update: 2007
**Agent:** BHT-3009-01 + Lipitor® (atorvastatin, Pfizer Ireland Pharmaceuticals Corp.)

**Purpose of study:** To control disease course and development of brain lesions

**Possible mechanism:** Designed to alter immune response to myelin basic protein (BHT-3009-01)/Promotes Th2 response (Lipitor)

**Study description:** Double blinded, crossover

**Dose/route:** BHT-3009 or PBO im in weeks 1, 3, 5, 9; Lipitor 80 mg/d or PBO po/d for weeks 1-13; patients who initially receive PBO will subsequently receive Rx

**Outcome parameters:** EDSS, MRI

**Type of MS:** RR, SP

**Number of Subjects:** 30

**Start date:** July 2004

**Observation period:** 1 year

**Investigators:** T. Vollmer and others

**Sites:** Barrow Neurological Institute, St. Joseph’s Hospital, Phoenix, AZ, and others

**Results/Publications:** Well tolerated; evidence of decreased immune responses against MBP; in subgroup, immune assay results suggest decreased production of inflammatory cytokines (Abstract #S02.003, #S02.004 AAN 2006)

**Funding:** Bayhill Therapeutics, Inc.

**ClinicalTrials.gov Identifier:** NCT00103974

Last update: 2006

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**Agent:** Bone marrow/peripheral stem cell transplantation (autologous)

**Purpose of study:** To control disease course and development of brain lesions

**Possible mechanism:** Rids the body of T cells that drive the immune attack against CNS

**Study description:** Open study

**Dose/route:** Stem cell mobilization with cyclophosphamide 4.5 g/m2 iv + G-CSF 10 g/kg/d G-CSF sc for 10 days; immunoablation with cyclophosphamide, busulfan, rATG

**Outcome parameters:** Clinical, MRI, immune function

**Type of MS:** Rapidly progressive

**Number of Subjects:** 24

**Start date:** February 2001

**Observation period:** 3 years

**Investigators:** M. Freedman and others

**Sites:** University of Ottawa and others

**Results/Publications:** No clinical attack in 11 transplanted patients (6 completed study); functional scales demonstrate stability or improvements; brain MRI in 5 patients with SP MS showed dramatic increase in rate of atrophy over 4 mos during which patients received immunoablative doses of chemotherapy and ASCT; in some, stabilized by 1 month post-transplant, and in others, after 4-6 mos; 3/4 patients tested with magnetization transfer ratio showed evidence of myelin repair (Abstract #P06.077, AAN 2002; Abstract #S11.006, AAN 2003; Abstracts #S60.005 and #S40.005, AAN 2004; Abstracts #S46.005 and #S46.006, AAN 2005; Abstract #SC2.013, AAN 2006)

**Funding:** MS Research Foundation, MS Society of Canada

**ClinicalTrials.gov Identifier:** Not available

Last update: 2006
Agent: Bone marrow/peripheral stem cell transplantation (autologous)
Purpose of study: To control development of brain lesions, also known as MIST study
Possible mechanism: Rids the body of T cells that drive the immune attack against CNS
Study description: Open, crossover
Dose/route: Cyclophosphamide 60 mg/kg/d for 2 days iv + rATG .5 mg/kg on day -5, 1 mg/kg on day -4, and 1.5 mg/kg on days -3,-2,-1 iv vs. standard therapy (interferons, Copaxone® or Novantrone®)
Outcome parameters: EDSS, number of relapses, ambulation index, timed ambulation, 9-hole peg test, PASAT, MRI, SF-36, MusiQOL, Neurological Rating Scale, survival
Type of MS: RR, active
Number of Subjects: 110
Start date: January 2006
Observation period: 5 years
Investigators: R. Burt and others
Sites: Northwestern University Feinberg School of Medicine, Chicago, and others
Results/Publications: Not available
Funding: Not available
ClinicalTrials.gov Identifier: NCT00273364
Last update: 2006

Agent: Bone marrow/peripheral stem cell transplantation (autologous)
Purpose of study: To control development of brain lesions, also known as HALT MS study
Possible mechanism: Rids the body of T cells that drive the immune attack against CNS
Study description: Open label
Dose/route: Carmustine 300 mg/m² iv, etoposide 100 mg/m² iv, cytarabine 100 mg/m² iv, melphalan 140 mg/m² iv, thymoglobulin 3.5 mg/kg iv, granulocyte-colony stimulating factor 5 mcg/kg/d sc, prednisone .5 mg/kg iv
Outcome parameters: EDSS, MSFC, MRI, relapse
Type of MS: RR, PR
Number of Subjects: 30
Start date: June 2006
Observation period: 5 years
Investigators: R. Nash and others
Sites: Fred Hutchinson National Cancer Center, Seattle, and others
Results/Publications: Not available
Funding: National Institute of Allergy and Infectious Disease
ClinicalTrials.gov Identifier: NCT00288626
Last update: 2006
**Agent:** Bone marrow/hematopoietic stem cell transplantation (autologous) vs. Novantrone® (mitoxantrone for injection concentrate, EMD Serono, Inc.)

**Purpose of study:** To prevent relapses, control or reverse disease progression, lesion development, and determine impact on immune function

**Possible mechanism:** Rids the body of T cells that drive the immune attack against CNS (NST)/Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion (Novantrone)

**Study description:** Stem cell transplantation vs. Novantrone

**Dose/route:** Cyclophosphamide and Campath with autologous hematopoietic bone marrow transplantation vs. Novantrone 12 mg/m2 iv

**Outcome parameters:** EDSS, Neurological Rating Scale, PASAT, timed ambulation, 9-hole peg test, MRI

**Type of MS:** Two clinical relapses or gadolinium enhancement on MRI despite 6 months of interferon

**Number of Subjects:** 92

**Start date:** April 2005

**Observation period:** 5 years

**Investigators:** R. Burt and others

**Sites:** Northwestern University Feinberg School of Medicine, Chicago, and others

**Results/Publications:** Not available

**Funding:** US FDA, National Institutes of Health GCRC

**ClinicalTrials.gov Identifier:** Not available

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**Agent:** Botox® (botulinum toxin A, Allergan, Inc.)

**Purpose of study:** To improve spasticity

**Possible mechanism:** Blocks neuromuscular transmission

**Study description:** Double blinded, placebo controlled

**Dose/route:** Botox 50-100 units per muscle im, depending on severity of spasticity and muscle size

**Outcome parameters:** Quality of life, functional assessments, pain assessments, spasticity measures

**Type of MS:** All types

**Number of Subjects:** 40

**Start date:** September 2005

**Observation period:** 12 weeks

**Investigators:** J. Preiningerova, B. Jabbari

**Sites:** Yale Center for MS Treatment and Research, New Haven, CT

**Results/Publications:** Not available

**Funding:** Allergan, Inc.

**ClinicalTrials.gov Identifier:** Not available

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Agent: Calcitriol (1,25-dihydroxyvitamin D3)  
**COMPLETED**

**Purpose of study:** To evaluate safety and tolerability  
**Possible mechanism:** Promotes suppressor T cells  
**Study description:** Open label, dose escalation  
**Dose/route:** 2.5 mcg/d po  
**Outcome parameters:** Frequency of relapse, EDSS  
**Type of MS:** RR  
**Number of Subjects:** 15  
**Start date:** 2000  
**Observation period:** 48 weeks  
**Investigators:** D. Wingerchuk and others  
**Sites:** University of Western Ontario, London, Ontario, Canada  
**Results/Publications:** 2 patients withdrew because of symptomatic hypercalcaemia resulting from persistent dietary indiscretion; diet-compliant patients experienced mild adverse effects; on-study exacerbation rate less than baseline (Journal of Neurology Neurosurgery and Psychiatry 2005;76(9):1294-6)  
**Funding:** MS Society of Canada  
**ClinicalTrials.gov Identifier:** Not available  
**Last update:** 2006

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Agent: Campath® (alemtuzumab, Genzyme Corporation) vs. Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.)  
**SUSPENDED**

**Purpose of study:** To control disease progression  
**Possible mechanism:** Targets CD52 antigen expressed on B and T lymphocytes (Campath)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)  
**Study description:** Open label  
**Dose/route:** Campath 12 mg/d iv for 5 days at mos 0, 12, 24 vs. Campath 24 mg/d iv for 5 days at mos 0, 12, 24 vs. Rebif 22 mcg tiw sc with dose increases over 4 wks to 44 mcg tiw sc for 36 mos  
**Outcome parameters:** Time to sustained accumulation of disability at 3 yrs  
**Type of MS:** RR  
**Number of Subjects:** 180  
**Start date:** November 2002  
**Observation period:** 36 months  
**Investigators:** Multiple  
**Sites:** Multicenter, United States and United Kingdom  
**Results/Publications:** Suspended 9/05, due to adverse events; 6 patients have developed idiopathic thrombocytopenic purpura (1 patient died) and 11.1% had thyroid adverse events compared with 1.9% on Rebif; interim analysis showed 75% reduction in relapse rate at 2 yrs in Campath group compared with Rebif (Genzyme press release, September 16, 2005; Abstract #P799, P800, ECTRIMS 2006; Abstracts #P06.087, S32.004, S12.004, AAN 2007)  
**Funding:** Genzyme Corporation  
**ClinicalTrials.gov Identifier:** NCT00050778  
**Last update:** 2007

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Agent: Cladribine
Purpose of study: To test safety, effectiveness, also known as CLARITY study
Possible mechanism: Lymphocyte reduction
Study description: Randomized, double blinded, placebo controlled
Dose/route: Cladribine 0.875 mg/kg/cycle po over 5 days per month, administered in 2-4 cycles per year vs. PBO po
Outcome parameters: Relapse rate, EDSS, MRI
Type of MS: RR
Number of Subjects: 1290
Start date: April 2005
Observation period: 2 years
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Enrollment completed (Merck Serono press release, January 16, 2007)
Funding: EMD Serono, Inc.
ClinicalTrials.gov Identifier: NCT00213135
Last update: 2007

Agent: Cladribine + Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.)
Purpose of study: To test safety, effectiveness of adding on cladribine to Rebif (FBS-free/HSA-free formulation), also known as ONWARD study
Possible mechanism: Lymphocyte reduction (Cladribine)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)
Study description: Randomized, double blinded, placebo controlled
Dose/route: Cladribine 0.875 mg/kg/cycle po for two consecutive cycles + Rebif 44 mcg tiw sc vs. Cladribine 0.875 mg/kg/cycle po for four consecutive cycles + Rebif 44 mcg tiw sc vs. Rebif + PBO po
Outcome parameters: EDSS, MRI
Type of MS: Relapsing forms
Number of Subjects: 260
Start date: December 2006
Observation period: 104 weeks
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: EMD Serono, Inc.
ClinicalTrials.gov Identifier: NCT00436826
Last update: 2007

Agent: CNTO 1275 (monoclonal antibody)  
Purpose of study: To test safety, impact on immune function  
Possible mechanism: Blocks IL-12 cytokine activity  
Study description: Randomized, double blinded, placebo controlled, dose ranging  
Dose/route: 30-200 mg monthly or bimonthly sc vs. PBO  
Outcome parameters: MRI  
Type of MS: RR  
Number of Subjects: 250  
Start date: July 2004  
Observation period: 71 weeks  
Investigators: Multiple  
Sites: Multicenter  
Results/Publications: Not available  
Funding: Centocor, Inc.  
ClinicalTrials.gov Identifier: NCT00207727  
Last update: 2006

Agent: Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.)  
Purpose of study: Long-term follow up of patients in original trial  
Possible mechanism: Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2  
Study description: Prospective, open label, multi-year follow-up of patients in original study  
Dose/route: 20 mg/d sc  
Outcome parameters: EDSS  
Type of MS: RR  
Number of Subjects: 232  
Start date: 1991  
Observation period: Ongoing  
Investigators: K. Johnson and others  
Sites: Multicenter, United States  
Results/Publications: 232 patients received at least 1 dose since 1991; ongoing patients (108) continued as of November 2003; 124 patients withdrew (50 returned for follow-up); for ongoing patients, 62% were stable/improved; and 24, 8 and 1% reached EDSS 4, 6 and 8, respectively; for withdrawn patients, 28% were stable/improved and 68, 50 and 10% reached EDSS 4, 6 and 8, respectively; Z4 (a composite measure of MRI metrics) appears to correlate with EDSS, predicting disability over next 4.5 yrs (Abstract #P06.079, AAN 2002; Abstract, ECTRIMS 2003; Abstract #S20.004, AAN 2004; Abstract #S22.001, AAN 2006; Multiple Sclerosis 2006;12:309-320)  
Funding: Teva Pharmaceutical Industries, Ltd.  
ClinicalTrials.gov Identifier: NCT00203021  
Last update: 2006
Agent: Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.)

Purpose of study: To evaluate effectiveness in delaying conversion to clinically definite MS, also known as PreCISe Study

Possible mechanism: Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2

Study description: Randomized, double blinded, placebo controlled, parallel group

Dose/route: 20 mg/d sc vs. PBO sc

Outcome parameters: Time to conversion to clinically definite MS, MRI

Type of MS: First clinical demyelinating event suggestive of MS

Number of Subjects: 480

Start date: November 2003

Observation period: 5 years

Investigators: G. Comi and others

Sites: Multicenter, worldwide

Results/Publications: Fully enrolled (communication with Teva Neuroscience)

Funding: Teva Neuroscience

ClinicalTrials.gov Identifier: Not available

Last update: 2007

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Agent: Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.)

Purpose of study: To evaluate safety and effectiveness of 20 mg vs. 40 mg

Possible mechanism: Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2

Study description: Randomized, double blinded, parallel group

Dose/route: 20 mg/d sc vs. 40 mg/d sc

Outcome parameters: Frequency of relapse, MRI

Type of MS: RR

Number of Subjects: 100

Start date: August 2003

Observation period: 9 months

Investigators: D. Wynn and others

Sites: Multicenter, United States

Results/Publications: Total number of Gd+ lesions at months 7, 8, and 9, showed a trend favoring the 40-mg group; the difference between the two dose groups emerged at month 3; trend favoring 40-mg group for relapse rate with benefit on proportion of relapse-free subjects and time to first relapse; injection site reactions and immediate postinjection reactions more common and severe with higher dose (Neurology 2007;68(12):939-44)

Funding: Teva Neuroscience

ClinicalTrials.gov Identifier: NCT00202982

Last update: 2007

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Agent: Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.)  
**Completed**

**Purpose of study:** To evaluate safety and effectiveness of oral administration, also known as CORAL study

**Possible mechanism:** Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** 5 mg/d po vs. 50 mg/d po vs. PBO po

**Outcome parameters:** Frequency of relapse, EDSS, MRI

**Type of MS:** RR

**Number of Subjects:** 1644

**Start date:** March 2000

**Observation period:** 56 weeks

**Investigators:** M. Filippi and others

**Sites:** Multicenter, worldwide

**Results/Publications:** Cumulative number of confirmed relapses did not differ between treatment and placebo groups; no drug effect seen for any secondary and tertiary endpoints; safe and well tolerated (Lancet Neurology 2006;5(3):213-20)

**Funding:** Teva Pharmaceutical Industries, Ltd.

**ClinicalTrials.gov Identifier:** Not available  
**Last update:** 2006

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Agent: Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.) + Novantrone® (mitoxantrone for injection concentrate, EMD Serono, Inc.)

**Purpose of study:** To evaluate safety, tolerability and effectiveness of pretreatment with Novantrone

**Possible mechanism:** Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)/Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion (Novantrone)

**Study description:** Randomized, two-arm, open label

**Dose/route:** Novantrone 12 mg/m²/mo iv for 2.5 mos followed by washout, then Copaxone 20 mg/d sc for 12.5 mos vs. Copaxone for 15 mos

**Outcome parameters:** Frequency of relapse, scoring technique, MRI, quality of life

**Type of MS:** RR, PR

**Number of Subjects:** 40

**Start date:** April 2003

**Observation period:** 15 months

**Investigators:** T. Vollmer and others

**Sites:** Multicenter, United States

**Results/Publications:** Novantrone/Copaxone produced 89% greater reduction in Gd+ lesions at months 6 and 9 (sustained at 15 months) compared to Copaxone alone; Gd+ lesion frequency decreased by 47% at 9 months and 87% at 15 months; mean relapse rate 0.16 in Novantrone/Copaxone group and 0.32 in Copaxone alone group; early decreases in volume of T1 and T2 lesions in Novantrone/Copaxone group sustained at 24 months of follow up (Abstract #62, ECTRIMS 2006; Abstracts #P06.096, P06.104, AAN 2007)

**Funding:** Teva Neuroscience

**ClinicalTrials.gov Identifier:** NCT00203073  
**Last update:** 2007

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Agent: Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.) + Novantrone® (mitoxantrone for injection concentrate, EMD Serono, Inc.) vs. Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.)

Purpose of study: To evaluate safety, tolerability and effectiveness in reducing disease activity

Possible mechanism: Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)/Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion (Novantrone)/Slows down immune response, possibly by interfering with T cell activation/movement across blood-brain barrier, and inducing suppressive T cells (Rebif)

Study description: Randomized, controlled, examining-MD blinded

Dose/route: Novantrone 12 mg/m2/mo iv given as short infusion monthly for 3 mos and 6mg/m2 quarterly for two further pulses + Copaxone 20 mg/d sc vs. Rebif 44 mcg tiw sc

Outcome parameters: MSIS, EDSS, annualised relapse rate, relapse free patients, time to first relapse, time to withdrawal

Type of MS: RR
Number of Subjects: 60
Start date: April 2005
Observation period: 36 months
Investigators: M. Boggild and J. Ramtahal
Sites: The Walton Centre for Neurology and Neurosurgery, Liverpool, UK and others, United Kingdom
Results/Publications: Not available
Funding: National Health Service
ClinicalTrials.gov Identifier: Not available
Last update: 2007

Agent: Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.) + prednisone

Purpose of study: To control disease course and development of brain lesions, also known as ASSERT Study

Possible mechanism: Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)/Closes damaged blood-brain barrier and reduces inflammation in CNS (prednisone)

Study description: Double blinded, placebo controlled

Dose/route: Copaxone 20 mg/d sc + prednisone po vs. Copaxone + PBO po

Outcome parameters: Change in brain volume using SIENA MRI technique

Type of MS: RR
Number of Subjects: 500
Start date: January 2005
Observation period: 36 months
Investigators: Multiple
Sites: Multicenter, United States and Canada
Results/Publications: Not available
Funding: Teva Neuroscience
ClinicalTrials.gov Identifier: NCT00203047
Last update: 2007
**Agent:** Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.) + Proventil® (albuterol, Schering Corporation)

**Purpose of study:** To control disease course and brain lesions, evaluate immune function

**Possible mechanism:** Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)/Decreases IL-12 activity (Proventil)

**Study description:** Double blinded, placebo controlled

**Dose/route:** Copaxone 20 mg/d sc + albuterol 4 mg/d po vs. Copaxone + PBO po

**Outcome parameters:** MSFC, time to relapse, number and severity of relapses, MRI, clinical scales, change in cytokine secretions and % of IL-12-producing monocytes

**Type of MS:** RR

**Number of Subjects:** 40

**Start date:** September 2001

**Observation period:** 2 years of follow-up

**Investigators:** S. Khoury

**Sites:** Brigham and Women's Hospital MS Center, Boston

**Results/Publications:** Closed to enrollment (communication with primary investigator)

**Funding:** NIH, National Institute of Allergy and Infectious Disease, Autoimmunity Centers of Excellence

**ClinicalTrials.gov Identifier:** NCT00039988

**Last update:** 2007

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**Agent:** Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.) vs. Avonex® (interferon beta-1a, Biogen Idec) vs. Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.) vs. Betaseron® (interferon beta-1b, Bayer HealthCare Pharmaceuticals, Inc.)

**Purpose of study:** To control disease relapses

**Possible mechanism:** Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex, Betaseron, Rebif)

**Study description:** Prospective, controlled, open label

**Dose/route:** Copaxone 20 mg/d sc vs. Avonex 30 mcg/wk im vs. Rebif 22 mcg tiw sc vs. Betaseron 250 mcg qod sc

**Outcome parameters:** Time course of effect on relapse rate

**Type of MS:** RR

**Number of Subjects:** 255

**Start date:** Not available

**Observation period:** Ongoing

**Investigators:** J. Haas

**Sites:** Judisches Krankenhaus Berlin, Abteilung für Neurologie, Germany

**Results/Publications:** Clinical benefit for Rx apparent at 6 mos, sustained at 12, 24; relapse rate (24 mos) reduced more for Copaxone (Abstract #P06.105, AAN 2003; European Journal of Neurology 2005;12(6):425-31)

**Funding:** Not available

**ClinicalTrials.gov Identifier:** Not available

**Last update:** 2006

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Agent: Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.) vs. Betaseron® (interferon beta-1b, Bayer HealthCare Pharmaceuticals, Inc.) vs. Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.)

**Purpose of study:** To compare safety, tolerability and effectiveness in reducing disease activity, also known as ACHIEVE study

**Possible mechanism:** Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Betaseron, Rebif)

**Study description:** Randomized, examining MD-blind, parallel groups

**Dose/route:** Copaxone 20 mg/d sc vs. Betaseron 250 mcg qod sc vs. Rebif 44 mcg tiw sc

**Outcome parameters:** Frequency of relapse, scoring technique, MRI

**Type of MS:** RR, PR

**Number of Subjects:** 850

**Start date:** February 2004

**Observation period:** 3 years

**Investigators:** P. Coyle and others

**Sites:** Multicenter, United States

**Results/Publications:** Terminated due to slow enrollment; data analysis ongoing (communication with Teva Neuroscience)

**Funding:** Teva Neuroscience

**ClinicalTrials.gov Identifier:** NCT00202995

**Last update:** 2007

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Agent: Cyclophosphamide

**Purpose of study:** To test safety and control disease progression, development of lesions

**Possible mechanism:** Alkylating agent, interferes with proliferating immune cells

**Study description:** Pilot, open label

**Dose/route:** 50 mg/kg/d iv for 4 days

**Outcome parameters:** Frequency of relapse, scoring technique, MRI

**Type of MS:** Aggressive RR

**Number of Subjects:** 20

**Start date:** October 2003

**Observation period:** 2 years

**Investigators:** D. Kerr and others

**Sites:** Johns Hopkins University, Baltimore

**Results/Publications:** 8 patients completed treatment; all developed transient severe neutropenia, followed by immune reconstitution in 10-17 days; all had reduction or elimination of new and enhancing lesions; brain atrophy slowed in several patients; no patient has had a relapse following treatment, and most had improvements in EDSS and MSFC (Abstract #P01.072, AAN 2006)

**Funding:** Johns Hopkins GCRC

**ClinicalTrials.gov Identifier:** Not available

**Last update:** 2006

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**Agent:** Cyclophosphamide vs. methylprednisolone

**Purpose of study:** To control disease progression, also known as PROMESS study

**Possible mechanism:** Alkylating agent, interferes with rapidly proliferating immune cells (cyclophosphamide)/Closes damaged blood-brain barrier, reducing inflammation in CNS (methylprednisolone)

**Study description:** Randomized, double blinded

**Dose/route:** Cyclophosphamide 750 mg/m² (if lymphocytes >1400) or 500 mg/m² (if lymphocytes <1400 and > 1000) or 400 mg/m² (if lymphocytes <900) every 4 wks for yr 1 and every 8 wks for yr 2 iv + ondansetron vs. methylprednisolone 1 g every 4 wks for yr 1 and every 8

**Outcome parameters:** EDSS, MSFC, frequency of relapse

**Type of MS:** SP

**Number of Subjects:** 360

**Start date:** November 2005

**Observation period:** 2 years

**Investigators:** B. Brochet and others

**Sites:** Multicenter, France

**Results/Publications:** Not available

**Funding:** French Health Ministry

**ClinicalTrials.gov Identifier:** NCT00241254

**Last update:** 2006

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**Agent:** Daclizumab

**Purpose of study:** To evaluate safety and effectiveness, also known as CHOICE trial

**Possible mechanism:** Limits T cell expansion by blocking signaling of cytokine IL-2

**Study description:** Randomized, double blinded, placebo controlled, dose ranging

**Dose/route:** 2 mg/kg sc every 2 wks vs. 1 mg/kg sc every 4 wks (alternates with PBO every 2 weeks) vs. PBO sc

**Outcome parameters:** Gd-MRI lesions, relapse rate, EDSS, MSFC

**Type of MS:** Active, relapsing

**Number of Subjects:** 270

**Start date:** April 2005

**Observation period:** 72 weeks

**Investigators:** Multiple

**Sites:** Multicenter, United States, Canada, Europe

**Results/Publications:** Patients receiving daclizumab showed significant reduction in Gd lesions at week 24; trial continuing to completion (Biogen Idec, Inc. and PDL BioPharma, Inc. press release, March 12, 2007)

**Funding:** Biogen Idec, Inc., PDL BioPharma, Inc.

**ClinicalTrials.gov Identifier:** NCT00109161

**Last update:** 2007
Agent: Daclizumab
Purpose of study: To evaluate safety and effectiveness, also known as ZAP MS study
Possible mechanism: Limits T cell expansion by blocking signaling of cytokine IL-2
Study description: Open label
Dose/route: 1 mg/kg/mo iv
Outcome parameters: MRI, clinical and immunological parameters
Type of MS: RR
Number of Subjects: 15
Start date: January 2004
Observation period: 20.5 months
Investigators: H. McFarland and others
Sites: National Institutes Health, Bethesda, MD
Results/Publications: Not available
Funding: NIH Intramural Research
ClinicalTrials.gov Identifier: NCT00071838 Last update: 2006

Agent: Dronabinol vs. cannabis
Purpose of study: To improve spasticity
Possible mechanism: Interacts with cannabinoid receptors on CNS cells, possibly impacting motor function, cognition and affect
Study description: Double blinded, placebo controlled
Dose/route: 1 cannabis cigarette per day + PBO po vs. dronabinol 10 mg/d po + smoked PBO vs. smoked PBO + PBO po
Outcome parameters: EDSS, Lido measurement of spasticity, Ashworth, MSFC, MSQLI
Type of MS: SP, PP
Number of Subjects: 60
Start date: April 2004
Observation period: Up to 5 months
Investigators: M. Agius and D. Richman
Sites: UC Davis Medical Center
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: NCT00260741 Last update: 2006
Agent: Estriol
Purpose of study: To control disease course
Possible mechanism: Pregnancy hormone that decreases Th1 response
Study description: Randomized, double blinded, placebo controlled
Dose/route: Copaxone 20 mg/d sc + estriol 8 mg/d po vs Copaxone + PBO
Outcome parameters: Relapse rate, MSFC, EDSS, MRI
Type of MS: RR, women
Number of Subjects: 130
Start date: June 2007
Observation period: 2 years
Investigators: R. Voskuhl and others
Sites: University of California at Los Angeles and others, United States
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: NCT00451204  Last update: 2007

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Agent: Fampridine-SR (4-aminopyridine, sustained release)  COMPLETED
Purpose of study: To test safety and effectiveness in improvement of walking ability in people with MS
Possible mechanism: Blocks potassium channels on axons, permitting demyelinated axon to transmit impulses
Study description: Double blinded, placebo controlled
Dose/route: po
Outcome parameters: Safety, Timed 25-Foot Walk, MS Walking Scale-12
Type of MS: All types
Number of Subjects: 301
Start date: June 2005
Observation period: 21 weeks
Investigators: Multiple
Sites: Multicenter, United States and Canada
Results/Publications: 283 patients completed the trial; a significantly higher proportion of fampridine group were "responders" who experienced consistently improved walking speed during 14 wks and significant improvement in MSWS-12 score; 2 serious adverse events attributed to fampridine that led to treatment discontinuation (anxiety, seizure during urosepsis) (Abstract #S32.003, AAN 2007)
Funding: Acorda Therapeutics, Inc.
ClinicalTrials.gov Identifier: NCT00127530  Last update: 2007

************************************************************************************
Agent: Fampridine-SR (4-aminopyridine, sustained release)

Purpose of study: To test safety and effectiveness in improvement of walking ability in people with MS

Possible mechanism: Blocks potassium channels on axons, permitting demyelinated axon to transmit impulses

Study description: Double blinded, placebo controlled

Dose/route: po

Outcome parameters: Timed 25-Foot Walk

Type of MS: All types

Number of Subjects: 200

Start date: June 2007

Observation period: 14 weeks

Investigators: Multiple

Sites: Multicenter, United States and Canada

Results/Publications: Not available

Funding: Acorda Therapeutics, Inc.

ClinicalTrials.gov Identifier: NCT00483652

Last update: 2007

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Agent: Fingolimod (FTY720)

Purpose of study: To test safety and effectiveness

Possible mechanism: Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue

Study description: Double blinded, placebo controlled

Dose/route: 1.25 mg po vs 5 mg po vs PBO po for 6 mos; in 6-mo extension, those on PBO randomized to 1.25 mg po vs 5 mg po

Outcome parameters: Frequency of relapse, MRI

Type of MS: RR

Number of Subjects: 255

Start date: 2004

Observation period: 6 months, with 18-month extension

Investigators: L. Kappos and others

Sites: Multicenter, Europe and Canada

Results/Publications: After 6 mos, number and volume of lesions and relapse rates significantly reduced in both Rx groups vs. PBO; at 6 mos extension, relapse rate reduced by 70% (in PBO patients who switched to 1.25 mg) and 86% (5 mg); significant reductions in active inflammation seen in both groups on MRI; more adverse events during extension in 5-mg groups (infections, increase in blood pressure, first dose heart rate reduction, alterations in liver function tests); one case of posterior reversible encephalopathy syndrome occurred after 10 weeks of treatment in the 5 mg group; those receiving FTY720 1.25 mg compared with PBO showed significant improvement in depression between baseline and 6 mos (Abstract #O141, ENS 2005; Abstracts #64,#P578,#682, ECTRIMS 2005; Abstract #S12.003, AAN 2006; NEJM 2006;355(11):1124-40; Abstract #P06.085, AAN 2007)

Funding: Novartis

ClinicalTrials.gov Identifier: Not available

Last update: 2007
Agent: Fingolimod (FTY720)

Purpose of study: To test safety and effectiveness

Possible mechanism: Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue

Study description: Double blinded, placebo controlled

Dose/route: 0.5 mg/d po vs. 1.25 mg/d po vs PBO

Outcome parameters: Frequency of relapse, disability progression, MRI, safety

Type of MS: RR

Number of Subjects: 2000

Start date: January 2006

Observation period: 2 years

Investigators: L. Kappos and others

Sites: Multicenter, Europe and North America

Results/Publications: Not available

Funding: Novartis

ClinicalTrials.gov Identifier: NCT00289978  Last update: 2006

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Agent: Fish oil

Purpose of study: To improve depression

Possible mechanism: Decreases cytokine levels

Study description: Double blinded, placebo controlled

Dose/route: 3 g bid po vs. PBO po

Outcome parameters: Becks Depression Inventory, Montgomery-Asberg Depression Rating Scale, cytokine measurements, red blood cell fatty acid analysis

Type of MS: All types

Number of Subjects: 60

Start date: August 2005

Observation period: 6 months

Investigators: L. Shinto, D. Bourdette

Sites: Oregon Health & Science University, Portland

Results/Publications: Not available

Funding: NIH

ClinicalTrials.gov Identifier: NCT00122954  Last update: 2006

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Agent: Fumaric acid esters
Purpose of study: To test safety and effectiveness
Possible mechanism: Upregulates Th2 response, immunomodulatory
Study description: Open label
Dose/route: 720 mg/d po until week 22; 360 mg/d po until week 70
Outcome parameters: MRI, EDSS, Ambulation Index, 9-Hole Peg Test, intracellular cytokine profiles
Type of MS: RR
Number of Subjects: 10
Start date: July 1997
Observation period: 70 weeks
Investigators: S. Schimrigk, N. Brune
Sites: MS Research Center, St. Josef Hospital, Ruhr University, Bochum, Germany
Results/Publications: 3 patients discontinued during first 3 wks of treatment; 6/7 experienced mild to moderate gastrointestinal discomfort that decreased gradually; Rx significantly reduced number and volume of Gd+ lesions after 18 wks; EDSS, Ambulation Index, and 9-Hole Peg Test remained stable or slightly improved in all patients; immunologic parameters suggest shift to Th2 (Abstract #S46.003, AAN 2005; European Journal of Neurology 2006;13(6):604-610)
Funding: Fumapharm AG, Swiss
ClinicalTrials.gov Identifier: Not available
Last update: 2007

Agent: Fumaric acid esters (BG00012)
Purpose of study: To test safety and effectiveness in controlling disease course and development of brain lesions
Possible mechanism: Upregulates Th2 response, immunomodulatory
Study description: Double blinded, placebo controlled
Dose/route: 120 mg/d po vs. 120 mg tid po vs. 240 mg tid po vs. PBO
Outcome parameters: MRI, EDSS, MSFC
Type of MS: RR
Number of Subjects: 260
Start date: November 2005
Observation period: 24 weeks + 24-week extension
Investigators: S. Schimrigk and others
Sites: MS Research Center, St. Josef Hospital, Ruhr University, Bochum, Germany, and others
Results/Publications: 225 patients entered safety extension, of which 15 (6.7%) discontinued treatment prematurely, 9 (4.0%) due to adverse events or study drug intolerance; most common adverse events were flushing (16.9%), MS relapse (16.0%), and nasopharyngitis (15.6%); compared with first 24 weeks, reductions in the proportions of patients relapsing were 18%, 26%, and 58% for the 120-mg/day, 360-mg/day group, and 720-mg/day groups, respectively (Abstract #P574, ENS 2005; Abstract #P06.086, AAN 2007)
Funding: Biogen Idec, Inc., Fumapharm AG
ClinicalTrials.gov Identifier: Not available
Last update: 2007
Agent: Fumaric acid esters (BG00012)
Purpose of study: To test safety and effectiveness in controlling disease course and development of brain lesions
Possible mechanism: Upregulates Th2 response, immunomodulatory
Study description: Double blinded, placebo controlled
Dose/route: 480 mg/d po vs. 720 mg/d po vs. PBO po
Outcome parameters: Frequency of relapse, EDSS, MSFC, MRI
Type of MS: RR
Number of Subjects: 1011
Start date: January 2007
Observation period: 2 years
Investigators: S. Schimrigk and others
Sites: MS Research Center, St. Josef Hospital, Ruhr University, Bochum, Germany, and others, worldwide
Results/Publications: Not available
Funding: Biogen Idec, Inc.
ClinicalTrials.gov Identifier: NCT00451451  Last update: 2007

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Agent: Ginseng
Purpose of study: To improve mental alertness and fatigue
Possible mechanism: Possible glucoregulatory and/or immunoregulatory properties
Study description: Double blinded, placebo controlled, crossover
Dose/route: 100 mg/d po increased to 400 mg/d as tolerated vs. PBO po
Outcome parameters: Activity Monitoring, Fatigue Severity Scale, Modified Fatigue Severity Scale, Beck Depression Inventory, Oddrill Stroop, Victoria Modified Stroop, MSFC, Sexual Function Questionnaire, Perceived Stress Scale, SF-36, Salivary Cortisol Levels
Type of MS: All types
Number of Subjects: 108
Start date: October 2005
Observation period: 17 weeks
Investigators: R. Whitham, L. Schaben
Sites: Oregon Health & Science University, Portland
Results/Publications: Not available
Funding: CVT Technologies
ClinicalTrials.gov Identifier: Not available  Last update: 2006

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Agent: Immunoglobulin

Purpose of study: To control disease course, also known as ESIMS Study

Possible mechanism: Binds complement, inhibits antibody production and B-cell differentiation, targets macrophages, modulates cytokine production

Study description: Double blinded, placebo controlled

Dose/route: 1 g/kg/mo iv vs. PBO iv

Outcome parameters: EDSS, MRI

Type of MS: SP

Number of Subjects: 318

Start date: September 1997

Observation period: 24 months

Investigators: O. Hommes and others

Sites: Multicenter, Europe

Results/Publications: No significant differences between treatment groups in clinical or MRI results (Lancet 2004 Sep 25;364(9440):1149-56; Multiple Sclerosis 2005;11(4):433-40)

Funding: Bayer AG

ClinicalTrials.gov Identifier: Not available

Last update: 2006

Agent: Interferon tau

Purpose of study: To test safety

Possible mechanism: Promotes shift from Th1 to Th2

Study description: Open label

Dose/route: 3 mg tid po

Outcome parameters: Safety, effectiveness

Type of MS: RR

Number of Subjects: 40

Start date: May 2004

Observation period: 15 months

Investigators: G. Buckle and others

Sites: Brigham and Women's Hospital, Boston, and others

Results/Publications: Data under analysis (communication with primary investigator)

Funding: Pepgen Corporation

ClinicalTrials.gov Identifier: Not available

Last update: 2007

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Agent: Lamictal® (lamotrigine, GlaxoSmithKline)
Purpose of study: To control disease course and prevent nervous system damage
Possible mechanism: Anticonvulsant, with possible impact on nerve impulse conduction
Study description: Randomized, double blinded, placebo controlled
Dose/route: Up to 400 mg/d po vs. PBO po
Outcome parameters: MRI, EDSS, MSFC
Type of MS: SP
Number of Subjects: 120
Start date: January 2006
Observation period: 24 months
Investigators: R. Kapoor and others
Sites: Institute of Neurology, National Hospital for Neurology and Neurosurgery and the Royal Free Hospital, London, UK
Results/Publications: Rationale and design described (Abstract #P794, ECTRIMS 2006)
Funding: MS Society of Great Britain and Northern Ireland
ClinicalTrials.gov Identifier: NCT00257855
Last update: 2007

Agent: Laquinimod (ABR-215062)
Purpose of study: To control disease course and development of brain lesions
Possible mechanism: Immunomodulatory
Study description: Randomized, double blinded, placebo controlled
Dose/route: 0.1 mg/d po vs. 0.3 mg/d po vs. PBO po
Outcome parameters: MRI, EDSS, MSFC
Type of MS: Relapsing
Number of Subjects: 209
Start date: April 2002
Observation period: 24 months
Investigators: C. Polman and others
Sites: VU Medical Centre, Amsterdam, and others, The Netherlands, Sweden, United Kingdom, Russia
Results/Publications: Mean cumulative number of active lesions reduced by 44% in .3 mg treatment group; in subgroup of patients with at least 1 one active lesion at baseline the reduction was slightly more pronounced (52%); no differences in relapses, disability found; well tolerated (Abstract #S12.005, AAN 2004; Neurology 2005;64:987-991)
Funding: Active Biotech AB
ClinicalTrials.gov Identifier: Not available
Last update: 2006
Agent: Laquinimod (ABR-215062)
Purpose of study: To control disease course and development of brain lesions
Possible mechanism: Immunomodulatory
Study description: Randomized, double blinded, placebo controlled
Dose/route: 0.3 mg/d po vs. 0.6 mg/d po vs. PBO po
Outcome parameters: MRI, relapse rate
Type of MS: RR
Number of Subjects: 306
Start date: March 2005
Observation period: 36 weeks
Investigators: G. Comi and others
Sites: Multiple
Results/Publications: In those taking 0.6 mg, active lesions decreased significantly compared with PBO, but not in those on 0.3 mg; trend toward reduction in relapse rate in 0.6-mg group; both doses tolerated with transient increases in liver enzymes (Abstract #S02.002, AAN 2007)
Funding: Teva Neuroscience
ClinicalTrials.gov Identifier: NCT00349193

Agent: Laquinimod (ABR-215062)
Purpose of study: To control disease course and development of brain lesions
Possible mechanism: Immunomodulatory
Study description: Randomized, double blinded, placebo controlled
Dose/route: 0.6 mg/d po vs. PBO po
Outcome parameters: Relapse rate, MSFC, EDSS, MRI
Type of MS: RR
Number of Subjects: 1000
Start date: December 2007
Observation period: 2 years
Investigators: Multiple
Sites: Multiple
Results/Publications: Not available
Funding: Teva Neuroscience
ClinicalTrials.gov Identifier: Not available

Last update: 2007

Last update: 2007
Agent: Lipitor® (atorvastatin, Pfizer Ireland Pharmaceuticals Corp.)
Purpose of study: To evaluate safety and effectiveness on decreasing or delaying clinical and MRI disease activity in patients with CIS
Possible mechanism: Promotes anti-inflammatory Th2 response
Study description: Randomized, double blinded, placebo controlled
Dose/route: 80 mg/d po vs. PBO po
Outcome parameters: Neurological and functional assessment tests, MRI, measure of metabolites
Type of MS: First clinical demyelinating event suggestive of MS
Number of Subjects: 152
Start date: January 2005
Observation period: 18 months
Investigators: S. Zamvil and others
Sites: University of California, San Francisco, and others, United States and Canada
Results/Publications: Not available
Funding: Immune Tolerance Network, National Institute of Allergy and Infectious Disease
ClinicalTrials.gov Identifier: NCT00094172
Last update: 2007

Agent: Lipitor® (atorvastatin, Pfizer Ireland Pharmaceuticals Corp.) and Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.)
Purpose of study: To delay time to definite MS in patients with clinically isolated syndrome
Possible mechanism: Promotes anti-inflammatory Th2 response (Lipitor)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)
Study description: Randomized, double blinded, placebo controlled
Dose/route: Rebif 44 mcg tiw sc + Lipitor 80 mg/d po vs. Rebif + PBO po
Outcome parameters: Frequency of relapse, EDSS, MRI
Type of MS: First clinical demyelinating event suggestive of MS
Number of Subjects: 30
Start date: April 2005
Observation period: 15 months
Investigators: S. Markovic-Plese
Sites: University of North Carolina, Chapel Hill
Results/Publications: Not available
Funding: Serono, Inc., Pfizer Inc.
ClinicalTrials.gov Identifier: NCT00137176
Last update: 2007

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**Agent:** Lipitor® (atorvastatin, Pfizer Ireland Pharmaceuticals Corp.) and Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.)

**Purpose of study:** To evaluate safety and effectiveness

**Possible mechanism:** Promotes anti-inflammatory Th2 response (Lipitor)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)

**Study description:** Double blinded, placebo controlled

**Dose/route:** Rebif 44 mcg tiw sc + Lipitor 80 mg/d po vs. Rebif + Lipitor 40 mg/d po vs. Rebif + PBO po

**Outcome parameters:** MRI, frequency and duration of relapse, blood & chemistry

**Type of MS:** RR

**Number of Subjects:** 45

**Start date:** February 2004

**Observation period:** 9 months

**Investigators:** G. Birnbaum

**Sites:** MS Treatment and Research Center, Minneapolis Clinic of Neurology

**Results/Publications:** 29 subjects enrolled; data analyzed for 24 subjects; 2 subjects on high dose Lipitor withdrew due to myalgias and elevated liver enzymes; new and enhancing MRI lesions and/or relapses in 9/13 on Lipitor, and in 1/9 subjects on PBO; new lesions occurred as early as 12 wks following Lipitor and continued up to 12 wks after stopping the drug (Abstract #P06.158, AAN 2005; Abstract #S32.005, AAN 2007)

**Funding:** Serono, Inc., Pfizer Inc.

**ClinicalTrials.gov Identifier:** Not available

**Last update:** 2007
Agent: Lymphocytapheresis (removal of immune cells), azathioprine® (azathioprine) + prednisone

Purpose of study: To control disease course and development of brain lesions

Possible mechanism: May down-regulate IL-2 production and CD4/8 ratio and up-regulate CD11b+CD8+ cells and neutrocytes (lymphocytapheresis)/Releases 6-MP and inhibits nucleic acid biosynthesis, preventing proliferation of cells that amplify immune response (azathioprine)/Closes damaged blood-brain barrier, reducing inflammation in CNS (prednisone)

Study description: Comparison with "best standard of care"

Dose/route: Year 1 - LCP tiw for 2-3 mos, every other week for 2-3 mos to achieve depletion + azathioprine 2.5 mg/kg po + prednisone 15 mg qod po; year 2 - LCP every 4 wks + azathioprine + prednisone, then wean

Outcome parameters: EDSS, MRI, quality of life, physician/patient global assessment, safety

Type of MS: SP

Number of Subjects: 42

Start date: Planned

Observation period: 3 years

Investigators: A. Reder and others

Sites: University of Chicago and others

Results/Publications: Not available

Funding: Private funding

ClinicalTrials.gov Identifier: Not available

Last update: 2007

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Agent: Lyrica® (pregabalin, Pfizer Inc.) vs. Paxil® (paroxetine, GlaxoSmithKline)

Purpose of study: To improve MS-related pain

Possible mechanism: GABA analogue, thought to act as Ca2+ channel modulator, decreasing Ca2+ influx into nerve cells, affecting release of pain neurotransmitters (Lyrica)/selective serotonin reuptake inhibitor (Paxil)

Study description: Randomized, open label

Dose/route: Paroxetine 50 mg/d po vs. pregabalin 600 mg bid po

Outcome parameters: Visual Analog Scale pain score, quality of life

Type of MS: All types, with neuropathic pain

Number of Subjects: 80

Start date: March 2006

Observation period: 8 weeks

Investigators: M. Melanson, M. Namaka, D. Turcotte

Sites: MS Clinic, Health Sciences Centre, Winnipeg, Manitoba, Canada

Results/Publications: Not available

Funding: Not available

ClinicalTrials.gov Identifier: NCT00291148

Last update: 2006

************************************************************************************
Agent: MBP8298 (synthetic myelin basic protein peptide)
Purpose of study: To control disease progression
Possible mechanism: Synthetic myelin basic protein peptide; induces immunological tolerance against a specific epitope of myelin
Study description: Double blinded, placebo controlled
Dose/route: 500 mg iv every 6 mos vs. PBO iv
Outcome parameters: EDSS
Type of MS: SP, PP
Number of Subjects: 32
Start date: Not available
Observation period: 2 years
Investigators: I. Catz, K. Warren
Sites: University of Alberta
Results/Publications: Results from all patients at 24 mos showed no significant difference between MBP8298 and PBO; statistically significant benefit of MBP8298 in 20 patients with HLA haplotypes DR2 and/or DR4; in this responder group, median time to progression was 78 mos, compared to 18 mos for PBO group (Abstract #S12.004, AAN 2006; European Journal of Neurology 2006;13(8):887-95)
Funding: BioMS Medical Corp.
ClinicalTrials.gov Identifier: Not available
Last update: 2007

Agent: MBP8298 (synthetic myelin basic protein peptide)
Purpose of study: To control disease activity and test safety, also known as MAESTRO-01
Possible mechanism: Synthetic myelin basic protein peptide; induces immunological tolerance against a specific epitope of myelin
Study description: Double blinded, placebo controlled
Dose/route: MBP8298 500 mg iv every 6 mos vs. PBO iv
Outcome parameters: EDSS, MSFC, relapse rates, MSQOL-54
Type of MS: SP
Number of Subjects: 550
Start date: December 2004
Observation period: 24 months
Investigators: M. Freedman and others
Sites: University of Alberta and others, Canada and Europe
Results/Publications: Data Safety Monitoring Board completed planned interim safety analysis and recommended that trial continue as per the protocol, based on assessment of first 100 patients enrolled who had completed 12 mos of treatment (Abstract #P01.084, AAN 2006; BioMS Medical Corp. press release, April 5, 2007)
Funding: BioMS Medical Corp.
ClinicalTrials.gov Identifier: Not available
Last update: 2007
Agent: MBP8298 (synthetic myelin basic protein peptide)
Purpose of study: To control disease activity and test safety, also known as MINDSET-01
Possible mechanism: Synthetic myelin basic protein peptide; induces immunological tolerance against a specific epitope of myelin
Study description: Double blinded, placebo controlled
Dose/route: MBP8298 500 mg iv; 5 single doses at baseline, and months 3,9,15,21
Outcome parameters: Frequency of relapse, scoring technique
Type of MS: RR
Number of Subjects: 215
Start date: November 2006
Observation period: 15 months
Investigators: Multiple
Sites: Multiple, Europe
Results/Publications: Enrollment completed (BioMS Medical Corp. press release, May 3, 2007)
Funding: BioMS Medical Corp.
ClinicalTrials.gov Identifier: Not available
Last update: 2007

Agent: MBP8298 (synthetic myelin basic protein peptide)
Purpose of study: To control disease activity and test safety, also known as MAESTRO-03
Possible mechanism: Synthetic myelin basic protein peptide; induces immunological tolerance against a specific epitope of myelin
Study description: Double blinded, placebo controlled
Dose/route: MBP8298 500 mg iv every 6 mos vs. PBO iv
Outcome parameters: EDSS
Type of MS: SP
Number of Subjects: 510
Start date: June 2007
Observation period: 24 months
Investigators: C. Markowitz and others
Sites: MS Center of the University of Pennsylvania, Philadelphia, and others, nationwide
Results/Publications: Not available
Funding: BioMS Medical Corp.
ClinicalTrials.gov Identifier: NCT00468611
Last update: 2007
Agent: Methylprednisolone
Purpose of study: To control development of brain lesions and treat disease relapses, also known as OMEGA study
Possible mechanism: Closes damaged blood-brain barrier, reducing inflammation in CNS
Study description: Double blinded, placebo controlled
Dose/route: 1000 mg iv vs. 1400 mg/d po, for 5 days
Outcome parameters: EDSS, MSFC, frequency of relapse, Targeted Neurological Deficit
Type of MS: Relapse in past 7 days
Number of Subjects: 140
Start date: October 2002
Observation period: 1 year
Investigators: F. Lublin and others
Sites: Mount Sinai Medical Center, and others in New York, NY
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: Not available

Agent: Methylprednisolone + Avonex® (interferon beta-1a, Biogen Idec)
Purpose of study: To control development of brain lesions and disease relapses, also known as MECOMBIN study
Possible mechanism: Closes damaged blood-brain barrier, reducing inflammation in CNS (methylprednisolone)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)
Study description: Placebo controlled
Dose/route: Methylprednisolone 500 mg/d po + Avonex 30 mcg/wk im vs. PBO po + Avonex
Outcome parameters: EDSS
Type of MS: RR
Number of Subjects: 387
Start date: October 2002
Observation period: 3 years
Investigators: M. Ravnborg and others
Sites: Multicenter, Denmark and Norway
Results/Publications: Not available
Funding: Biogen Idec, Inc.
ClinicalTrials.gov Identifier: NCT00168766

Last update: 2007
Agent: Minocycline

**Purpose of study:** To control development of brain lesions

**Possible mechanism:** Inhibits matrix metalloproteinases

**Study description:** Open label, after 3-month untreated run-in observation

**Dose/route:** 100 mg bid po

**Outcome parameters:** MRI

**Type of MS:** RR

**Number of Subjects:** 10

**Start date:** October 2001

**Observation period:** 36 months

**Investigators:** L. Metz

**Sites:** University of Calgary, Alberta

**Results/Publications:** Despite moderately high pretreatment relapse rate (1.3/year pre-enrolment) prior to treatment, no relapses occurred between months 6 and 24; despite active MRI activity pretreatment (19/40 Gd+ scans), one patient (half-dose group) had Gd+ lesions at 12 and 24 months; levels of p40 subunit of IL-12 were elevated with treatment; matrix metalloproteinase-9 decreased (Abstract #S31.001, AAN 2003, Annals of Neurology 2004;55(5):756; Abstract #S32.006, AAN 2005; Abstract #P239, ECTRIMS 2005; Multiple Sclerosis 2007;13(4):517-26)

**Funding:** Canadian Institute of Health Research

**ClinicalTrials.gov Identifier:** Not available

**Last update:** 2007

Agent: Minocycline + Avonex® (interferon beta-1a, Biogen Idec)

**Purpose of study:** To control development of brain lesions

**Possible mechanism:** Inhibits matrix metalloproteinases (minocycline)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)

**Study description:** Open label

**Dose/route:** Avonex 30 mcg/wk im + minocycline 100 mg bid po

**Outcome parameters:** Frequency of relapse, EDSS, MSFC, MRI

**Type of MS:** RR

**Number of Subjects:** 20

**Start date:** June 2003

**Observation period:** 15 months

**Investigators:** R. Bashir, D. Kirby

**Sites:** Creighton University, Bellevue, NE

**Results/Publications:** 11 patients completed 1 year on study and 2 patients dropped out (reversible hair loss, depression); side effects included vaginal candidiasis, nausea, dizziness, headache, depression; 6 patients had increased hepatic enzymes (minimal and transient in four, two requiring Avonex dose adjustment); none of 5 patients completing the study so far had enhancing brain lesions on MRI (Abstract #S03, CMSC 2005)

**Funding:** Biogen Idec, Inc.

**ClinicalTrials.gov Identifier:** Not available

**Last update:** 2006
Agent: Minocycline + Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.)

**Purpose of study:** To control disease course

**Possible mechanism:** Inhibits matrix metalloproteinases (minocycline)/ Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** Copaxone 20 mg/d sc + minocycline po vs. Copaxone + PBO po

**Outcome parameters:** MRI

**Type of MS:** RR

**Number of Subjects:** 44

**Start date:** Not available

**Observation period:** 9 months

**Investigators:** L. Metz and others

**Sites:** University of Calgary, Alberta, and others

**Results/Publications:** Trend to reductions in Gd+ lesions, new T2 lesions and relapse risk (Abstract #S02.003, AAN 2007)

**Funding:** Teva Pharmaceutical Industries, Ltd.

**ClinicalTrials.gov Identifier:** NCT00203112

**Last update:** 2007

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Agent: MN-166

**Purpose of study:** To test safety and control disease course

**Possible mechanism:** Inhibits leukotriene activity, phosphodiesterases and nitric oxide synthase

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** MN-166 20 mg tid po vs. MN-166 10 mg tid vs. PBO po

**Outcome parameters:** MRI, frequency of relapse, EDSS

**Type of MS:** RR, SP

**Number of Subjects:** 300

**Start date:** July 2005

**Observation period:** 24 months

**Investigators:** Multiple

**Sites:** Multicenter, Eastern Europe

**Results/Publications:** Data Safety Monitoring Board recommended continuing study based on safety and benefits to MRI and relapses (MediciNova, Inc. press release, March 29, 2007)

**Funding:** MediciNova, Inc.

**ClinicalTrials.gov Identifier:** Not available

**Last update:** 2007
Agent: Namenda® (memantine, Forest Pharmaceuticals)
Purpose of study: To improve cognitive function
Possible mechanism: Blocks NMDA receptors
Study description: Double blinded, placebo controlled
Dose/route: 5 mg/d po increased in 5-mg increments to 20 mg/d over 4 wks vs. PBO po
Outcome parameters: PASAT, California Verbal Learning Test II, Controlled Oral Word Association Test, Stroop Color and Word Test, Symbol Digit Modalities Test, Delis-Kaplan Executive Function System, Perceived Deficit Questionnaire, MS Screening Neuropsychological Questionnaire
Type of MS: All types
Number of Subjects: 146
Start date: April 2004
Observation period: 16 weeks
Investigators: D. Bourdette and others
Sites: Oregon Health & Science University, Portland, and others, United States
Results/Publications: Not available
Funding: Forest Laboratories, Inc.
ClinicalTrials.gov Identifier: NCT00300716 Last update: 2006

Agent: NBI-5788 (altered peptide ligand) COMPLETED
Purpose of study: To test safety and control disease course and development of brain lesions
Possible mechanism: Modified portion of myelin basic protein, induces immune response to regulate pathogenic cells
Study description: Double blinded, placebo controlled
Dose/route: 5 mg/wk sc for 5 wks, then every 4 wks for 32 wks vs. PBO sc
Outcome parameters: MRI, EDSS
Type of MS: RR, SP
Number of Subjects: 150
Start date: August 2003
Observation period: 46 weeks
Investigators: J. Antel and others
Sites: Multicenter, United States and Canada
Results/Publications: Clinical trial did not meet its primary endpoint and did not demonstrate efficacy although safe and well tolerated; company has discontinued development for MS (Neurocrine Biosciences, Inc. press release, March 8, 2006)
Funding: Neurocrine Biosciences, Inc.
ClinicalTrials.gov Identifier: NCT00079495 Last update: 2006

************************************************************************************
Agent: NeuroVax™ (a trivalent T cell receptor peptide vaccine, Orchestra Therapeutics)

Purpose of study: To evaluate safety and effect on disease course

Possible mechanism: Stimulates regulatory (protective) T cells

Study description: Open label

Dose/route: 300 mcg im every 4 wks

Outcome parameters: Number of TCR peptide-reactive T cells in peripheral blood mononuclear cells; FOXP3 expression on CD4+CD25+ T cells by western blots/RT-PCR

Type of MS: RR, SP

Number of Subjects: 40

Start date: January 2003

Observation period: 1 year

Investigators: D. Bourdette and A. Vandenbark

Sites: Oregon Health & Science University, Portland

Results/Publications: Diminished FOXP3 levels pre-treatment; post-treatment, striking increase in frequency of TCR-reactive T cells in peripheral blood mononuclear cells that produced high levels of anti-inflammatory cytokine IL-10, as well as normalized expression of FOXP3 in CD4+CD25+ T cells (Multiple Sclerosis 2005;11(5):552-61; Journal of Neuroscience Research 2005;81(1):45-52; Abstract #P651, ECTRIMS 2005; Abstract #S32.002, AAN 2006)

Funding: Immune Tolerance Network, Immune Response Corporation

ClinicalTrials.gov Identifier: Not available

Last update: 2006

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Agent: NeuroVax™ (a trivalent T cell receptor peptide vaccine, Orchestra Therapeutics)

Purpose of study: To evaluate safety and effect on disease course

Possible mechanism: Stimulates regulatory (protective) T cells

Study description: Randomized, double blinded, placebo controlled

Dose/route: NeuroVax™ 300 mcg im every 4 wks for 44 wks

Outcome parameters: MRI

Type of MS: RR

Number of Subjects: 200

Start date: March 2007

Observation period: 48 weeks

Investigators: K. Selmaj and others, Europe

Sites: Multicenter, Europe

Results/Publications: Not available

Funding: Orchestra Therapeutics, Inc.

ClinicalTrials.gov Identifier: Not available

Last update: 2007

************************************************************************************

50
Agent: Novantrone® (mitoxantrone for injection concentrate, EMD Serono, Inc.)
Purpose of study: To evaluate long-term safety, also known as RENEW study
Possible mechanism: Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion
Study description: Registry to evaluate open-label therapy
Dose/route: 12 mg/m2 iv every 3 mos up to a cumulative dose of 140 mg/m2
Outcome parameters: Drug-related adverse events, left ventricular ejection fraction, menstrual history, relapse rate
Type of MS: Worsening RR, and SP
Number of Subjects: 500
Start date: February 2001
Observation period: 5 years
Investigators: Multiple
Sites: Multicenter
Results/Publications: Follow-up data being collected for 361 patients (104 receiving mitoxantrone) plus patients who discontinued mitoxantrone (257); 301 relapses in 221 patients; median time to first relapse, 155 days; 95 patients experienced 158 adverse events, most frequently infectious (34%) and cardiac (23%); 7 deaths, 2 possibly related to treatment; 1 therapy-related leukemia reported (Abstract #P06.083, AAN 2004; Abstract #P01.068, AAN 2006; Abstract #P759, ECTRIMS 2006; Abstract #P06.080, AAN 2007)
Funding: EMD Serono Inc.
ClinicalTrials.gov Identifier: Not available
Last update: 2007

Agent: Novantrone® (mitoxantrone for injection concentrate, EMD Serono, Inc.)
Purpose of study: To assess quality of life and cost of disease in people with MS treated with Novantrone in RENEW study
Possible mechanism: Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion
Study description: Prospective study
Dose/route: 12 mg/m2 iv every 3 mos up to a cumulative dose of 140 mg/m2
Outcome parameters: Health Survey (SF-12 v2), Health Utilities Index, Patient Determined Disease Steps
Type of MS: RR, SP
Number of Subjects: 252
Start date: Based on enrollment in RENEW study
Observation period: 5 years
Investigators: T. Vollmer
Sites: Barrow Neurological Institute, St. Joseph's Hospital, Phoenix, AZ
Results/Publications: Not available
Funding: EMD Serono Inc.
ClinicalTrials.gov Identifier: Not available
Last update: 2006

************************************************************************************
Agent: Novantrone® (mitoxantrone for injection concentrate, EMD Serono, Inc.)
Purpose of study: To determine long-term safety
Possible mechanism: Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion
Study description: Annual assessment of safety profile
Dose/route: Monthly for 6 mos vs. every 3 mos; median cumulative dose, 73 mg/m2
Outcome parameters: Safety profile
Type of MS: RR, SP, PP
Number of Subjects: 802
Start date: 2000
Observation period: 5 years
Investigators: G. Edan and others
Sites: CHU de Rennes, France, and others
Results/Publications: Follow-up duration of 5361 patient-years; 1 patient presented with acute congestive heart failure; 39 patients experienced at least one asymptomatic LVEF reduction under 50%; persisting in 10 patients; 2 cases of therapy-related leukemia (1 death and 1 remission); 17.3% of 317 women treated before 45 years old developed persistent amenorrhea (Abstract #P06.93, AAN 2004; Abstract #S02.006, AAN 2006; Abstract #P738, ECTRIMS 2006)
Funding: Not available
ClinicalTrials.gov Identifier: Not available
Last update: 2007

Agent: Novantrone® (mitoxantrone for injection concentrate, EMD Serono, Inc.)
Purpose of study: To evaluate safety and to control disease course
Possible mechanism: Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion
Study description: Randomized, double blinded, three arms
Dose/route: 5 mg/m2 iv vs. 9 mg/m2 vs. 12 mg/m2 every 3 mos up to 24 mos
Outcome parameters: EDSS, change of ambulation index, time to first relapse requiring corticoid treatment, MRI
Type of MS: SP
Number of Subjects: 336
Start date: March 2005
Observation period: 5 years
Investigators: Multiple
Sites: Multicenter, Germany
Results/Publications: Not available
Funding: Wyeth Pharma GmbH, Germany
ClinicalTrials.gov Identifier: NCT00146159
Last update: 2006

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52
Agent: Novantrone® (mitoxantrone for injection concentrate, EMD Serono, Inc.) + Avonex® (interferon beta-1a, Biogen Idec) or Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.)

Purpose of study: To evaluate safety and to control disease course

Possible mechanism: Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion (Novantrone)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)

Study description: Open label

Dose/route: Novantrone 12 mg/m2 every 3 mos (4 times) + Avonex 30 mcg/wk im vs. Novantrone + Copaxone 20 mg/d sc

Outcome parameters: Safety, scoring technique, MRI

Type of MS: RR, SP

Number of Subjects: 50

Start date: September 2001

Observation period: 12 months

Investigators: P. Calabresi and others

Sites: University of Maryland, College Park, and others

Results/Publications: Preliminary results -- no difference between groups; approximately 25% of patients had reduction in left ventricular ejection fraction of 10% or greater after 4 doses of Novantrone (Abstract #S12.006, AAN 2004)

Funding: EMD Serono Inc.

ClinicalTrials.gov Identifier: Not available

Last update: 2006

Agent: Novantrone® (mitoxantrone for injection concentrate, EMD Serono, Inc.) + Betaseron® (interferon beta-1b, Bayer HealthCare Pharmaceuticals, Inc.)

Purpose of study: To control disease course using pretreatment with Novantrone

Possible mechanism: Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion (Novantrone)/Slows down immune response, possibly by interfering with T cell activation and movement across BBB, and inducing suppressive T cells (Betaseron)

Study description: Physician blinding

Dose/route: Novantrone 20 mg/mo iv + methylprednisolone 20 mg (6 mos), then Betaseron 250 mcg qod sc vs. methylprednisolone + Betaseron (6 mos), then all Betaseron

Outcome parameters: Frequency of relapse, EDSS, MRI

Type of MS: RR

Number of Subjects: 220

Start date: January 1999

Observation period: 3 years

Investigators: G. Edan

Sites: Multicenter, France and Italy

Results/Publications: Not available

Funding: French Health Ministry, Schering AG

ClinicalTrials.gov Identifier: NCT00219908

Last update: 2007

************************************************************************************
Agent: Novantrone® (mitoxantrone for injection concentrate, EMD Serono, Inc.) + Betaseron® (interferon beta-1b, Bayer HealthCare Pharmaceuticals, Inc.)

Purpose of study: To control development of brain lesions and disease course

Possible mechanism: Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion (Novantrone)/Slows down immune response, possibly by interfering with T cell activation and movement across BBB, and inducing suppressive T cells (Betaseron)

Study description: Open label

Dose/route: Novantrone 12 mg/m² (mo 1), 5 mg/m² (mo 2, 3 and every 3rd mos) + Betaseron 250 mcg qod sc

Outcome parameters: MRI, relapse rates, EDSS

Type of MS: RR, SP

Number of Subjects: 10

Start date: Not available

Observation period: 6 months

Investigators: D. Jeffery and others

Sites: Wake Forest, Winston-Salem, NC

Results/Publications: Mean enhancing lesion frequency decreased 90% at month 7 and enhancing lesion volume decreased by 96%; relapse rates decreased 64%; T2 lesion burden and T1 hypointense lesion burden increased slightly during baseline phase and decreased following combination, but not significantly; no serious adverse events and no drop-outs due to toxicity (Abstract #S23.004, AAN 2002; Abstract, ECTRIMS 2003, *Multiple Sclerosis* 2005;11(3):296-301)

Funding: Berlex Laboratories, Inc., Immunex Corporation

ClinicalTrials.gov Identifier: Not available Last update: 2007

Agent: Pixantrone (BBR 2778)

Purpose of study: To test safety, control development of brain lesions and determine impact on immune function, also known as PIXAMS study

Possible mechanism: Intercalates DNA, inhibits topoisomerase II, cytotoxic

Study description: Open label

Dose/route: 4 courses Pixantrone 120 mg/m² iv at 3-week intervals

Outcome parameters: Immunosuppressive effects, Gd+ lesion evolution, safety

Type of MS: Aggressive RR or SP MS

Number of Subjects: 20

Start date: Fall 2007

Observation period: 2 years

Investigators: R. Gonsette and others

Sites: Belgium National Centre for Multiple Sclerosis, Melsbroek, Belgium, and others, Europe

Results/Publications: Not available

Funding: Fondation-Charcot-Stichting

ClinicalTrials.gov Identifier: Not available Last update: 2007

************************************************************************************
Agent: Plasmapheresis (plasma exchange)
Purpose of study: To assess the effect of plasma exchange in accelerating the clearance of natalizumab
Possible mechanism: Removes circulating antibodies
Study description: Open label
Dose/route: 3 plasma exchanges qod iv, over 5 days
Outcome parameters: Natalizumab concentration; VLA-4 receptor saturation; leukocyte migration across a synthetic blood-brain barrier
Type of MS: RR
Number of Subjects: 12
Start date: May 2007
Observation period: 24 weeks
Investigators: R. Fox; B. Khatri; G. Giovannoni
Sites: Mellen Center, Cleveland Clinic, Cleveland, OH; St. Luke’s Medical Center of Aurora Health Care, Milwaukee, WI
Results/Publications: Not available
Funding: Biogen Idec, Inc.
ClinicalTrials.gov Identifier: NCT00424788

Agent: Pravachol® (pravastatin, Bristol-Myers Squibb Company)
Purpose of study: To test tolerability and effectiveness in controlling disease course
Possible mechanism: Promotes anti-inflammatory Th2 response
Study description: Double blinded, placebo controlled
Dose/route: 40 mg/d po vs. PBO po
Outcome parameters: MRI, MSFC
Type of MS: RR
Number of Subjects: 40
Start date: November 2005
Observation period: 6 months
Investigators: D. Laplaud and others
Sites: University Hospital, Nantes, France
Results/Publications: Not available
Funding: Public Funds
ClinicalTrials.gov Identifier: NCT00200655

Last update: 2007
Last update: 2006
Agent: Progesterone + estradiol
Purpose of study: To prevent postpartum MS relapses, also known as POPARTMUS study
Possible mechanism: Promotes anti-inflammatory Th2 response
Study description: Randomized, double blinded, placebo controlled
Dose/route: Progesterone 10 mg/d po + esttradiol 75 mcg/wk pc vs. PBO po + PBO pc
Outcome parameters: Rate of relapse 12 wks after delivery
Type of MS: Relapsing, women
Number of Subjects: 300
Start date: June 2005
Observation period: 6 months
Investigators: C. Confavreux and others
Sites: Hospices Civils de Lyon, and others, Europe
Results/Publications: Not available
Funding: French Ministry of Health, The Myelin Project, European Leukodystrophy Association, Association pour la Recherche sur la Sclérose en Plaques
ClinicalTrials.gov Identifier: NCT00127075
Last update: 2006

Agent: Provigil® (modafinil, Cephalon, Inc.) + Avonex® (interferon beta-1a, Biogen Idec)
Purpose of study: To treat breakthrough cognitive symptoms
Possible mechanism: Increases neuronal activation (Provigil)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)
Study description: Randomized, parallel-group, pilot, evaluator blinding
Dose/route: Provigil 200 mg/d po + Avonex 30 mcg/wk im vs. Avonex
Outcome parameters: Neuropsychological battery, side effects, multivariate analyses of covariance
Type of MS: RR
Number of Subjects: 59
Start date: August 2002
Observation period: 4 months
Investigators: J. A. Wilken and others
Sites: Veterans Affairs Medical Center, Washington, DC, and others
Results/Publications: Patients in the combination therapy group demonstrated significant improvement from baseline on neurocognitive, fatigue, mood, and QOL measures at 4 months; side effects mild (Abstract #P02.123, AAN 2003; Abstract #P05.141, AAN 2005; Abstract #P01.078, AAN 2006, Abstract #P419, ECTRIMS 2006)
Funding: Biogen Idec, Inc., Cephalon, Inc.
ClinicalTrials.gov Identifier: NCT00210301
Last update: 2007
Agent: Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.)

**COMPLETED**

**Purpose of study:** To control disease course, new lesions; follow-up to PRISMS study

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells

**Study description:** Placebo controlled

**Dose/route:** 44 mcg tiw sc vs. 22 mcg tiw sc

**Outcome parameters:** EDSS, MRI

**Type of MS:** RR

**Number of Subjects:** 560

**Start date:** 1994

**Observation period:** 8 years

**Investigators:** Multiple

**Sites:** Multicenter, Australia, Canada, Europe

**Results/Publications:** 68.2% of the original study cohort included, of whom 72.0% were still receiving Rebif; patients originally randomized to Rebif showed lower EDSS progression, relapse rate and T2 burden up to 8 years compared with those in the late treatment group; no differences in brain parenchymal volume; 19.7% progressed to SP MS; no new safety concerns were identified (Neurology 2001;56:1628-1636; Abstract #P06.112, AAN 2003; Abstract #P02.118, AAN 2004; Neurology 2006;67:944-953)

**Funding:** Serono, Inc.

**ClinicalTrials.gov Identifier:** Not available

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Agent: Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.)

**Purpose of study:** To test safety and antigenicity of FBS-free/HSA-free formulation

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells

**Study description:** Open label

**Dose/route:** 44 mcg tiw sc

**Outcome parameters:** Neutralizing antibodies (NAbs) assessment

**Type of MS:** RR

**Number of Subjects:** 230

**Start date:** January 2005

**Observation period:** 96 weeks

**Investigators:** Multiple

**Sites:** Multicenter

**Results/Publications:** At week 48, 227/260 patients (87.3%) remained on new formulation; compared with historical data for EVIDENCE, PRISMS, and SPECTRIMS, incidence of injection site reactions was 30% vs. 84%; cytopenia, 10% vs. 12%; depression and suicidal ideation, 6% vs. 20%; hepatic disorders, 13% vs. 17%; skin rashes, 5% vs. 12%; thyroid disorders, 2% vs. 5%; and hypersensitivity reactions, 5% vs. 3%; flu-like symptoms, 71% vs. 48%; persistent NAbs (2.5% vs. 14.3%) (Abstract #P675, ECTRIMS 2006; Abstract #P06.077, AAN 2007)

**Funding:** EMD Serono, Inc.

**ClinicalTrials.gov Identifier:** NCT00110396

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Agent: Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.) + estroprogestins

Purpose of study: To control disease course and development of new lesions

Possible mechanism: Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)/Immunomodulatory (estroprogestins)

Study description: Randomized, examining MD-blind

Dose/route: Rebif 44 mcg tiw sc vs. Rebif + desogestrel 150 mcg po + etinilestradiol 20 mcg po vs. Rebif + desogestrel 25 mcg + etinilestradiol 40 mcg

Outcome parameters: Frequency of relapse, EDSS, MSFC, MRI

Type of MS: RR, women

Number of Subjects: 180

Start date: May 2004

Observation period: 24 months

Investigators: C. Pozzilli and others

Sites: MS Centre, San Andrea Hospital, University “La Sapienza”, Rome, and others

Results/Publications: Not available

Funding: University “La Sapienza”

ClinicalTrials.gov Identifier: NCT00151801

Last update: 2006

Agent: Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer Inc.) vs. Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries Ltd.)

Purpose of study: To compare effectiveness in controlling disease course

Possible mechanism: Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)

Study description: Open label, randomized

Dose/route: Rebif 44 mcg tiw sc vs. Copaxone 20 mg/d sc

Outcome parameters: Time to first relapse, MRI, neurological exams, hematology, clinical chemistry, urinalysis, antibodies, adverse events

Type of MS: RR

Number of Subjects: 10

Start date: February 2004

Observation period: 96 weeks

Investigators: J. Guarnaccia and others

Sites: MS Treatment Center at Griffin Hospital, Derby, CT

Results/Publications: Not available

Funding: Serono, Inc.

ClinicalTrials.gov Identifier: Not available

Last update: 2006

************************************************************************************
Agent: Rehabilitation
Purpose of study: To improve symptoms following acute relapses
Possible mechanism: Comprehensive program of aerobic exercise and fatigue-minimizing strategies
Study description: Physician blinding
Dose/route: Intensive outpatient rehabilitation vs. usual care
Outcome parameters: Injury Severity Score, Health Status Questionnaire (SF-36), other scales
Type of MS: RR, SP
Number of Subjects: 160
Start date: February 2000
Observation period: 12 months
Investigators: F. Bethoux, D. Miller
Sites: Cleveland Clinic Foundation
Results/Publications: No significant differences; 11 patients dropped out before randomization, and 24 afterward; these 24 were significantly younger than those who completed study, more likely to have RR MS, and were significantly less disabled (Abstract #S22, CMSC 2004, progress report to NMSS)
Funding: National MS Society
ClinicalTrials.gov Identifier: Not available
Last update: 2006

Agent: Rehabilitation
Purpose of study: To determine whether exercise can improve depression
Possible mechanism: Effects on brain dopamine, noradrenaline and serotonin transmission
Study description: Trained examiner blinded
Dose/route: Home exercise program, motivational interview and telephone follow-up vs. delayed treatment
Outcome parameters: Structured Clinical Interview for DMS-III-R, Hamilton Depression Rating Scale, Hopkins Symptom Checklist
Type of MS: All types
Number of Subjects: 108
Start date: February 2005
Observation period: 6 months
Investigators: C. Bombardier and others
Sites: University of Washington MS Rehabilitation Research & Training Center
Results/Publications: Not available
Funding: National Institute on Disability and Rehabilitation Research
ClinicalTrials.gov Identifier: Not available
Last update: 2006
Agent: Rehabilitation
Purpose of study: To improve function and participation
Possible mechanism: Improves physical function, decreases pain, and improves participation in life activities
Study description: Trained examiner blinded
Dose/route: Motivational interview, physical therapy, and home exercise program with telephone follow-up vs. no treatment
Outcome parameters: MSFC, Ashworth Spasticity Index, Brief Pain Inventory, Community Integration Questionnaire
Type of MS: All types
Number of Subjects: 120
Start date: June 2004
Observation period: Until September 2008
Investigators: J. Bowen and others
Sites: University of Washington MS Rehabilitation Research & Training Center
Results/Publications: Not available
Funding: National Institute on Disability and Rehabilitation Research
ClinicalTrials.gov Identifier: Not available

Agent: Rehabilitation (memory retraining)
Purpose of study: To improve new learning and memory
Possible mechanism: Engages additional cortical regions in encoding new information into long-term memory
Study description: Double blinded, placebo controlled
Dose/route: Memory retraining protocol comprising 10 sessions vs. control protocol comprising 10 sessions
Outcome parameters: Memory tests; reports of emotional functioning, memory functioning, and quality of life
Type of MS: RR, progressive
Number of Subjects: 200
Start date: February 2005
Observation period: 8 months
Investigators: N. Chiaravalloti
Sites: Kessler Medical Rehabilitation Research and Education Center, West Orange, NJ
Results/Publications: Not available
Funding: National Institutes of Health
ClinicalTrials.gov Identifier: NCT00166283
Last update: 2007
Agent: Rehabilitation (robotic locomotor training)
Purpose of study: To improve walking ability
Possible mechanism: May help restore strength, balance, recognition of sensory cues and other factors that make walking possible
Study description: Treadmill training using a robot vs. non-treadmill exercise program
Dose/route: Treadmill training using a robot vs. non-treadmill exercise program three times weekly for 12 wks
Outcome parameters: Overground walking speed, performance on 6-minute walk
Type of MS: PP, SP
Number of Subjects: 40
Start date: April 2006
Observation period: 12 weeks
Investigators: B. Giesser
Sites: The Marilyn Hilton MS Achievement Center at UCLA
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: Not available
Last update: 2007

Agent: RG2077
Purpose of study: To test safety and immune mechanisms
Possible mechanism: Antibody (immunoglobulin) to CTLA4, blocks costimulation
Study description: Open label
Dose/route: Single infusion, 2.0 mg/kg, 10.0 mg/kg, 20.0 mg/kg, or 35.0 mg/kg; and multi-dose of 10 mg/kg iv
Outcome parameters: Safety, immunologic/mechanistic studies
Type of MS: RR
Number of Subjects: 16
Start date: March 2003
Observation period: 5 months
Investigators: S. Khoury and others
Sites: Harvard Medical School, Boston, and others
Results/Publications: Data shows no safety issues and evidence of a biologic effect; manuscript in preparation (Abstract #S46.004, AAN 2005; communication with principal investigator)
Funding: Immune Tolerance Network
ClinicalTrials.gov Identifier: NCT00076934
Last update: 2007
Agent: Rituxan® (rituximab, Genentech and Biogen Idec)
Purpose of study: To control development of brain lesions
Possible mechanism: Binds to CD20 antigen on B cells and induces B-cell lysis
Study description: Open label, neuroradiologist blinding
Dose/route: 375 mg/m2 iv (4 times)
Outcome parameters: MRI
Type of MS: RR, not responsive to standard immunomodulatory treatment
Number of Subjects: 30
Start date: March 2002
Observation period: 1 year
Investigators: A. Cross
Sites: Washington University, St. Louis
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: Not available
Last update: 2007
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Agent: Rituxan® (rituximab, Genentech and Biogen Idec)
Purpose of study: To evaluate tolerability, effect on disease activity
Possible mechanism: Binds to CD20 antigen on B cells and induces B-cell lysis
Study description: Randomized, double blinded, placebo controlled
Dose/route: 1 g/d iv (eight times) vs. PBO iv
Outcome parameters: Time to confirmed disease progression, MRI
Type of MS: PP
Number of Subjects: 435
Start date: April 2004
Observation period: 30 months
Investigators: Multiple
Sites: Multicenter, United States and Canada
Results/Publications: Not available
Funding: Genentech, Inc.
ClinicalTrials.gov Identifier: NCT00087529
Last update: 2007
************************************************************************************
Agent: Rituxan® (rituximab, Genentech and Biogen Idec)
Purpose of study: To evaluate tolerability, effect on disease activity
Possible mechanism: Binds to CD20 antigen on B cells and induces B-cell lysis
Study description: Randomized, double blinded, placebo controlled
Dose/route: 1 g/d iv (on day 1 and day 15) vs. PBO iv
Outcome parameters: Frequency of relapse, scoring technique, MRI
Type of MS: RR
Number of Subjects: 104
Start date: December 2004
Observation period: 48 weeks
Investigators: Multiple
Sites: Multicenter, United States and Canada
Results/Publications: 91% reduction in gd+ lesion count and reduced proportion of patients with relapses vs. PBO; with the exception of infusion-associated events, rates of adverse and serious adverse events were comparable (Abstract #S12.003, AAN 2007; Genentech press release, May 1, 2007)
Funding: Genentech, Inc.
ClinicalTrials.gov Identifier: NCT00097188

Agent: RTL1000
Purpose of study: To test safety
Possible mechanism: Recombinant T-cell receptor ligands that bind to T cells, inducing a switch from inflammatory to anti-inflammatory
Study description: Double blinded, placebo controlled, dose escalation
Dose/route: In each cohort of 6 subjects, 4 subjects will receive a single dose of RTL1000 (2 mg, 6 mg, 20 mg, 60 mg, or 200 mg) iv and 2 will receive PBO iv
Outcome parameters: EDSS, 25-foot walk, 9-hole peg test, MRI
Type of MS: RR, SP
Number of Subjects: 36
Start date: January 2007
Observation period: 3 months
Investigators: V. Yadav and others
Sites: MS Center of Oregon, Oregon Health & Science University, Portland, and others, United States
Results/Publications: Not available
Funding: Artielle ImmunoTherapeutics, Inc.
ClinicalTrials.gov Identifier: NCT00411723
Agent: Sativex® (tetrahydrocannabinol and cannabidiol, GW Pharmaceuticals)

Purpose of study: To improve pain

Possible mechanism: Interacts with cannabinoid receptors on CNS cells, possibly relating to motor function, cognition and affect

Study description: Randomized, double blinded, placebo controlled

Dose/route: 2.7 mg/2.5 mg of tetrahydrocannabinol/cannabidiol per spray, directed under tongue or inside cheeks; patients can gradually self-titrate to a maximum of 48 sprays in 24 hours

Outcome parameters: Neuropathic Pain Scale, sleep NRS-11, UK Neurological Disability Scale, HADS, Brief Repeatable Battery of Neuropsychological Tests, Patient’s Global Impression of Change

Type of MS: All types, with central neuropathic pain

Number of Subjects: 66

Start date: March 2002

Observation period: 5 weeks

Investigators: D. Rog and others

Sites: Walton Centre for Neurology and Neurosurgery, Liverpool, United Kingdom

Results/Publications: Sativex reduced mean intensity of pain and sleep disturbance significantly more than PBO; more patients on Sativex than PBO reported dizziness, dry mouth and somnolence, and cognitive side effects in long-term memory storage (Neurology 2005;65(6):812-9)

Funding: GW Pharmaceuticals, Inc.

ClinicalTrials.gov Identifier: Not available

Last update: 2006

Agent: Sativex® (tetrahydrocannabinol and cannabidiol, GW Pharmaceuticals)

Purpose of study: To improve pain when added to existing treatment regimen

Possible mechanism: Interacts with cannabinoid receptors on CNS cells, possibly relating to motor function, cognition and affect

Study description: Randomized, double blinded, placebo controlled

Dose/route: 100 microliters of tetrahydrocannabinol/cannabidiol per spray, directed under tongue or inside cheeks; patients can self-titrate to a maximum of 48 sprays in 24 hours

Outcome parameters: Pain (Numeric Rating Scale), Neuropathic Pain Scale, QOL, safety

Type of MS: All types, with central neuropathic pain

Number of Subjects: 174

Start date: July 2006

Observation period: 15 weeks

Investigators: Multiple

Sites: Multiple, Canada and Europe

Results/Publications: Not available

Funding: GW Pharmaceuticals, Inc.

ClinicalTrials.gov Identifier: NCT00391079

Last update: 2007
Agent: Sativex® (tetrahydrocannabinol and cannabidiol, GW Pharmaceuticals)

Purpose of study: To improve bladder dysfunction

Possible mechanism: Interacts with cannabinoid receptors on CNS cells, possibly relating to motor function, cognition and affect

Study description: Randomized, double blinded, placebo controlled

Dose/route: 100 microliters of tetrahydrocannabinol/cannabidiol per spray, directed under tongue or inside cheeks; patients can self-titrate to a maximum of 24 sprays in 24 hours

Outcome parameters: Reduction in daily episodes of urgency incontinence, incidence of nocturia and urgency, overall bladder condition, daytime frequency, quality of life, patient’s global impression of change, volume voided

Type of MS: All types, with bladder dysfunction

Number of Subjects: 135

Start date: 2006

Observation period: 10 weeks

Investigators: C. Constantinescu and others

Sites: University Hospital Nottingham, UK, and others in United Kingdom, Belgium, Romania

Results/Publications: Trend toward decrease in daily episodes of incontinence and in number of urgency episodes in favour of Sativex group but not significant; significant reduction of nocturia episodes and daytime voids in Sativex group, along with significant improvement of patient’s opinion of bladder symptom severity and patient's global impression of change (Abstract #P411, ECTRIMS 2006)

Funding: GW Pharmaceuticals, Inc.

ClinicalTrials.gov Identifier: Not available

Last update: 2007
**Agent:** Sativex® (tetrahydrocannabinol and cannabidiol, GW Pharmaceuticals)

**Purpose of study:** To improve spasticity

**Possible mechanism:** Interacts with cannabinoid receptors on CNS cells, possibly relating to motor function, cognition and affect

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** 2.7 mg/2.5 mg of tetrahydrocannabinol/cannabidiol per spray, directed under tongue or inside cheeks; patients can gradually self-titrature to a maximum of 48 sprays in 24 hours

**Outcome parameters:** NRS, Ashworth Score, subjective measure of spasm

**Type of MS:** All types, with spasticity

**Number of Subjects:** 189

**Start date:** April 2002

**Observation period:** 6 weeks

**Investigators:** C. Collin and others

**Sites:** Royal Berkshire and Battle NHS Trust, Reading, UK, and others, UK

**Results/Publications:** NRS score significantly better for Sativex than PBO; secondary efficacy measures were all in favour of active preparation but not statistically significant; CNS effects (dizziness, impaired balance, attention disturbance, blurred vision) more common in Sativex group (European Journal of Neurology 2007;14(3):290-6)

**Funding:** GW Pharmaceuticals, Inc.

**ClinicalTrials.gov Identifier:** Not available  
**Last update:** 2007

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**Agent:** SB-683699

**Purpose of study:** To investigate safety and effectiveness

**Possible mechanism:** Reduces the number of active white blood cells entering the brain

**Study description:** Randomized, double blinded, placebo controlled, parallel group, dose ranging

**Dose/route:** po

**Outcome parameters:** MRI

**Type of MS:** RR

**Number of Subjects:** 350

**Start date:** January 2007

**Observation period:** 6 months

**Investigators:** Multiple

**Sites:** Multiple, Canada and Europe

**Results/Publications:** Not available

**Funding:** GlaxoSmithKline

**ClinicalTrials.gov Identifier:** NCT00395317  
**Last update:** 2007

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Agent: Stress management program
Purpose of study: To determine ability of stress management program to control MS inflammatory activity
Possible mechanism: Improves glucocorticoid receptor function on immune cells
Study description: Longitudinal, evaluator blinded
Dose/route: Intensive cognitive behavioral stress management program (16 meetings with behavioral medicine specialist) vs. condensed cognitive behavioral stress management program (1-day workshop)
Outcome parameters: Frequency of relapse, EDSS, MRI
Type of MS: RR, SP
Number of Subjects: 112
Start date: March 2005
Observation period: 12 months
Investigators: D. Mohr
Sites: University of California, San Francisco; MS Hub
Results/Publications: Not available
Funding: NICHD
ClinicalTrials.gov Identifier: NCT00147446
Last update: 2006

Agent: T cell vaccination
Purpose of study: To control disease progression and lesion development
Possible mechanism: Induces immunity against myelin-attacking T cells
Study description: Double blinded
Dose/route: 4 ml sc
Outcome parameters: EDSS, MSFC, MRI
Type of MS: RR
Number of Subjects: 30
Start date: Spring 2002
Observation period: 1 year
Investigators: D. Karussis and others
Sites: Hadassah Hospital, Jerusalem, Israel
Results/Publications: Not available
Funding: Grant for TCV
ClinicalTrials.gov Identifier: Not available
Last update: 2007
Agent: T cell vaccination
Purpose of study: To prevent development of clinically definite MS
Possible mechanism: Induces immunity against myelin-attacking T cells
Study description: Double blinded, placebo controlled
Dose/route: 3 immunizations every 6 wks (up to 60 million cells per immunization), followed by 2 boosters given every 6 mos
Outcome parameters: Second relapse, MRI, evoked potentials
Type of MS: First clinical demyelinating event suggestive of MS
Number of Subjects: 76
Start date: July 2003
Observation period: 1 year
Investigators: A. Achiron, M. Mandel
Sites: MS Center, Sheba Medical Center, Tel-Hashomer, Israel
Results/Publications: Not available
Funding: Horowitz Foundation
ClinicalTrials.gov Identifier: NCT00228228

Agent: Teriflunomide
Purpose of study: To control lesion development, disease progression and relapses
Possible mechanism: Modulates responses of T-cells within the immune system by impairing DNA synthesis
Study description: Randomized, double blinded, placebo controlled
Dose/route: 7 mg/d po vs. 14 mg/d po vs. PBO
Outcome parameters: MRI, EDSS, relapses
Type of MS: RR, SP
Number of Subjects: 180
Start date: 2000
Observation period: 9 months
Investigators: P. O'Connor and others
Sites: Multicenter, Canada
Results/Publications: Significantly fewer active lesions in Rx group vs. PBO during double-blind phase; treated patients had significantly fewer T1 and T2 lesions per scan; 14 mg/d group had significantly reduced T2 disease burden, and significantly fewer in this group demonstrated disability increase than those on PBO; well tolerated (Abstract #P06.063, AAN 2004; Neurology 2006;66:894-900)
Funding: Aventis Pharmaceuticals
ClinicalTrials.gov Identifier: Not available
Agent: Teriflunomide
Purpose of study: To control lesion development, disease progression and relapses, also known as TEMPO study
Possible mechanism: Modulates responses of T-cells within the immune system by impairing DNA synthesis
Study description: Double blinded, placebo controlled
Dose/route: Teriflunomide 7 mg/d po vs. 14 mg/d po vs. PBO po
Outcome parameters: Frequency of relapse, EDSS, MRI
Type of MS: RR
Number of Subjects: 1050
Start date: Fall 2004
Observation period: 2 years
Investigators: P. O'Connor and others
Sites: St. Michael's Hospital, University of Toronto, and others, North America and Europe
Results/Publications: Not available
Funding: Sanofi Aventis
ClinicalTrials.gov Identifier: NCT00134563

Agent: Tovaxin™ (T cell vaccination, Opexa Therapeutics)  COMPLETED
Purpose of study: To determine safety and ability to control disease course and development of brain lesions
Possible mechanism: Induces immunity against myelin-attacking T cells
Study description: Open label, dose escalation
Dose/route: Up to 13 vaccinations sc
Outcome parameters: Frequency of relapse, EDSS, MRI
Type of MS: RR, SP
Number of Subjects: 15
Start date: September 2004
Observation period: 130 weeks
Investigators: B. Loftus
Sites: Diagnostic Clinics of Houston
Results/Publications: Myelin-reactive T cells depleted in dose-dependent manner; all patients in dose 2 group had 100% reduction in myelin-reactive T cell counts at week 5; strong correlation with physical component of MSIS and trend to improved EDSS; 1 exacerbation was observed in dose 1 group; minimal adverse events and no dose-limiting toxicities (Abstract #P618, ECTRIMS 2005)
Funding: Opexa Therapeutics
ClinicalTrials.gov Identifier: Not available

Last update: 2006
Agent: Tovaxin™ (T cell vaccination, Opexa Therapeutics)

**Purpose of study:** To delay conversion to clinically definite MS, or control disease course and development of brain lesions, also known as TERMS study

**Possible mechanism:** Induces immunity against myelin-attacking T cells

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** 5 injections of 30-45 million T cells sc at 0, 4, 8, 12, 24 wks

**Outcome parameters:** MRI, frequency of relapse, EDSS, MSFC

**Type of MS:** First clinical demyelinating event suggestive of MS, RR

**Number of Subjects:** 150

**Start date:** April 2006

**Observation period:** 12 months

**Investigators:** E. Fox and others

**Sites:** Central Texas Neurology, Austin, and others, United States

**Results/Publications:** Not available

**Funding:** Opexa Therapeutics

**ClinicalTrials.gov Identifier:** NCT00245622

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**Agent:** Trimethoprim + vitamin C

**Purpose of study:** To prevent urinary tract/bladder infections, thus reducing MS relapses

**Possible mechanism:** Reduces bacteriuria

**Study description:** Double blinded, placebo controlled

**Dose/route:** Trimethoprim 100 mg qhs + vitamin C 500 mg bid po vs. PBO po + routine bladder care

**Outcome parameters:** Relapses

**Type of MS:** RR, SP, female

**Number of Subjects:** 100

**Start date:** December 1999

**Observation period:** 24 months

**Investigators:** A. Cross, D. Derrington

**Sites:** Washington University, St. Louis

**Results/Publications:** Terminated due to enrollment issues; data analysis ongoing (communication with principal investigator)

**Funding:** National MS Society

**ClinicalTrials.gov Identifier:** Not available

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Last update: 2006

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Last update: 2007
**Agent:** Tysabri® (natalizumab, Biogen Idec and Elan Pharmaceuticals, Inc.) **COMPLETED**

**Purpose of study:** To control disease course, also known as AFFIRM study

**Possible mechanism:** Interferes with movement of immune cells across the blood-brain barrier by attaching to alpha 4-integrin

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** Tysabri 300 mg every 4 wks iv vs. PBO iv

**Outcome parameters:** EDSS, MSFC, frequency of relapse, MRI

**Type of MS:** RR

**Number of Subjects:** 942

**Start date:** December 2001

**Observation period:** 2 years

**Investigators:** C. Polman and others

**Sites:** Multicenter, worldwide

**Results/Publications:** Rx group had reduction in risk of disability progression (42%), reduced clinical relapse rate (67%) (Abstracts #S16.004, #S16.005, AAN 2005; Abstracts #P01.086, #S02.005, #S32.004, #S42.007, #S52.005 AAN 2006; *The New England Journal of Medicine* 2006;354:899-910)

**Funding:** Biogen Idec, Inc., Elan Corporation, plc

**ClinicalTrials.gov Identifier:** NCT000273000

**Last update:** 2006

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**Agent:** Tysabri® (natalizumab, Biogen Idec and Elan Pharmaceuticals, Inc.) **COMPLETED**

+ Avonex® (interferon beta-1a, Biogen Idec)

**Purpose of study:** To control disease course, also known as SENTINEL study

**Possible mechanism:** Interferes with movement of immune cells across the blood-brain barrier by attaching to alpha 4-integrin (Tysabri)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** Tysabri 300 mg iv every 4 wks + Avonex 30 mcg/wk im vs. PBO iv + Avonex

**Outcome parameters:** MRI, EDSS

**Type of MS:** RR

**Number of Subjects:** 1171

**Start date:** 2002

**Observation period:** 128 weeks

**Investigators:** Multiple

**Sites:** Multicenter, United States and Europe

**Results/Publications:** Combination reduced disability progression by 24% and relapses by 54% over Avonex alone (Abstract # S36.001, AAN 2005; Biogen Idec press releases, 2/28/05, 4/13/05; *The New England Journal of Medicine* 2006;354:911-923; Abstracts P01.086, S32.004, S42.007, S52.005, AAN 2006)

**Funding:** Biogen Idec, Inc., Elan Corporation, plc

**ClinicalTrials.gov Identifier:** NCT00030966

**Last update:** 2006

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Agent: Zenvia™ (dextromethorphan/quinidine, Avanir Pharmaceuticals)

Purpose of study: To improve pseudobulbar affect (pathological laughing/criing)
Possible mechanism: Antagonist of NMDA receptor, suppresses excitatory neurotransmitters

Study description: Double blinded, placebo controlled
Dose/route: 1 capsule bid po for 12 wks vs. PBO bid po
Outcome parameters: Emotional lability scale, patient diary, Visual Analog Scale, Pain Intensity Rating Scale
Type of MS: All types, with pseudobulbar affect
Number of Subjects: 150
Start date: December 2002
Observation period: 3 months
Investigators: Multiple
Sites: Multicenter, United States

Results/Publications: Rx group had significantly greater reductions in lability scale scores than PBO group at all clinic visits, fewer crying or laughing episodes, lower pain intensity scores, and improved quality of life and quality of relationships scores; Rx was well tolerated; dizziness occurred with greater frequency than with PBO (Abstract #S46.001, AAN 2005, Abstract #P04.022, AAN 2006; Annals of Neurology 2006;59:780-787)
Funding: Avanir Pharmaceuticals
ClinicalTrials.gov Identifier: NCT00050232
Last update: 2006

Agent: Zenvia™ (dextromethorphan/quinidine, Avanir Pharmaceuticals)

Purpose of study: To improve pseudobulbar affect (pathological laughing/criing)
Possible mechanism: Antagonist of NMDA receptor, suppresses excitatory neurotransmitters

Study description: Open label
Dose/route: 1 capsule bid po for 12 wks vs. PBO bid po
Outcome parameters: Emotional lability scale, patient diary, Visual Analog Scale, Pain Intensity Rating Scale
Type of MS: All types, with pseudobulbar affect
Number of Subjects: 600
Start date: February 2003
Observation period: 12 months
Investigators: Multiple
Sites: Multicenter, United States
Results/Publications: Not available
Funding: Avanir Pharmaceuticals
ClinicalTrials.gov Identifier: NCT00056524
Last update: 2006
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