LARGE PHASE 3 TRIALS IN RR MS X

updated August 2012

Abbreviations Key:
AAN – American Academy of Neurology
ECTRIMS – European Committee of Treatment and Research in MS
IM – intramuscular, injected into muscle
IV – intravenous, injected into vein
PP - primary progressive
PR - progressive relapsing
RR - relapsing-remitting
SC – subcutaneous, injected under the skin
SP - secondary progressive

AGENT	PURPOSE OF STUDY	POSSIBLE MECHANISM	HOW DRUG IS TAKEN	TYPE OF MS/ NUMBER OF SUB-JECTS	RESULTS
Alemtuzumab (Genzyme Corporation) vs. interferon beta-1a (Rebif®, Serono Pfizer)	To compare effect on progression of disability and relapse rate (CARE-MS I)	Targets CD52 antigen expressed on B and T lymphocytes/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier	IV, SC	RR/581	Reduced relapse rates by 55% over Rebif; no statistically significant difference in slowing disease progression or EDSS increase (Abstract 151, ECTRIMS 2011; read more here http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=5695 and here http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6496)
Alemtuzumab (Genzyme Corporation) vs. interferon beta-1a (Rebif®, Serono Pfizer)	To test 2 doses versus Rebif on pro-gression and relapse rate, also (CARE-	Targets CD52 antigen expressed on B and T cells/ Slows down immune response, possibly interfering with T cell activation and movement across blood-	IV, SC	RR/ 700	Relapse rate reduced by 49% compared to Rebif; risk of disability progression reduced by 42% (Abstract S01.004, AAN 2012; read more here http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6377 and here http://www.nationalmssociety.org/news/news-

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	MS II)	brain barrier			detail/index.aspx?nid=6496).
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	Upregulates Th2 response, immune-modulatory	Oral, SC	RR/ 1431	Reduced average annual relapses by 44 to 51% over placebo (Abstract P04.136, AAN 2012; read more here http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6377 and here http://nationalmssociety.org/news/news-detail/index.aspx?nid=6015).
BG-12 (dimethyl fumarate) vs. glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries, Ltd.)	To test safety and effectiveness in controlling disease course and develop-ment of brain lesions, also known as DEFINE study	Upregulates Th2 response, immune-modulatory	Oral, SC	RR/ 1431	Achieved statistical significance on all primary and secondary outcomes (Abstract 95, ECTRIMS 2012; read more here http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=5695 and here http://nationalmssociety.org/news/news-detail/index.aspx?nid=6015).
BIIB017 (PEGylated interferon beta-1a)	To reduce relapses	Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells	SC	RR/ 1260	Ongoing, not recruiting; read more http://clinicaltrials.gov/ct2/show/NCT00906399.

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Daclizumab High Yield Process (DAC HYP) vs. interferon beta-1a (Avonex®, Biogen Idec)	To evaluate safety and effective-ness, also known as the DECIDE study	Limits T cell expansion by blocking signaling of cytokine IL-2	IM, SC	RR/ 1800	Ongoing; read more http://clinicaltrials.gov/ct2/show/NCT01064401.
Daclizumab High Yield Process (DAC HYP)	Testing the use of a prefilled syringe, also known as the OBSERVE study	Limits T cell expansion by blocking signaling of cytokine IL-2	SC	RR/ 100	Ongoing; read more http://clinicaltrials.gov/ct2/show/NCT01462318.
Fingolimod (Gilenya™, Novartis)	To test safety and effective-ness, also known as FREEDOMS II study	Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue	Oral	RR/ 778	Reduced relapse rate by 48% compared with placebo (Abstract 5LB00.015, AAN 2012; read more here http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6377 and here http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6269).

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Glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries Ltd.)	To test less frequent dosing, also known as GALA Study	Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2	SC	RR/ 1350	Reduced average annual relapse rate by 34.4% compared to placebo (Teva Pharmaceutical Industries press release, June 14, 2012).
Glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries Ltd.)	To test safety and effective-ness of new formulation	Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2	SC	RR/ 1400	Ongoing, read more http://clinicaltrials.gov/ct2/show/NCT01578785.
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	Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2	IM, SC	RR/ 1000	No significant difference in reducing clinical relapses or progression (Abstracts S11.002 and PL02.003, AAN 2012; read more http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6377).

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Laquinimod vs. interferon beta-1a (Avonex®, Biogen Idec)	To control disease course and develop-ment of brain lesions, also known as BRAVO study	Immunomodulatory/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells	Oral, IM	RR/ 1200	Did not reduce annualized relapse rate significantly more than placebo (Abstract 148, AAN 2012; read more http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=5695).
Methylprednisolone	To compare oral versus intra-venous, also known as OMEGA study	Closes damaged blood-brain barrier, reducing inflammation in CNS	oral, IV	RR/ 140	Ongoing, read more http://clinicaltrials.gov/ct2/show/NCT00418145.
NU100 (recombinant human interferon beta-1b)	To control disease course and development of brain lesions	Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells	SC	RR/ 500	Ongoing; read more http://clinicaltrials.gov/ct2/show/NCT01464905.
Ocrelizumab vs. interferon beta-1a (Rebif®, Serono Pfizer)	To evaluate safety and effective-ness in reducing disease activity, also known as ORA-TORIO study	Binds to CD20 antigen on B cells and induces B-cell lysis/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells	IV, SC	RR/ 800	Ongoing; read more http://clinicaltrials.gov/ct2/show/NCT01247324.

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Teriflunomide (HMR1726)	To control lesion develop-ment, disease progression and relapses, also known as TOPIC study	Modulates responses of T-cells within the immune system by impairing DNA synthesis	Oral	CIS/ 780	Ongoing; read more http://clinicaltrials.gov/ct2/show/NCT00622700. Approved 9/12/12 to treat MS; read more http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6864.
Teriflunomide (HMR1726)	To control lesion develop-ment, disease progression and relapses, also known as TOWER study	Modulates responses of T-cells within the immune system by impairing DNA synthesis	Oral	RR/ 1110	Reduced relapses compared with placebo over at least 48 weeks (Genzyme/Sanofi-Aventis press release, June 4, 2012; read more http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6456). Approved 9/12/12 to treat MS; read more http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6864.
Teriflunomide (HMR1726) and interferon beta-1a	To test safety and effective-ness of combination therapy	Modulates responses of T-cells within the immune system by impairing DNA synthesis /Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier	Oral, IM	Re-lapsing/ 1455	Did not reach primary endpoint (Genzyme/Sanofi-Aventis press release, December 20, 2011; read more http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=5801). Approved 9/12/12 to treat MS; read more http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6864.