

Newer developments in the management of multiple sclerosis and other neuroinflammatory diseases

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Neuroimmunology and MS Clinic:

Outpatient & Day Clinic, Neuroimmunology & Neurooncology Ward

8 physicians, 3 nurses, 1 neuropsychologist

- 2800 patients on file
- > 3000 frequencies (2012)

Neuroimmunology and MS Research Unit:

Research Lab (M. Reindl) & CSF Lab (F. Deisenhammer)

1 molecular biologist, 6 PhD students, 8 technicians

- Biomarkers in MS / NMO / immunoneuropathies
- Antidrug antibodies in MS
- Treatment trials

Disclosures

Thomas Berger has participated in meetings sponsored by and received honoraria (lectures, advisory boards, consultations) from pharmaceutical companies marketing treatments for multiple sclerosis: Allergan, AOP, Baxter, Bayer (Schering), Biogen Idec, Biotest, CSL Behring, Genzyme, Merck (Serono), Novartis, ratiopharm, Sanofi Aventis, TEVA.

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Learning objectives

- Differential diagnosis of a first demyelinating event
- Expectations on new treatments in MS
- Treatment concepts in MS
- New treatments along these concepts
- Benefit-risk evaluations
- Individual treatment strategy and pathway

Cases 1-4: *The Histories*

1. GW, m, 35y; since 1 week ascending hypesthesia, finally up to right fingers. *CTS left some years ago.*

2. WJ, m, 58y; since 1 week progressive hypesthesia/weakness right UL, now also right LL. *Hypertension; trauma right shoulder 10 days ago.*

3. SC, f, 49y; since 1 week progressive hypesthesia/pain/weakness left UL, then also right UL and both LL. *CTS right; absolute vertebrostenosis C6/7.*

4. ES, f, 30y; since 1 week progressive hypesthesia/weakness both LL, urinary incontinence. *UTI 4 weeks ago.*

DD acute (transverse-) myelitis

Cases 1-4: *The Evoked Potentials*

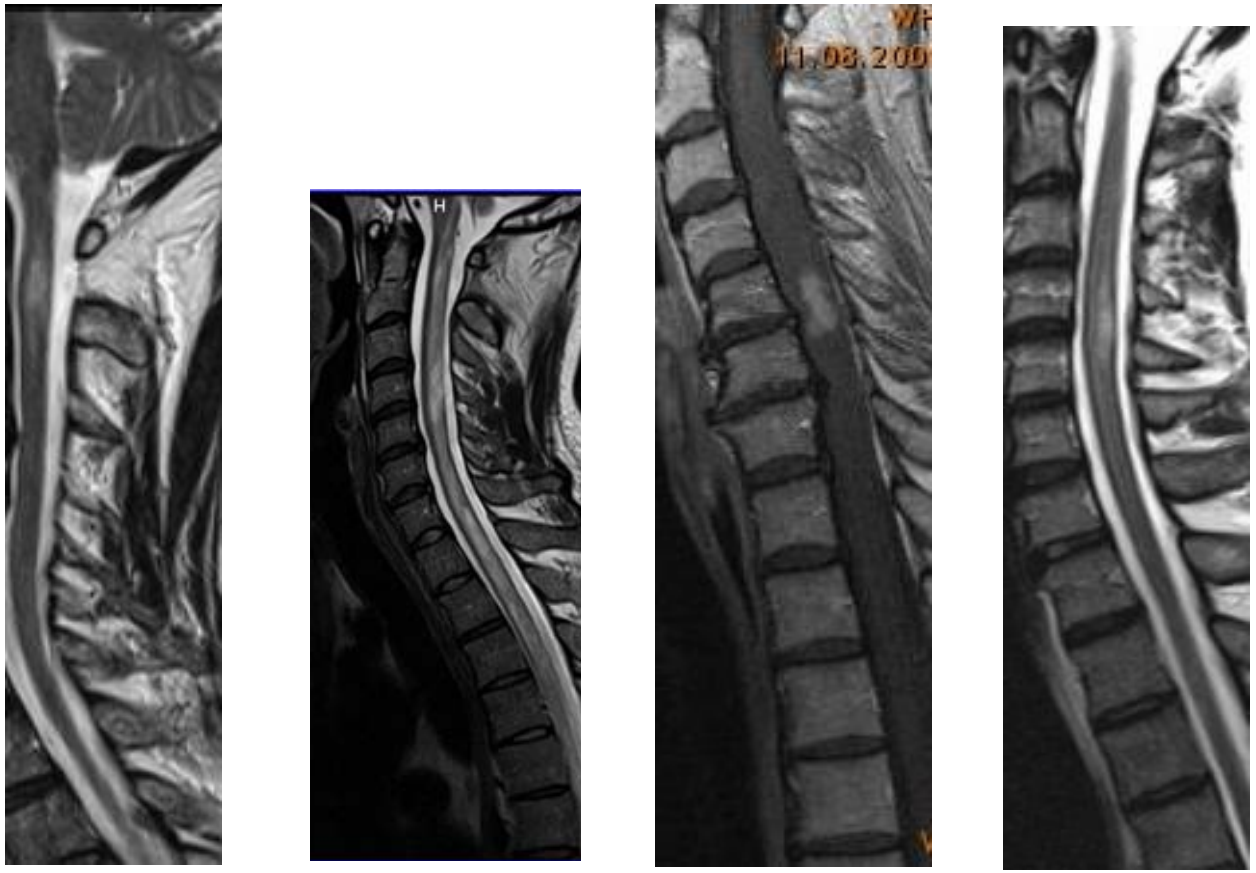
1. GW, m, 35y; pathological: Tib SEP right; MEP LL left; VEP right

2. WJ, m, 58y; pathological: Med/Tib SEP both; VEP n.d.

3. SC, f, 49y; pathological: Med SEP left

4. ES, f, 30a; pathological: Med/Tib SEP both; MEP UL/LL both; VEP both

Cases 1-4: *The MRI Findings*



Case 1

GW, m, 35y

History: since 1 week ascending hypesthesia, finally up to right fingers.

CTS left some years ago.

N-exam: incomplete SC syndrome C8

EVP: pathological: Tib SEP right; MEP LL left; VEP right

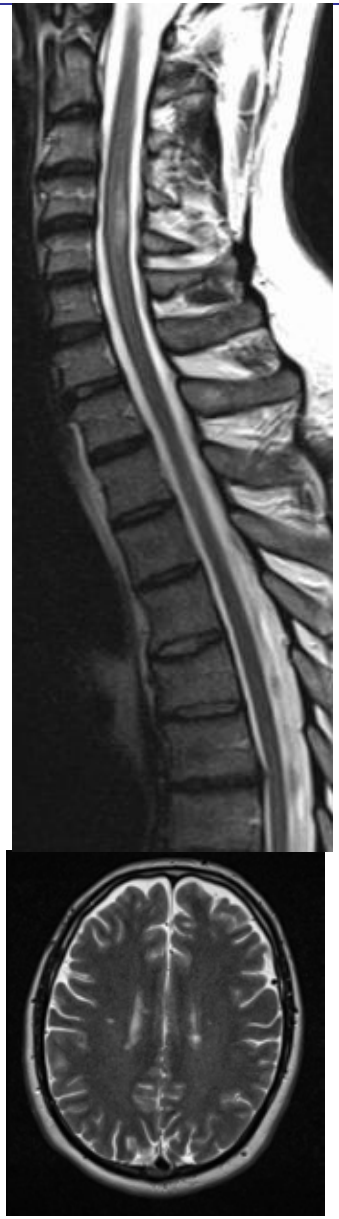
CSF:

cc 15/µl, some lympho; protein 54; IgG-index 1.06; OCB+

other findings:

anti-AQP-4 antibodies negative; all other lab exams negative

diagnosis: multiple sclerosis



Case 2

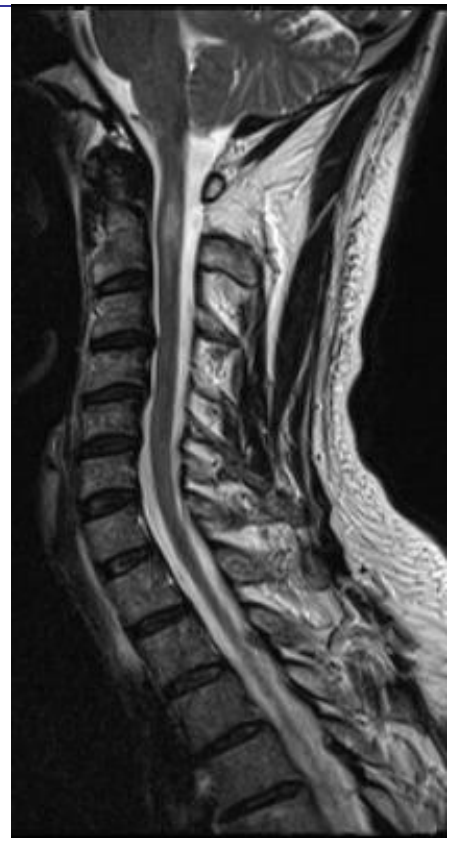
WJ, m, 58y

History: since 1 week progressive hypesthesia/weakness right UL, now also right LL.

Hypertension; trauma right shoulder 10 days ago.

N-exam: weakness C6 right, hypesthesia C5-7 right

EVP: pathological: Med/Tib SEP both; VEP n.d.



CSF:

cc 23/µl, some lympho; protein 36; IgG-index 0.62; OCB+

other findings:

all normal/negative

diagnosis: acute transverse myelitis

Case 3

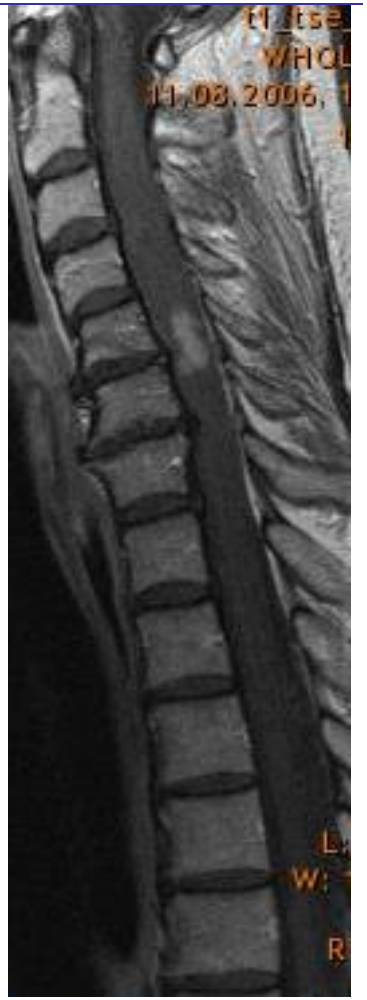
SC, f, 49y

History: since 1 week progressive hypesthesia/pain/weakness left UL, then also right UL and both LL.

CTS right; absolute vertebrostenosis C6/7.

N-exam: incomplete SC syndrome C5

EVP: pathological: Med SEP left



CSF:

1) cc 6/µl, some lympho; protein 48; IgG-index 0.45; OCB-

2) cc 7/µl, some lympho; protein 72; IgG-index 0.62; OCB-

other findings:

serum ACE 75 U/l; FDG-PET: pathological mediastinal LN; CT chest: multiple enlarged LN; LN biopsy: granulomatous lymphadenitis, granulomas with epitheloid cells

diagnosis: (neuro-) sarcoidosis

Case 4

ES, w, 30y

History: since 1 week progressive hypesthesia/weakness both LL, urinary incontinence.

UTI 4 weeks ago.

N-exam: complete SC syndrome D6, neurogenic bladder dysfunction

EVP: pathological Med/Tib SEP both; MEP UL/LL both; VEP both

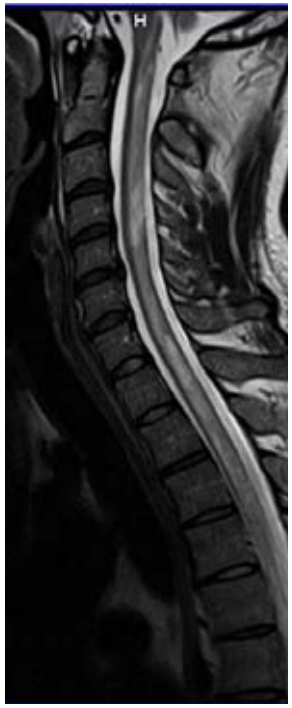
CSF:

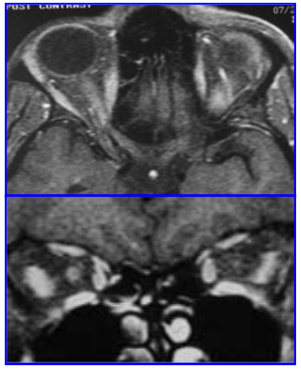
cc 9/µl, some lympho; protein 42; IgG-index n.d.; OCB-

other findings:

anti-AQP-4 antibodies positiv, 1:40.960

diagnosis: neuromyelitis optica





DDx: CIS / ADEM / NMO

	CIS	ADEM	NMO-spectrum
age	adults >> children	children >> adults	any age
symptoms & disease course	mainly mono-symptomatic; moderate relapse, good remission	impaired consciousness, fever, meningeal signs (children), seizures; often polysymptomatic; often dramatic severe onset, usually good remission	ON, myelitis, rarely other CNS symptoms; usually severe relapses, early disability
MRI	periventricular, ovoid lesions („Dawson fingers“)	large (tumour-like) lesions (white and grey matter), often reversible	LETM (≥3 segments, white and grey matter), brainstem, hypothalamus
CSF	cell count: <50/µl; OCB pos. (permanent)	cell count variable; OCB rarely pos. (transient)	cell count variable; OCB rarely pos. (transient)
other issues		post-infectious/-vaccine MOG antibodies (?)	AQP-4 antibodies MOG antibodies (?)
diagnostic criteria	McDonald (2010)	NMSS Task Force (2008)	Wingerchuk (2006)
treatment	Acute: HDMP (PLEX) DMT: IFNß-1a/b, GLAT	Acute: HDMP – PLEX DMT: not necessary	Acute: HDMP – PLEX DMT: AZA, α-CD20 mAb

Current & future MS treatment

Considerations

- Change of expectations
- Immunopathogenetic rationales
- Prognosis & risks
- Treatment options / concepts
- Patients‘ expectations & adherence
- Benefit-risk evaluation
- Disease & treatment monitoring

à Individual treatment desicion

Communication

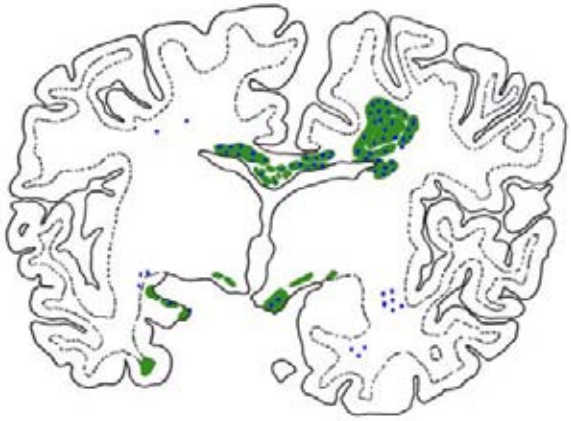
Neuropathology of MS

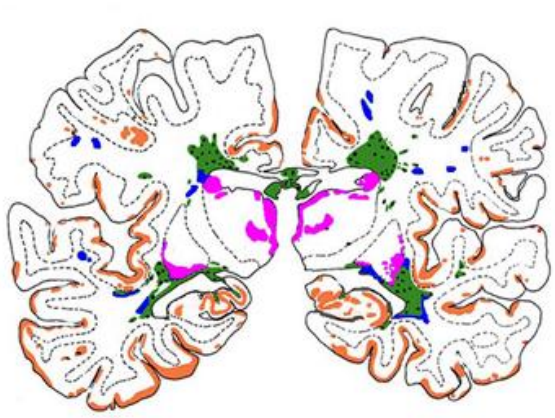
Pathological differences between RRMS and CPMS (SPMS, PPMS)

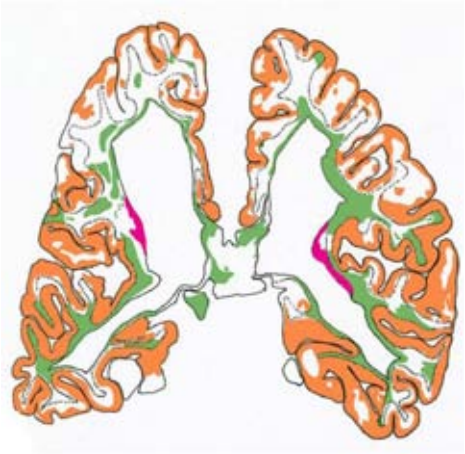
RRMS RPMS SPMS / PPMS

- New waves of inflammation entering the CNS from circulation
- Focal demyelinating lesions with variable axonal injury and blood brain barrier injury mainly in the WM

- Compartmentalized inflammation in CNS
- Slow expansion of pre-existing WM lesions
- Diffuse inflammation and axonal injury in NAWM
- Extensive cortical demyelination



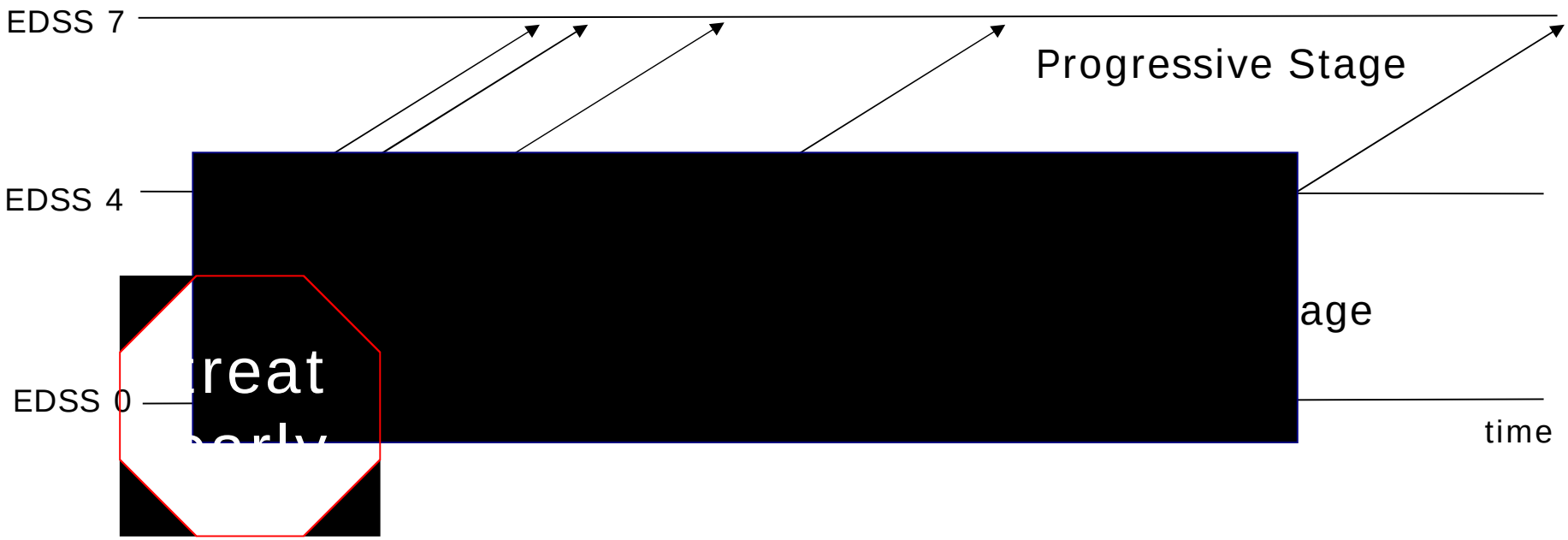




Kutzelnigg et al 2005, Hochmeister et al 2006, Frischer et al 2009

Treatment

rationale – concept #1 („the classical way“)



Progression from EDSS 0-4 (inflammatory phase): 1-32 years

Progression from EDSS 4-7 (degenerative phase): 7-11 years

Confavreux et al., NEJM 2000

DMTs in RRMS:
treatment effects

NNT calculations

Annualized relapse rate over 2 years					
Trial	Placebo	DMT	Absolute reduction		Relative reduction
IM IFN?P1a 30 µg qw (Jacobs 1996)	0.90	0.61	0.29		0.32
SC IFN?x1a 22 µg tiw (PRISMS 1998)	1.28	0.91	0.37		0.29
SC IFN?O1a 44 µg tiw (PRISMS 1998)	1.28	0.87	0.41		0.32
IFN?&1b 250 µg qod (IFNMSSG 1993)	1.27	0.84	0.43		0.34
GA 20 mg qd (Johnson 1995)	0.84	0.59	0.25		0.30

Treatment

New approved DMT's in RRMS

FDA NEWS RELEASE

For Immediate Release: Sept. 12, 2012
Media Inquiries: Sandy Walsh, 301-796-4669, sandy.walsh@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves new multiple sclerosis treatment Aubagio

The U.S. Food and Drug Administration today approved Aubagio (teriflunomide), a once-a-day tablet for the treatment of adults with relapsing forms of multiple sclerosis (MS).

Paris, France – August 30, 2013 – Sanofi (EURONEXT: SAN and NYSE: SNY) and its subsidiary Genzyme announced today that the European Commission has granted marketing authorization for Aubagio® (teriflunomide) 14 mg, a once-daily, oral therapy indicated for the treatment of adult patients with relapsing remitting multiple sclerosis (RRMS).

FDA NEWS RELEASE

For Immediate Release: March 27, 2013
Media Inquiries: Stephanie Yao, 301-796-0394, stephanie.yao@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves new multiple sclerosis treatment: Tecfidera

The U.S. Food and Drug Administration today approved Tecfidera (dimethyl fumarate) capsules to treat adults with relapsing forms of multiple sclerosis (MS).

On 21 March 2013, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Tecfidera 120 mg and 240 mg, gastro-resistant hard capsules, intended for the treatment of adult patients with relapsing remitting multiple sclerosis.

Teriflunomide

Phase III clinical trial: TEMSO

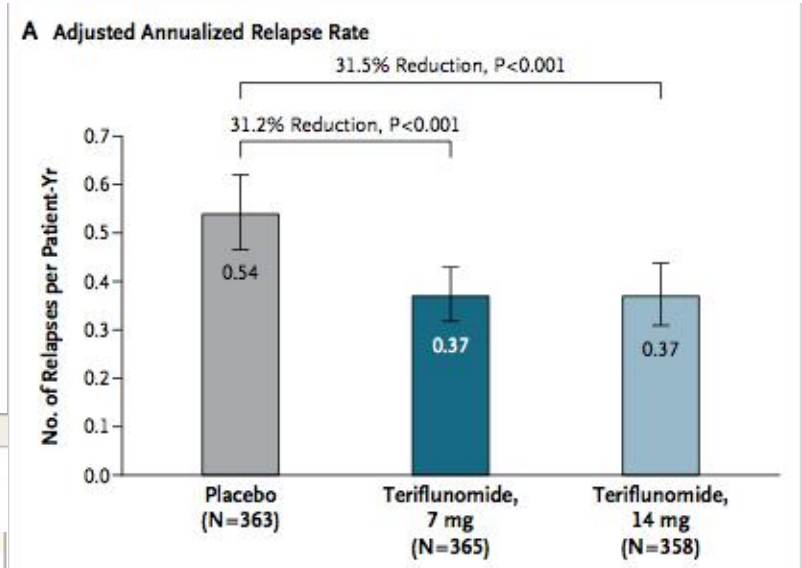
N Engl J Med 2011;365:1293-303.

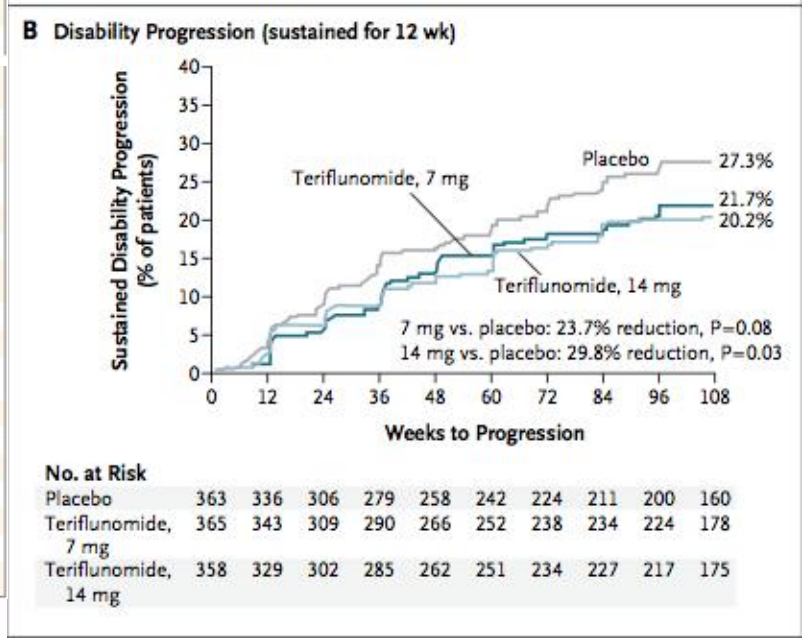
Randomized Trial of Oral Teriflunomide for Relapsing Multiple Sclerosis

Paul O'Connor, M.D., Jerry S. Wolinsky, M.D., Christian Confavreux, M.D., Giancarlo Comi, M.D., Ludwig Kappos, M.D., Tomas P. Olsson, M.D., Ph.D., Hadj Benzerdjeb, M.D., Philippe Truffinet, M.D., Lin Wang, Ph.D., Aaron Miller, M.D., and Mark S. Freedman, M.D., for the TEMSO Trial Group*

Table 2. Clinical and MRI Results.*

Variable	Placebo (N=363)	Teriflunomide, 7 mg (N=365)	Teriflunomide, 14 mg (N=358)	P Value: Teriflunomide, 7 mg, vs. Placebo	P Value: Teriflunomide, 14 mg, vs. Placebo
MRI outcomes					
Total lesion volume					
Change from baseline — ml	2.21±7.00	1.31±6.80	0.72±7.59	0.03	<0.001
Relative reduction vs. placebo — %**		39.4	67.4		
Volume of hypointense lesions on T_1-weighted images					
Change from baseline — ml	0.53±1.06	0.50±1.15	0.33±1.01	0.19	0.02
Relative reduction vs. placebo — %**		16.7	31.3		
Volume of hyperintense lesion components on T_2-weighted images††					
Change from baseline — ml	1.67±6.47	0.81±6.18	0.39±6.90	0.04	<0.001
Relative reduction vs. placebo — %**		44.0	76.7		
Gadolinium-enhancing lesions per T_1-weighted scan¶					
Estimated no. (95% CI)	1.33 (1.06–1.67)	0.57 (0.43–0.75)	0.26 (0.17–0.41)	<0.001	<0.001
Relative risk (95% CI)		0.43 (0.31–0.59)	0.20 (0.12–0.32)		
Absence of gadolinium-enhancing lesions on T_1-weighted images — no. of patients (%)‡‡	135 (39.0)	180 (51.4)	218 (64.1)	<0.001	<0.001
Unique active lesions per scan¶					
Estimated no. (95% CI)	2.46 (2.10–2.89)	1.29 (1.07–1.54)	0.75 (0.58–0.99)	<0.001	<0.001
Relative risk (95% CI)		0.52 (0.42–0.65)	0.31 (0.23–0.41)		
Brain parenchymal fraction§§					
Change from baseline‖	−0.004±0.001	−0.003±0.001	−0.003±0.001	0.19	0.35
Difference vs. placebo‖		0.001±0.001	0.001±0.001		
Relative reduction vs. placebo — %		25.0	25.0		





Dimethylfumarate (BG-12)

Phase III clinical trial: DEFINE

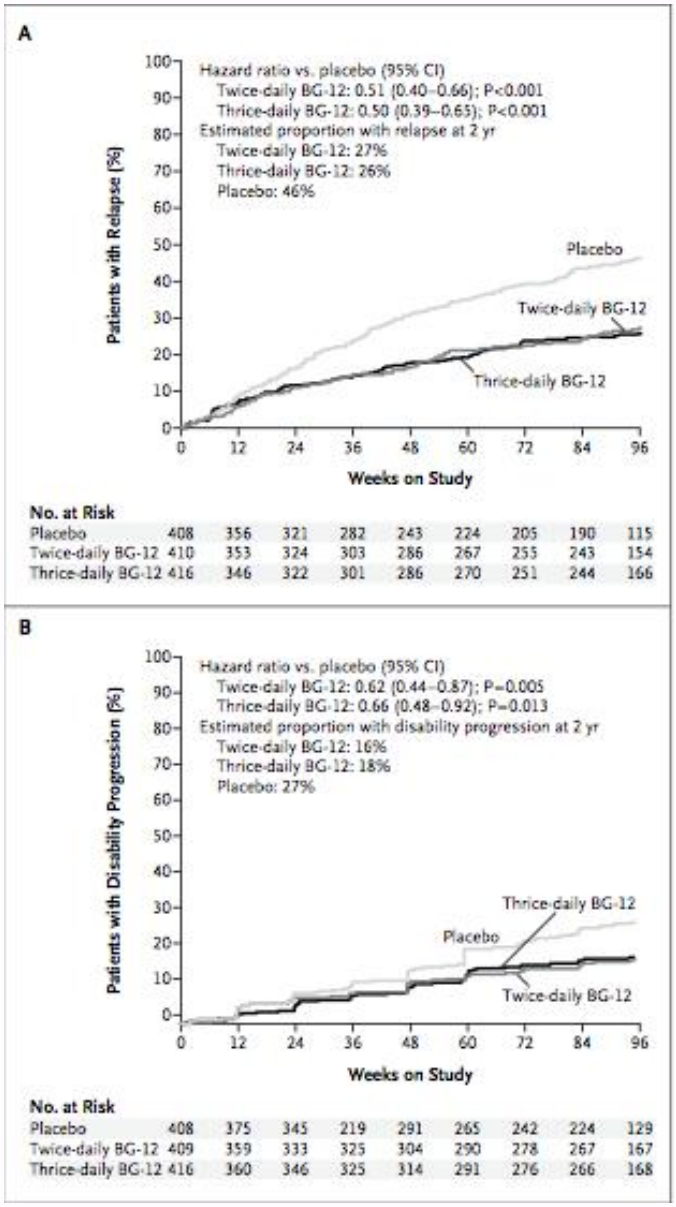
N Engl J Med 2012;367:1098-107.

Placebo-Controlled Phase 3 Study of Oral BG-12 for Relapsing Multiple Sclerosis

Ralf Gold, M.D., Ludwig Kappos, M.D., Douglas L. Arnold, M.D., Amit Bar-Or, M.D., Gavin Giovannoni, M.D., Krzysztof Selmaj, M.D., Carlo Tornatore, M.D., Marianne T. Sweetser, M.D., Ph.D., Minhua Yang, M.S., Sarah I. Sheikh, M.D., and Katherine T. Dawson, M.D., for the DEFINE Study Investigators*

Table 2. Clinical and MRI End Points during the 96-Week Study.*

End Point	Placebo (N=408)	Twice-Daily BG-12 (N=410)	Thrice-Daily BG-12 (N=416)
Patients with relapse at 2 yr — %†	46	27	26
Hazard ratio vs. placebo (95% CI)	—	0.51 (0.40–0.66)‡	0.50 (0.39–0.65)‡
Odds ratio vs. placebo (95% CI)§	—	0.42 (0.31–0.57)‡	0.41 (0.30–0.56)‡
Time to first relapse, 25th percentile — wk¶	38	87	91
Annualized relapse rate at 2 yr			
Adjusted relapse rate (95% CI)‖	0.36 (0.30–0.44)	0.17 (0.14–0.21)	0.19 (0.15–0.23)
Rate ratio vs. placebo (95% CI)	—	0.47 (0.37–0.61)‡	0.52 (0.40–0.67)‡
Confirmed progression of disability at 2 yr			
Patients with progression sustained for 12 wk — %†	27	16**	18
Hazard ratio vs. placebo (95% CI)		0.62 (0.44–0.87)††	0.66 (0.48–0.92)‡‡
MRI assessments			
New or newly enlarging T_2-weighted lesions at 2 yr as compared with baseline			
Adjusted mean no. of lesions (95% CI)	17.0 (12.9–22.4)	2.6 (2.0–3.5)	4.4 (3.2–5.9)
Ratio of adjusted mean no. of lesions in treatment group to adjusted mean no. in placebo group (95% CI)		0.15 (0.10–0.23)‡	0.26 (0.17–0.38)‡
Gadolinium-enhancing T_1-weighted lesions at 2 yr			
Mean no.	1.8±4.2	0.1±0.6	0.5±1.7
Odds ratio vs. placebo (95% CI)	—	0.10 (0.05–0.22)‡	0.27 (0.15–0.46)‡



Dimethylfumarate (BG-12)

Phase III clinical trial: CONFIRM

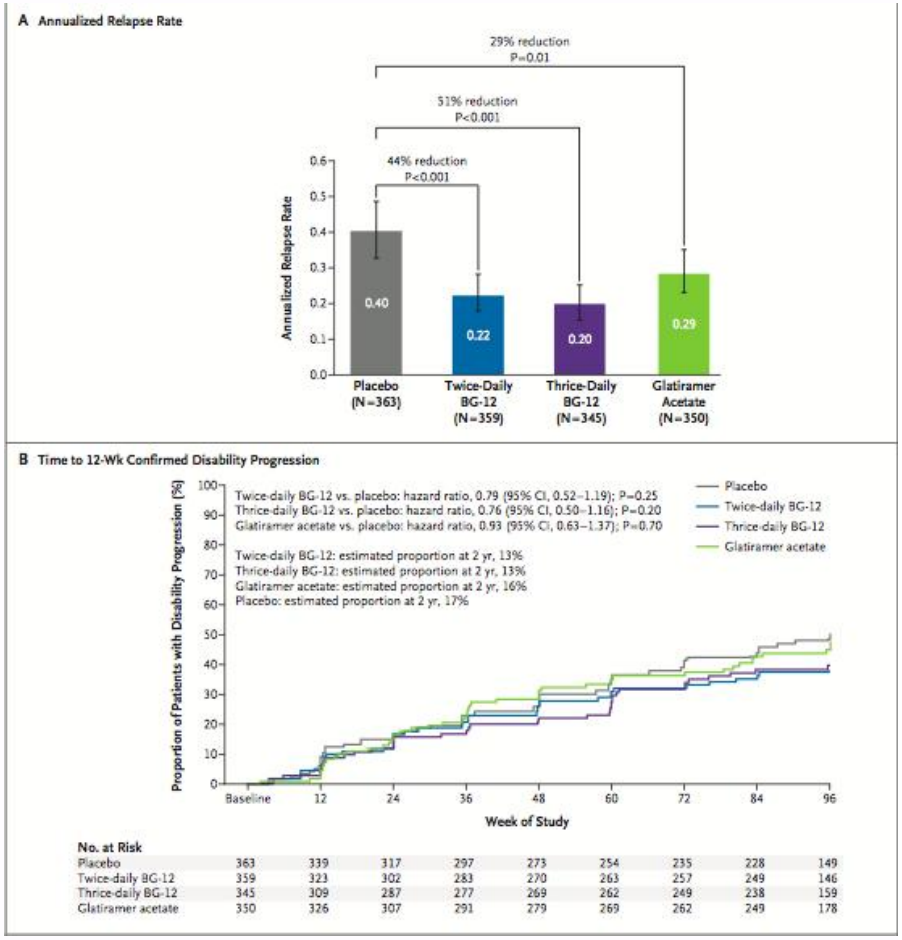
N Engl J Med 2012;367:1087-97.

Placebo-Controlled Phase 3 Study of Oral BG-12 or Glatiramer in Multiple Sclerosis

Robert J. Fox, M.D., David H. Miller, M.D., J. Theodore Phillips, M.D., Ph.D., Michael Hutchinson, F.R.C.P., Eva Havrdova, M.D., Mariko Kita, M.D., Minhua Yang, M.S., Kartik Raghupathi, M.S., Mark Novas, M.D., Marianne T. Sweetser, M.D., Ph.D., Vissia Viglietta, M.D., Ph.D., and Katherine T. Dawson, M.D., for the CONFIRM Study Investigators*

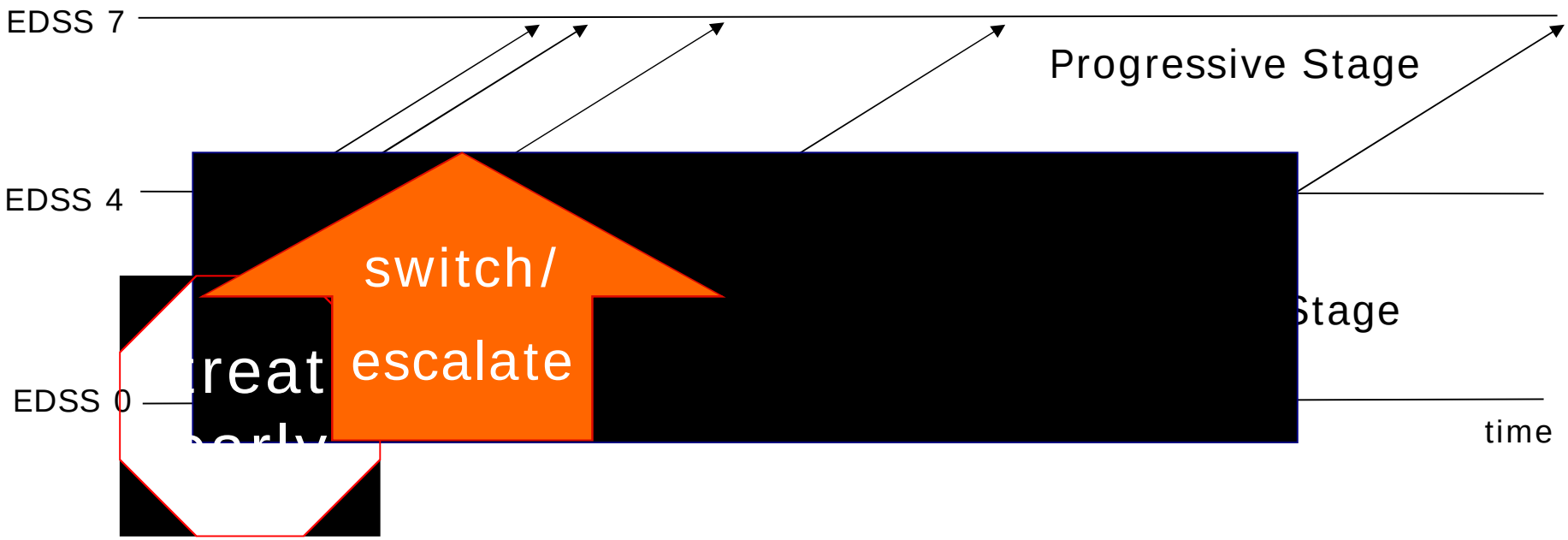
Table 2. Clinical End Points (ITT Population) and MRI End Points (MRI Cohort) during the Study.*

End Point	Placebo (N=363)	Twice-Daily BG-12 (N=359)	Thrice-Daily BG-12 (N=345)	Glatiramer Acetate (N=350)
Annualized relapse rate at 2 yr†				
Rate (95% CI)	0.40 (0.33–0.49)	0.22 (0.18–0.28)	0.20 (0.16–0.25)	0.29 (0.23–0.35)
Percentage reduction vs. placebo (95% CI)		44.0 (26.0–57.7)‡	50.5 (33.8–63.1)‡	28.6 (6.9–45.2)§
Time to first confirmed relapse, 25th percentile — wk¶	30	72	NA‖	57
Estimated proportion of patients with a relapse at 2 yr				
Proportion — %¶	41	29	24	32
Hazard ratio vs. placebo (95% CI)**		0.66 (0.51–0.86)††	0.55 (0.42–0.73)‡	0.71 (0.55–0.92)††
Disability progression at 2 yr				
Estimated proportion of patients with progression confirmed at least 12 wk later — %¶	17	13	13	16
Hazard ratio vs. placebo (95% CI)‡‡		0.79 (0.52–1.19)	0.76 (0.50–1.16)	0.93 (0.63–1.37)
New or enlarging T_2-weighted hyperintense lesions at 2 yr§§				
No. of patients evaluated	139	140	140	153
Adjusted mean no. of lesions (95% CI)	17.4 (13.5–22.4)	5.1 (3.9–6.6)	4.7 (3.6–6.2)	8.0 (6.3–10.2)
Ratio of mean no. of lesions in active-treatment group to mean no. in placebo group (95% CI)		0.29 (0.21–0.41)‡	0.27 (0.20–0.38)‡	0.46 (0.33–0.63)‡
New T_1-weighted hypointense lesions at 2 yr§§				
No. of patients evaluated	139	140	140	154
Adjusted mean no. of lesions (95% CI)	7.0 (5.3–9.2)	3.0 (2.3–4.0)	2.4 (1.8–3.2)	4.1 (3.2–5.3)
Ratio of mean no. of lesions in active-treatment group to mean no. in placebo group (95% CI)		0.43 (0.30–0.61)‡	0.35 (0.24–0.49)‡	0.59 (0.42–0.82)‡
Gadolinium-enhancing lesions at 2 yr§§				
No. of patients evaluated	144	147	144	161
No. of lesions	2.0±5.6	0.5±1.7	0.4±1.2	0.7±1.8
Odds ratio vs. placebo (95% CI)		0.26 (0.15–0.46)‡	0.35 (0.20–0.59)‡	0.39 (0.24–0.65)‡



Treatment

rationale – concept #2 („escalation“)



Progression from EDSS 0-4 (inflammatory phase): 1-32 years

Progression from EDSS 4-7 (degenerative phase): 7-11 years

Confavreux et al., NEJM 2000

Treatment

switch & escalation rationales & options

Rationales:

1) non-responders
2) AE‘s and (increasing) risks
3) non-adherence
4) patient‘s request

Options

- IFNß to IFNß
- IFNß to GLAT and vice versa
- IFNß/GLAT to oral treatment (DMF, TERI, LAQ)
- treatment escalation (Mito, NTZ, FTY, AZM, RXM)
- treatment de-escalation

Multiple Sclerosis Registry
Austrian Society of Neurology (ÖGN)

NTZ treated patients = 1010 (as of May 6, 2013)

females = 70.8%; age = 35.7 years; MS duration = 8.0 years

EDSS 3.3; relapses 12 months prior NTZ start = 2.4

FTY treated patients = 203 (as of May 6, 2013)

females = 76.4%; age = 39.2 years; MS duration = 9.4 years

EDSS 2.6; relapses 12 months prior FTY start = 2.3

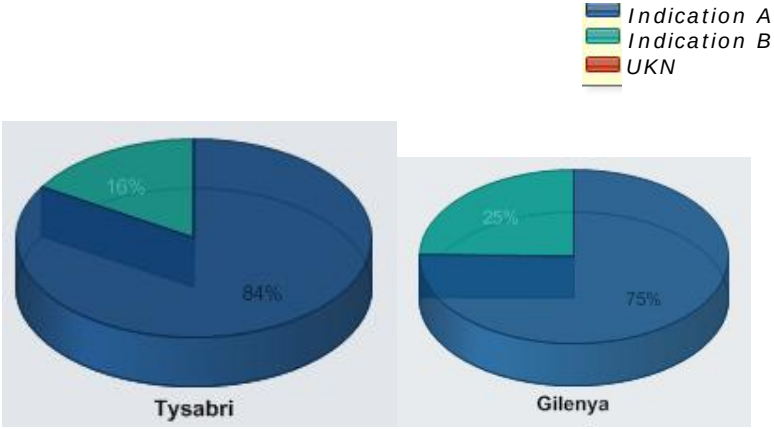


Fig. 2: Annual relapse rate

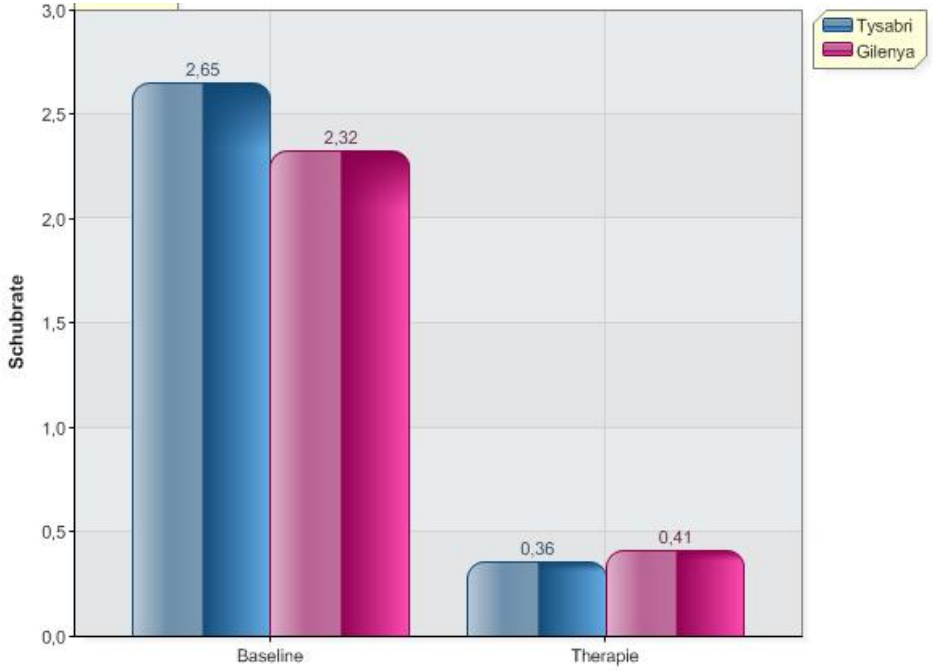
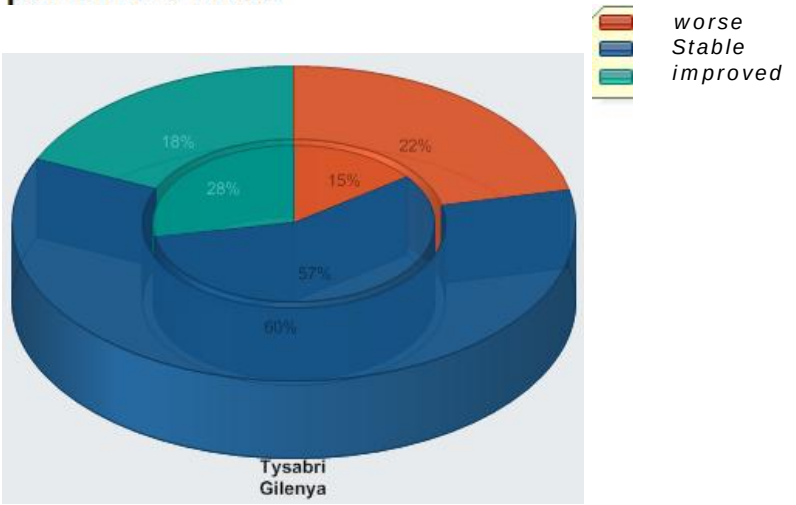
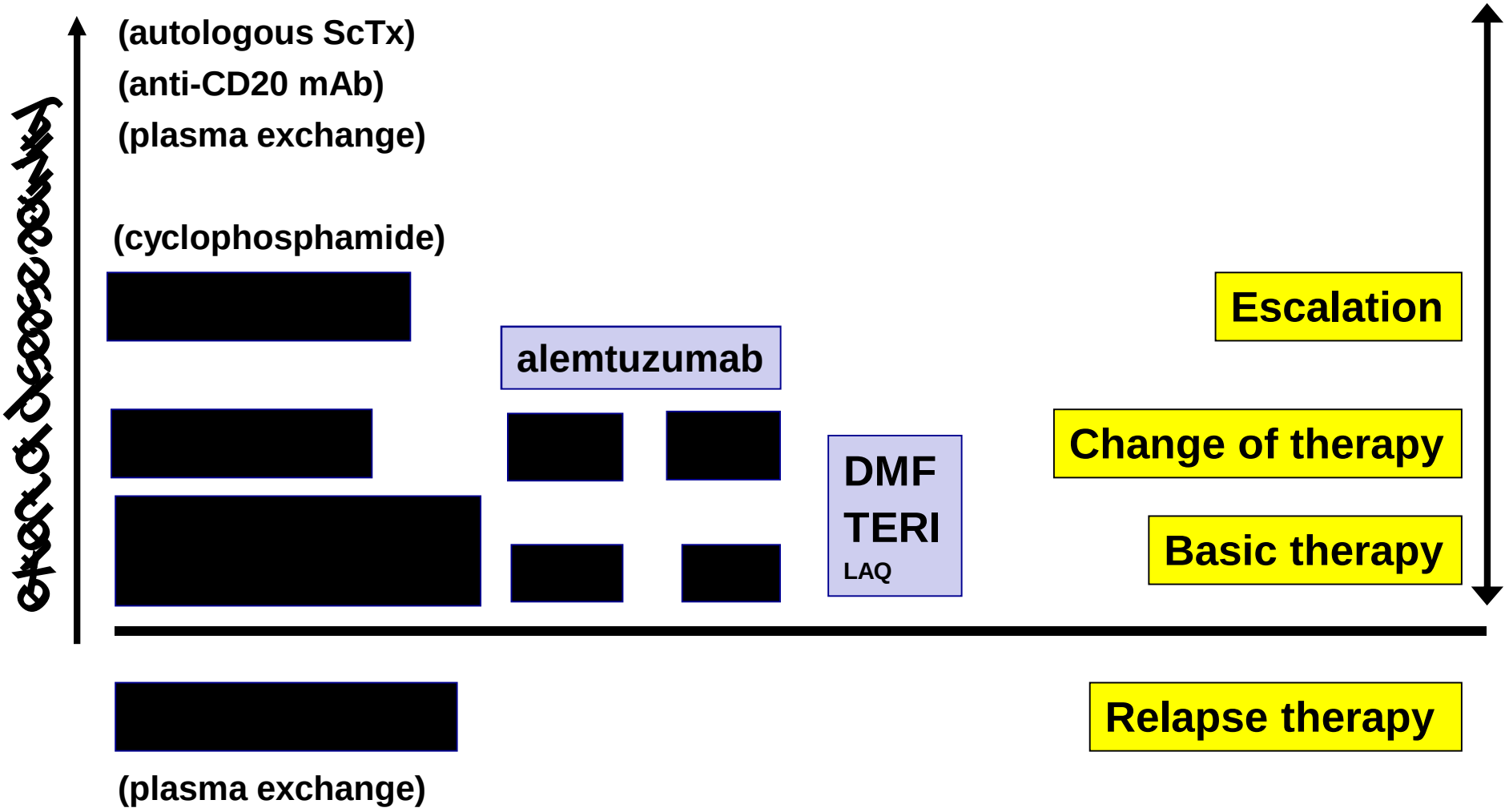


Fig. 4: Change of more than one point in the EDSS



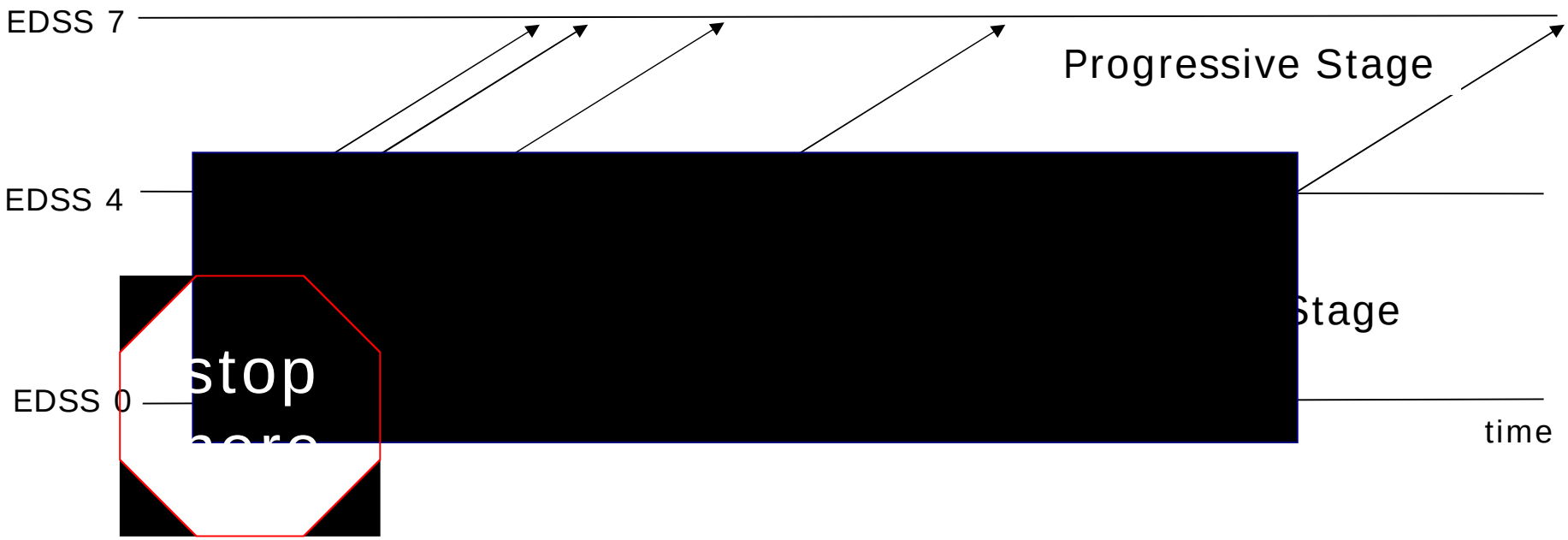
Treatment

Disease modifying therapies



Treatment

rationale – concept #3 („induction“)



Progression from EDSS 0-4 (inflammatory phase): 1-32 years

Progression from EDSS 4-7 (degenerative phase): 7-11 years

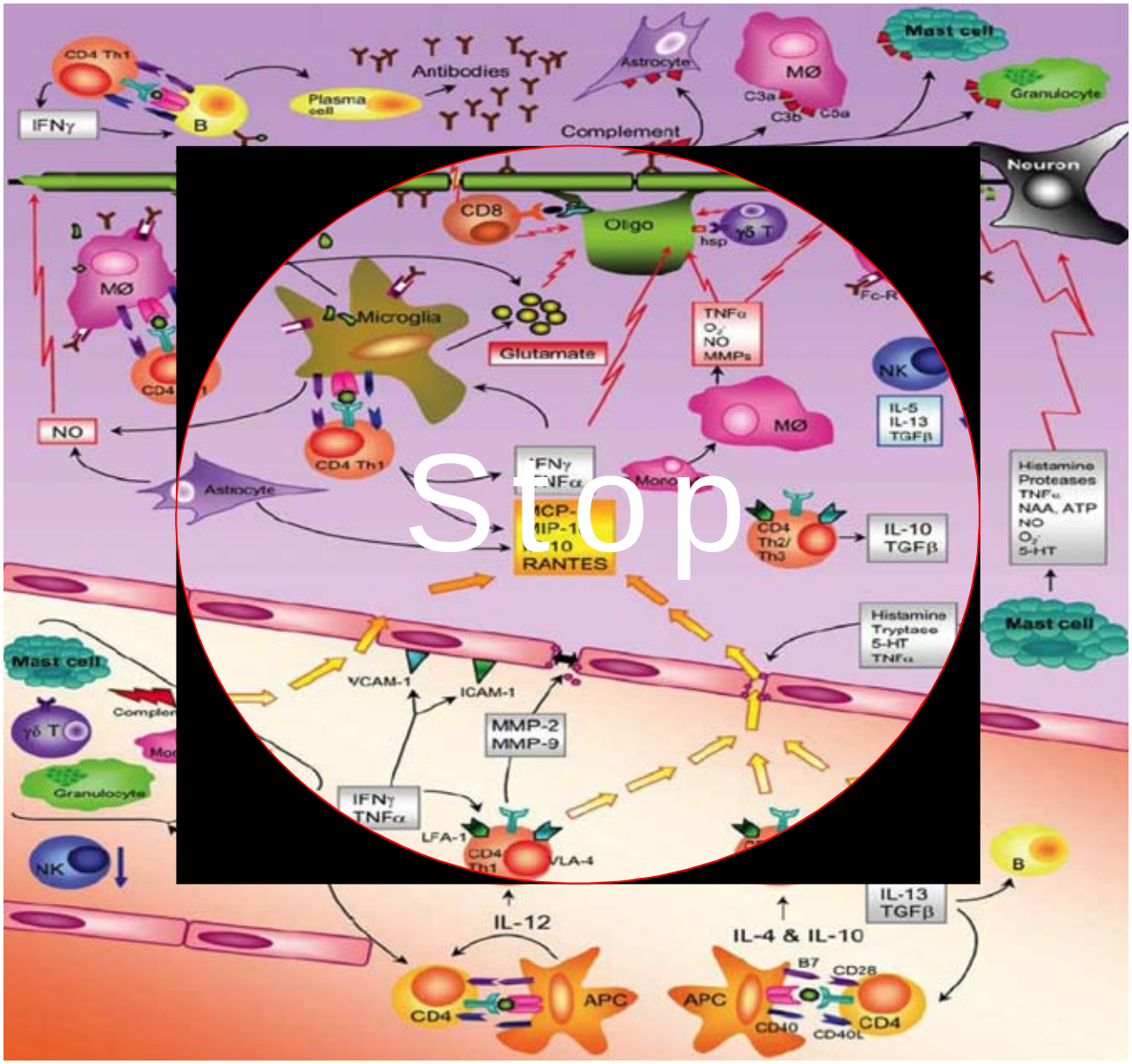
Confavreux et al., NEJM 2000

Immunological rationale of induction tx

Intense Immunosuppression (e.g. Alemtuzumab)

vs

Generation of a new immune repertoire (AHScTx)



Treatment

New approved DMT's in RRMS

European Commission Approves Genzyme's Multiple Sclerosis Treatment Lemtrada™ (alemtuzumab)

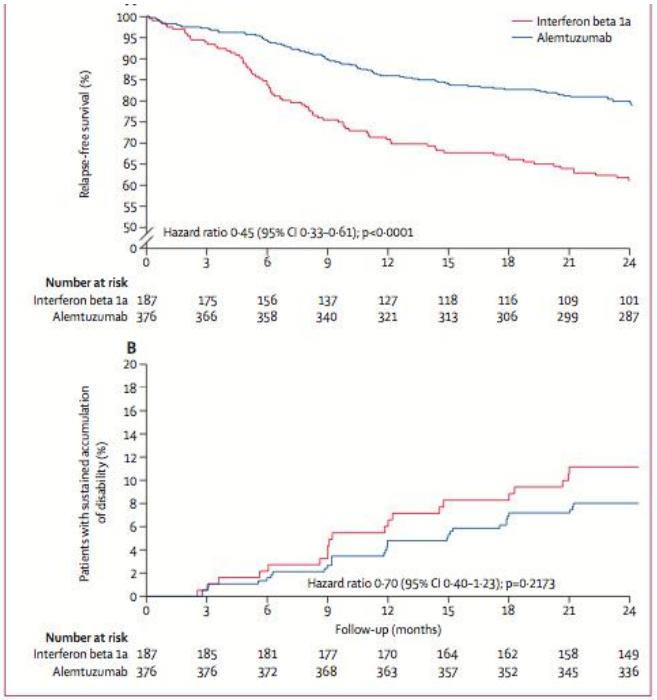
Paris, France – September 17, 2013

Lemtrada is indicated for the treatment of adult patients with relapsing remitting multiple sclerosis (RRMS) with active disease defined by clinical or imaging features. Lemtrada 12 mg has a novel dosing and administration schedule of two annual treatment courses. The first treatment course of Lemtrada is administered via intravenous infusion on five consecutive days, and the second course is administered on three consecutive days, 12 months later.

Lancet 2012; 380: 1819–28

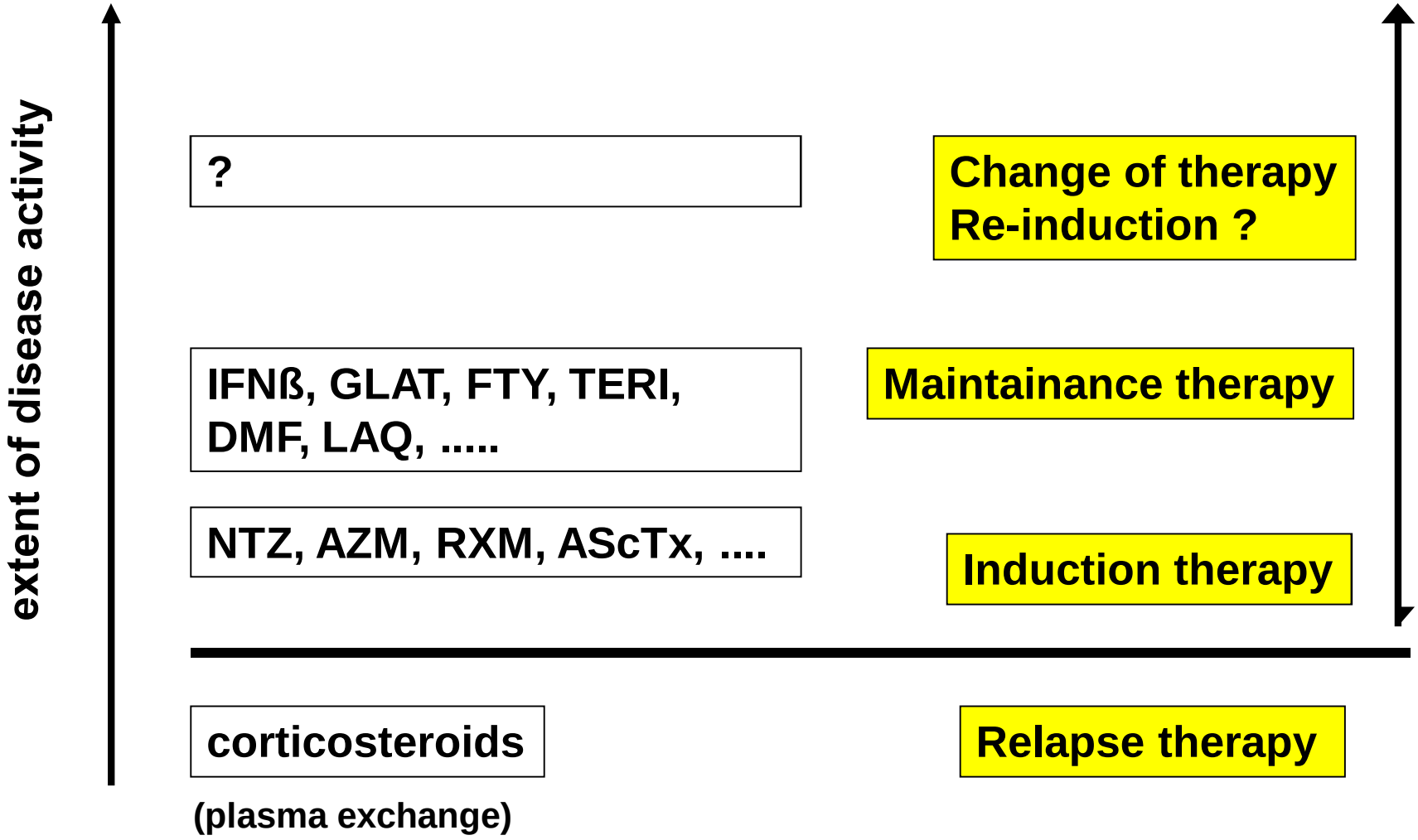
Alemtuzumab versus interferon beta 1a as first-line treatment for patients with relapsing-remitting multiple sclerosis: a randomised controlled phase 3 trial

Jeffrey A Cohen, Alasdair J Coles*, Douglas L Arnold, Christian Confavreux, Edward J Fox, Hans-Peter Hartung, Eva Havrdova, Krzysztof W Selmaj, Howard L Weiner, Elizabeth Fisher, Vesna V Brinar, Gavin Giovannoni, Miroslav Stojanovic, Bella I Ertik, Stephen L Lake, David H Margolin, Michael A Panzara, D Alastair S Compston, for the CARE-MS I investigators†*



Treatment

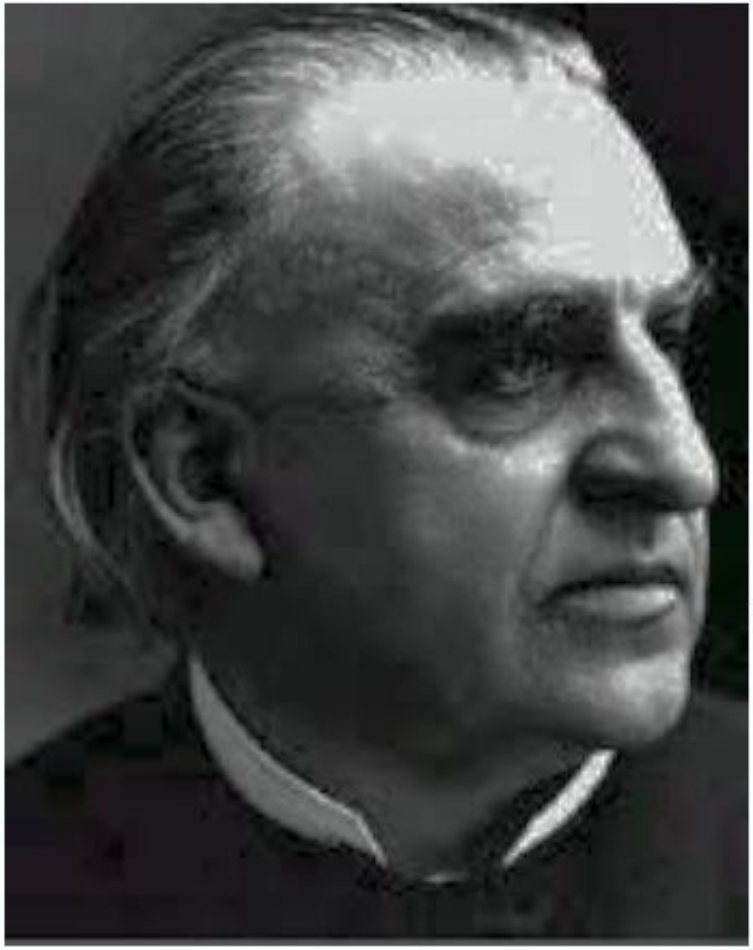
Disease modifying therapies



MS treatments: *Benefit-risk evaluation*

How to capture the benefit and minimize the risks ?

Diagnosis



To learn how to treat disease, one must learn how to recognize it. The diagnosis is the best trump in the scheme of treatment.

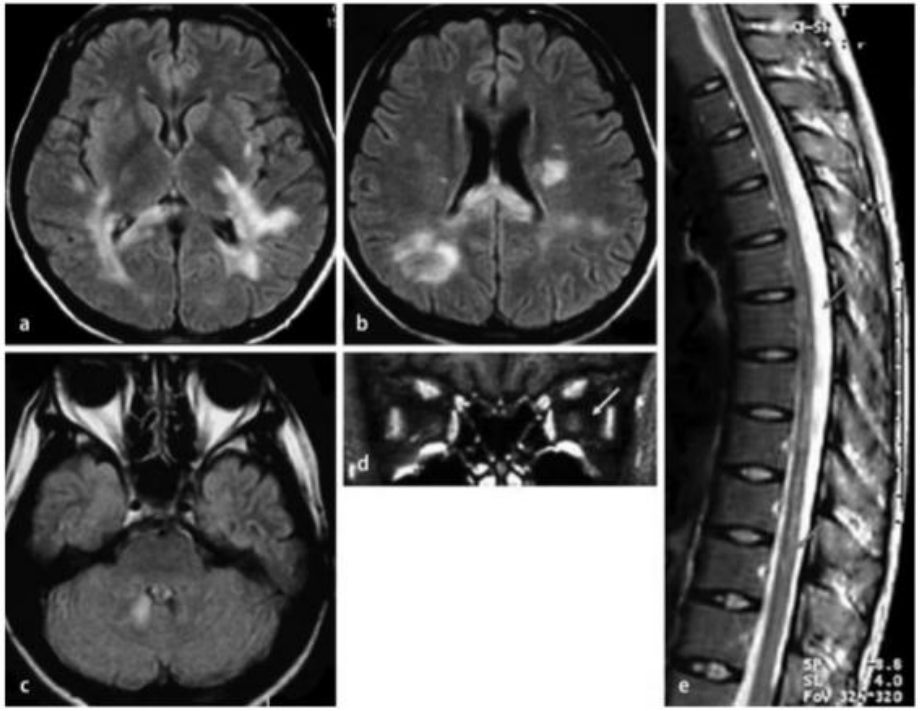
Jean Martin Charcot
1825-1893

Neuromyelitis optica:
DMT - interferon ß

J Neurol (2008) 255:305–307

Yuko Shimizu
Kazumasa Yokoyama
Tatsuro Misu
Toshiyuki Takahashi
Kazuo Fujihara
Seiji Kikuchi
Yasuto Itoyama
Makoto Iwata

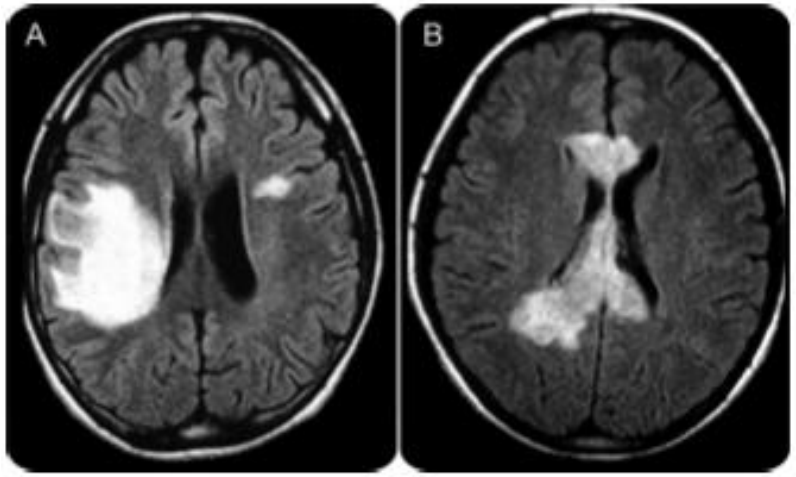
Development of extensive brain lesions following interferon beta therapy in relapsing neuromyelitis optica and longitudinally extensive myelitis



Neurology® 2010;75:1423-1427

IFNβ-1b may severely exacerbate Japanese optic-spinal MS in neuromyelitis optica spectrum

J. Shimizu, Y. Hatanaka, M. Hasegawa, et al.



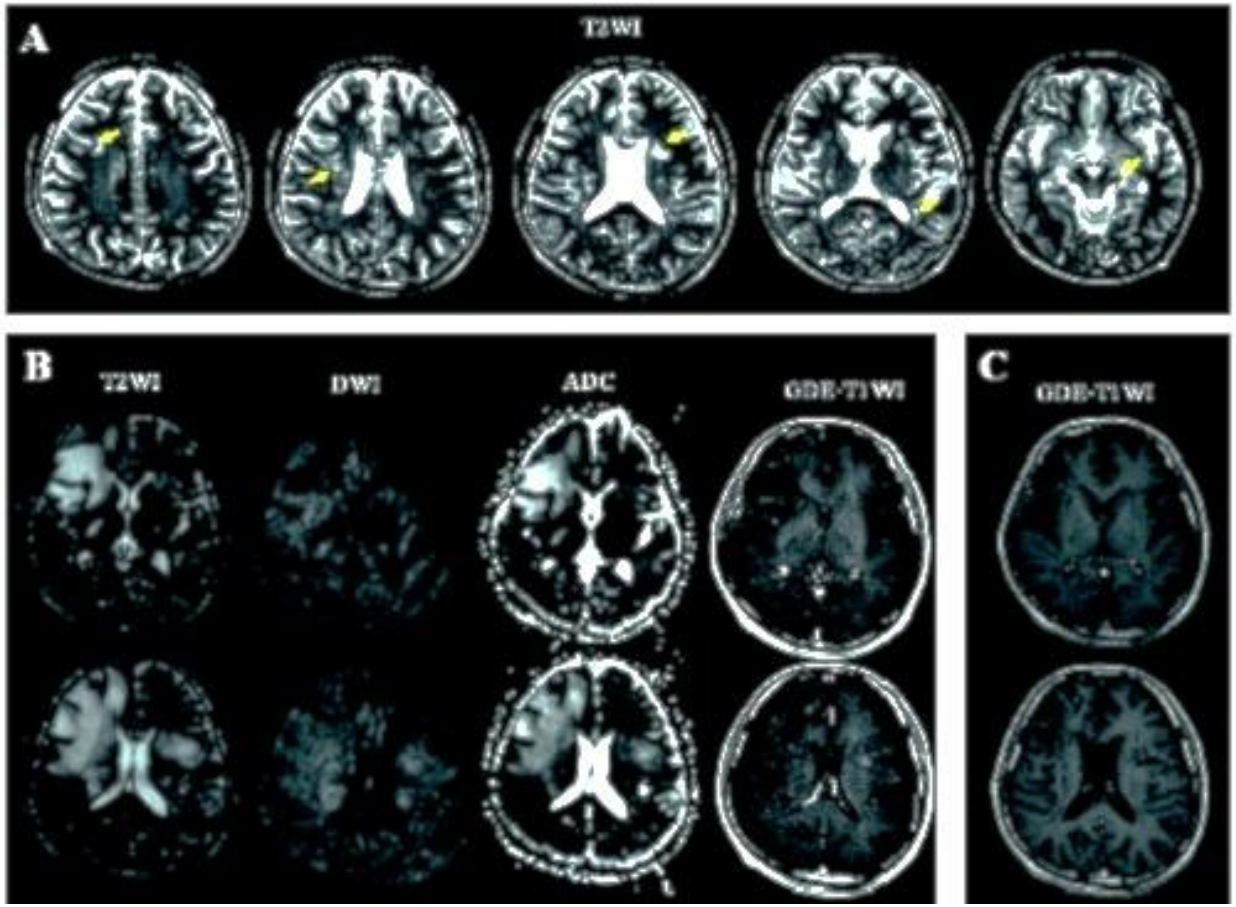
Neuromyelitis optica

DMT – Fingolimod

Development of extensive brain lesions following fingolimod (FTY720) treatment in a patient with neuromyelitis optica spectrum disorder

Ju-Hong Min, Byoung Joon Kim and Kwang Ho Lee

Mult Scler 2012 18: 113 originally published online 6 December 2011



Treatment

Individual benefit-risk evaluation

[redacted]

[redacted]

Drugs don't work in patients who don't take them.

— C. Everett Koop, M.D.

Therapeutic monoclonal antibodies

AE's and risks

Natalizumab	secondary activation of latent DNS virus - PML
Rituximab	reactivation of DNA virus - PML reactivation of Enterovirus - encephalitis
Alemtuzumab	„reconstitution autoimmunity": ITP, thyroiditis, GPS reactivation of latent DNA virus, measles virus, CMV toxoplasmosis increased bacterial and fungal infections neoplasm ?
Daclizumab	reactivation of latent DNA virus - CMV bacterial and fungal infections (brain abscess)

Oral MS treatments

AE‘s and risks

Fingolimod (FTY720) *Cohen et al, NEJM 2010* *Kappos et al NEJM 2010*	lymphopenia reactivation of latent DNA virus - VZV, HSV cardiovascular disorders (bradycardia, AV-block I ° /II ° , hypertension) maculaedema (neoplasms) teratogenic
Laquinimod *Comi et al, NEJM 2012*	abdominal/back pain
Teriflunomide *O‘Connor et al, NEJM 2011*	lymphopenia hair loss teratogenic
DMF (BG-12) *Fox et al, NEJM 2012* *Gold et al, NEJM 2012*	Flushing GI (diarrhea, nausea, vomiting, abdominal pain)

Multiple sclerosis & pregnancy
teratogenic DMT's

FTY classified as FDA pregnancy risk category C

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use GILENYA™ safely and effectively. See full prescribing information for GILENYA.

etal risk: Women of childbearing potential should use effective
traception during and for two months after stopping GILENYA com
nt. (5.6) *treatme*

TERI classified as FDA pregnancy risk category X

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use AUBAGIO® safely and effectively. See full prescribing information for AUBAGIO.

AUBAGIO® (teriflunomide) tablets for oral administration.

Initial U.S. Approval: 2012

Risk of Teratogenicity

Based on animal data, AUBAGIO may cause major birth defects if used during pregnancy. Pregnancy must be excluded before starting AUBAGIO. AUBAGIO is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. Pregnancy must be avoided during AUBAGIO treatment or prior to the completion of an accelerated elimination procedure after AUBAGIO treatment *[see Contraindications*

Multiple Sclerosis Registry
Austrian Society of Neurology

Aims & Goals

- uniform quality standard in Austria
- documentation of:
  - *indication and treatment monitoring*
  - *benchmarks of efficiacy (ARR, EDSS)*
  - *(signals of) adverse events*
  - *sequential therapies*
  - *treatment frequency and adherence*
- transparent informations for MS centers
- Expert Statements
- product informations/news

Treatment

rationale – the ultimative concept

Personalized MS treatment

Giving the right drug to the right patient

at the right dose at the right time

MS treatment decisions

Individual treatment road map

The only way to predict the future is to create the future

A. Morita