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Centre d'Esclerosi Múltiple de Catalunya

What are the real choices? Therapy options for people with MS in 2013 and beyond

Jaume Sastre-Garriga

Servei de Neurologia / Neuroimmunologia

Centre d'Esclerosi Múltiple de Catalunya – Cemcat

Hospital Universitari Vall d'Hebron, Barcelona

Vall d'Hebron Hospital

FEM Fundació Esclerosi Múltiple

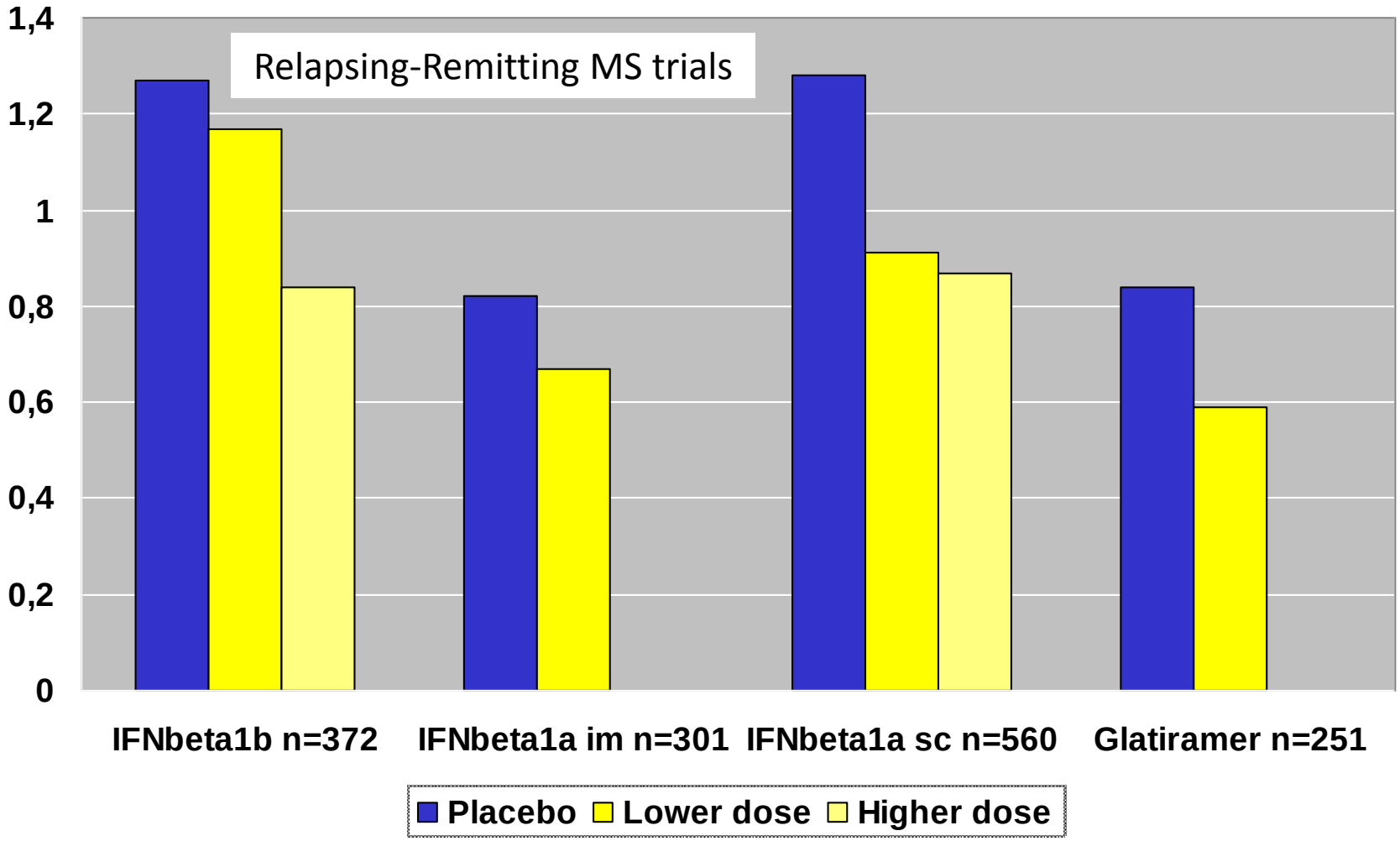
Outline of the talk

- Disease Modifying Drugs
  - Present therapies
    - "First line"
    - "Second line"
  - Future Therapies
    - Oral therapies
    - Monoclonal antibodies
- Conclusions

Disease modifying therapies

Present drugs

Interferons & Glatiramer



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Interferons & Glatiramer

Effects of oral glatiramer acetate on clinical and MRI-monitored disease activity in patients with relapsing multiple sclerosis: a multicentre, double-blind, randomised, placebo-controlled study

*Massimo Filippi, Jerry S Wolinsky, Giancarlo Comi, the CORAL Study Group**

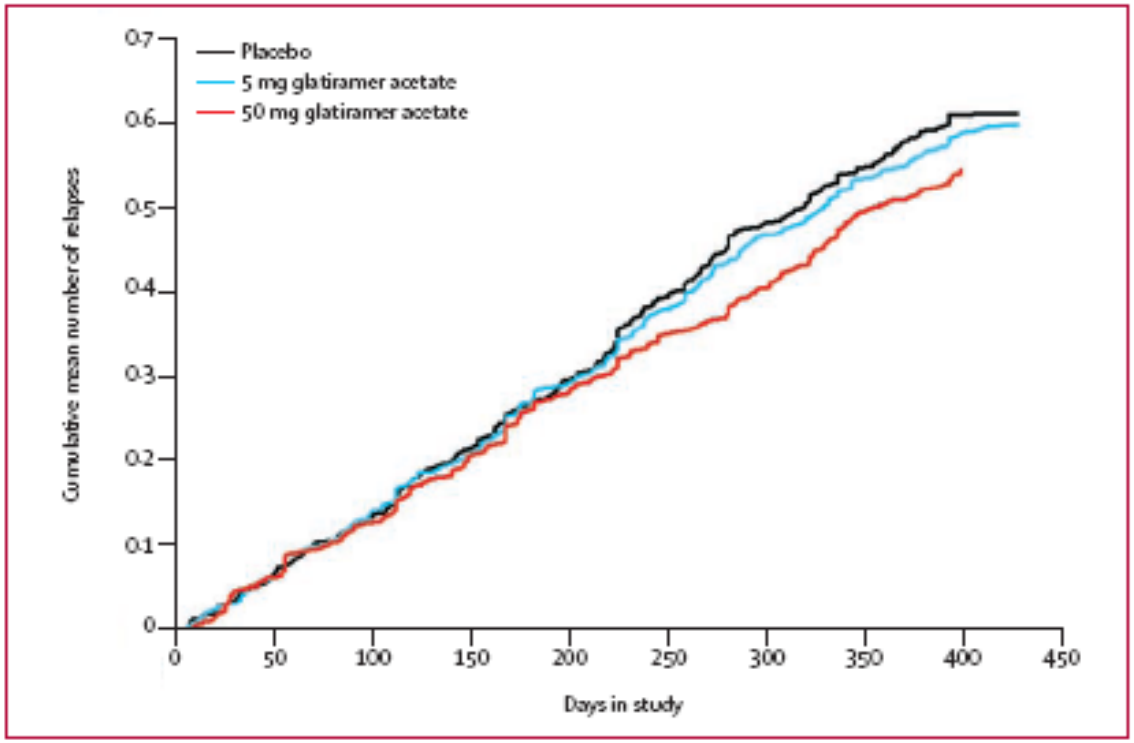

Figure 2: Mean cumulative number of confirmed relapses during the 56-week trial duration, displayed as a function of the number of days the patients in each group were in the study

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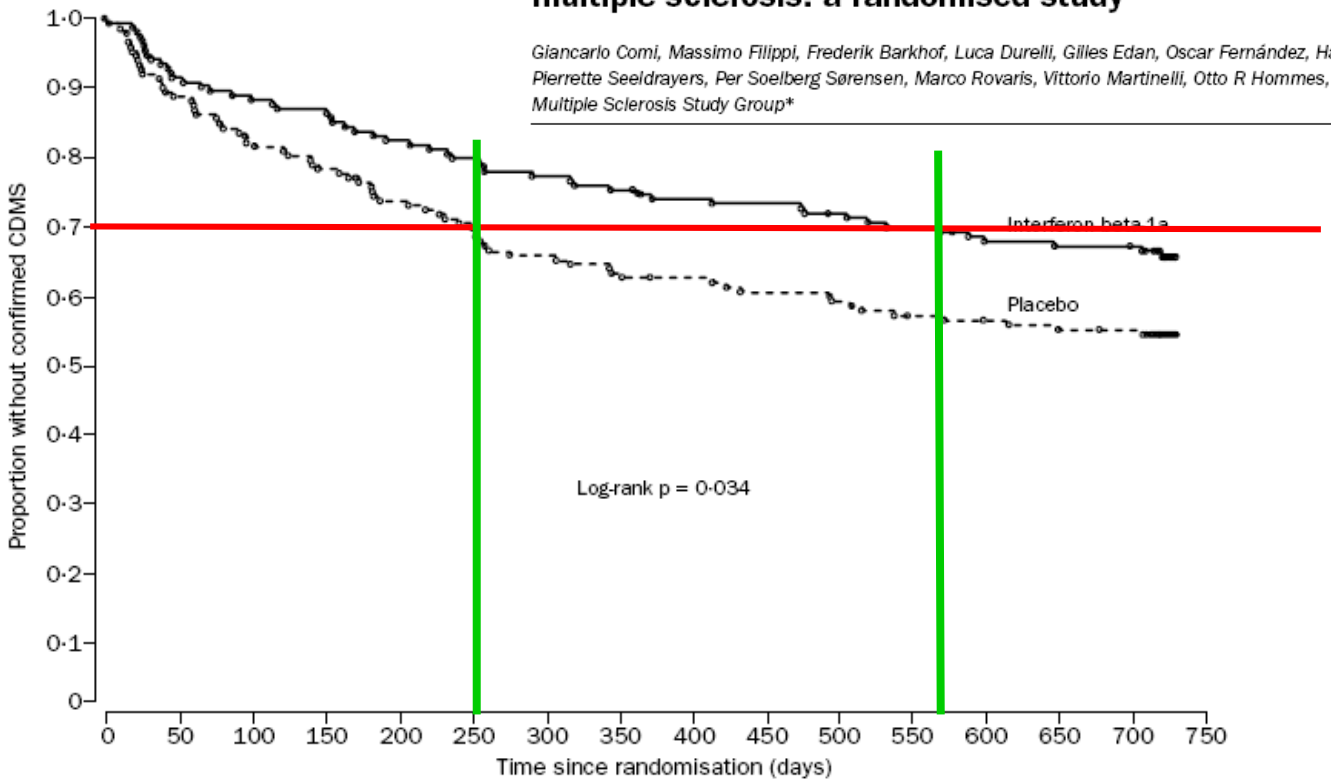
Early MS: first attacks

ARTICLES

Effect of early interferon treatment on conversion to definite multiple sclerosis: a randomised study

*Giancarlo Comi, Massimo Filippi, Frederik Barkhof, Luca Durelli, Gilles Edan, Oscar Fernández, Hans-Peter Hartung, Pierrette Seeldrayers, Per Soelberg Sørensen, Marco Rovaris, Vittorio Martinelli, Otto R Hommes, and the Early Treatment of Multiple Sclerosis Study Group**



Number of patients at risk

Interferon beta-1a	154	129	114	105	99
Placebo	154	115	96	86	81

Figure 2: **Kaplan–Meier survival curve of probability of no conversion to clinically definite multiple sclerosis (CDMS) over 2 years**

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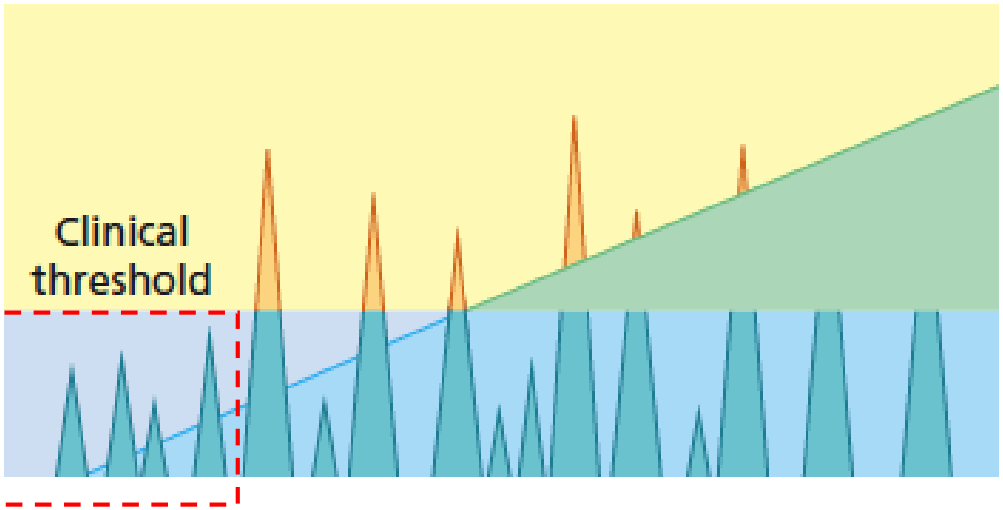
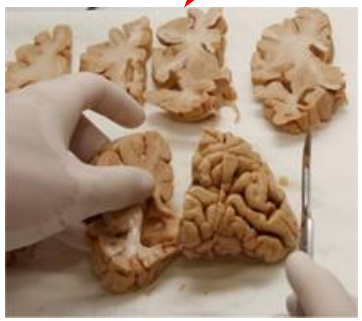
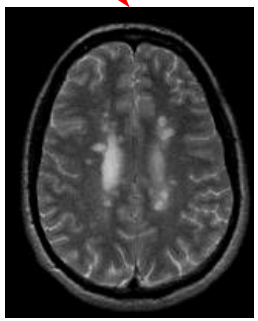
Very early MS: preclinical stage



Preclinical phase





Subclinical multiple sclerosis can be defined as the presence of asymptomatic lesions typical of MS on an MRI performed for reasons other than suspecting MS

‘Subclinical MS’: follow-up of four cases

B. Hakiki, B. Goretti, E. Portaccio, V. Zipoli and M. P. Amato
Department of Neurology, University of Florence, Florence, Italy

Unexpected multiple sclerosis: follow-up of 30 patients with magnetic resonance imaging and clinical conversion profile

C Lebrun,[1] C Bensa,[2] M Debouverie,[3] J De Seze,[4] S Wiertlievski,[5] B Brochet,[6] P Clavelou,[7] D Brassat,[8] P Labauge,[9] E Roullet,[2] on behalf of CFSEP

Association Between Clinical Conversion Sclerosis in Radiologically Isolated Syndrome and Magnetic Resonance Imaging, Cerebrospinal Fluid and Visual Evoked Potential

Follow-up of 70 Patients

Christine Lebrun, MD; Caroline Bensa, MD; Marc Debouverie, MD; Sandrine Wiertlevski, MD; David Brassat, MD; Jerome de Seze, MD; Lucien Rumbach, MD; Jean Pelletier, MD; Pierre Labauge, MD; Bruno Brochet, MD; Ayman Tourbah, MD; Pierre Clavelou, MD; for the Club Francophone de la Sclérose en Plaques

Incidental MRI anomalies suggestive of multiple sclerosis

The radiologically isolated syndrome

D.T. Okuda, MD
E.M. Mowry, MD
A. Beheshtian, MD
E. Waubant, MD, PhD
S.E. Baranzini, PhD
D.S. Goodin, MD
S.L. Hauser, MD

ABSTRACT

Background: The discovery and broad application of MRI in medicine has led to an in awareness in the number of patients with incidental white matter pathology in the CNS. R encountered in clinical practice, the natural history or evolution of such individuals with res their risk of developing multiple sclerosis (MS) is unclear.

Objective: To investigate the natural history of patients who exhibit incidental imaging

Asymptomatic spinal cord lesions predict disease progression in radiologically isolated syndrome

D.T. Okuda, E.M. Mowry, B.A.C. Cree, et al.

Multiple sclerosis risk in radiologically uncove asymptomatic possible inflammatory-demyelinating disease

A Siva[1], S Saip[1], A Altintas[1], A Jacob[2,], BM Keegan[3] and OH Kantarci[3]*

Cognitive function in radiologically isolated syndrome

Improving the Characterization of Radiologically Isolated Syndrome Suggestive of Multiple Sclerosis

Nicola De Stefano[1]*, Maria Laura Stromillo[1], Francesca Rossi[1], Marco Battaglini[1], Antonio Giorgio[1], Emilio Portaccio[2], Bahia Hakiki[2], Gianmichele Maria Letizia Bartolozzi[6], Maria Pia Sormani[7],

Impact of pregnancy on conversion to clinically isolated syndrome in a radiologically isolated syndrome cohort

Christine Lebrun[1], Frederic Blanc[2], David Brassat[3], Hélène Zephir[4] and Jerome de Seze[2] on behalf of CFSEP

Lesiones incidentales desmielinizant magnética: estudio de 11 casos con s clinicorradiológico y revisión de la bi

Alba Sierra-Marcos, Raquel Mitjana, Joaquín Castilló, Mari Carmen
Mar Tintoré, Jordi Río-Izquierdo, Cristina Auger-Acosta, Àlex Rovira,

Cortical lesions in radiologically isolated syndrome

C Lebrun[1], E Le Page[1], O Kantarci[2], A Siva[3], D Pelletier[4], DT Okuda[5], on behalf of the Club Francophone de la Sclerose en Plaques (CFSEP) and the Radiologically Isolated Syndrome Consortium (RISC) Group

A. Giorgio, MD
M.L. Stromillo, MD
F. Rossi, MD
M. Battaglini, PhD
B. Hakiki, MD
E. Portaccio, MD
A. Federico, MD
M.P. Amato, MD
N. De Stefano, MD

ABSTRACT

Objective: To assess the presence of cortical lesions (CLs) as detectec radiologically isolated syndrome (RIS).

Methods: Fifteen subjects with RIS underwent an MRI examination, inc recovery sequence for CL assessment. T2-hyperintense white matter (W normalized volumes of brain and cortex were also obtained.

Results: Thirty-four CLs were identified in 6 of 15 (40%) subjects wit distributed in frontotemporal lobes. CLs were frequent in subjects with G oligoclonal bands on CSF, cervical cord lesions, and dissemination in t

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Secondary progressive MS

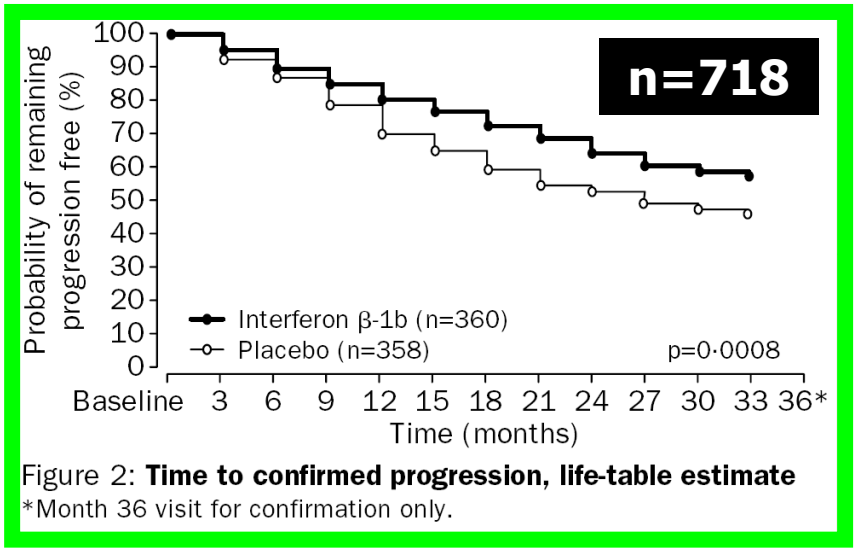
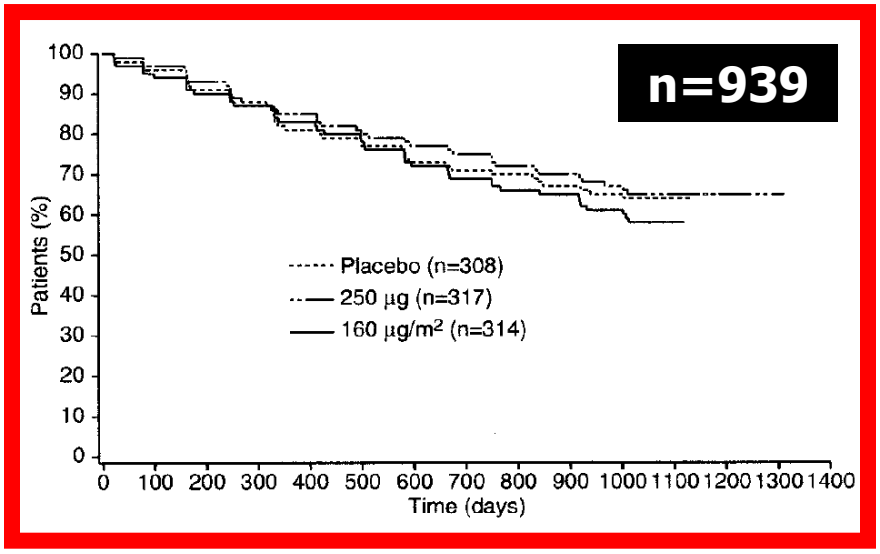
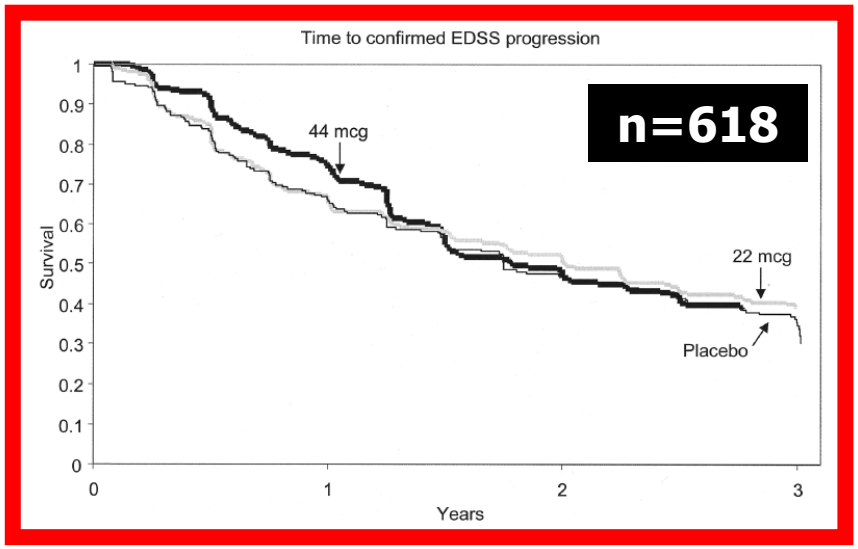
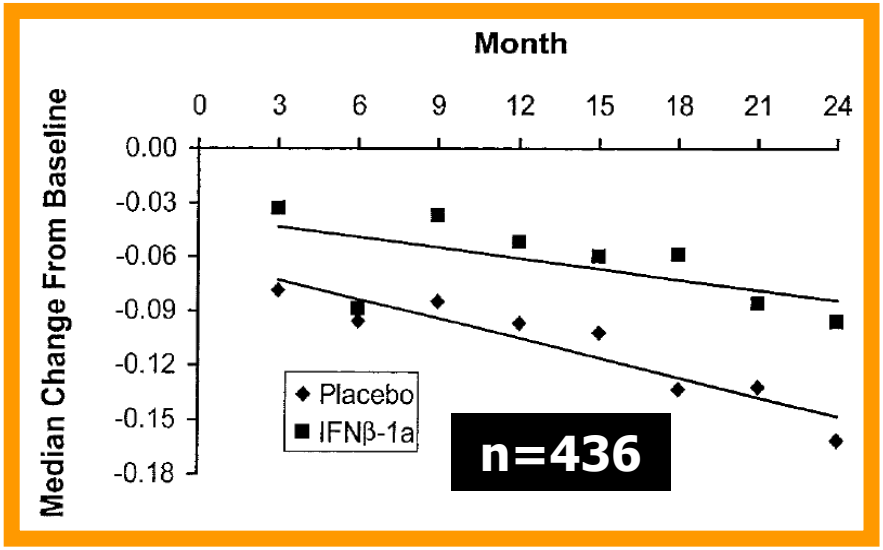


Figure 2: **Time to confirmed progression, life-table estimate**
*Month 36 visit for confirmation only.







Primary progressive MS

Glatiramer Acetate in Primary Progressive Multiple Sclerosis: Results of a Multinational, Multicenter, Double-Blind, Placebo-Controlled Trial

Jerry S. Wolinsky, MD,[1] Ponnada A. Narayana, PhD,[2] Paul O'Connor, MD,[3] Patricia K. Coyle, MD,[4] Corey Ford, MD,[5] Kenneth Johnson, MD,[6] Aaron Miller, MD,[7] Lillian Pardo, MD, MHSA,[8] Shaul Kadosh, MBA,[9] David Ladkani, PhD,[9] and the PROMiSe Trial Study Group

ORIGINAL ARTICLES

Rituximab in Patients with Primary Progressive Multiple Sclerosis

Results of a Randomized Double-Blind Placebo-Controlled Multicenter Trial

Kathleen Hawker, MD,[1] Paul O'Connor, MD,[2] Mark S. Freedman, MD,[3] Peter A. Calabresi, MD,[4] Jack Antel, MD,[5] Jack Simon, MD,[6] Stephen Hauser, MD,[7] Emmanuelle Waubant, MD,[7] Timothy Vollmer, MD,[8] Hillel Panitch, MD,[9] Jiameng Zhang, PhD,[10] Peter Chin, MD,[10] and Craig H. Smith, MD,[10] for the OLYMPUS trial group

A single-center, randomized, double-blind, placebo-controlled study of interferon beta-1b on primary progressive and transitional multiple sclerosis

X Montalban[1], J Sastre-Garriga[1], M Tintoré[1], L Brieva[1], FX Aymerich[2], J Río[1], J Porcel[1], C Borràs[1], C Nos[1] and À Rovira[2]

Interferon β-1a in primary progressive MS

An exploratory, randomized, controlled trial

S.M. Leary, MRCP; D.H. Miller, FRCP; V.L. Stevenson, MRCP; P.A. Brex, MRCP; D.T. Chard, MRCP; and A.J. Thompson, FRCP

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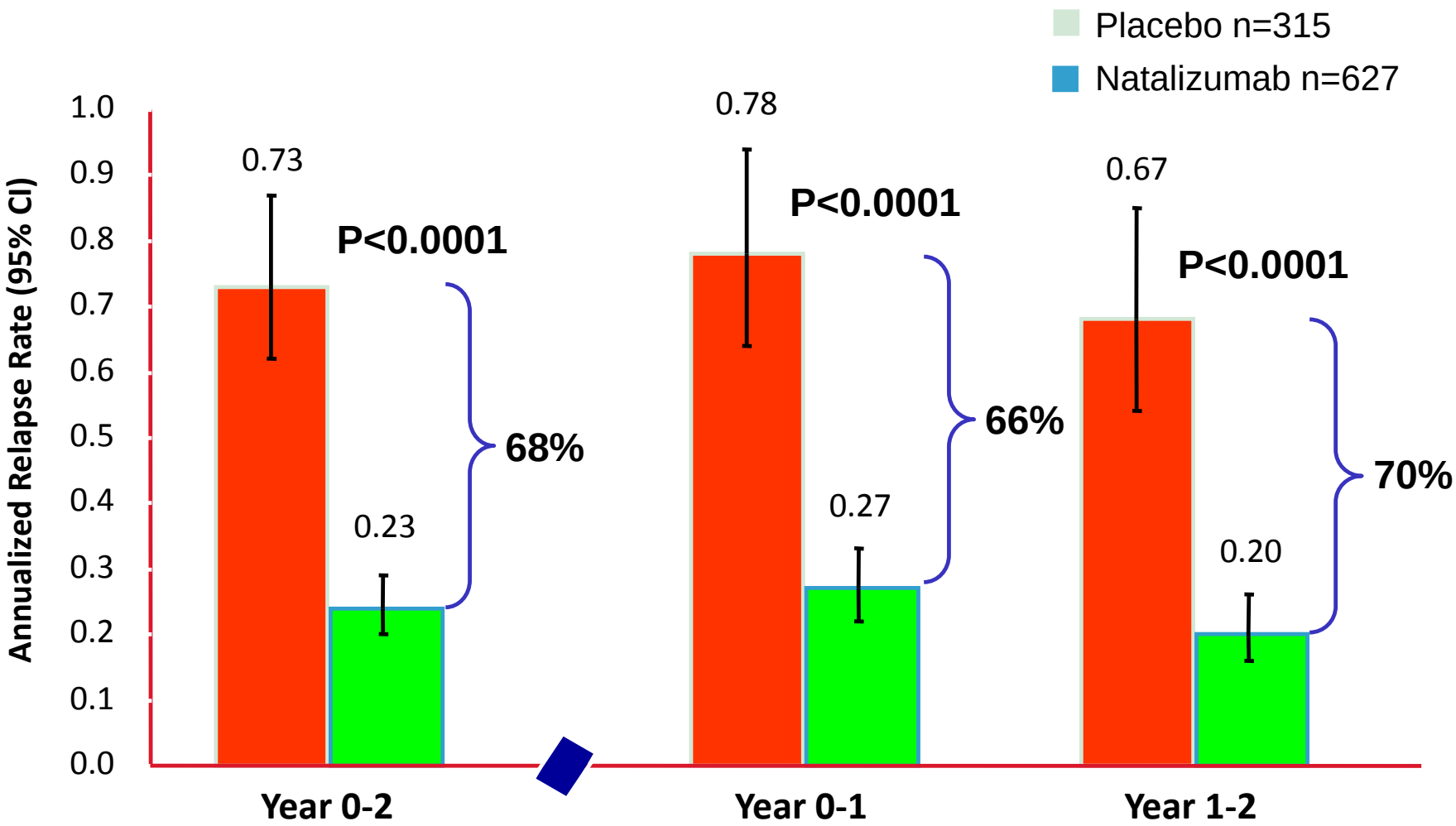
Natalizumab



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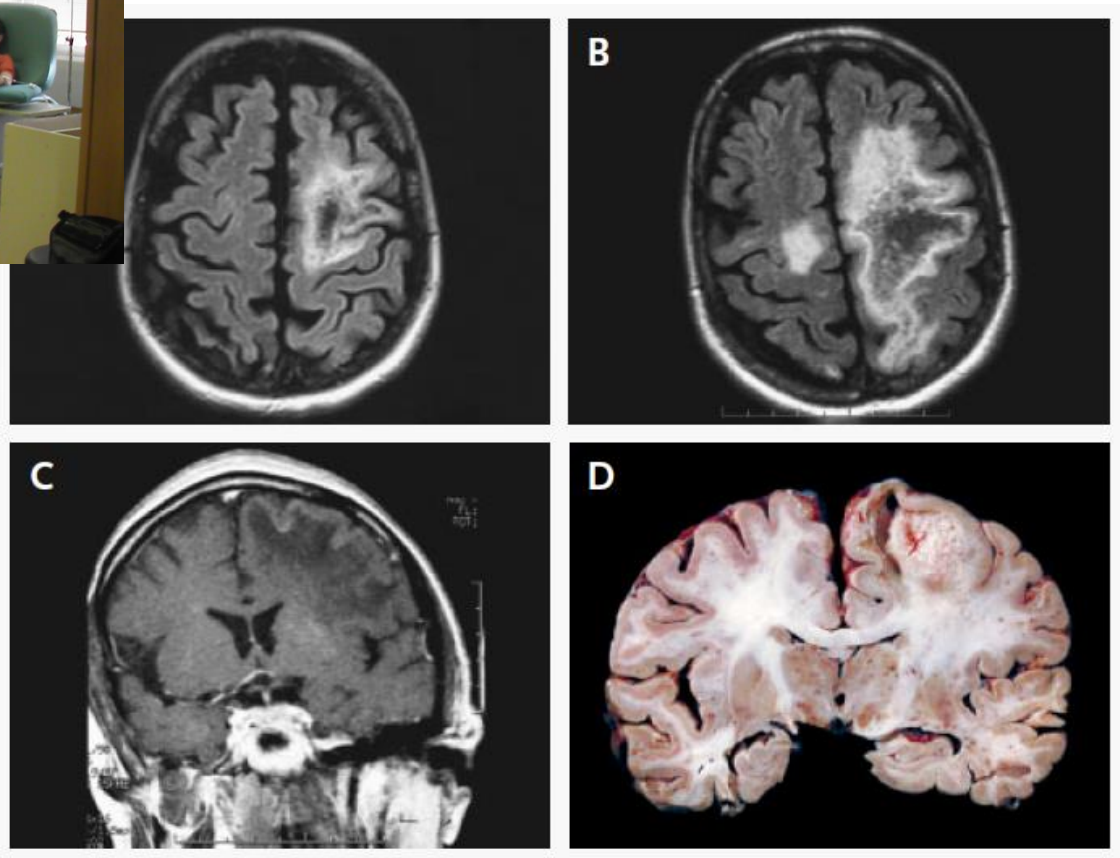
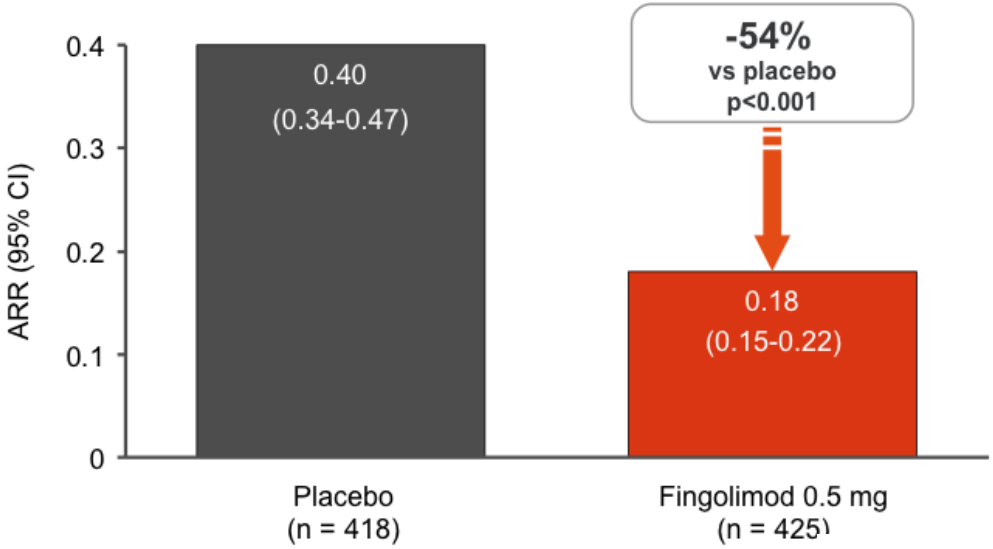
Natalizumab

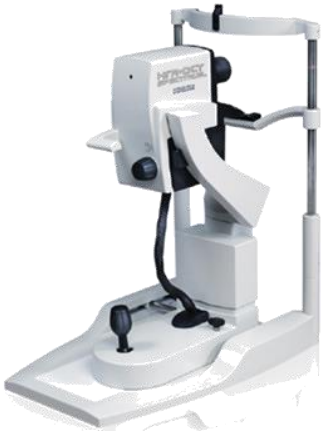


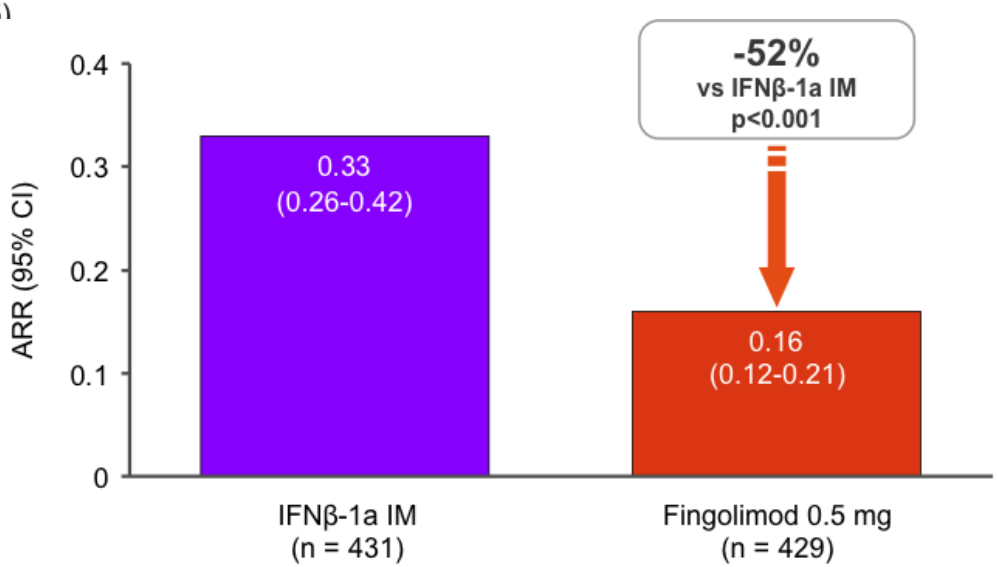
Fingolimod


INSTRUCTIONS FOR USE
Opening Instructions:
GILENYA
(fingolimod)
capsules
0.5 mg
To open kit:
Press firmly 1
To open: While pressing tab 1 firmly, pull on tab 2.
Pull
Closing Instructions:
GILENYA
(fingolimod)
capsules
0.5 mg

Fingolimod







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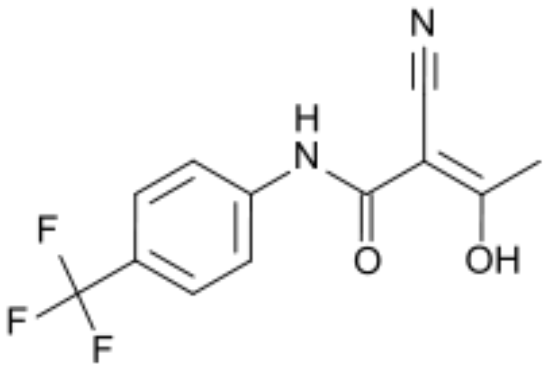
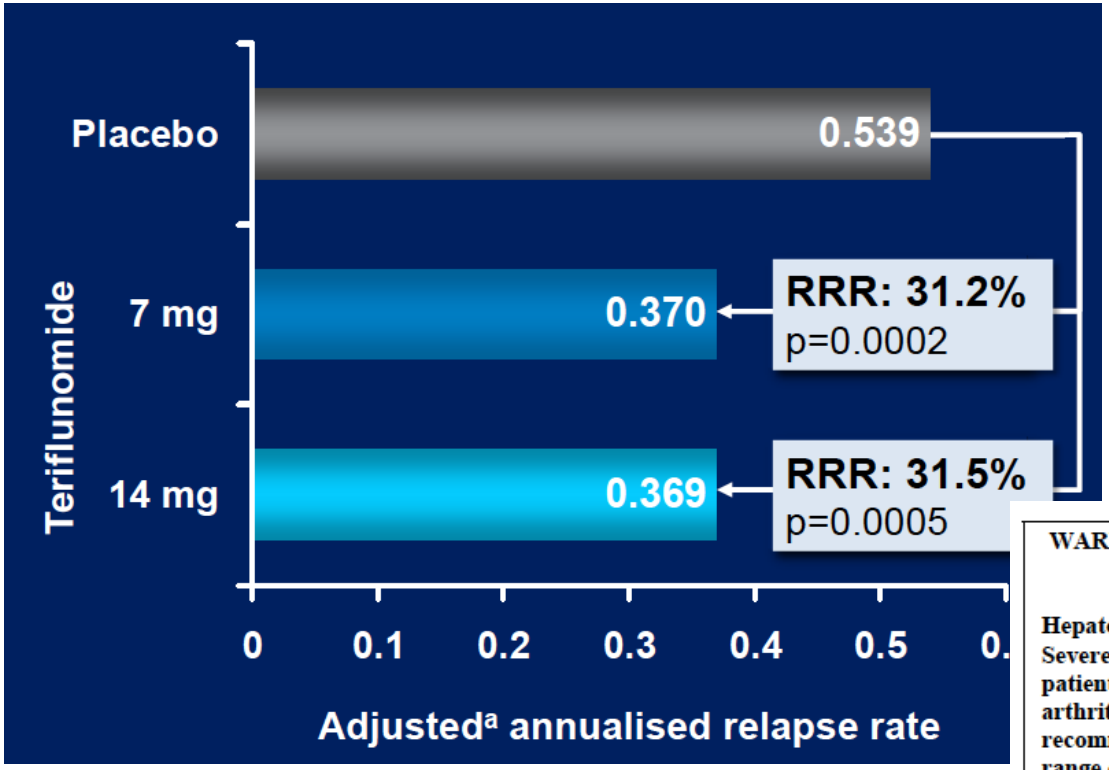
Disease modifying therapies

Future drugs

Teriflunomide



Teriflunomide



WARNING: HEPATOTOXICITY and RISK OF TERATOGENICITY

See full prescribing information for complete boxed warning

Hepatotoxicity

Severe liver injury including fatal liver failure has been reported in patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. Obtain transaminase and bilirubin levels within 6 months before initiation of AUBAGIO and monitor ALT levels at least monthly for six months (5.1). If drug induced liver injury is suspected, discontinue AUBAGIO and start accelerated elimination procedure (5.3).

Risk of Teratogenicity

Based on animal data, AUBAGIO may cause major birth defects if used during pregnancy. AUBAGIO is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. Pregnancy must be avoided during AUBAGIO treatment. (4.2, 5.2)

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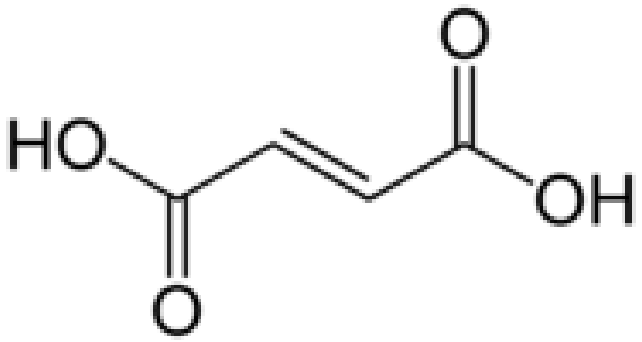
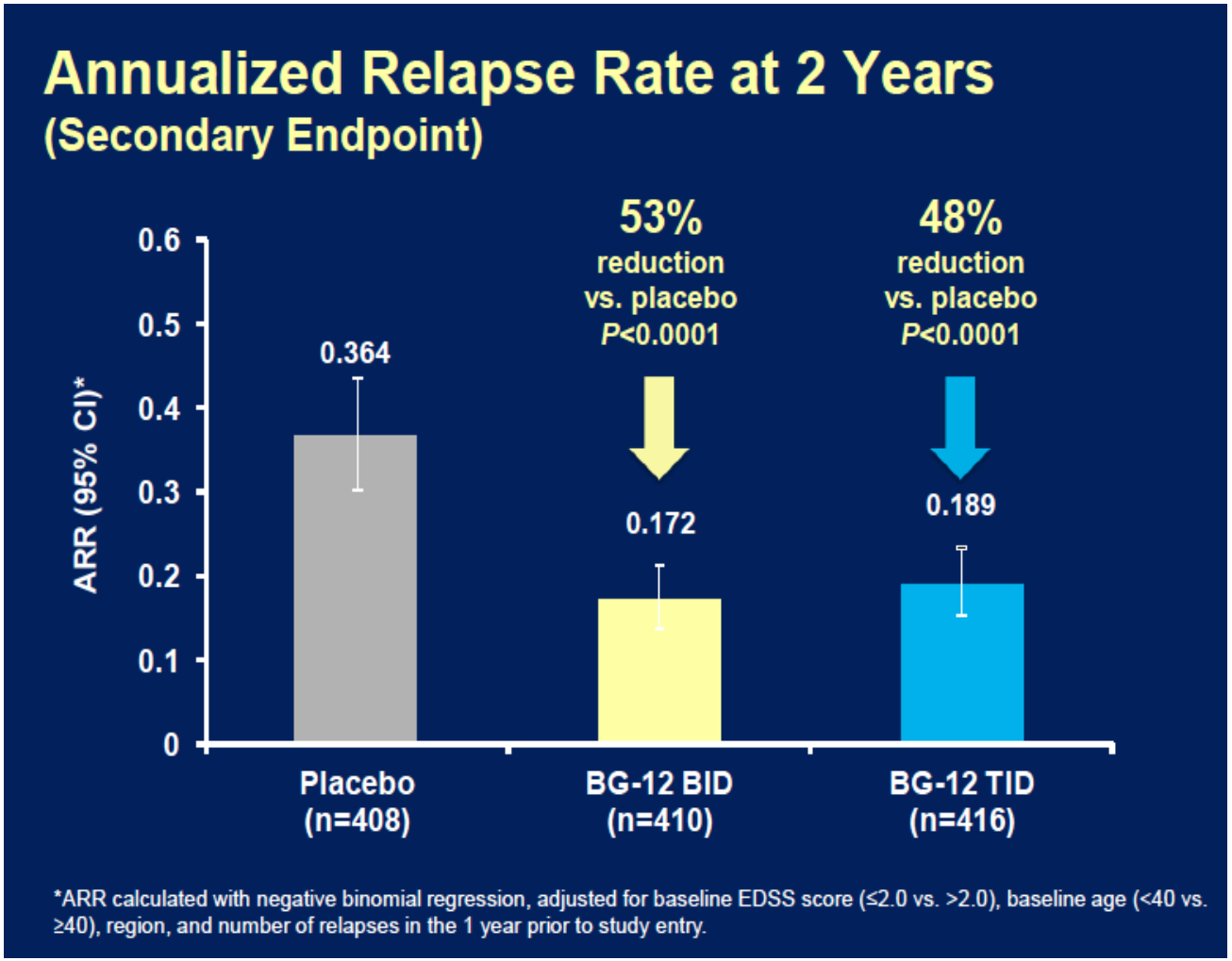
Dimethyl-fumarate (BG-12)



Tecfidera
[dimethyl fumarate]

Dimethyl-fumarate (BG-12)



- ✓ FLUSHING

- ✓ ABDOMINAL PAIN
- ✓ DIARRHEA
- ✓ NAUSEA

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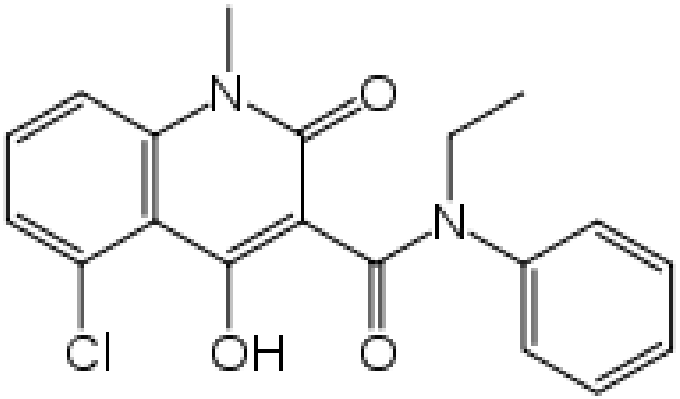
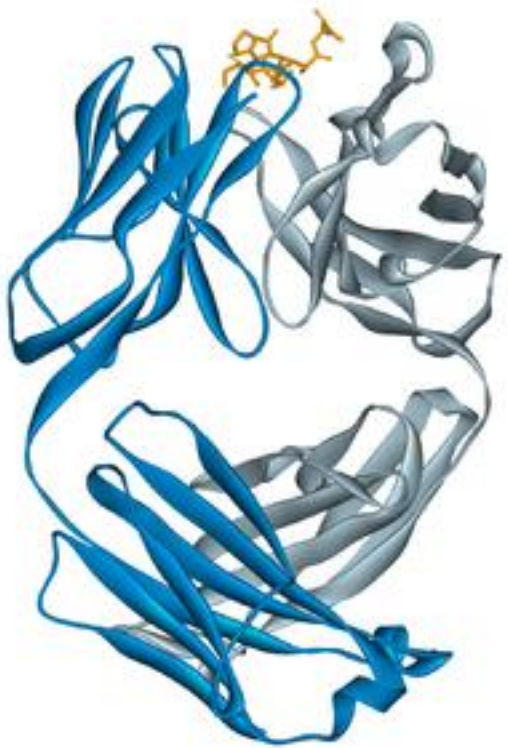
Forthcoming drugs: laquinimod

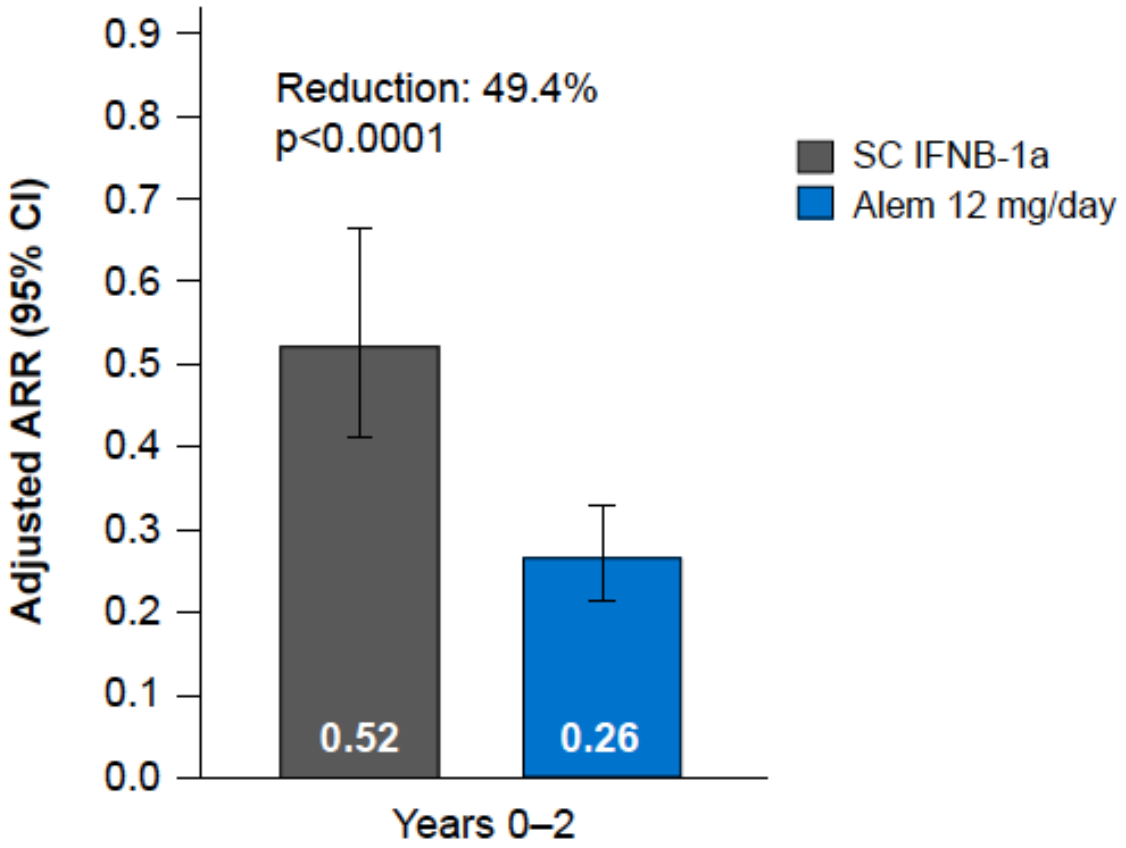


PRESS RELEASE:

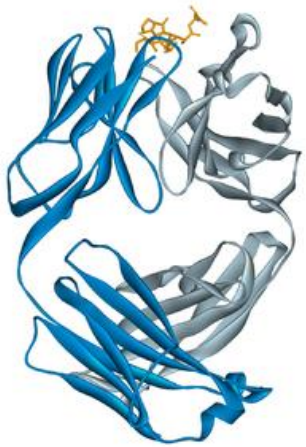
TEVA TO INITIATE THIRD PHASE III TRIAL OF ORAL LAQUINIMOD FOR THE TREATMENT OF RELAPSING REMITTING MULTIPLE SCLEROSIS

Forthcoming drugs: alemtuzumab





Forthcoming drugs: alemtuzumab



Autoimmune Adverse Events

N (%)	SC IFNB-1a n=202	Alemtuzumab 12 mg/day n=435	Alemtuzumab 24 mg/day n=161
Thyroid AEs	10 (5.0)	69 (15.9)	31 (19.3)
Serious Thyroid AEs	0	2 (0.5)	2 (1.2)
ITP AEs	0	4 (0.9)	3 (1.9)
Serious ITP AEs	0	3 (0.7)	2 (1.2)

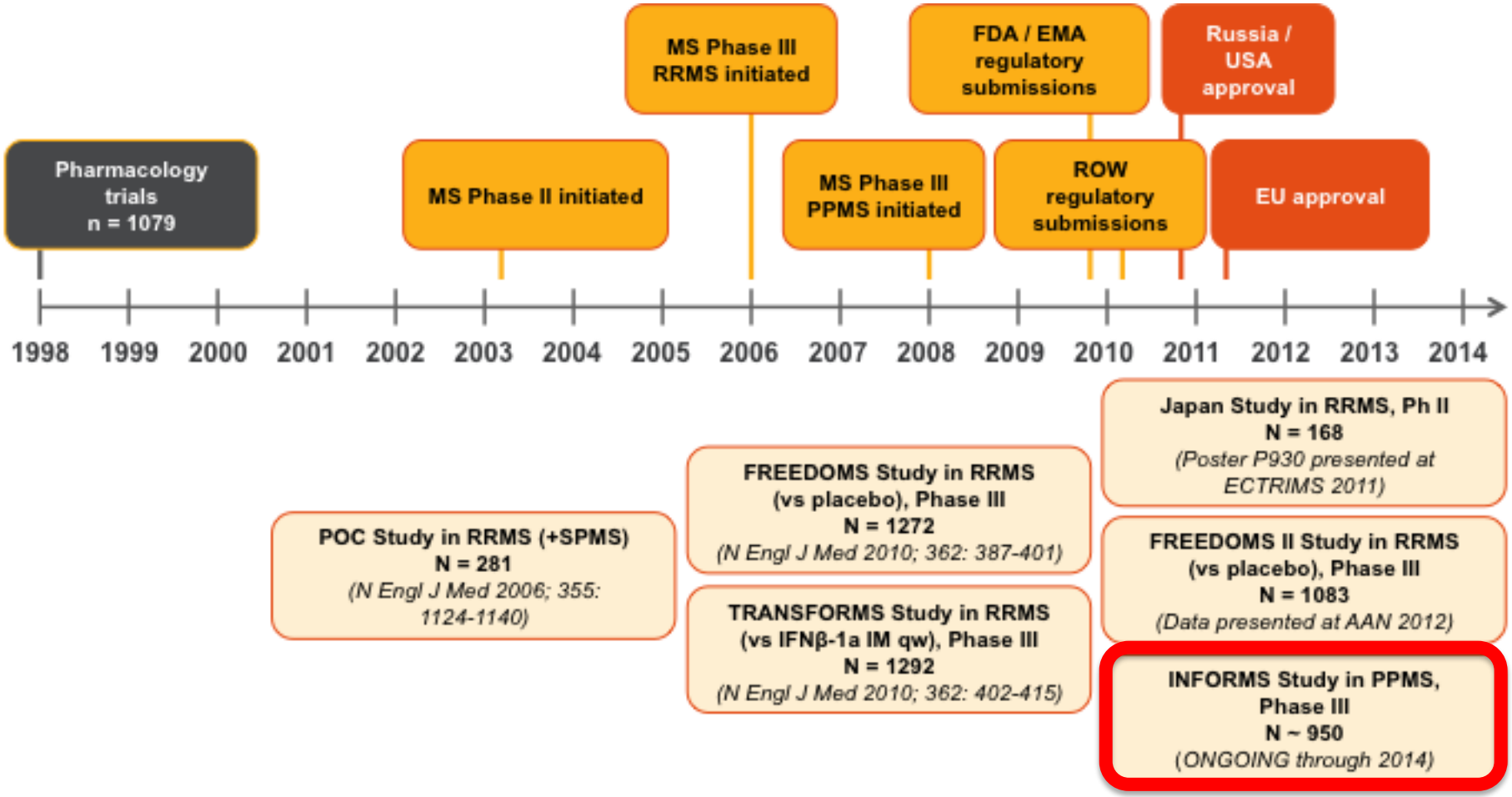
- Thyroid disorders
  - 94.3% mild or moderate in severity
  - Responded to standard treatment
  - No ophthalmopathy or thyrotoxicosis
- Immune thrombocytopenia
  - Detected through clinical and laboratory monitoring
  - Most responded to first-line treatment with prompt and sustained responses; 1 patient underwent splenectomy during the extension study

CARE-MS II

Forthcoming drugs: alemtuzumab

Alemtuzumab for multiple sclerosis: who and when to treat?

Primary Progressive: fingolimod



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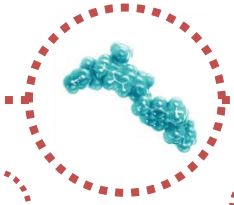
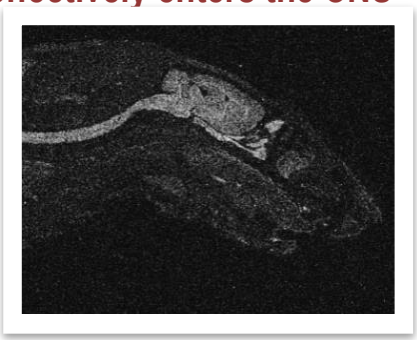
Primary Progressive: ocrelizumab

Patient population	Relapsing multiple sclerosis (RMS)		Primary progressive multiple sclerosis (PPMS)
Phase/study	**Phase III OPERA I**	**Phase III OPERA II**	**Phase III ORATORIO**
# of patients	N=800	N=800	N=630
Design	• 96-week treatment period: ▪ **ARM A:** Ocrelizumab 2x 300 mg IV every 24 weeks ▪ **ARM B:** Rebif® (interferon β-1a)	• 96-week treatment period: ▪ **ARM A:** Ocrelizumab 2x 300 mg IV every 24 weeks ▪ **ARM B:** Rebif® (interferon β-1a)	• 120-week treatment period: ▪ **ARM A:** Ocrelizumab 2x 300 mg IV every 24 weeks ▪ **ARM B:** Placebo
Primary endpoint	▪ Annualized relapse rate at 96 weeks versus Rebif	▪ Annualized relapse rate at 96 weeks versus Rebif	▪ Sustained disability progression versus placebo by Expanded Disability Status Scale (EDSS)
Status	▪ Expect FPI Q3 2011	▪ Expect FPI Q3 2011	▪ FPI Q1 2011

Secondary Progressive: siponimod

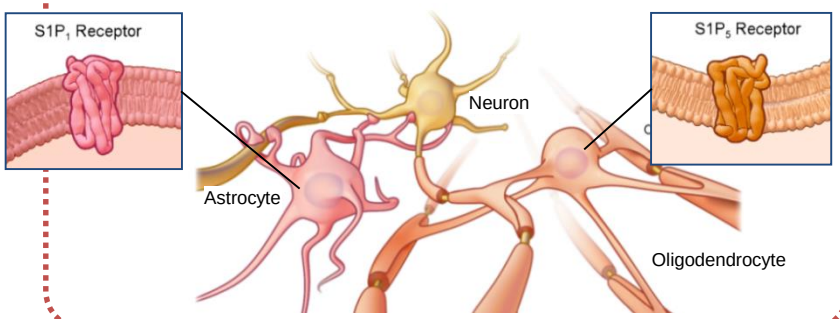


Preclinical data confirms siponimod effectively enters the CNS *



** Clinical significance not yet known*

Siponimod may modulate central $S1P_{1,5}$ receptors to impact CNS inflammation, degeneration, and/or repair mechanisms



30 countries

EXPAND

1530 SPMS patients

Phase III program designed to evaluate the potential of siponimod as a daily oral therapy to delay progression of disability in patients with SPMS

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Secondary Progressive: natalizumab

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Example: "Heart attack" AND "Los Angeles"
Search for studies: Search
Advanced Search | Help | Studies by Topic | Glossary

Find Studies | About Clinical Studies | Submit Studies | Resources | About This Site

Home > Find Studies > Study Record Detail

Text Size

A Clinical Study of the Efficacy of Natalizumab on Reducing Disability Progression in Subjects With SPMS (ASCEND in SPMS)

This study is currently recruiting participants.

Verified April 2013 by Biogen Idec

Sponsor:
Biogen Idec

Collaborator:
Elan Pharmaceuticals

Information provided by (Responsible Party):
Biogen Idec

ClinicalTrials.gov Identifier:
NCT01416181

First received: July 21, 2011
Last updated: April 20, 2013
Last verified: April 2013
History of Changes

Remyelination

Anti-Lingo-1

Still to go into phase II

Histamine 3 Receptor Antagonist

Ongoing phase II trial

Mesenchymal stem cell transplantation

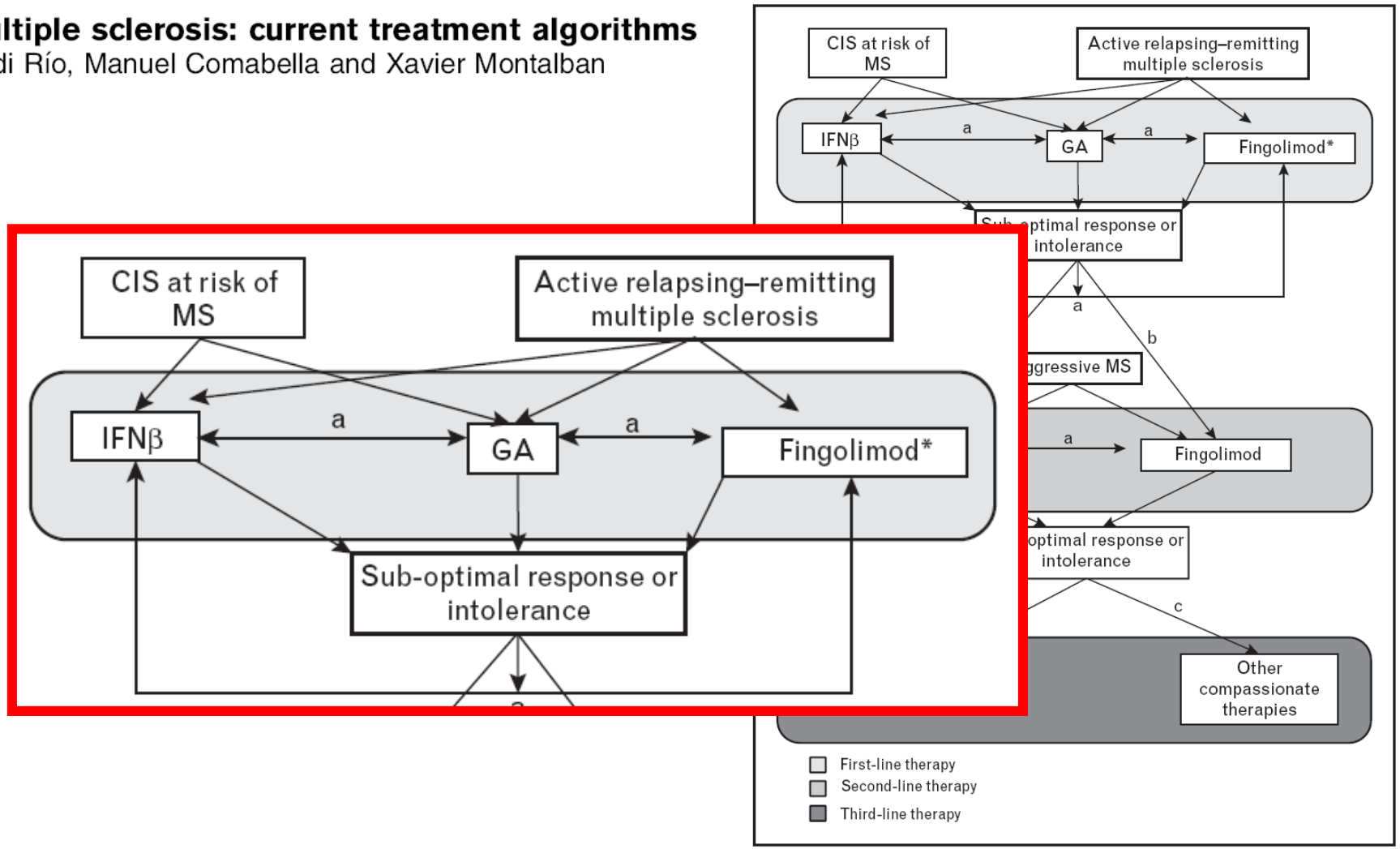
Autologous mesenchymal stem cells for the treatment of secondary progressive multiple sclerosis: an open-label phase 2a proof-of-concept study

Peter Connick, Madhan Kolappan,* Charles Crawley, Daniel J Webber, Rickie Patani, Andrew W Michell, Ming-Qing Du, Shi-Lu Luan, Daniel R Altmann, Alan J Thompson, Alastair Compston, Michael A Scott, David H Miller, Siddharthan Chandran*

Conclusions

Conclusions: treatment algorithms

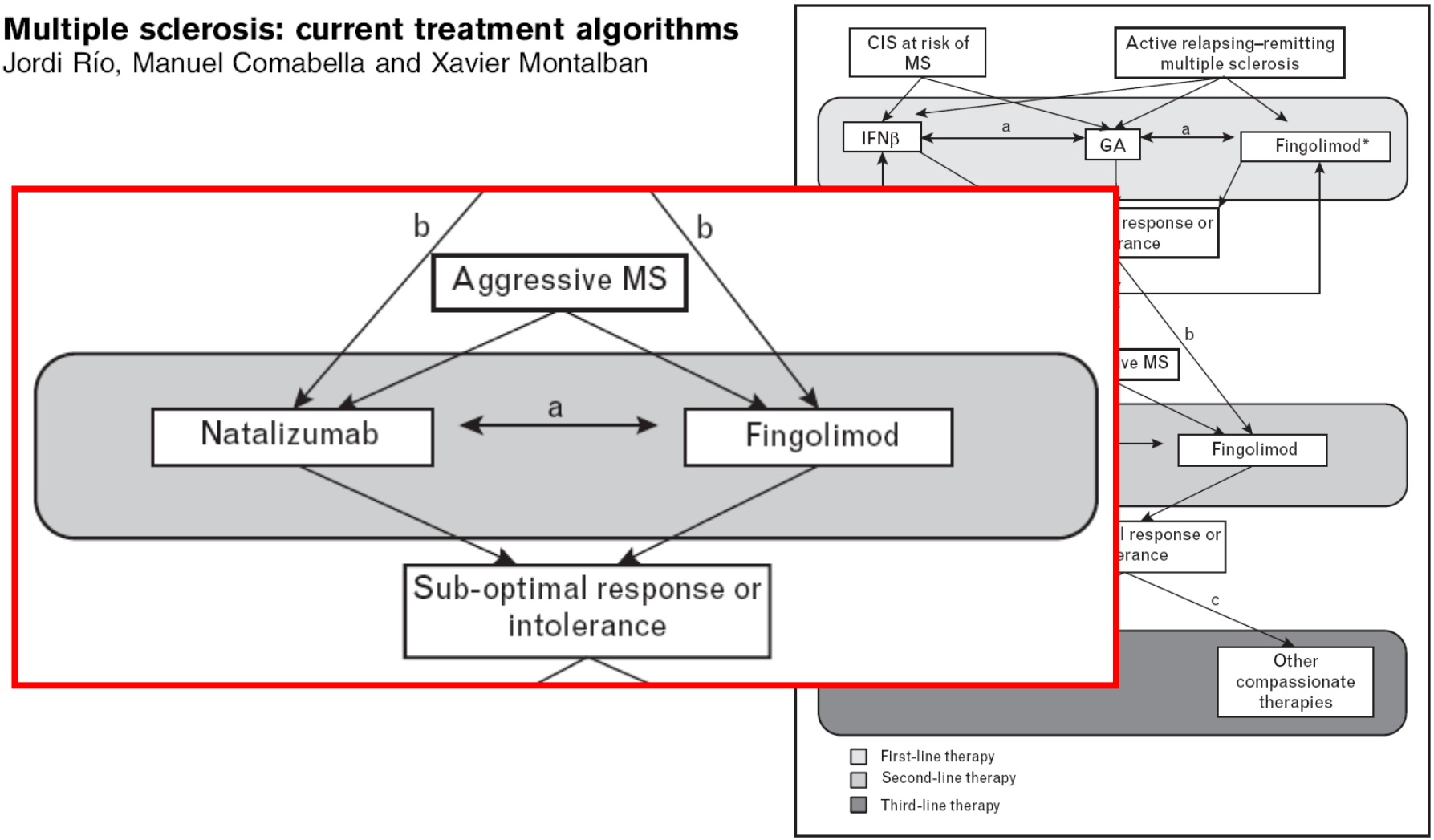
Multiple sclerosis: current treatment algorithms
Jordi Río, Manuel Comabella and Xavier Montalban



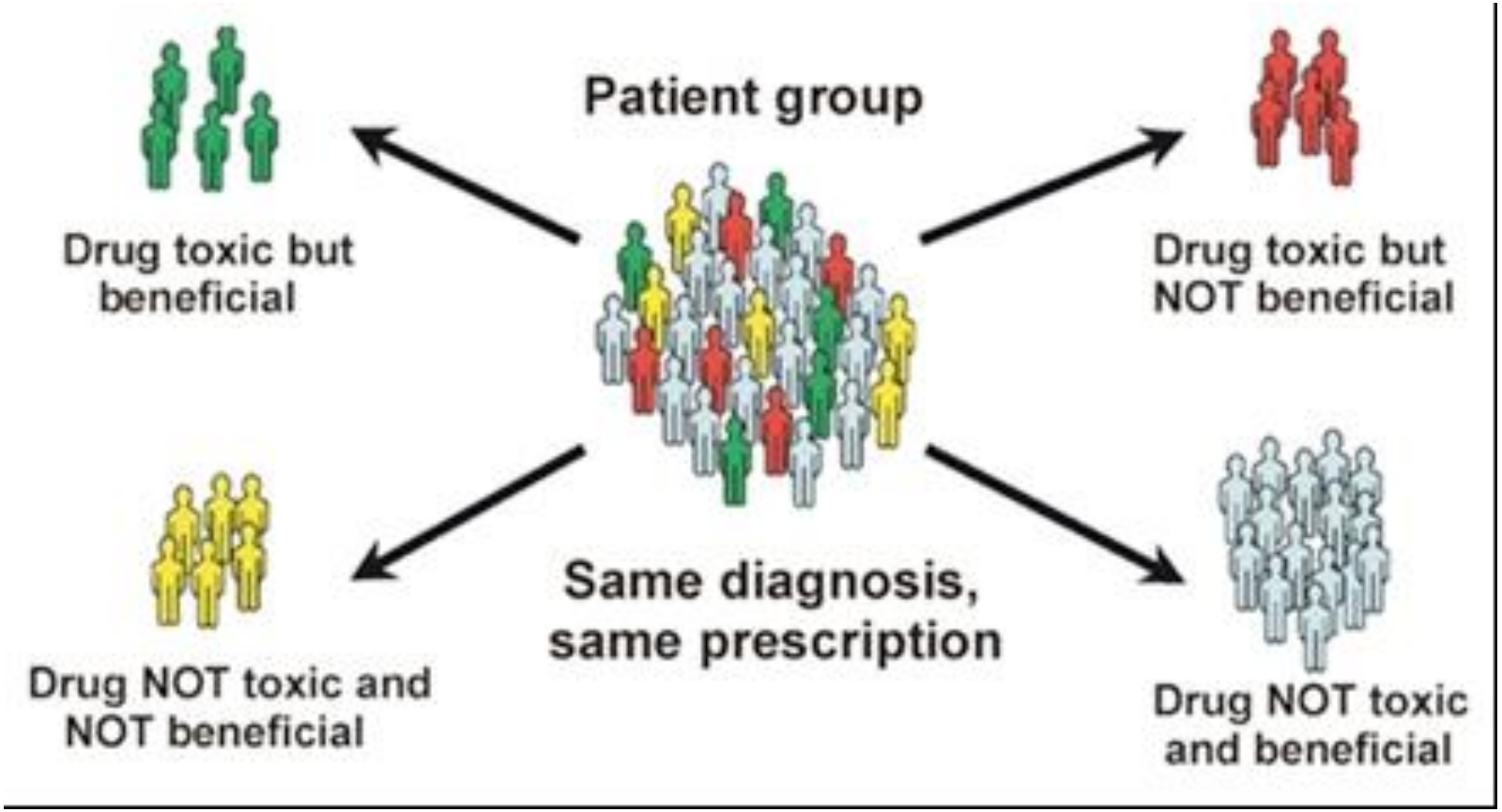
Current Opinion in Neurology 2011, 24:230–237

Conclusions: treatment algorithms

Multiple sclerosis: current treatment algorithms
Jordi Río, Manuel Comabella and Xavier Montalban



Personalized medicine



From: http://mytorontocanadambastudentexperience.blogspot.com.es/2012/10/personalized-medicine-or-p4-medicine.html

Many thanks to Xavier Montalban, Mar Tintoré & everybody at

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Centre d'Esclerosi Múltiple de Catalunya

UNiC 2010

UNeR 2008

CARM 2010

IDI INSTITUT DE DIAGNÒSTIC PER LA IMATGE

Vall d'Hebron Institut de Recerca

Vall d'Hebron Hospital

Fundació Esclerosi Múltiple

UAB Universitat Autònoma de Barcelona

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Centre d'Esclerosi Múltiple de Catalunya

What are the real choices? Therapy options for people with MS in 2013 and beyond

Jaume Sastre-Garriga

Servei de Neurologia / Neuroimmunologia

Centre d'Esclerosi Múltiple de Catalunya – Cemcat

Hospital Universitari Vall d'Hebron, Barcelona

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