Clinical Trials in Multiple Sclerosis 2011:
Planned, In Progress, Recently Completed

This listing is prepared by the National Multiple Sclerosis Society from materials provided by principal investigators and from information gathered from published literature and public presentations. While we strive for accuracy, this list cannot be considered to include all MS trials, and there may be inaccuracies due to changes in protocol for selected studies.

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; trials that are not marked as completed may have completed observing participants, but are engaged in data analyses/preparing for publication. 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.

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A database of trials recruiting people with MS is available at:
http://www.nationalmssociety.org/trialsrecruiting.
This database is searchable by state, type of MS, and keyword, and includes a list of international studies.

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We are committed to a world free of multiple sclerosis. Our global support of MS research and treatment focuses on three key areas: STOPPING the progression of disease, RESTORING function that's been lost, and ENDING the disease forever.

Large Phase III Trials

AGENT	PURPOSE OF STUDY	HOW DRUG IS TAKEN	TYPE OF MS	NUMBER OF SUBJECTS
Alemtuzumab (Genzyme Corporation) vs. interferon beta-1a (Rebif®, Serono Pfizer)	To compare effect on progression of disability and relapse rate, also known as CARE-MS I, CAMMS 323	intravenous, subcutaneous	RR	581
Alemtuzumab (Genzyme Corporation) vs. interferon beta-1a (Rebif®, Serono Pfizer)	To test 2 doses of alemtuzumab versus interferon beta-1a on progression of disability and relapse rate, also known as CARE-MS II, CAMMS 324	intravenous, subcutaneous	RR	700
BG-12 (dimethyl fumarate) vs. glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries, Ltd.)	To test safety and effectiveness in controlling disease course and development of brain lesions, also known as CONFIRM study	oral, subcutaneous	RR	1431
BIIB017 (PEGylated interferon beta-1a)	To reduce relapses	subcutaneous	RR	1260
Botulinum toxin A (Botox®, Allergan, Inc.)	To improve bladder dysfunction, also known as Dignity Study	injected into bladder	All types, stable for ≥ 3 mos; EDSS ≤ 6.5	405
Cannabis extract (dronabinol)	To determine ability to prevent disease progression, also known as CUPID trial	oral	PP, SP	493
Cyclophosphamide vs. methylprednisolone	To control disease progression, also known as PROMESS study	intravenous	SP	360
Daclizumab High Yield Process (DAC HYP) vs. interferon beta-1a (Avonex®, Biogen Idec)	To evaluate safety and effectiveness	intramuscular, subcutaneous	RR	1500
Fingolimod (Gilenya™, Novartis)	To test safety and effectiveness, also known as FREEDOMS II study	oral	RR	1080

AGENT	PURPOSE OF STUDY	HOW DRUG IS TAKEN	TYPE OF MS	NUMBER OF SUBJECTS
Fingolimod (Gilenya™, Novartis)	To test safety and effectiveness, also known as INFORMS study	oral	PP	654
Glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries Ltd.)	To test less frequent dosing, also known as GALA Study	subcutaneous	RR	1350
Interferon beta-1a (Avonex®, Biogen Idec) + glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries Ltd.)	To test combination therapy on brain lesion load and underlying disease course, also known as CombiRx Study	intramuscular, subcutaneous	RR	1000
Laquinimod vs. interferon beta-1a (Avonex®, Biogen Idec)	To control disease course and development of brain lesions, also known as BRAVO study	oral, intramuscular	RR	1200
Ocrelizumab	To evaluate safety and effectiveness in reducing disease activity, also known as ORATORIO study	intravenous	PP	630
Teriflunomide (HMR1726)	To control lesion development, disease progression and relapses, also known as TOPIC study	oral	CIS	780
Teriflunomide (HMR1726)	To control lesion development, disease progression and relapses, also known as TOWER study	oral	RR	1110
Teriflunomide (HMR1726) and interferon beta-1a	To test safety and effectiveness of combination therapy	oral, intramuscular	Relapsing	1455

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Abbreviations Key

AAN – American Academy of Neurology
BBB - blood brain barrier
bid - twice daily
biw - twice weekly
CMSC – Consortium of MS Centers
ECTRIMS – European Committee of Treatment and Research in MS
EDSS - Expanded Disability Status Scale
G-CSF - granulocyte colony-stimulating factor
Gd - gadolinium
im - intramuscular
iv - intravenous
MSFC - Multiple Sclerosis Functional Composite
MSIS - Multiple Sclerosis Impact Scale
MSQLI - Multiple Sclerosis Quality of Life Inventory
MSQOL-54 - Multiple Sclerosis Quality of Life-54
NIH – National Institutes of Health
NRS - Scripps Neurological Rating Scale
PASAT - Paced Auditory Serial Addition Test
PBO - placebo
pc - percutaneous
po - oral
PP - primary progressive
PR - progressive relapsing
qhs - at bedtime
qhs - every night
qod - every other day
rATG - rabbit antithymocyte globulin
RR - relapsing-remitting
sc - subcutaneous
SF-36 - Short Form-36 derived from General Health Survey of Medical Outcomes Study
SP - secondary progressive
tid - three times daily
tiw - three times weekly

Clinical Trials in Multiple Sclerosis 2011

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
Study phase: III
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: P. Cesaro and others
Sites: Hôpital Henri-Mondor-France, Creteil, and others, France
Results/Publications: Not available
Funding: French Health Ministry
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00190268
Last update: 2011
****

Agent: Abatacept
Purpose of study: To evaluate saftey and effect on disease activity, also known as the ACCLAIM study
Possible mechanism: Prevents T cell stimulation through CD28-B7 pathway
Study description: Randomized, double blinded, placebo controlled
Study phase: II
Dose/route: Abatacept (500 mg, 750 mg, or 1 kg, depending on weight) iv vs. PBO iv at weeks 0, 2, 4, and then every 4 weeks through week 24
Outcome parameters: MRI
Type of MS: RR
Number of Subjects: 123
Start date: November 2010
Observation period: 64 weeks
Investigators: S. Khoury
Sites: Brigham and Women's Hospital, Boston, and others
Results/Publications: Not available
Funding: NIH
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01116427
Last update: 2011
****

Agent: ACT-128800
Purpose of study: To evaluate saftey and effect on disease activity
Possible mechanism: S1P1 selective receptor agonist; reduces number of circulating lymphocytes by preventing exit from lymphatic tissue
Study description: Randomized, double blinded, placebo controlled
Study phase: II
Dose/route: 10 mg/d po vs. 20 mg/d po vs. 40 mg/d po vs. PBO po
Outcome parameters: MRI, relapse, EDSS
Type of MS: RR
Number of Subjects: 400
Start date: August 2009
Observation period: 32 weeks
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Actelion Pharmaceuticals, Ltd.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01006265
Last update: 2010
****

Agent: Alemtuzumab (Genzyme Corporation) vs. interferon beta-1a (Rebif®, Serono Pfizer)
Purpose of study: To compare effect on progression of disability and relapse rate, also known as CARE-MS I, CAMMS 323
Possible mechanism: Targets CD52 antigen expressed on B and T lymphocytes (alemtuzumab)/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: Examining MD blind, open label
Study phase: III
Dose/route: Alemtuzumab 12 mg/d iv for 5 days at mos 0, 12 vs. Rebif 44 mcg tiw sc for 2 yrs
Outcome parameters: Time to sustained accumulation of disability and relapse rate at 2 yrs
Type of MS: RR
Number of Subjects: 581
Start date: September 2007
Observation period: 2 years
Investigators: Multiple
Sites: Multicenter, North America, Europe, Latin America, Australia
Results/Publications: Rationale and design described (Abstract #P02.171, AAN 2008)
Funding: Genzyme Corporation, Bayer HealthCare
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00530348
Last update: 2010
****

Agent: Alemtuzumab (Genzyme Corporation) vs. interferon beta-1a (Rebif®, Serono Pfizer)
Purpose of study: To test 2 doses of alemtuzumab versus interferon beta-1a on progression of disability and relapse rate, also known as CARE-MS II, CAMMS 324
Possible mechanism: Targets CD52 antigen expressed on B and T lymphocytes (alemtuzumab)/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, rater-blinded
Study phase: III
Dose/route: Alemtuzumab 12 mg/d iv for 5 days at mo 0 and 3 days at mo 12 vs. alemtuzumab 24 mg/d iv for 5 days at mo 0 and 3 days at mo 12 vs. Rebif 44 mcg tiw sc for 2 yrs
Outcome parameters: Time to sustained accumulation of disability and relapse rate at 2 yrs
Type of MS: RR
Number of Subjects: 700
Start date: October 2007
Observation period: 2-4 years
Investigators: Multiple
Sites: Multicenter, North America, Europe, Latin America, Australia
Results/Publications: Rationale and design described (Absract #P02.150, AAN 2008)
Funding: Genzyme Corporation, Bayer HealthCare
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00548405
Last update: 2010
****

Agent: Aspirin
Purpose of study: To improve fatigue
Possible mechanism: Inhibits prostaglandins
Study description: Double blinded, placebo controlled
Study phase: III
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: http://clinicaltrials.gov/ct2/show/NCT00467584
Last update: 2011
****

Agent: Atacicept **TERMINATED**
Purpose of study: To evaluate safety and effectiveness in reducing disease activity
Possible mechanism: Blocks B cell maturation, function, survival
Study description: Randomized, double blinded, placebo controlled
Study phase: II
Dose/route: Atacicept 150 mg biw sc (4 wks), then 150 mg/wk sc (32 wks) vs. atacicept 75 mg biw sc (4 wks), then 75 mg/wk sc (32 wks) + 25 mg biw sc (4 wks), then 25 mg/wk sc (32 wks) vs. PBO sc
Outcome parameters: MRI, EDSS, MSFC
Type of MS: RR
Number of Subjects: 292
Start date: June 2008
Observation period: 48 weeks
Investigators: Multiple
Sites: Multicenter, United States
Results/Publications: Discontinued based on recommendation of independent data monitoring committee that observed increase in disease activity in treatment arm (Zymogenetics SEC filing, September 28, 2010)
Funding: EMD Serono
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00624468
Last update: 2010
****

Agent: Atorvastatin (Lipitor®, Pfizer Ireland Pharmaceuticals Corp.) **COMPLETED**
Purpose of study: To evaluate safety and effectiveness on decreasing or delaying clinical and MRI disease activity in patients with CIS, also known as STAyCIS study
Possible mechanism: Promotes anti-inflammatory Th2 response
Study description: Randomized, double blinded, placebo controlled
Study phase: II
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 (CIS)
Number of Subjects: 81
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: Study was underpowered to detect the planned effect size due to discontinuation of enrollment at 81 subjects and did not meet primary endpoint; proportion of patients who did not develop new T2 lesions up to month 12 or to starting Avonex was 55.3% (Rx) and 27.6% (PBO) (Abstract #132, ECTRIMS 2009; Abstract #S21.005, AAN 2010)
Funding: Immune Tolerance Network, National Institute of Allergy and Infectious Disease
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00094172
Last update: 2010
****

Agent: Atorvastatin (Lipitor®, Pfizer Ireland Pharmaceuticals Corp.) and interferon beta-1a (Rebif®, Serono Pfizer)
Purpose of study: To delay time to definite MS in patients with CIS
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
Study phase: Not available
Dose/route: Rebif 44 mcg tiw sc + Lipitor 80 mg/d po vs. Rebif + PBO po
Outcome parameters: Gene expression, safety, efficacy
Type of MS: First clinical demyelinating event suggestive of MS
Number of Subjects: 30
Start date: October 2004
Observation period: 15 months
Investigators: S. Markovic-Plese
Sites: University of North Carolina, Chapel Hill
Results/Publications: Combination was safe and well tolerated; no significant difference in the clinical or MRI outcome; gene expression analysis revealed differentially expressed genes that are under further analysis (Communication with investigator)
Funding: University of North Carolina, Chapel Hill
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00137176
Last update: 2011
****

Agent: ATX-MS-1467
Purpose of study: To assess safety and biological activity
Possible mechanism: Consists of four short peptides derived from myelin basic protein, to induce immunological tolerance
Study description: Open label, proof of principle
Study phase: I
Dose/route: Open label upward titration over 5 dose levels using two routs of administration (ID and SC)
Outcome parameters: Adverse events, MRI, injection site reactions, immunology
Type of MS: Relapsing, HLA DRB1*15 positive
Number of Subjects: 40
Start date: March 2010
Observation period: 48 weeks
Investigators: Multiple
Sites: Multicenter, United Kingdom
Results/Publications: Not available
Funding: Apitope Technology (Bristol) Ltd., Merck Serono
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01097668
Last update: 2011
****

Agent: BAF312
Purpose of study: To test safety and effect on disease activity
Possible mechanism: Sphingosine-1-phosphate receptor binder; inhibits lymphocytes from exiting lymphatic tissue
Study description: Randomized, double blinded, placebo controlled, dose ranging
Study Phase: II
Dose/route: BAF312 0.5 mg/d po vs. BAF312 2.0 mg/d po vs. BAF312 10.0 mg/d po vs. PBO po; then dose adjustment for active arms vs. PBO
Outcome parameters: MRI
Type of MS: RR
Number of Subjects: 275
Start date: May 2009
Observation period: Not available
Investigators: Not available
Sites: Not available
Results/Publications: Not available
Funding: Novartis
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00879658
Last update: 2011
****

Agent: BG-12 (dimethyl fumarate)
Purpose of study: To test safety and effectiveness in controlling disease course and development of brain lesions, also known as DEFINE study
Possible mechanism: Upregulates Th2 response, immunomodulatory
Study description: Double blinded, placebo controlled
Study phase: III
Dose/route: 480 mg/d po vs. 720 mg/d po vs. PBO po
Outcome parameters: Proportion of relapsing patients, frequency of relapse, EDSS, MSFC, MRI
Type of MS: RR
Number of Subjects: 1237
Start date: March 2007
Observation period: 2 years
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: In both groups taking BG-12, significant reduction in proportion of people experiencing relapses at 2 years, relapse rate, disease activity on MRI scans, and EDSS scores; adverse events included abdominal pain, flushing, headache, fatigue, and feeling hot (Biogen Idec press release, April 11, 2011)
Funding: Biogen Idec, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00420212
Last update: 2011
****

Agent: BG-12 (dimethyl fumarate) vs. glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries, Ltd.)
Purpose of study: To test safety and effectiveness in controlling disease course and development of brain lesions, also known as CONFIRM study
Possible mechanism: Upregulates Th2 response, immunomodulatory (BG0012)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)
Study description: Double blinded, placebo controlled
Study phase: III
Dose/route: BG00012 480 mg/d po vs. 720 mg/d po vs. Copaxone 20 mg/d sc vs. PBO
Outcome parameters: Proportion of relapsing patients, relapse rate, EDSS, MSFC, MRI
Type of MS: RR
Number of Subjects: 1431
Start date: July 2007
Observation period: 2 years
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Baseline characteristics presented (Abstract #P06.158, AAN 2010)
Funding: Biogen Idec, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00451451
Last update: 2010
****

Agent: BG-12 (dimethyl fumarate) and interferon beta or glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries, Ltd.)
Purpose of study: To test safety and effectiveness in controlling disease course and development of brain lesions, also known as EXPLORE study
Possible mechanism: Upregulates Th2 response, immunomodulatory (BG0012)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (interferon beta)/ Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)
Study description: Open label
Study phase: III
Dose/route: BG00012 240 mg/tid po + interferon vs. BG00012 240 mg/tid po + Copaxone 20 mg/d sc
Outcome parameters: Safety and tolerability, relapse, MRI
Type of MS: RR
Number of Subjects: 100
Start date: May 2010
Observation period: 8 months
Investigators: Multiple
Sites: Multicenter, United States
Results/Publications: Not available
Funding: Biogen Idec, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01156311
Last update: 2011
****

Agent: BIIB017 (PEGylated interferon beta-1a)
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
Study description: Randomized, double blinded, placebo controlled, parallel group
Study phase: III
Dose/route: BIIB017 125 mcg sc vs. PBO sc (every 2-4 wks)
Outcome parameters: Annualized relapse rate
Type of MS: RR
Number of Subjects: 1260
Start date: June 2009
Observation period: 2 years
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Biogen Idec
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00906399
Last update: 2010
****

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
Study phase: II
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, *Multiple Sclerosis* International Quality of Life Questionnaire, 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: http://clinicaltrials.gov/ct2/show/NCT00273364
Last update: 2010
****

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
Study phase: II
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, GCSF 5 mcg/kg/d sc, prednisone 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: First 7 people followed for an average of 9.5 months had no further relpases; EDSS stable (n=2), improved (n=3), worsened by 0.5 points (n=1); no new lesions on MRI; 1 case each of graft-versus-host disease, pseudo-relapse and MRSA infection occurred transiently (Abstract #P02.179, AAN 2008; Abstract #P07.133, AAN 2009)
Funding: National Institute of Allergy and Infectious Disease
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00288626
Last update: 2011
****

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
Study phase: Not available
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: 1-8 years
Investigators: M. Freedman and others
Sites: University of Ottawa and others
Results/Publications: 6/16 patients with ≥1.5 year of follow-up showed sustained EDSS improvements (3/16 worsened and 7/16 unchanged); those showing earliest changes also had shortest disease course; no Gd enhancing lesions; T2 lesion volumes remained stable in 7/16; 9/16 showed overall reductions compared to baseline (Abstracts #S60.005 and #S40.005, AAN 2004; Abstracts #S46.005 and #S46.006, AAN 2005; Abstract #SC2.013, AAN 2006; Abstract #73, ECTRIMS 2007; Abstract P02.145, AAN 2009)
Funding: MS Scientific Research Foundation
ClinicalTrials.gov Identifier: Not available
Last update: 2011
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Agent: Botulinum toxin A (Botox®, Allergan, Inc.)
Purpose of study: To improve bladder dysfunction, also known as Dignity Study
Possible mechanism: Blocks neuromuscular transmission
Study description: Double blinded, placebo controlled, parallel-group study
Study phase: III
Dose/route: Botox 200 units injected into bladder vs. Botox 300 units injected into bladder vs. PBO injected into bladder, at least 12 wks apart
Outcome parameters: Number of incontinence episodes
Type of MS: All types, stable for ≥ 3 mos; EDSS ≤ 6.5
Number of Subjects: 405
Start date: August 2006
Observation period: up to 3 years
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Allergan, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00311376
Last update: 2010
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Agent: Botulinum toxin A (Botox®, Allergan, Inc.)
Purpose of study: To improve bladder and respiratory dysfunction, also known as Dignity TOO Study
Possible mechanism: Blocks neuromuscular transmission
Study description: Double blinded, placebo controlled
Study phase: III
Dose/route: Botox 200 units injected into bladder vs. Botox 300 units injected into bladder vs. PBO injected into bladder; up to 2 treatments 12 wks apart
Outcome parameters: Number of incontinence episodes, safety, pulmonary function
Type of MS: All types, stable for ≥ 3 mos; EDSS 7.0 ≤ 8.0
Number of Subjects: 135
Start date: May 2007
Observation period: up to 52 weeks
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Allergan, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00439140
Last update: 2010
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Agent: C-105 (l-amphetamine sulfate) **COMPLETED**
Purpose of study: To evaluate effects on cognitive function
Possible mechanism: Central nervous system stimulant
Study description: Double blinded, placebo controlled
Study phase: II
Dose/route: C-105 5 mg/d po titrated to 30 mg/d po over one month vs. PBO po
Outcome parameters: Safety, cognitive testing
Type of MS: RR, SP, with cognitive dysfunction
Number of Subjects: 151
Start date: 2006
Observation period: 1.5 months
Investigators: Multiple
Sites: Multicenter, United States
Results/Publications: Primary outcomes (processing speed and executive function) not met; significant improvement in secondary outcomes (measures of total learning and delayed recall) at highest dose (30 mg/d); no severe or serious adverse events reported; adverse events occurring more frequently in treatment group included visual disturbance (8.3% vs. 0.0% for PBO) and fatigue (9.3% vs. 4.7% for PBO) (*Journal of Neurology* 2009 Jul;256(7):1095-102)
Funding: Cognition Pharmaceuticals
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00529581
Last update: 2010
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Agent: Cannabis extract (cannador)
Purpose of study: To improve pain and muscle stiffness, also known as MUSEC trial
Possible mechanism: May inhibit neurotransmitter release, affect immune function, be neuroprotetive
Study description: Randomized, double blinded, placebo controlled
Study phase: III
Dose/route: Cannador 5 mg/d po (individual dose titration of 5 mg every 3 days to 25 mg/d, administered as 2 equal doses based on tolerability) vs. PBO po
Outcome parameters: Likert Scale (pain severity)
Type of MS: All types, stable for at least 6 mos
Number of Subjects: 279
Start date: June 2006
Observation period: 12 weeks
Investigators: J. Zajicek and others
Sites: Peninsula Medical School, Plymouth, and others, United Kingdom
Results/Publications: Muscle stiffness improved by 29.4% in cannabis group vs. 15.7% in PBO group; similar improvements noted in body pain, spasms and sleep quality; most frequent adverse events were urinary tract infections, dizziness, dry mouth, and headache (Abstract #881, ECTRIMS 2009)
Funding: Weleda AG and IKF
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00552604
Last update: 2010
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Agent: Cannabis extract (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
Study phase: I, II
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: http://clinicaltrials.gov/ct2/show/NCT00682929
Last update: 2010
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Agent: Cannabis extract (dronabinol)
Purpose of study: To determine ability to prevent disease progression, also known as CUPID trial
Possible mechanism: May reduce neuronal damage mediated through an interaction with cannabinoid type 1 and opioid receptors
Study description: Randomized, double blinded, placebo controlled, parallel group
Study phase: III
Dose/route: Dronabinol 3.5-28 mg/d po in two divided doses titrated according to body weight and adverse events vs. PBO po
Outcome parameters: EDSS, MSIS-29 physical impact scale
Type of MS: PP, SP
Number of Subjects: 493
Start date: May 2006
Observation period: 3 years
Investigators: J. Zajicek and others
Sites: Peninsula Medical School, Plymouth, and others, United Kingdom
Results/Publications: Not available
Funding: Medical Research Council (UK), MS Society (UK) and MS Trust (UK)
ClinicalTrials.gov Identifier: Not available
Last update: 2010
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Agent: Cannabis extract (tetrahydrocannabinol and cannabidiol, Sativex®, GW Pharm.)
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
Study phase: III
Dose/route: 100 microliters of tetrahydrocannabinol/cannabidiol per spray, directed under tongue or inside cheeks; patients can gradually self-titrate to a maximum of 24 sprays/24 hrs
Outcome parameters: Pain (Numeric Rating Scale), Neuropathic Pain Scale, QOL, safety
Type of MS: All types, with central neuropathic pain
Number of Subjects: 339
Start date: July 2006
Observation period: 15 weeks
Investigators: Multiple
Sites: Multiple, Canada and Europe
Results/Publications: Primary/secondary endpoints not significant; large placebo response (GW Pharmaceuticals press release, April 8, 2008)
Funding: GW Pharmaceuticals, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00391079
Last update: 2010
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Agent: Cannabis extract (tetrahydrocannabinol/cannabidiol, Sativex®, GW Pharm.)**COMPLETED**
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
Study phase: III
Dose/route: 100 microliters of tetrahydrocannabinol/cannabidiol per spray, directed under tongue or inside cheeks, added to current antispasticity therapy; up to12 sprays/d vs. PBO
Outcome parameters: Numerical Rating Scale and other scales
Type of MS: RR, P, with spasticity
Number of Subjects: 572
Start date: January 2008
Observation period: 56 weeks
Investigators: Multiple
Sites: Multiple, Europe
Results/Publications: 241 responders in first phase were randomly assigned to receive either Sativex or placebo for 12 weeks; spasticity on NRS improved significantly more in the Sativex group , as did sleep disruption, spasm frequency, the ability to complete activities of daily living, and the clinician/caregiver's impressions of improvement; most common adverse events in the Sativex group were vertigo, fatigue, muscle spasms and urinary tract infection (*European Journal of Neurology* 2011 Mar 1. [Epub ahead of print])
Funding: GW Pharmaceuticals, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00681538
Last update: 2011
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Agent: CCSVI (chronic cerebrospinal venous insufficiency) treatment; evaluation of angioplasty
Purpose of study: To evaluate safety and effectiveness of CCSVI treatment
Possible mechanism: May relieve narrowing or blockages in the internal jugular or azygos veins
Study description: Double blinded, parallel group
Study phase: I
Dose/route: Angioplasty vs. sham comparator
Outcome parameters: QOL, EDSS, relapse rates, Timed 25-Foot Walk
Type of MS: EDSS 3-6, with stenosis of internal jugular or azygos vein
Number of Subjects: 130
Start date: August 2010
Observation period: 24 months
Investigators: G. Siskin
Sites: Albany Medical Center, New York, Image Care Latham, New York
Results/Publications: Not available
Funding: Community Care Physicians, P.C.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01201701
Last update: 2011
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Agent: CCSVI (chronic cerebrospinal venous insufficiency) treatment; evaluation of venoplasty
Purpose of study: To evaluate safety and effectiveness of CCSVI treatment
Possible mechanism: May relieve extracranial venous obstructive lesions
Study description: Single center, multispecialty, randomized, double blind, placebo control, feasibility clinical trial
Study phase: I
Dose/route: Venoplasty vs. sham comparator
Outcome parameters: Adverse events, neurological assessment, MRI/MRA, mortality
Type of MS: EDSS 0-7, with 50% or more stenosis of the extracranial veins
Number of Subjects: 600
Start date: August 2010
Observation period: 1 year
Investigators: M. Mehta
Sites: The Vascular Group, PLLC, Albany, NY
Results/Publications: Not available
Funding: The Vascular Group, PLLC, Albany, NY
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01089686
Last update: 2011
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Agent: CDP323 **TERMINATED**
Purpose of study: To evaluate safety, tolerability and effects of two doses
Possible mechanism: VLA-4 inhibitor, blocking entry of immune cells into CNS
Study description: Double blinded, placebo controlled
Study phase: II
Dose/route: CDP323 500 mg/d po vs. 500 mg bid po vs. PBO po
Outcome parameters: MRI
Type of MS: RR, SP with superimposed relapses
Number of Subjects: 234
Start date: May 2007
Observation period: 40 weeks
Investigators: Multiple
Sites: Multicenter, US and Europe
Results/Publications: Preliminary analysis showed no benefit compared with PBO, study discontinued; 13 subjects had temporarily elevated liver enzymes (5x upper limit of normal); common non-disease-related adverse events included headache, nasopharyngitis, and nausea (Abstract #S21.002, AAN 2010)
Funding: UCB and Biogen Idec
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00484536
Last update: 2010
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Agent: Cladribine **COMPLETED**
Purpose of study: To test safety, effectiveness, also known as CLARITY study
Possible mechanism: Lymphocyte reduction
Study description: Randomized, double blinded, placebo controlled
Study phase: III
Dose/route: Cladribine 0.875 mg/kg vs. PBO po
Outcome parameters: Relapse rate, EDSS, MRI
Type of MS: RR
Number of Subjects: 1326
Start date: April 2005
Observation period: 2 years
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Relapse rate reduced by 58% (low-dose) and 55% (high-dose) vs. PBO; proportion of relapse-free patients significantly higher in Rx groups vs. PBO; Rx groups had more than 30% reduction in EDSS vs. PBO and at least 70% reduction in Gd lesions, active T2 lesions, and combined unique lesions; 4 malignancies (cervical stage 0, melanoma, ovarian and pancreatic) and 1 case of choriocarcinoma (in pregnancy 6 months post-study) reported in Rx groups; common adverse events were headaches, upper respiratory tract infections, nasopharyngitis, nausea, and lymphopenia; herpes zoster in 2.3% of Rx groups (*The New England Journal of Medicine* 2010;362:416-26)
Funding: EMD Serono, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00213135
Last update: 2010
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Agent: Cladribine + interferon beta-1a (Rebif® [fetal bovine serum-free/human serum albumin-free formulation], Serono Pfizer)
Purpose of study: To test safety, effectiveness, 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
Study phase: II
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, safety
Type of MS: RR, SP with relapses
Number of Subjects: 200
Start date: December 2006
Observation period: 104 weeks
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Rationale and design described (Abstract #P809, ECTRIMS 2007)
Funding: EMD Serono, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00436826
Last update: 2010
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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
Study phase: III
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: http://clinicaltrials.gov/ct2/show/NCT00241254
Last update: 2011
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Agent: Daclizumab + interferon beta **COMPLETED**
Purpose of study: To evaluate safety and effectiveness, also known as CHOICE study
Possible mechanism: Limits T cell expansion by blocking signaling of cytokine IL-2
Study description: Randomized, double blinded, placebo controlled, dose ranging
Study phase: II
Dose/route: 2 mg/kg sc every 2 wks vs. 1 mg/kg sc every 4 wks (alternates with PBO every 2 weeks) + interferon beta vs. PBO sc + interferon beta
Outcome parameters: Gd-MRI lesions, relapse rate, EDSS, MSFC, effects on immune cells
Type of MS: Active, relapsing
Number of Subjects: 230
Start date: April 2005
Observation period: 72 weeks
Investigators: Multiple
Sites: Multicenter, United States, Canada, Europe
Results/Publications: Gd-MRI lesions significantly reduced by 72% in 2-mg group and by 25% in 1-mg group compared with IFN/PBO; no significant changes in T cells, B cells, natural killer cells, or T-cell proliferative response in Rx groups compared with IFN/PBO, but number of CD56bright natural killer cells 7x-8x higher in daclizumab groups (*Lancet Neurology* 2010;February 16, 2010)
Funding: Biogen Idec, Inc., Facet Biotech
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00109161
Last update: 2010
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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
Study phase: II
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: http://clinicaltrials.gov/ct2/show/NCT00071838
Last update: 2010
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Agent: Daclizumab High Yield Process (DAC HYP) vs. interferon beta-1a (Avonex®, Biogen Idec)
Purpose of study: To evaluate safety and effectiveness
Possible mechanism: Limits T cell expansion by blocking signaling of cytokine IL-2 (DAC HYP)/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, active control
Study phase: III
Dose/route: Avonex 30 mcg/wk im + PBO sc vs. DAC HYP 150 mg/every 4 wks SC + PBO im
Outcome parameters: Relapse rate
Type of MS: RR
Number of Subjects: 1500
Start date: May 2010
Observation period: 96 to 144 weeks
Investigators: Multiple, worldwide
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Biogen Idec, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01064401
Last update: 2011
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Agent: dalfampridine (Ampyra®, Acorda Therapeutics) **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
Study phase: III
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: Proportion of timed walk responders higher in Rx group (42.9%) compared to PBO group (9.3%); average improvement in walking speed among responders during 8-weeks was 24.7%; mean improvement at last on-treatment visit was 25.7%; UTI, insomnia, headache, asthenia, dizziness, nausea, back pain, balance disorder, and paresthesia each reported >50% higher in Rx group (*Annals of Neurology* 2010;68(4):494-502)
Funding: Acorda Therapeutics, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00483652
Last update: 2011
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Agent: Dextromethorphan/quinidine (Zenvia™, Avanir Pharm.) **COMPLETED**
Purpose of study: To improve pseudobulbar affect (pathological laughing/crying), also known as STAR trial
Possible mechanism: Dextromethorphan/quinidine capsules, Antagonist of NMDA receptor, suppresses excitatory neurotransmitters
Study description: Randomized, double blinded, placebo controlled
Study phase: III
Dose/route: 30 (dextromethorphan)/10 (quinidine) capsules bid po for 12 wks vs. 20/10 capsules bid po vs PBO bid po
Outcome parameters: Patient record episodes, Center for Neurologic Studies Lability Scale
Type of MS: All types, with pseudobulbar affect, and amyotrophic lateral sclerosis
Number of Subjects: 326
Start date: December 2007
Observation period: 168 days
Investigators: Multiple
Sites: Multicenter, United States and Latin America
Results/Publications: Both doses significantly reduced episode rates compared to PBO; those on higher dosage showed improved social functioning and mental health; more frequent adverse events included dizziness, nausea and diarrhea; 7 deaths among participants with ALS, all of which were likely due to respiratory problems related to ALS (*Annals of Neurology* 2010;68(5):693-702)
Funding: Avanir Pharmaceuticals
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00573443
Last update: 2011
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Agent: Dirucotide (formerly MBP8298) **COMPLETED**
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
Study phase: II, III
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: Did not meet primary endpoint, no statistically significant differences in secondary endpoints (Eli Lilly and Company/BioMS Medical Corp. press release, July 27, 2009)
Funding: BioMS Medical Corp.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00869726
Last update: 2010
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Agent: Dirucotide (formerly MBP8298) **TERMINATED**
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
Study phase: III
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, United States
Results/Publications: Discontinued upon Maestro-01 negative results (Eli Lilly and Company/BioMS Medical Corp. press release, July 27, 2009)
Funding: BioMS Medical Corp.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00468611
Last update: 2010
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Agent: Donepezil (Aricept®, Eisai Co.) **COMPLETED**
Purpose of study: To improve memory, also known as AIMS study
Possible mechanism: Cholinesterase inhibitor
Study description: Randomized, double blinded, placebo controlled
Study phase: III
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, self-reported memory change, brief repeatable battery and tests, Clinical Impression of Change
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 Brook, NY, and others
Results/Publications: No benefit relative to placebo on primary or secondary outcome measures (*Neurology* 2011;76(17):1500-7)
Funding: NIH
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00062972
Last update: 2011
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Agent: Duloxetine hydrochloride (Cymbalta®, Lilly)
Purpose of study: To decrease central neuropathic pain due to MS
Possible mechanism: Inhibits serotonin and norepinephrine reuptake in CNS, leading to modulation of central sensitization and neuroplasticity
Study description: Double blinded, placebo controlled
Study phase: III
Dose/route: 60 mg/d po for 6 wks followed by 60, 90, or 120 mg/d po for up to 12 wks vs. PBO
Outcome parameters: Likert Scale (pain severity)
Type of MS: All types, with central neuropathic pain
Number of Subjects: 238
Start date: November 2008
Observation period: Up to 20 weeks
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Eli Lilly and Company
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00755807
Last update: 2011
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Agent: Epigallocatechin-gallate (Sunphenon®, Taiyo International Food) vs. glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries, Ltd.)
Purpose of study: To protect nerves and affect immune function, known as SuniMS study
Possible mechanism: May interfere with T cell growth and function, and protect against neuronal injury (Sunphenon)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)
Study description: Double blinded, placebo controlled
Study phase: II
Dose/route: Sunphenon 200 mg bid po for 3 mos, then 400 mg bid po + Copaxone 20 mg/d sc vs. PBO po + Copaxone 20 mg/d sc
Outcome parameters: MRI
Type of MS: RR
Number of Subjects: 100
Start date: September 2007
Observation period: 18 months
Investigators: F. Zipp
Sites: Cecilie-Vogt-Clinic for Neurology and NeuroCure Clinical Research Center, Charité University Hospital, Berlin
Results/Publications: Not available
Funding: IIT
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00525668
Last update: 2010
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Agent: ELND002
Purpose of study: To evaluate safety and tolerability
Possible mechanism: May interfere with movement of immune cells across the blood-brain barrier by inhibiting **a**lpha-4 integrin
Study description: Dose escalating, randomized, placebo controlled, double blinded
Study phase: IIb
Dose/route: ELND002 weekly or monthly every 4 wks for 12 wks sc
Outcome parameters: Safety and tolerability
Type of MS: RR
Number of Subjects: 125
Start date: May 2010
Observation period: 68 weeks
Investigators: Multiple
Sites: Multicenter, United States and Canada
Results/Publications: Not available
Funding: Elan Pharmaceuticals
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01144351
Last update: 2011
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Agent: Estriol + glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries, Ltd.)
Purpose of study: To control disease course
Possible mechanism: Pregnancy hormone that decreases Th1 inflammatory immune response
Study description: Randomized, double blinded, placebo controlled
Study phase: II, III
Dose/route: Estriol 8 mg/d po + Copaxone 20 mg/d sc 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, NIH, others
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00451204
Last update: 2011
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Agent: Fingolimod (Gilenya™, Novartis) **COMPLETED**
Purpose of study: To test safety and effectiveness, also known as FREEDOMS study
Possible mechanism: Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue
Study description: Randomized, double blinded, placebo controlled
Study phase: III
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: 1272
Start date: January 2006
Observation period: 2 years
Investigators: L. Kappos and others
Sites: Multicenter, Europe and North America
Results/Publications: Relapse rates were 0.18 for the lower dose, 0.16 with the higher dose, and 0.40 for those on placebo (a reduction of 54% and 60% over placebo, respectively); both doses showed slower progression over those on placebo; both Rx doses superior to PBO with regard to MRI-related measures; adverse events that led to discontinuation of the study medication were more common with fingolimod at a dose of 1.25 mg (occurring in 14.2% of patients) than with 0.5 mg (7.5%) or PBO (7.7%); most common serious adverse events, each reported for eight patients, were bradycardia, MS relapse, and basal-cell carcinoma (*The New England Journal of Medicine* 2010 Feb 4;362(5):387-401)
Funding: Novartis
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00289978
Last update: 2010
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Agent: Fingolimod (Gilenya™, Novartis)
Purpose of study: To test safety and effectiveness, also known as FREEDOMS II study
Possible mechanism: Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue
Study description: Randomized, double blinded, placebo controlled
Study phase: III
Dose/route: 0.5 mg/d po vs. 1.25 mg/d po vs PBO po
Outcome parameters: Frequency of relapse
Type of MS: RR
Number of Subjects: 1080
Start date: June 2006
Observation period: 24 months
Investigators: D. Huang and others
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Novartis
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00355134
Last update: 2011
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Agent: Fingolimod (Gilenya™, Novartis)
Purpose of study: To test safety and effectiveness, also known as INFORMS study
Possible mechanism: Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue
Study description: Randomized, double blinded, placebo controlled, parallel group
Study phase: IIIb
Dose/route: 1.25 mg/d po vs PBO po
Outcome parameters: Scoring technique, MRI, frequency of relapse
Type of MS: PP
Number of Subjects: 654
Start date: January 2009
Observation period: 3-4.5 years
Investigators: Multiple
Sites: Multicenter, United States
Results/Publications: Not available
Funding: Novartis
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00731692
Last update: 2011
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Agent Fingolimod (Gilenya™, Novartis) vs. Avonex® (interferon beta-1a, Biogen Idec)
COMPLETED
Purpose of study: To test safety and effectiveness, also known as TRANSFORMS study
Possible mechanism: Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue (fingolimod)/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, parallel group
Study phase: III
Dose/route: 0.5 mg/d po vs. 1.25 mg/d po vs Avonex 30 mcg/wk im
Outcome parameters: Frequency of relapse
Type of MS: RR
Number of Subjects: 1153
Start date: May 2006
Observation period: 12 months
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Annualized relapse rate reduced by 52% in .5-mg group and by 38% in 1.25-mg group compared to Avonex; both doses reduced MRI activity; no difference in time to sustained disability progression; two fatal infections in 1.25-mg group (disseminated primary varicella zoster, herpes simplex encephalitis); nonfatal herpesvirus infections, bradycardia, atrioventricular block, hypertension, macular edema, skin cancer, elevated liver-enzymes (*The New England Journal of Medicine* 2010;362:402-15.)
Funding: Novartis
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00340834
Last update: 2010
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Agent: Firategrast (SB-683699) **COMPLETED**
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
Study phase: II
Dose/route: Firategrast 150 mg po vs. 600 mg po vs. 900 mg (females)/1200 mg (males) po vs. PBO po
Outcome parameters: MRI at 6 months
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: Primary outcome statistically significant for highest dose vs. PBO: 49% decrease in Gd+ lesions; significant decrease in new T2 lesions observed in 900/1200mg group; no evidence of PML observed up to 1 year post treatment (Abstract #113, ECTRIMS 2010)
Funding: GlaxoSmithKline
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00395317
Last update: 2011
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Agent: Flupirtine maleate
Purpose of study: To examine neuroprotective ability, also known as FLORIMS study
Possible mechanism: non-opioid analgesic; activates K+ channels and indirectly antagonizes NMDA receptors; reduces apoptosis and necrosis induced by noxious stimuli
Study description: Double blinded, placebo controlled
Study phase: II
Dose/route: 300 mg/d po vs. PBO po
Outcome parameters: MRI, clinical scales, frequency of relapse, optical coherence tomography
Type of MS: RR
Number of Subjects: 80
Start date: December 2007
Observation period: 12 months
Investigators: P. Friedemann
Sites: NeuroCure Clinical Research Center, Charite Universitätsmedizin, Berlin, and University of Göttingen, Department of Neurology Recruiting, Göttingen, Germany
Results/Publications: Not available
Funding: IIT, Bayer Schering
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00623415
Last update: 2010
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Agent: Ginkgo biloba **COMPLETED**
Purpose of study: To improve cognitive function
Possible mechanism: Alter neural function
Study description: Double blinded, placebo controlled
Study phase: II
Dose/route: 120 mg bid po vs. PBO po
Outcome parameters: Battery of neuropsychological tests
Type of MS: RR, P
Number of Subjects: 158
Start date: January 2009
Observation period: 12 weeks
Investigators: D. Bourdette, J. Haselkorn
Sites: Portland VA Medical Center, VA Puget Sound Health Care System
Results/Publications: After 12 weeks, no differences were seen between ginkgo and PBO groups in any outcomes (Abstract #S41.004, AAN 2011)
Funding: VA Rehabilitation Research and Development Service
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00841321
Last update: 2011
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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
Study phase: Not available
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, Doodrill 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, E. Kim
Sites: Oregon Health & Science University, Portland
Results/Publications: No significant imrovement in primary or secondary endpoints (Abstract #S21.006, AAN 2009)
Funding: CVT Technologies
ClinicalTrials.gov Identifier: Not available
Last update: 2011
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Agent: Glatiramer acetate (Copaxone®, 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 original study
Study phase: IV
Dose/route: 20 mg/d sc
Outcome parameters: EDSS
Type of MS: RR
Number of Subjects: 100
Start date: 1991
Observation period: Ongoing
Investigators: K. Johnson and others
Sites: Multicenter, United States
Results/Publications: Results on 100 people with mean disease duration of 22 years administering GA for up to 15 years showed reduced relapse rates and decreased disability progression and transition to SPMS; no long-term safety issues (*Multiple Sclerosis* 2010;16;342)
Funding: Teva Pharmaceutical Industries, Ltd.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00203021
Last update: 2010
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Agent: Glatiramer acetate (Copaxone®, Teva Pharm. Industries Ltd.) **COMPLETED**
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
Study phase: III
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: 481
Start date: November 2003
Observation period: 5 years
Investigators: G. Comi and others
Sites: Multicenter, worldwide
Results/Publications: Risk of developing clinically definite MS reduced by 45% versus PBO; time for 25% to development of definite MS delayed by 386 days compared to PBO; proportion of patients who developed MS was 43% in PBO group vs. 25% in Copaxone group; NAA levels significantly higher in people taking Copaxone in a subgroup of 34 people at 1 year; label extended to include CIS and MRI consistent with MS (*Lancet* 2009 Oct 31;374(9700):1503-11)
Funding: Teva Neuroscience
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00666224
Last update: 2010
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Agent: Glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries Ltd.)
Purpose of study: To evaluate neuroprotective ability in MS
Possible mechanism: Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2
Study description: Randomized, double blinded, placebo controlled
Study phase: IIIb
Dose/route: 20 mg/d sc vs. PBO sc
Outcome parameters: Retinal nerve fiber layer, additional optical coherence tomography parameters
Type of MS: First episode of optic neuritis
Number of Subjects: 200
Start date: February 2009
Observation period: 6 months
Investigators: P. Calabresi and others
Sites: Johns Hopkins University, Baltimore, and others, United States
Results/Publications: Not available
Funding: Teva Pharmaceuticals Industries, Ltd.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00856635
Last update: 2010
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Agent: Glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries Ltd.)
COMPLETED
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
Study phase: III
Dose/route: 20 mg/d sc vs. 40 mg/d sc
Outcome parameters: Relapses
Type of MS: RR
Number of Subjects: 1155
Start date: September 2006
Observation period: 12 months
Investigators: G. Comi and others
Sites: Multicenter, worldwide
Results/Publications: Both doses safe and well-tolerated, with no gain in effectiveness for the higher dose (*Annals of Neurology* 2011;69(1):75-82)
Funding: Teva Pharmaceuticals Industries, Ltd.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00337779
Last update: 2011
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Agent: Glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries Ltd.)
Purpose of study: To test less frequent dosing, also known as GALA Study
Possible mechanism: Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2
Study description: Double blinded, placebo controlled
Study phase: III
Dose/route: Copaxone 40 mg tiw sc vs. PBO sc
Outcome parameters: frequency of relapse, MRI
Type of MS: RR
Number of Subjects: 1350
Start date: June 2010
Observation period: 12 months
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Teva Pharmaceuticals Industries, Ltd.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01067521
Last update: 2011
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Agent: Glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries Ltd.) + albuterol (Proventil®, Schering Corporation) **COMPLETED**
Purpose of study: To control disease course, development of brain lesions and evaluate impact on immune function
Possible mechanism: Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)/Decreases activity of cytokine IL-12 (Proventil)
Study description: Double blinded, placebo controlled
Study phase: Not available
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: 44
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: Improvement in MSFC observed in albuterol group at 6 months and 12 months, but not at 24 months; delay in time to first relapse observed in albuterol group; IL-13 and IFN-gamma production decreased in both treatment groups; 3 moderate or severe adverse events related to treatment (injection site reaction, leg weakness, chest tightness)(*Archives of Neurology* 2010 ;67(9):1055-61)
Funding: NIH, National Institute of Allergy and Infectious Disease, Autoimmunity Centers of Excellence
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00039988
Last update: 2011
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Agent: Glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries Ltd.) + prednisone **TERMINATED**
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
Study phase: IV
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: 506
Start date: January 2005
Observation period: 36 months
Investigators: Multiple
Sites: Multicenter, United States, Canada, Australia
Results/Publications: Terminated due to lack of efficacy of the prednisone/placebo (clinicaltrials.gov)
Funding: Teva Neuroscience
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00203047
Last update: 2011
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Agent: Helminth-induced immunomodulation therapy
Purpose of study: To determine safety and effectiveness in reducing disease activity, also known as HINT 1 Study
Possible mechanism: May stimulate protective immune response
Study description: Baseline versus treatment design, radiologists blinded to treatment status
Study phase: I
Dose/route: Solution containing the eggs of the helminth, every 2 wks po
Outcome parameters: Gd lesions on serial MRI scans, EDSS, MSFC, relapes, gastrointestinal symptoms, immunology
Type of MS: RR
Number of Subjects: 20
Start date: March 2008
Observation period: 7 months
Investigators: J. Fleming
Sites: University of Wisconsin, Madison
Results/Publications: No significant adverse effects observed; favorable trends in MRI and immunological assessments in first phase of 5 people (*Multiple Sclerosis Journal* 2011 Mar 3. [Epub ahead of print])
Funding: National MS Society
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00645749
Last update: 2011
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Agent: Helminth-induced immunomodulation therapy (Trichuris suis ova)
Purpose of study: To determine safety
Possible mechanism: May stimulate protective immune response
Study description: Open label, crossover
Study phase: II
Dose/route: 2500 eggs per dose, every 2 wks po for 12 wks
Outcome parameters: MRI
Type of MS: RR, SP
Number of Subjects: 10
Start date: March 2010
Observation period: 5 months
Investigators: P. Sørensen, A. Voldsgaard
Sites: Danish MS Research Center, Rigshospitalet, Denmark
Results/Publications: Not available
Funding: Danish MS Society, Danish Medical Research Council, Danish MS Research Center
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01006941
Last update: 2010
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Agent: Ibudilast (MN-166) **COMPLETED**
Purpose of study: To test safety and control disease course
Possible mechanism: Inhibits leukotriene activity, phosphodiesterases and nitric oxide synthase; may be neuroprotective
Study description: Randomized, double blinded, placebo controlled
Study phase: II
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: 292
Start date: July 2005
Observation period: 12 months with 12-month extension
Investigators: Multiple
Sites: Multicenter, Eastern Europe
Results/Publications: Mean number of active lesions and relapse rate did not differ between treatment arms; reduction in % brain volume change in the 60-mg group compared with PBO; post hoc analysis showed reduction in proportion of active lesions that evolved into persistent black holes for Rx groups compared with PBO; over 2 years, fewer patients with confirmed progression on EDSS in Rx groups; dose related increase in gastrointestinal adverse events -- 10% (placebo to 30 mg/d), 12% (placebo to 60 mg/d), 17% (30 mg/d), and 18% (60 mg/d) (Abstract #52, ECTRIMS 2007; Abstract #P48, World Congress of MS 2009; *Neurology* 2010;74:1–1)
Funding: MediciNova, Inc.
ClinicalTrials.gov Identifier: Not available
Last update: 2010
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Agent: Idebenone
Purpose of study: To determine effect on disease activity
Possible mechanism: Acts as a potent antioxidant and facilitates mitochondrial electron flux and energy production; potentially also anti-inflammatory
Study description: Double blinded, placebo controlled
Study phase: I, II
Dose/route: 900 mg/d po for first month, then 2250 mg/d po for remainder of study
Outcome parameters: MRI, clinical scales
Type of MS: PP
Number of Subjects: 66
Start date: July 2009
Observation period: 3 years
Investigators: B. Bielekova
Sites: National Institutes of Health, Bethesda, MD
Results/Publications: Not available
Funding: NINDS
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00950248
Last update: 2010
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Agent: Interferon beta-1a (Avonex®, Biogen Idec) + glatiramer acetate (Copaxone®, 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
Study phase: III
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, MSQLI, 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: Baseline information on 907 participants (Abstract #S21.005, AAN 2009)
Funding: NINDS, agents provided by Biogen Idec, Inc. and Teva Neuroscience
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00211887
Last update: 2011
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Agent: Interferon beta-1a (Avonex®, Biogen Idec) + methylprednisolone**COMPLETED**
Purpose of study: To control development of brain lesions and disease relapses, also known as MECOMBIN 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)/Closes damaged blood-brain barrier, reducing inflammation in CNS (methylprednisolone)
Study description: Placebo controlled
Study phase: IV
Dose/route: Avonex 30 mcg/wk im+Methylprednisolone 500 mg/d po vs. Avonex+ PBO
Outcome parameters: EDSS
Type of MS: RR
Number of Subjects: 341
Start date: October 2002
Observation period: 3 years
Investigators: M. Ravnborg and others
Sites: Multicenter, Denmark and Norway
Results/Publications: 38% reduction in relapse rate in combination group; no difference in time to sustained progression; significant improvements in MSFC, EDSS, MSIS, T1/T2 lesion volume and new/enlarging T2 lesions; no difference in BPF; osteopenia found in 2/6 patients receiving MP/PBO; adverse events included insomnia, distorted taste, hypertension, flushing (Abstract #LB3.002, AAN 2009; Abstracts 51, P800, ECTRIMS 2009)
Funding: Biogen Idec, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00168766
Last update: 2010
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Agent: Interferon beta-1a (Rebif® [FBS-free/HSA-free formulation], EMD Serono/Pfizer)
Purpose of study: To improve quality of life
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: Randomized, two-arm, open label
Study phase: III
Dose/route: 44 mcg tiw vs. 8.8 mcg tiw for 2 wks, 22 mcg tiw for 2 wks, then 44 mcg tiw
Outcome parameters: Quality of Life, tolerability, injection site reactions, depression, fatigue, impact on analgesic use, safety, compliance
Type of MS: Relapsing forms
Number of Subjects: 180
Start date: April 2007
Observation period: 12 weeks
Investigators: Multiple
Sites: Multicenter, United States
Results/Publications: Not available
Funding: EMD Serono, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00472797
Last update: 2010
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Agent: Interferon beta-1a (Rebif® [FBS-free/HSA-free formulation], EMD Serono and Pfizer Inc.) **COMPLETED**
Purpose of study: To evaluate safety and effectiveness, also known as IMPROVE 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: Randomized, double-blinded, placebo-controlled
Study phase: IIb
Dose/route: PBO for 16 wks then Rebif 44 mcg tiw for 24 wks vs. Rebif 44 mcg tiw for 40 wks
Outcome parameters: MRI, biomarkers
Type of MS: RR
Number of Subjects: 180
Start date: December 2006
Observation period: 40 weeks
Investigators: N. De Stefano
Sites: Multicenter, Canada and Europe
Results/Publications: At week 16, mean number of combined unique active lesions (primary endpoint) was significantly lower in Rebif group than PBO; mean cumulative number of CUA lesions was lower by week 4 (Abstract #P07.145, AAN 2009; *Multiple Sclerosis* OnlineFirst, March 3, 2010)
Funding: EMD Serono, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00441103
Last update: 2010
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Agent: Interferon beta-1a (Rebif®, EMD Serono 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
Study phase: II
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: http://clinicaltrials.gov/ct2/show/NCT00151801
Last update: 2010
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Agent: Interferon beta-1b (Betaseron®, 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
Study phase: Not available
Dose/route: 250 mcg qod sc
Outcome parameters: Clinical parameters, MSFC, EuroQoL 5-Dimensions
Type of MS: RR
Number of Subjects: 3566
Start date: 2003
Observation period: 5 years
Investigators: L. Kappos and others
Sites: University Hospitals, Basel, Switzerland, and others, worldwide
Results/Publications: By 12/05, 3566 people recruited; 65.5% have continued treatment for 4 years; of these, 83.7% had no disease progression and 55.7% reduction in relpase rate compared with pre-baseline (Abstract #P595, ECTRIMS 2004; Abstract #P694, ECTRIMS 2006; Abstract #P86, World Congress of MS 2008)
Funding: Bayer HealthCare Pharmaceuticals, Inc.
ClinicalTrials.gov Identifier: Not available
Last update: 2011
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Agent: Interferon beta-1a (Avonex®, Biogen Idec) vs. interferon beta-1a (Rebif®, EMD Serono and Pfizer Inc., vs. interferon beta-1b (Betaseron®, Bayer HealthCare) vs. glatiramer acetate (Copaxone®, Teva Pharmaceuticals)
Purpose of study: To examine compliance/adherence, also known as TOP MS 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, Rebif, Betaseron)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)
Study description: Open label
Study phase: IV
Dose/route: Avonex 30 mcg/wk im vs. Rebif 44 mcg tiw sc vs. Betaseron 250 mcg qod sc vs. Copaxone 20 mg/d sc
Outcome parameters: Therapy adherence, relapse, disability, QOL, productivity
Type of MS: Active RR
Number of Subjects: 3000
Start date: December 2008
Observation period: 24 months
Investigators: Study managers at specialty pharmacies
Sites: Diplomat Specialty Pharmacy, BioScrip, Medmark, a Walgreens Specialty Pharmacy
Results/Publications: Not available
Funding: Teva Neuroscience
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00819000
Last update: 2010
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Agent: Interferon tau **COMPLETED**
Purpose of study: To test safety
Possible mechanism: Promotes shift from Th1 to Th2
Study description: Open label
Study phase: Not available
Dose/route: 3 mg tid po
Outcome parameters: Safety, effectiveness
Type of MS: RR
Number of Subjects: 25
Start date: May 2004
Observation period: 15 months
Investigators: G. Buckle and others
Sites: Brigham and Women's Hospital, Boston, and others
Results/Publications: Trend in favor of active treatment, which was not statistically significant in terms of the primary outcome measure (Communication with investigator)
Funding: Pepgen Corporation
ClinicalTrials.gov Identifier: Not available
Last update: 2011
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Agent: IPX056 (extended release baclofen) vs. immediate release baclofen
Purpose of study: To improve MS spasticity
Possible mechanism: Acts on central nervous system to relieve spasms, cramping, and tightness of muscles caused by spasticity
Study description: Double blinded
Study phase: II
Dose/route: IPX056 bid po vs. baclofen tablets tid po
Outcome parameters: Morning Stiffness Score, Nighttime Awakening Score
Type of MS: All types, with spasticity
Number of Subjects: 28
Start date: April 2009
Observation period: 6 weeks
Investigators: Multiple
Sites: Multicenter, United States
Results/Publications: Not available
Funding: Impax Pharmaceuticals
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00914290
Last update: 2010
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Agent: Lamotrigine (Lamictal®, GlaxoSmith Kline) **COMPLETED**
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
Study phase: II
Dose/route: Up to 400 mg/d po vs. PBO po
Outcome parameters: MRI, EDSS, MSFC, MSIS
Type of MS: SP
Number of Subjects: 120
Start date: January 2006
Observation period: 24 months
Investigators: R. Kapoor and others
Sites: National Hospital for Neurology and Neurosurgery and Royal Free Hospital, London
Results/Publications: No difference in primary outcome (rate of change of central cerebral volume over 24 months); lamotrigine associated with greater central cerebral volume loss than PBO first year, and volume increased partially after treatment stopped; lamotrigine reduced deterioration of timed 25-foot walk but not other secondary clinical outcome measures; rash and dose-related deterioration of gait and balance experienced more in lamotrigine group than the placebo group (*Lancet Neurology* 2010;9(7):681-8)
Funding: MS Society of Great Britain and Northern Ireland
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00257855
Last update: 2011
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Agent: Laquinimod **COMPLETED**
Purpose of study: To control disease course and development of brain lesions, also known as ALLEGRO study
Possible mechanism: Immunomodulatory
Study description: Randomized, double blinded, placebo controlled
Study phase: III
Dose/route: 0.6 mg/d po vs. PBO po
Outcome parameters: Frequency of relapse
Type of MS: RR
Number of Subjects: 1000
Start date: December 2007
Observation period: 2 years
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Laquinimod reduced annual relapse rate by 23%, compared to PBO; laquinimod reduced the risk of disease progression (by 36%) and brain atrophy (by 33.8%), and reduced accumulation of brain lesions detected with MRI; no serious infections reported; most common adverse events were back pain and abdominal pain, and elevations in liver enzymes, but no serious liver damage reported (Latebreaking abstract, AAN 2011)
Funding: Teva Neuroscience
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00509145
Last update: 2011
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Agent: Laquinimod vs. interferon beta-1a (Avonex®, Biogen Idec)
Purpose of study: To control disease course and development of brain lesions, also known as BRAVO study
Possible mechanism: Immunomodulatory
Study description: Randomized, blinded, placebo controlled
Study phase: III
Dose/route: 0.6 mg/d po vs. PBO po vs. Avonex 30 mcg/wk im
Outcome parameters: Frequency of relapse
Type of MS: RR
Number of Subjects: 1200
Start date: April 2008
Observation period: 24 months
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Teva Neuroscience
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00605215
Last update: 2011
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Agent: Lipoic acid
Purpose of study: To study how participants absorb and break down supplement
Possible mechanism: Activates cAMP signaling pathways
Study description: Open label
Study phase: I
Dose/route: 1200 mg po
Outcome parameters: Biochemical changes
Type of MS: RR, PP
Number of Subjects: 20
Start date: January 2010
Observation period: 48 hours
Investigators: D. Carr and others
Sites: Portland VA Medical Center and Oregon Health & Science University, Portland, OR
Results/Publications: Not available
Funding: Veterans Affairs
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00997438
Last update: 2010
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Agent: Lipoic acid
Purpose of study: To relieve optic nerve injury
Possible mechanism: Activates cAMP signaling pathways
Study description: Randomized, double blinded, parallel group
Study phase: I
Dose/route: Lipoic acid 1200 mg/d po vs. PBO po
Outcome parameters: Retinal nerve fiber layer (RNFL) thickness of the affected optic nerve, as determined by optical coherence tomography
Type of MS: Optic neuritis
Number of Subjects: 54
Start date: January 2011
Observation period: 24 weeks
Investigators: V. Yadav
Sites: Oregon Health & Science University, Portland, OR
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01294176
Last update: 2011
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Agent: Low fat diet
Purpose of study: To control development of brain lesions
Possible mechanism: Plant-based diet
Study description: Randomized, controlled, physician blinding
Study phase: I
Dose/route: low fat diet vs. regular diet
Outcome parameters: MRI, relapse, EDSS
Type of MS: RR
Number of Subjects: 54
Start date: February 2009
Observation period: 12 months
Investigators: V. Yadav
Sites: Oregon Health & Science University, Portland, OR
Results/Publications: Not available
Funding: The McDougall Education Foundation
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00852722
Last update: 2011
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Agent: LY2127399
Purpose of study: To control disease course and development of brain lesions
Possible mechanism: BAFF antibody
Study description: Double blinded, placebo controlled
Study phase: II
Dose/route: 4 mg sc vs 12 mg sc vs 40 mg sc vs. 120 mg sc vs. 120 mg sc at wks 0,12 + PBO sc at wks 4, 8, 16, and 20 vs. PBO, dosing every 4 wks
Outcome parameters: MRI, frequency of relapse, clinical scales
Type of MS: RR
Number of Subjects: 245
Start date: April 2009
Observation period: 72 weeks
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Eli Lilly and Company
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00882999
Last update: 2010
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Agent: Memantine (Namenda®, Forest Pharmaceuticals) **COMPLETED**
Purpose of study: To improve cognitive function
Possible mechanism: Blocks NMDA receptors
Study description: Double blinded, placebo controlled
Study phase: II, III
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, additional neuropsychological tests and questionnaires
Type of MS: All types
Number of Subjects: 126
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: No significant differences on PASAT or other cognitive tests; subjects on memantine had no serious adverse events but had more fatigue and neurological adverse events, as well as, per family members' reports, less cognitive improvement and greater neuropsychiatric symptoms than subjects on PBO (*Multiple Sclerosis Journal* 2010;16(6):715-23)
Funding: Forest Laboratories, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00300716
Last update: 2011
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Agent: Mesenchymal stem cells
Purpose of study: To assess safety, feasibility, tolerability
Possible mechanism: May inhibit immune mechanisms and augment intrinsic tissue repair
Study description: Open label
Study phase: I
Dose/route: Single infusion of autologous, culture-expanded, bone marrow-derived mesenchymal stem cells at dose of 2 x 106 cells/kg
Outcome parameters: MRI, evoked potentials, optical coherence tomography, relapse rate
Type of MS: RR, SP, PR
Number of Subjects: 24
Start date: Spring 1010
Observation period: 8 months
Investigators: J. Cohen and others
Sites: Cleveland Clinic Mellen MS Center, University Hospitals Case Medical Center, National Center for Stem Cell and Regenerative Medicine, Cleveland, OH
Results/Publications: Not available
Funding: Department of Defense Congressionally Directed Medical Research Program
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00813969
Last update: 2010
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Agent: Methylprednisolone
Purpose of study: To compare oral versus intravenous delivery 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
Study phase: III
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: T. DeAngelis and others
Sites: Mount Sinai Medical Center, and others in New York, NY
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00418145
Last update: 2011
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Agent: Minocycline
Purpose of study: To delay conversion to clinically definite MS
Possible mechanism: Inhibits matrix metalloproteinases
Study description: Randomized, double blinded, placebo controlled
Study phase: III
Dose/route: Minocycline 100 mg bid po vs. PBO po
Outcome parameters: Conversion to MS defined by McDonald Criteria
Type of MS: CIS
Number of Subjects: 100
Start date: April 2008
Observation period: 2 years
Investigators: L. Metz and others
Sites: Multiple, Canada
Results/Publications: Not available
Funding: MS Society of Canada
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00666887
Last update: 2010
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Agent: MIS416
Purpose of study: To examine safety
Possible mechanism: A construct of microparticle and naturally occurring, non-immunogenic, cytosolically-active TLR-9 and NOD-2 ligands
Study description: Open label, dose escalation
Study phase: II
Dose/route: MSI416 (one of four doses) administered once weekly iv for up to 24 weeks
Outcome parameters: Safety, maximum tolerated dose, pharmacodynamic assessments, MRI assessments, clinical status
Type of MS: CP
Number of Subjects: 0
Start date: August 2010
Observation period: 24 weeks
Investigators: A. Luckey, T. Anderson
Sites: Primorus Clinical Trials, Christchurch, NZ
Results/Publications: Not available
Funding: Innate Therapeutics Limited, Fast Forward LLC
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01191996
Last update: 2011
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Agent: Mitoxantrone for injection concentrate
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
Study phase: IV
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: 509 patients enrolled and received at least 1 dose of mitoxantrone; 172 completed 5-year trial; mean cumulative dose, 69.8 mg/m2; mean treatment duration, 1.5 years; LVEF 50% of baseline reported in 27/509 patients during treatment phase and 14/250 (5.6%) patients during observation phase; 25 patients reported cardiac-related serious adverse events, with the most common SAE being reduced LVEF; 2 deaths from cardiac-related events (Abstract #P01.171, AAN 2010)
Funding: EMD Serono Inc.
ClinicalTrials.gov Identifier: Not available
Last update: 2010
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Agent: Mitoxantrone for injection concentrate **COMPLETED**
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
Study phase: Not available
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: Cohort followed for 5354 patient-years (mean); 1/802 patients had acute congestive heart failure and 39/794 patients had asymptomatic left ventricular ejection fraction reduction under 50%; 2 cases of therapy-related leukaemia detected 20 months after Rx start; of 317 women treated before the age of 45, 17.3% developed persistent age-dependant amenorrhea (*Multiple Sclerosis* 2011 Feb 15 [Epub ahead of print])
Funding: Not available
ClinicalTrials.gov Identifier: Not available
Last update: 2011
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Agent: Mitoxantrone for injection concentrate **+ g**latiramer acetate (Copaxone®, Teva Pharmaceutical Industries Ltd.) **COMPLETED**
Purpose of study: To evaluate safety and effectiveness of induction with mitoxantrone
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 (mitoxantrone)
Study description: Randomized, two-arm, open label
Study phase: II
Dose/route: Mitoxantrone 12 mg/m2/mo iv + Copaxone 20 mg/d sc vs. Copaxone
Outcome parameters: Frequency of relapse, scoring technique, MRI, quality of life
Type of MS: RR, PR
Number of Subjects: 30
Start date: April 2003
Observation period: 60 months
Investigators: T. Vollmer and others **Sites:** Multicenter, United States
Results/Publications: Gd lesions/T1 black holes reduced (*Multiple Sclerosis* 2008;14:663-70)
Funding: Teva Neuroscience
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00203073
Last update: 2010
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Agent: Mitoxantrone for injection concentrate **+g**latiramer acetate (Copaxone®, Teva Pharm. Ind. Ltd.) vs. interferon beta-1a (Rebif®, EMD Serono/Pfizer) **COMPLETED**
Purpose of study: To evaluate safety and effectiveness of induction with mitoxantrone
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 (mitoxantrone)/ 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, controlled, examining-MD blinded
Study phase: I
Dose/route: Mitoxantrone 12 mg/m2/mo iv for 3 mos and 6mg/m2 quarterly for two pulses + Copaxone 20 mg/d sc vs. Rebif 44 mcg tiw sc
Outcome parameters: MSIS, EDSS, annualised relapse rate, relapse free patients
Type of MS: RR
Number of Subjects: 60 (only 30 randomized)
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, UK
Results/Publications: Study underpowered due to slow recruitment (30 randomized); well tolerated; no significant differences in primary outcomes; significant increase in number of relapse-free patients at 12, 24 months in induction group (Abstract #P842, ECTRIMS 2010)
Funding: National Health Service
ClinicalTrials.gov Identifier: Not available
Last update: 2011
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Agent: Mitoxantrone for injection concentrate + interferon beta-1b (Betaseron®, Bayer HealthCare Pharmaceuticals, Inc.) **COMPLETED**
Purpose of study: To evaluate safety and effectiveness of induction with mitoxantrone
Possible mechanism: Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion (mitoxantrone)/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
Study phase: II
Dose/route: Mitoxantrone 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: Induction group had significant delay in EDSS progression, reduced relapse rate, and Gd+ lesions at month 9 and T2 lesion accumulation at each time point (*Journal of Neurology Neurosurgery and Psychiatry* 2011 Mar 24. [Epub ahead of print])
Funding: French Health Ministry, Schering AG
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00219908
Last update: 2011
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Agent: Mycophenolate mofetil (CellCept®, Roche Laboratories, Inc.) + interferon beta-1a (Avonex®, Biogen Idec) **COMPLETED**
Purpose of study: To test safety and tolerability
Possible mechanism: Inhibits proliferation of T and B cells, suppresses antibody formation (CellCept)/Slows down immune response, possibly by interfering with T cell activation/movement across blood-brain barrier, and inducing suppressive T cells (Avonex)
Study description: Randomized, double blinded, placebo controlled
Study phase: II, III
Dose/route: Avonex 30 mcg/wk im + CellCept 250-1000 mg bid po vs. Avonex + PBO
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: No differences in patient-reported adverse events, MRI metrics, or lab abnormalities (*Therapeutic Advances in Neurological Disorders* 2010;3:3)
Funding: Biogen Idec, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00223301
Last update: 2010
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Agent: Mycophenolate mofetil (CellCept®, Roche Laboratories, Inc.) + interferon beta-1a (Avonex®, Biogen Idec) **COMPLETED**
Purpose of study: To test safety and tolerability
Possible mechanism: Inhibits proliferation of T and B cells, suppresses antibody formation (CellCept)/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, open label, parallel group
Study phase: II, III
Dose/route: Avonex 30 mcg/wk or CellCept 500-1000 mg bid po 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: 35
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: No difference on primary safety MRI endpoints; mycophenolate group showed trend toward lower accumulation of combined active lesions, Gd and T2 lesions; both well tolerated (*Therapeutic Advances in Neurological Disorders* 2010;3:15)
Funding: Aspreva Pharmaceuticals
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00324506
Last update: 2010
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Agent: Low dose naltrexone **COMPLETED**
Purpose of study: To test effect on quality of life
Possible mechanism: Semi-synthetic opiate antagonist
Study description: Placebo controlled, double blinded, crossover
Study phase: II
Dose/route: 4.5 mg/d po vs. PBO po for 8 wks, 1 wk washout, then crossover
Outcome parameters: MSQLI
Type of MS: All types
Number of Subjects: 60
Start date: June 2007
Observation period: 17 weeks
Investigators: B. Cree, E. Kornyeyeva, D. Goodin
Sites: University of California, San Francisco
Results/Publications: High rate of subject dropout and data management errors reduced statistical power; no serious adverse events; naltrexone associated with significant improvement on mental health quality of life measures (*Annals of Neurology* 2010;68(2):145-50)
Funding: Private funding
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00501696
Last update: 2010
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Agent: Natalizumab (Tysabri®, Biogen Idec and Elan)
Purpose of study: To reduce fatigue, also known as ENER-G study
Possible mechanism: Interferes with movement of immune cells across the blood-brain barrier by attaching to alpha 4-integrin
Study description: Open label
Study phase: IV
Dose/route: Tysabri 300 mg every 4 wks iv
Outcome parameters: Visual Analog Scale for fatigue, Modified Fatigue Impact Scale, Fatigue Severity Scale, Automated Neuropsychology Assessment Metrics
Type of MS: Relapsing forms
Number of Subjects: 200
Start date: September 2007
Observation period: 12 months
Investigators: Multiple
Sites: Multicenter, United States
Results/Publications: In preliminary results on 44 patients, significant improvement in fatigue on all three scales, for up to 48 weeks of treatment (Abstract #P06.142, AAN 2010)
Funding: Biogen Idec, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00464074
Last update: 2010
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Agent: Natalizumab (Tysabri®, Biogen Idec and Elan)
Purpose of study: To determine effects of treatment on vaccination response
Possible mechanism: Interferes with movement of immune cells across the blood-brain barrier by attaching to alpha 4-integrin
Study description: Randomized, open label
Study phase: IV
Dose/route: Tysabri 300 mg iv every 4 weeks for at least 9 mos, along with 3 immunizations of keyhole limpet hemocyanin sc at Day 168, 182, 196 and immunization of tetanus diphtheria vaccine im at Day 168 vs. 3 immunizations of keyhole limpet hemocyanin sc at Day 0, 14, 28 and immunization with tetanus diphtheria vaccine im at Day 0
Outcome parameters: Effect of Tysabri on antibody response and circulating lymphocyte subsets, alpha-4 saturation/expression
Type of MS: Relapsing forms
Number of Subjects: 46
Start date: November 2007
Observation period: 8 months
Investigators: Multiple
Sites: Multicenter, United States
Results/Publications: Natalizumab treatment did not significantly affect primary or secondary IgG antibody responses to KLH or Td; no deleterious effect on ability to generate immune response to recall antigen/neoantigen (Abstract #S51.001, AAN 2011)
Funding: Biogen Idec
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00536120
Last update: 2011
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Agent: Natalizumab (Tysabri®, Biogen Idec and Elan) **COMPLETED**
Purpose of study: To determine effects on MS-related fatigue
Possible mechanism: Interferes with movement of immune cells across the blood-brain barrier by attaching to alpha 4-integrin
Study description: Open label
Study phase: IV
Dose/route: Tysabri 300 mg every 4 wks iv
Outcome parameters: Fatigue Severity Scale; Modified Fatigue Impact Scale
Type of MS: RR
Number of Subjects: 42
Start date: July 2006
Observation period: 6 months
Investigators: N. Putzki and others
Sites: University Clinic Essen, Germany
Results/Publications: Significant reductions in fatigue noted at month six; no impact on fatigue at month 3; no correlation between decreases in imaging measures of disease activity and fatigue scores (Journal of the Neurological Sciences 2009;285:109-113)
Funding: Biogen Idec
ClinicalTrials.gov Identifier: Not available
Last update: 2010
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Agent: Natalizumab (Tysabri®, Biogen Idec and Elan)
Purpose of study: Tysabri Global ObseRvational Program In Safety, also known as TYGRIS
Possible mechanism: Interferes with movement of immune cells across the blood-brain barrier by attaching to alpha 4-integrin
Study description: Open label, observational cohort
Study phase: IV
Dose/route: 300 mg every 4 wks iv
Outcome parameters: Long-term safety data
Type of MS: Relapsing forms
Number of Subjects: 5111
Start date: January 2007
Observation period: 5 years
Investigators: Multiple
Sites: Multicenter, United States and Canada
Results/Publications: 5111 patients enrolled; serious adverse even incidence was 4%, most frequently hypersensitivity reactions and infections; 2 cases of PML in Tygris population (6 post-marketing cases overall as of 5/8/09) (Abstract #S11.005, AAN 2009)
Funding: Biogen Idec
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00477113
Last update: 2010
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Agent: Nerispirdine **COMPLETED**
Purpose of study: To evaluate effects on visual function
Possible mechanism: Sodium/potassium channel blocker
Study description: Randomized, double blinded, placebo controlled, crossover
Study phase: II
Dose/route: Nerispirdine 50 mg/d po vs. 400 mg/d po vs. PBO
Outcome parameters: Visual evoked potential
Type of MS: All types, with history of optic neuritis
Number of Subjects: 30
Start date: November 2008
Observation period: 5 weeks
Investigators: Multiple
Sites: Multicenter, United States
Results/Publications: No longer under study for MS (communication with company)
Funding: Sanofi
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00772525
Last update: 2011
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Agent: Ocrelizumab
Purpose of study: To evaluate safety and effectiveness in reducing disease activity, also known as ORATORIO study
Possible mechanism: Binds to CD20 antigen on B cells and induces B-cell lysis
Study description: Randomized, double blinded, placebo controlled, parallel group
Dose/route: Ocrelizumab 600 mg iv + methylprednisolone 100 mg iv 30 minutes prior to ocrelizumab infusion vs. PBO iv + methylprednisolone 100 mg iv 30 minutes prior to PBO infusion
Outcome parameters: Time to onset of sustained disability progression, timed 25-foot walk, MRI, safety and tolerability
Type of MS: PP
Number of Subjects: 630
Start date: January 2011
Observation period: 120 weeks
Investigators: Multiple
Sites: Multicenter, Canada and Europe
Results/Publications: Study design presented (Abstract #P.04.186, AAN 2011)
Funding: Hoffman-La Roche
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/showNCT01194570
Last update: 2011
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Agent: Ocrelizumab vs. interferon beta-1a (Avonex®, Biogen Idec)
Purpose of study: To evaluate safety and effectiveness in reducing disease activity
Possible mechanism: Binds to CD20 antigen on B cells and induces B-cell lysis
Study description: Randomized, parallel-group, partially blinded
Study phase: II
Dose/route: Ocrelizumab 1000 mg iv vs. 300 mg iv vs. PBO IV vs. Avonex 30 mcg/wk im
Outcome parameters: MRI
Type of MS: RR
Number of Subjects: 200
Start date: June 2008
Observation period: 3 years
Investigators: Multiple
Sites: Multicenter, United States
Results/Publications: Significant reduction in relapse rate and increase in proportion of relapse -free paitents through week 48; 1 person died at week 14 due to brain edema, after occurrence of systemic inflammatory response syndrome with multi-organ failure at week 12; serious infection rates were similar in Rx and PBO; no opportunistic infections were reported; higher incidence of infusion-related events observed on first exposure to ocrelizumab, but was significantly lower in subsequent infusions (Abstract #S41.001, AAN 2011)
Funding: Genentech, Inc., F. Hoffman-Laroche Ltd.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00676715
Last update: 2011
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Agent: Omega-3 fatty acid **COMPLETED**
Purpose of study: To improve depression
Possible mechanism: Decreases cytokine levels
Study description: Double blinded, placebo controlled
Study phase: I, II
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, MSFC
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: Both groups improved on MADRS, but no significant difference between groups; Rx group showed greater improvement in Paced Auditory Serial Addition Test score; no serious adverse events occurred. (Abstract #S21.007, AAN 2010)
Funding: NIH, others
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00122954
Last update: 2010
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Agent: ONO-4641
Purpose of study: To decrease brain lesions
Possible mechanism: Sphingosine-1-phosphate receptor binder; inhibits lymphocytes from exiting lymphatic tissue
Study description: Double blinded, placebo controlled
Study phase: II
Dose/route: ONO-4641 0.5 mg/d po vs. 0.10 mg/d po vs 0.15 mg/d po vs PBO po
Outcome parameters: T1 lesions
Type of MS: RR
Number of Subjects: 376
Start date: March 2010
Observation period: 26 weeks
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Ono Pharmaceuticals Co., Ltd.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01081782
Last update: 2011
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Agent: Phenytoin
Purpose of study: To prevent optic nerve injury
Possible mechanism: Anti-convulsive, blocks entry of sodium ions into nerve fibers
Study description: Randomized, double blinded, placebo controlled
Study phase: II
Dose/route: Phenytoin 15 mg/kg/d po for 3 days, followed by 14 mg/kg/d po for 14 wks
Outcome parameters: Retinal nerve fiber layer (RNFL) thickness of the affected optic nerve, as determined by optical coherence tomography
Type of MS: Optic neuritis
Number of Subjects: 90
Start date: April 2011
Observation period: 6 months
Investigators: R. Kapoor and others
Sites: Multicenter, United Kingdom
Results/Publications: Not available
Funding: National MS Society & MS Society of Great Britain and Northern Ireland
ClinicalTrials.gov Identifier: Pending
Last update: 2011
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Agent: PI-2301 (co-polymer)
Purpose of study: To evaluate safety, tolerability, dosing, and pharmacokinetics
Possible mechanism: Immunomodulation via the MHC Class II receptor
Study description: Randomized, double blinded, placebo controlled, multiple doses
Study phase: I
Dose/route: PI-2301/wk sc (4 doses) vs PBO/wk sc for 8 wks; then open label for 4 wks
Outcome parameters: Safety, tolerability, MRI, EDSS, immunological markers
Type of MS: SP
Number of Subjects: 50
Start date: May 2008
Observation period: 14 weeks
Investigators: G. Edan and others
Sites: Multiple, France
Results/Publications: Transient, mild, and self-limited injection site reactions occurred; circulating levels detected in serum of subjects in 10-, 30- and 60-mg groups; evidence of immune priming (PI-2301-specific IL-13 and IFN-g T-cell detection in ELISpot assay) observed (Abstract #P422, ECTRIMS 2009)
Funding: Peptimmune
ClinicalTrials.gov Identifier: Not available
Last update: 2010
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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
Study phase: I, II
Dose/route: Pixantrone 120 mg/m² iv every 3 wks for 12 wks
Outcome parameters: Immunosuppressive effects, Gd+ lesion evolution, safety
Type of MS: Aggressive RR or SP MS
Number of Subjects: 20
Start date: Fall 2008
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, Belgium
ClinicalTrials.gov Identifier: Not available
Last update: 2011
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Agent: Polyphenon E
Purpose of study: To test safety and neuroprotective effects
Possible mechanism: Antioxidant/neuroprotective
Study description: Open label
Study phase: II
Dose/route: 400 mg bid po
Outcome parameters: MRI, EDSS, MSFC, MSQLI, cognitive battery
Type of MS: RR, SP
Number of Subjects: 10
Start date: March 2009
Observation period: 6 months
Investigators: J. Lovera
Sites: Louisiana State University Health Sciences Center, New Orleans
Results/Publications: Not available
Funding: National Center for Complementary and Alternative Medicine (NIH)
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00836719
Last update: 2010
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Agent: Pregabalin (Lyrica®, Pfizer, Inc.) vs. paroxetine (Paxil®, GlaxoSmith Kline)
Purpose of study: To improve MS-related pain
Possible mechanism: GABA analogue, thought to act as Ca++ channel modulator, decreasing Ca++ influx into nerve cells, affecting release of pain neurotransmitters (Lyrica)/ selective serotonin reuptake inhibitor (Paxil)
Study description: Randomized, open label
Study phase: III
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: http://clinicaltrials.gov/ct2/show/NCT00291148
Last update: 2010
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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
Study phase: III
Dose/route: Progesterone 10 mg/d po + estgradiol 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: http://clinicaltrials.gov/ct2/show/NCT00127075
Last update: 2010
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Agent: Rehabilitation
Purpose of study: To determine whether home exercise program can improve depression
Possible mechanism: Effects on brain dopamine, noradrenaline and serotonin transmission
Study description: Trained examiner blinded
Study phase: Not available
Dose/route: Home exercise program, motivational interview and telephone follow-up vs. delayed treatment
Outcome parameters: Structured Clinical Interview for DSM-III-R, Hamilton Depression Rating Scale, Hopkins Symptom Checklist
Type of MS: All types
Number of Subjects: 101
Start date: February 2005
Observation period: 6 months
Investigators: C. Bombardier and others
Sites: University of Washington MS Rehabilitation Research & Training Center
Results/Publications: Significant improvement on Structured Clinical Interview, Hamilton scale, and MFIS at 12 wks in Rx group but not controls; nonsignificant trend for exercise to improve more in Rx vs. control group (Abstract #P13, CMSC 2008)
Funding: National Institute on Disability and Rehabilitation Research
ClinicalTrials.gov Identifier: Not available
Last update: 2010
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Agent: Rehabilitation
Purpose of study: To use motivational counseling to improve function and participation
Possible mechanism: Improves physical function, decreases pain, and improves participation in life activities
Study description: Randomized, trained examiner blinded
Study phase: Not available
Dose/route: Motivational interview and home exercise program with periodic 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: 123
Start date: June 2004
Observation period: 2 years
Investigators: J. Bowen and others
Sites: University of Washington MS Rehabilitation Research & Training Center
Results/Publications: Motivational interviewing increased amount of strengthening/flexibility exercise at 2 yrs, but did not lead to changes in fatigue, pain, or depression (Abstract #S05, CMSC 2008)
Funding: National Institute on Disability and Rehabilitation Research
ClinicalTrials.gov Identifier: Not available
Last update: 2010
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Agent: Rehabilitation
Purpose of study: Educational session to promote physical activity, also known as Project Workout On Wheels
Possible mechanism: Improves physical function
Study description: Randomized, parallel-group, open label
Study phase: Not available
Dose/route: Educational session, goal setting, self monitoring of daily engagement in physical activity vs. Self-guided education manual about adopting physical activity, self monitor daily engagement in physical activity
Outcome parameters: Weekly exercise participation over 12-month period
Type of MS: People with MS or other disorders who require use of wheelchair as primary method of mobility outside the home
Number of Subjects: 130
Start date: August 2006
Observation period: 1 year
Investigators: K. Froehlich-Grobe
Sites: University of Kansas
Results/Publications: Not available
Funding: National Institute of Child Health and Development (NIH)
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00866112
Last update: 2010
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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
Study phase: Not available
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: http://clinicaltrials.gov/ct2/show/NCT00166283
Last update: 2011
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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
Study phase: I, II
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: Preliminary data suggest a potentially beneficial effect on cognitive performance (Abstract #P08.165, AAN 2009)
Funding: National MS Society
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00607126
Last update: 2011
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Agent: Rehabilitation (aerobic exercise)
Purpose of study: To improve cognitive function
Possible mechanism: May improve brain function
Study description: Single blinded, parallel group
Study phase: II
Dose/route: Training on recumbent cross trainer 20-30 minutes, 3 times/week for 6 months vs. stretching for 20-30 minutes, 3 times/week for 6 months
Outcome parameters: PASAT, Symbol Digit Modalities Test, V)2 Max, long latency cognitive event related potentials
Type of MS: All types, cognitive problems
Number of Subjects: 50
Start date: July 2010
Observation period: 6 months
Investigators: B. Giesser
Sites: University of California at Los Angeles and California State University at Northridge
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01219647
Last update: 2011
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Agent: Rehabilitation (constraint-induced movement therapy)
Purpose of study: To rehabilitate extremity use
Possible mechanism: Concentrated form of physical therapy directed at more impaired arm that is believed to cause growth of certain brain regions to improve arm use
Study description: Randomized, single blinded
Study phase: II
Dose/route: Constraint-induced movement therapy (3.5 hours of therapy per day for 10 consecutive weekdays) vs. complementary and alternative medicine techniques including aquatic therapy, relaxation exercises, massage, and music therapy (3.5 hours of therapy per day)
Outcome parameters: MRI
Type of MS: RR, SP, PP
Number of Subjects: 66
Start date: February 2010
Observation period: 6 months
Investigators: V. Mark and others
Sites: University of Alabama at Birmingham
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01081275
Last update: 2011
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Agent: Rehabilitation (multi-modal exercise program vs. minimal exercise)
Purpose of study: To reduce progresion of mobility disability
Possible mechanism: Improves aerobic capacity, muscle strength, balance
Study description: Randomized, controlled
Study phase: I
Dose/route: Balanced amounts of aerobic, resistance, and balance modes of training delivered 3 times/wk vs. stretching delivered 3 times/wk
Outcome parameters: Clinical, kinematic, patient-rated and physiological measures of mobility disability
Type of MS: All types
Number of Subjects: 40
Start date: April 2011
Observation period: 6 months
Investigators: R. Motl
Sites: University of Illinois at Urbana-Champaign
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: Not available
Last update: 2011
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Agent: Rehabilitation (leg cycling)
Purpose of study: To reduce spasticity
Possible mechanism: Reduces muscle hypertonia
Study description: People with MS vs. controls without MS
Study phase: I
Dose/route: 8 laboratory sessions of control conditions (sitting on the cycle without pedaling) or leg cycling of 10 or 20 minutes, and of light, moderate or hard intensity
Outcome parameters: Modified Ashworth Scale, fatigue, muscle weakness, postural control, gait
Type of MS: With spasticity
Number of Subjects: 30
Start date: April 2011
Observation period: 2 years
Investigators: J. Sosnoff
Sites: University of Illinois at Urbana-Champaign
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: Not available
Last update: 2011
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Agent: Riluzole (Rilutek®, Sanofi)
Purpose of study: To evaluate neuroprotective ability in MS
Possible mechanism: Inhibits glutamate toxicity to nerve cells
Study description: Double blinded, placebo controlled
Study phase: II
Dose/route: Rilutek 50 mg/d po vs. PBO po for one month; Avonex 30 mcg/wk im added after 3 mos if liver function normal
Outcome parameters: Frequency and duration of relapse, safety, evoked potentials, MRI
Type of MS: early MS, CIS
Number of Subjects: 40
Start date: July 2006
Observation period: 2 years
Investigators: E. Waubant
Sites: University of California, San Francisco
Results/Publications: 10 patients have completed more than 3 months on combined therapy; a few have reported transient mild dizziness (Abstract #P530, World Congress of MS 2009)
Funding: National MS Society
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00501943
Last update: 2011
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Agent: Rituximab (Rituxan®, Genentech and Biogen Idec) **COMPLETED**
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
Study phase: II
Dose/route: 375 mg/m2 iv (4 times), added to immunomodulatory treatment
Outcome parameters: MRI
Type of MS: RR, not responsive to standard immunomodulatory treatment
Number of Subjects: 26
Start date: March 2002
Observation period: 1 year
Investigators: A. Cross
Sites: Washington University, St. Louis
Results/Publications: At 24 weeks, EDSS unchanged, MSFC improved over baseline (driven by performance on PASAT); treatment depleted T cells as well as B cells (Abstracts #31,P476 World Congress of MS 2008; *Archives of Neurology* 2010;67(6):707-14)
Funding: National MS Society
ClinicalTrials.gov Identifier: Not available
Last update: 2011
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Agent: Rituximab (Rituxan®, Genentech and Biogen Idec) **COMPLETED**
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
Study phase: II, III
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: Time to confirmed disease progression at 96 weeks not significantly different between rituximab and PBO; planned subgroup analysis indicates time to progression was significantly increased in rituximab-treated patients younger than 51 years, and those with Gd lesions compared with PBO group; serious infections occurred in 4.5% rituximab versus <1.0% of PBO (*Annals of Neurology* 2009;66[4]:460-471)
Funding: Genentech, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00087529
Last update: 2011
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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
Study phase: I
Dose/route: In each cohort of 6 subjects, 4 subjects received a single dose of RTL1000 (2 mg, 6 mg, 20 mg, 60 mg, or 200 mg) iv and 2 received PBO iv
Outcome parameters: EDSS, 25-foot walk, 9-hole peg test, MRI
Type of MS: RR, SP
Number of Subjects: 34
Start date: January 2007
Observation period: 3 months
Investigators: A. Vandenbark and others
Sites: MS Center of Oregon, Oregon Health & Science Univ., Portland, and others, U.S.
Results/Publications: All subjects tolerated the 2- to 60-mg doses; doses ≥ 100mg caused hypotension and diarrhea in 3/4 subjects; no evidence of disease worsening (EDSS, 25 foot timed walk, 9-hole peg test, brain MRI); half-life of RTL1000 in plasma was <5 minutes, possibly due to rapid partitioning to blood cells; drug dose-dependent cytokine changes occurred in plasma and blood mononuclear cells (Abstract #S21.003, AAN 2010)
Funding: Artielle ImmunoTherapeutics, Inc.
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00411723
Last update: 2010
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Agent: Simvastatin + interferon beta-1a (Avonex®, Biogen Idec Inc.)**COMPLETED**
Purpose of study: To determine safety and effectiveness in reducing disease activity, also known as SIMCOMBIN
Possible mechanism: Immunomodulatory
Study description: Randomized, double blinded, placebo controlled, parallel
Study phase: IV
Dose/route: Simvastatin 40 mg bid po + Avonex 30 mcg/wk im vs. PBO po + Avonex 30 mcg/wk im
Outcome parameters: Frequency of relapse
Type of MS: RR
Number of Subjects: 307
Start date: February 2006
Observation period: Up to 24 months
Investigators: P. Sorensen and others
Sites: Multicenter, Denmark, Norway, Sweden, and Finland
Results/Publications: No beneficial effect; trend toward simvastatin being less effective than PBO on all primary/secondary endpoints (Abstract #134, ECTRIMS 2010)
Funding: Biogen Idec
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00492765
Last update: 2011
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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
Study phase: II
Dose/route: Intensive cognitive behavioral stress management program (16 meetings with behavioral medicine specialist) vs. condensed 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, CA; MS Center at Evergreen, Seattle, WA; Northwestern University, Chicago, IL
Results/Publications: Not available
Funding: NICHD
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00147446
Last update: 2010
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Agent: T cell vaccination (Tovaxin®, Opexa Therapeutics) **COMPLETED**
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
Study phase: IIb
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: Significant reduction in EDSS for Tovaxin group (28.1%) vs. PBO (5.6%); adjusted relapse rate reduced by 55% vs. PBO; Timed 25 foot Walk showed a benefit for Tovaxin over PBO; brain atrophy reduced by 88% and Gd lesions progressing to black holes by 20% in Tovaxin group; no serious adverse events; in post-hoc analysis of treatment-naïve patients, Tovaxin-treated patients had an ARR of 0.18, 64% lower than the ARR (0.50) among placebo patients, and 76% were relapse-free at one year, compared with 60% of placebo group (Abstract #P06.132, AAN 2009; Abstract #P07.192, AAN 2011)
Funding: Opexa Therapeutics
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00245622
Last update: 2011
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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, sham control
Study phase: II
Dose/route: 4 ml sc autologous, tailored irradiated vaccine vs. sham injection
Outcome parameters: EDSS, MSFC, MRI
Type of MS: RR
Number of Subjects: 26
Start date: Spring 2002
Observation period: 1 year
Investigators: D. Karussis and others
Sites: Hadassah Hospital, Jerusalem, Israel
Results/Publications: Mean EDSS change from baseline to year 1 was +0.39 in PBO group and -0.44 in Rx group; mean annualized number of relapses in Rx group was reduced from a mean of 0.82 during the year prior to 0.06 after vaccination, and remained unchanged (1.0) in PBO group; no significant difference in MRI (Abstract #P06.134, AAN 2010)
Funding: Grant for TCV
ClinicalTrials.gov Identifier: Not available
Last update: 2010
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Agent: Teriflunomide (HMR1726) **COMPLETED**
Purpose of study: To control lesion development, disease progression and relapses, also known as TEMSO study
Possible mechanism: Modulates responses of T-cells within the immune system by impairing DNA synthesis
Study description: Double blinded, placebo controlled
Study phase: III
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, Worldwide
Results/Publications: Teriflunomide significantly reduced relapse rates, disability progression and MRI disease activity (at the higher dose) with an additional one-in-ten patients progression-free and an additional one-in-four patients free of gadolinium-enhanced T1 lesions compared with placebo, after 108 weeks' treatment (Abstracts #S41.002, #S41.003, PD6.001, AAN 2011)
Funding: Sanofi
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00134563
Last update: 2011
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Agent: Teriflunomide (HMR1726)
Purpose of study: To control lesion development, disease progression and relapses, also known as TOPIC study
Possible mechanism: Modulates responses of T-cells within the immune system by impairing DNA synthesis
Study description: Randomized, double blinded, placebo controlled, parallel group
Study phase: III
Dose/route: Teriflunomide 7 mg/d po vs. 14 mg/d po vs. PBO po
Outcome parameters: Conversion to clinically definite MS
Type of MS: CIS
Number of Subjects: 780
Start date: February 2008
Observation period: 2 years
Investigators: A. Miller and others
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Sanofi
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00622700
Last update: 2011
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Agent: Teriflunomide (HMR1726)
Purpose of study: To control lesion development, disease progression and relapses, also known as TOWER study
Possible mechanism: Modulates responses of T-cells within the immune system by impairing DNA synthesis
Study description: Randomized, double blinded, placebo controlled, parallel group
Study phase: III
Dose/route: Teriflunomide 7 mg/d po vs. 14 mg/d po vs. PBO po
Outcome parameters: EDSS, FIS
Type of MS: RR
Number of Subjects: 1110
Start date: September 2008
Observation period: 3 years, 4 months
Investigators: W. Byrnes and others
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Sanofi
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00751881
Last update: 2011
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Agent: Teriflunomide (HMR1726) vs. glatiramer acetate (Copaxone®, Teva)
Purpose of study: To test safety and effectiveness of combination therapy
Possible mechanism: Modulates responses of T-cells within the immune system by impairing DNA synthesis (teriflunomide)/ Peptide copolymer synthesized to mimic myelin basic protein, induces shift to Th2 (Copaxone)
Study description: Randomized, double blinded, placebo controlled, parallel group
Study phase: III
Dose/route: Teriflunomide 7 mg/d po + Copaxone 20 mg/d sc vs. 14 mg/d po + Copaxone 20 mg/d sc vs. PBO po + Copaxone 20 mg/d sc
Outcome parameters: MRI, EDSS, fatigue impact scale, safety
Type of MS: RR, SP, PR
Number of Subjects: 120
Start date: May 2007
Observation period: 24 weeks
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: 7 adverse events led to discontinuation in combo Rx groups; 6 patients with increased liver enzymes; proportion of patients with adverse events related to immunosuppression (white blood cell counts, infections) balanced among groups; T1-Gd lesions reduced significantly more in combo Rx groups (Abstract #S21.001, AAN 2010)
Funding: Sanofi
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT00475865
Last update: 2010
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Agent: Teriflunomide (HMR1726) and interferon beta-1a
Purpose of study: To test safety and effectiveness of combination therapy
Possible mechanism: Modulates responses of T-cells within the immune system by impairing DNA synthesis (teriflunomide) / Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (interferon)
Study description: Randomized, double blinded, placebo controlled, parallel group
Study phase: III
Dose/route: Teriflunomide 7 mg/d po + interferon im vs. 14 mg/d po + interferon im vs. PBO po + interferon im
Outcome parameters: Relapse rate, EDSS, MRI
Type of MS: Relapsing
Number of Subjects: 1455
Start date: February 2011
Observation period: 48 to 172 weeks
Investigators: Multiple
Sites: Multicenter, worldwide
Results/Publications: Not available
Funding: Sanofi
ClinicalTrials.gov Identifier: http://clinicaltrials.gov/ct2/show/NCT01252355
Last update: 2011
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Agent: Vitamin D + glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries, Ltd.)
Purpose of study: To test safety and effectiveness in reducing disease activity
Possible mechanism: Multiple immune mechanisms postulated (enhances macrophage phagocytosis, enhancesA activity of natural killer cells, inhibits production of Th1 cytokines, exhibits anti-tumor activity, inhibits transcription of IFN-gamma target genes)
Study description: Randomized, double blinded
Study phase: Not available
Dose/route: Vitamin D 5,000 IU/d po + Copaxone 20 mg/d sc vs. vitamin D 600 IU/d po + Copaxone 20 mg/d sc
Outcome parameters: Relapse rate, EDSS, MSFC, vision, MRI, QOL
Type of MS: RR
Number of Subjects: 172
Start date: July 2011
Observation period: 2 years
Investigators: E. Mowry and others
Sites: Johns Hopkins University, Baltimore, and others, United States
Results/Publications: Not available
Funding: National MS Society
ClinicalTrials.gov Identifier: Not available
Last update: 2011
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Glossary

ADVERSE REACTION
Also called Adverse Event. An unwanted effect caused by the administration of drugs. Onset could be sudden or develop over time. (See also Side Effects)

APPROVED DRUGS
In the United States, the Food and Drug Administration (FDA) must approve a substance as a drug before it can be marketed and administered. The approval process involves several steps including pre-clinical laboratory and animal studies, clinical trials for safety and efficacy, filing of a New Drug Application by the manufacturer of the drug, FDA review of the application, and FDA approval or rejection of the application. (See also Food and Drug Administration)

ARM
Any of the treatment groups in a randomized trial. Most randomized trials have two "arms," but some have three "arms," or even more. (See also Randomized Trial)

BASELINE
The initial time point in a clinical trial, just before a participant starts to receive the experimental treatment being tested. Safety and efficacy of a drug often are determined by monitoring changes from the baseline values.

BIAS
When a point of view prevents impartial judgment on issues relating to the subject of that point of view. In clinical studies, bias is controlled by blinding and randomization. (See also Blind and Randomization)

BLIND
A randomized trial is "Blind" if the participant is not told which arm of the trial they are on. A clinical trial is "Blind" if participants are unaware whether they are in the experimental or control arm of the study. Also called "masked." (See also Single Blind Study and Double Blind Study)

CLINICAL
Pertaining to or founded on observation and treatment of participants, as distinguished from theoretical or basic science.

CLINICAL TRIAL
A clinical trial is a research study to answer specific questions about vaccines, new therapies, or new ways of using known treatments. Clinical trials (also called medical research and research studies) are used to determine whether new drugs or treatments are both safe and effective. Carefully conducted clinical trials are the fastest and safest way to find treatments that work in people.

Trials are in four phases (See also Phase I, II, III, and IV Trials):

Phase I tests a new drug or treatment in a small group.
Phase II expands the study to a larger group of people.
Phase III expands the study to an even larger group of people.
Phase IV takes place after the drug or treatment has been licensed and marketed.

COHORT
A group of individuals with some characteristics in common.

COMPASSIONATE USE
A method of providing experimental therapeutics prior to final FDA approval for use in humans. This procedure is used with very sick individuals who have no other treatment options. Often, case-by-case approval must be obtained from the FDA for "compassionate use" of a drug or therapy.

COMPLEMENTARY AND ALTERNATIVE THERAPY
Broad range of healing philosophies, approaches, and therapies that Western (conventional) medicine does not commonly use to promote wellbeing or treat health conditions. Examples include acupuncture and herbs.

COMPLETED
The study has concluded normally. Participants are no longer being examined or treated, i.e., last patient's last visit has occurred. (See also Recruitment Status)

CONTRAINDICATION
A specific circumstance when the use of certain treatments could be harmful.

CONTROL GROUP
The standard by which experimental observations are evaluated. In many clinical trials, one group of patients will be given an experimental drug or treatment, while the control group is given either a standard treatment for the illness or a placebo. (See also Placebo and Standard Treatment)

CONTROLLED TRIALS
Control is a standard against which experimental observations might be evaluated. In clinical trials, one group of participants is given an experimental drug, while another group (i.e., the control group) is given either a standard treatment for the disease or a placebo.

CHRONIC-PROGRESSIVE (CP) MS
Former "catch-all" term for progressive forms of MS, now categorized as two separate forms of disease. (See also Secondary-Progressive MS and Primary-Progressive MS)

CROSSOVER
A study design that has each patient in two or more treatments in a specified order.

DATA SAFETY AND MONITORING BOARD (DSMB)
An independent committee composed of community representatives and clinical research experts that reviews data while a clinical trial is in progress to ensure that participants are not

exposed to undue risk. A DSMB could recommend that a trial be stopped due to safety concerns or if the trial objectives have been achieved.

DOSE-RANGING STUDY
A clinical trial in which two or more doses of an agent (such as a drug) are tested against each other to determine which dose works best and is least harmful.

DOUBLE-BLIND STUDY
A clinical trial design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug and which are receiving a placebo (or another therapy). Double-blind trials are thought to produce objective results, because the expectations of the doctor and the participant about the experimental drug do not affect the outcome. Also called double-masked study. (See also Blinded Study, Single-Blind Study, and Placebo)

DRUG-DRUG INTERACTION
A modification of the effect of a drug when administered with another drug. The effect could be an increase or a decrease in the action of either substance, or it could be an adverse effect that is not normally associated with either drug.

EFFICACY
Of a drug or treatment. The maximum ability of a drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed. In the procedure mandated by the FDA, Phase II clinical trials gauge efficacy and Phase III trials confirm it. (See also Food and Drug Administration (FDA), Phase II and III Trials)

ELIGIBILITY CRITERIA
Summary criteria for participant selection. Includes Inclusion and Exclusion criteria. (See also Inclusion/Exclusion Criteria)

EMPIRICAL
Based on experimental data, not on a theory.

ENDPOINT
Overall outcomes that the protocol is designed to evaluate. Common endpoints are time to first relapse, toxicity, or disease progression. (See also Outcome Measure)

ENROLLING
The act of signing up participants into a study. Generally this process involves evaluating a participant with respect to the eligibility criteria of the study and going through the informed consent process.

EPIDEMIOLOGY
The branch of medical science that deals with the study of incidence, distribution, and control of a disease in a population.

EXPERIMENTAL DRUG
A drug that is not FDA licensed for use in humans or as a treatment for a particular condition. (See also Off-Label Use)

FOOD AND DRUG ADMINISTRATION (FDA)
The U.S. Department of Health and Human Services agency responsible for ensuring the safety and effectiveness of all drugs, biologics, vaccines, and medical devices.

HYPOTHESIS
A supposition or assumption advanced as a basis for reasoning or argument, or as a guide to experimental investigation.

INCLUSION/EXCLUSION CRITERIA
The medical or social standards determining whether a person might or might not be allowed to enter a clinical trial. Those criteria are based on factors such as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. It is important to note that inclusion and exclusion criteria are not used to reject people personally, but rather to identify appropriate participants and keep them safe.

INFORMED CONSENT
The process of learning the key facts about a clinical trial before deciding whether or not to participate. It is also a continuing process throughout the study to provide information for participants. To help someone decide whether or not to participate, the doctors and nurses involved in the trial explain the details of the study.

INFORMED CONSENT DOCUMENT
A document that describes the rights of the study participants and includes details about the study, such as its purpose, duration, required procedures, and key contacts. Risks and potential benefits also are explained in the informed consent document. Based on the informed consent document, the individual decides whether or not to sign the form and participate in the study. Informed consent is not a contract, and the participant may withdraw from the trial at any time.

INSTITUTIONAL REVIEW BOARD (IRB)
A committee of physicians, statisticians, researchers, community advocates, and others who ensure that a clinical trial is ethical and that the rights of study participants are protected. All clinical trials in the United States must be approved by an IRB before they begin. Every institution that conducts or supports biomedical or behavioral research involving human participants must, by federal regulation, have an IRB that initially approves and periodically reviews the research to protect the rights of human participants.

INTENT TO TREAT
Analysis of clinical trial results that includes all data from participants in the groups to which they were randomized (See also Randomization) even if they never received the treatment.

INTERVENTIONS
Primary interventions being studied. Types of interventions are Drug, Gene Transfer, Vaccine, Behavior, Device, or Procedure.

INTRADERMAL (ID)
Introduced into the skin.

INTRAMUSCULAR (IM)
Injected into the muscle.

INTRAVENOUS (IV)
Injected into the vein.

INVESTIGATIONAL NEW DRUG
A new drug, antibiotic drug, or biological drug that is used in a clinical investigation. It also includes a biological product used in vitro for diagnostic purposes.

MRI
Magnetic resonance imaging. A non-invasive process of producing an image, especially of internal soft tissues of the body, from electromagnetic energy. MRI is used in MS to reveal lesions in the brain and spinal cord. It is used to confirm a diagnosis of MS and to track disease progression during clinical trials.

MULTICENTER STUDY
A clinical trial involving patients at more than one site open-label study—a study in which all patients receive the experimental treatment.

MULTIPLE SCLEROSIS, MAJOR FORMS
Although potential exists for the course of multiple sclerosis to progress from one pattern to a more severe one, the clinical course of MS usually falls within one of the following categories: relapsing-remitting, primary-progressive, progressive-relapsing, secondary-progressive.

NEW DRUG APPLICATION (NDA)
An application submitted by the manufacturer of a drug to the FDA—after clinical trials have been completed—for a license to market the drug for a specified indication.

OBJECTIVE
The reason for performing a trial in terms of the scientific questions to be answered by the data collected during the trial. The primary objective is the main question to be answered and drives any statistical planning for the trial (e.g., the sample size). Secondary and tertiary objectives are goals of a trial that will provide further information on the use of the treatment.

OFF-LABEL USE
A drug prescribed for conditions other than those approved by the FDA.

OPEN-LABEL TRIAL
A clinical trial in which doctors and participants know which drug or vaccine is being administered.

ORAL
Taken by mouth.

ORPHAN DRUGS
An FDA category that refers to medications used to treat diseases and conditions that occur rarely. There is little financial incentive for the pharmaceutical industry to develop medications for these diseases or conditions. Orphan drug status gives a manufacturer specific financial incentives to develop and provide such medications.

OUTCOME MEASURE
Measurement unit used to assess the effectiveness of a program or intervention, such as measures of disease activity, progression, or changes in MRI scans. Read more about Clinical Study Measures used in MS trials.

PEER REVIEW
Review of a clinical trial by experts chosen by the study sponsor. Those experts review the trials for scientific merit, participant safety, and ethical considerations.

PHARMACOKINETICS
The processes (in a living organism) of absorption, distribution, metabolism, and excretion of a drug or vaccine.

PHASE I TRIALS
Initial studies to determine the metabolism and pharmacologic actions of drugs in humans, to observe the side effects associated with increasing doses, and to gain early evidence of effectiveness. Could include healthy participants and/or patients.

PHASE II TRIALS
Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks.

PHASE III TRIALS
Expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained. Phase III trials are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide and adequate basis for physician labeling.

PHASE IV TRIALS
Post-marketing studies to delineate additional information including the drug's risks, benefits, and optimal use.

PILOT STUDY
An early, small-to-moderate sized study, also known as a Phase 2 study. A pilot study follows the Phase 1 study, or "safety study," and is designed to begin determining the effectiveness of the experimental treatment.

PLACEBO
A placebo is an inactive pill, liquid, or powder that has no treatment value. In clinical trials, experimental treatments often are compared with placebos to assess the treatment's effectiveness. (See also Placebo Controlled Study)

PLACEBO CONTROLLED STUDY
A method of investigation of drugs in which an inactive substance (the placebo) is given to one group of participants, while the drug being tested is given to another group. The results obtained in the two groups are then compared to see whether the investigational treatment is more effective in treating the condition.

PLACEBO EFFECT
A physical or emotional change, occurring after a substance is taken or administered, that is not the result of any special property of the substance. The change could be beneficial, reflecting the expectations of the participant and often the expectations of the person giving the substance.

PRECLINICAL
Refers to the testing of experimental drugs in the test tube or in animals—the testing that occurs before trials in humans may be carried out.

PRIMARY-PROGRESSIVE (PP) MS
Form of MS characterized by disease progression from onset, with occasional plateaus (leveling of condition) and temporary minor improvements possible.

PROGRESSIVE-RELAPSING (PR) MS
Form of MS characterized by progressive disease from onset, with acute relapses, with or without full recovery. Periods between relapses characterized by continuing progression. Considered to be a rare clinical course.

PROTOCOL
A study plan on which all clinical trials are based. The plan is carefully designed to safeguard the health of the participants as well as answer specific research questions. A protocol describes what types of people may participate in the trial. The length of the study as well as the schedule of tests, procedures, medications, and dosages. While in a clinical trial, participants following a protocol are seen regularly by the research staff to monitor their health and to determine the safety and effectiveness of their treatment. (See also Inclusion/Exclusion Criteria)

QUALITY OF LIFE TRIALS
Also called Supportive Care trials. Refers to trials that explore ways to improve comfort and quality of life for individuals with a chronic illness.

RANDOMIZATION
A method based on chance by which study participants are assigned to a treatment group. Randomization minimizes the differences among groups by equally distributing people with particular characteristics among all the trial arms. The researchers do not know which

treatment is better. From what is known at the time, any one of the treatments chosen could be of benefit to the participant. (See also Arm)

RANDOMIZED TRIAL
A study in which participants are randomly (i.e., by chance) assigned to one of two or more treatment arms of a clinical trial. Occasionally placebos are utilized. (See also Arm and Placebo)

RECRUITMENT STATUS
Indicates the current stage of a trial, whether it is planned, ongoing, or completed. Possible values include:

Not yet recruiting—Participants are not yet being recruited or enrolled.
Recruiting—Participants are currently being recruited and enrolled.
Enrolling by invitation—Participants are being (or will be) selected from a predetermined population.
Active, not recruiting—Study is ongoing (i.e., patients are being treated or examined), but enrollment has completed.
Completed—The study has concluded normally. Participants are no longer being examined or treated (i.e., last patient's last visit has occurred).
Suspended—Recruiting or enrolling participants has halted prematurely but potentially will resume.
Terminated—Recruiting or enrolling participants has halted prematurely and will not resume. Participants are no longer being examined or treated.
Withdrawn—Study halted prematurely, prior to enrollment of first participant.

RELAPSE
A sudden worsening of preexisting symptoms, or the development of new neurologic symptoms, which lasts at least 24 hours. Synonymous with "exacerbation" or "acute attack."

RELAPSING-PROGRESSIVE MS
Former name for progressive-relapsing MS.

RELAPSING-REMITTING (RR) MS
Form of MS characterized by clearly defined disease relapses (flare-ups) with full recovery or with sequelae (resulting conditions) and residual deficit upon recovery. Periods between disease relapses characterized by a lack of disease progression (gradual worsening).

RISK-BENEFIT RATIO
The risk to individual participants versus the potential benefits. The risk/benefit ratio could differ depending on the condition being treated.

SECONDARY-PROGRESSIVE (SP) MS
Form of MS characterized by initial RR disease course followed by progression with or without occasional relapses, minor remissions (some recovery), and plateaus (leveling of condition).

SINGLE-BLIND STUDY
A study in which one party, either the investigator or participant, is unaware of what medication the participant is taking. Also called single-masked study. (See also Blind and Double-Blind Study).

STANDARD TREATMENT
A treatment currently in wide use and approved by the FDA, considered to be effective in the treatment of a specific disease or condition.

STATISTICAL SIGNIFICANCE
The probability that an event or difference occurred by chance alone. In clinical trials, the level of statistical significance depends on the number of participants studied and the observations made, as well as the magnitude of differences observed.

SUBCUTANEOUS (SC)
Injected under the skin.

SUSPENDED
Recruiting or enrolling participants has halted prematurely but potentially will resume. (See also Recruitment Status)

TERMINATED
Recruiting or enrolling participants has halted prematurely and will not resume. Participants are no longer being examined or treated. (See also Recruitment Status)

TOXICITY
An adverse effect produced by a drug that is detrimental to the participant's health. The level of toxicity associated with a drug will vary depending on the condition which the drug is used to treat.

TREATMENT IND
IND stands for Investigational New Drug application, which is part of the process to get approval from the FDA for marketing a new prescription drug in the United States. It makes promising new drugs available to desperately ill participants as early in the drug development process as possible. Treatment INDs are made available to participants before general marketing begins, typically during Phase III studies. To be considered for a treatment IND a participant cannot be eligible to be in the definitive clinical trial.

WITHDRAWN
Study halted prematurely, prior to enrollment of first participant. (See also Recruitment Status)

This information is adapted from ClinicalTrials.gov, a service of the National Institutes of Health and developed by the National Library of Medicine.