XXXVI
CONGRESSO NAZIONALE
SIFO

Catania,
Centro Congressuale Fieristico
Culturale "Le Ciminiere"
22-25 OTTOBRE 2015

XXXVI
CONGRESSO
NAZIONALE
SIFO

"Sessione plenaria: cronicità e terapie innovative"

Catania, 24 ottobre 2015

Impatto terapeutico, economico ed organizzativo dei nuovi farmaci per la sclerosi multipla

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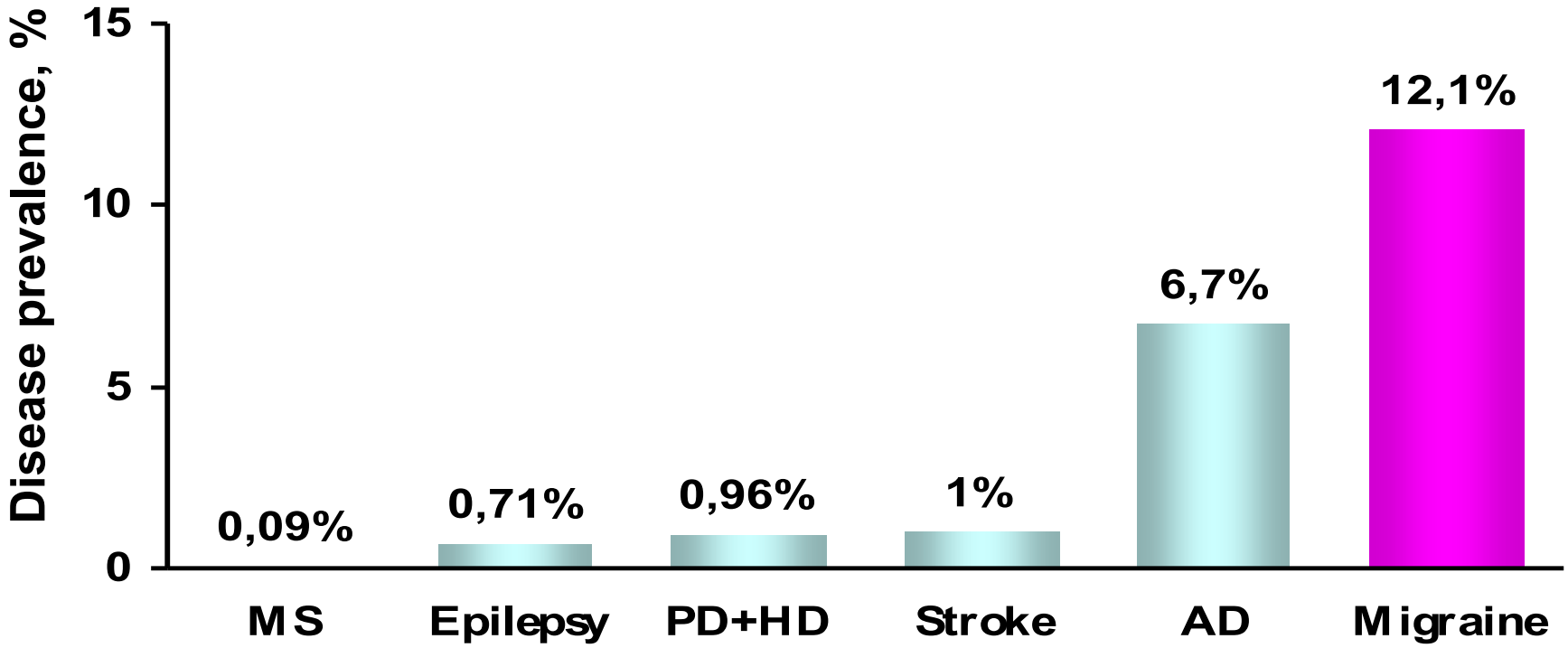
Centro Sclerosi Multipla
C.S.M.

Prevalenza delle malattie neurologiche



MS = multiple sclerosis; PD+HD = Parkinson disease + Huntington disease; AD = Alzheimer's disease.

1. Hirtz D. et al. *Neurology*. 2007;68:326–337.

2. *National Institute of Neurological Disorders and Stroke*. Available at: www.ninds.nih.gov. Accessed May 17, 2007.

Costi sanitari diretti annuali per paziente

	Costo sanitario diretto	Costo medicinale	Costo sanitario	Costo recidive	Inizializzazione
fingolimod	€ 21.004	€ 20.272	€ 680	€ 52	€ 570
natalizumab	€ 23.476	€ 22.185	€ 1281	€ 10	
IFN beta 1A (Avonex)	€ 10.291	€ 9.864	€ 323	€ 104	
IFN beta 1A (Rebif 22)	€ 10.706	€ 10.279	€ 323	€ 104	
IFN beta 1A (Rebif 44)	€ 14.248	€ 13.821	€ 323	€ 104	
IFN beta 1b (Betaferon)	€ 6.327	€ 5.900	€ 323	€ 104	
IFN beta 1B (Extavia)	€ 6.327	€ 5.900	€ 323	€ 104	
glatiramer acetato	€ 9.949	€ 9.522	€ 323	€ 104	
teriflunomide	€ 10.406	€ 9.947	€ 355	€ 104	
dimetil fumarato	€ 12.646	€ 12.187	€ 355	€ 104	
alemtuzumab	€ 29.301	€ 28.432	€ 859	€ 10	

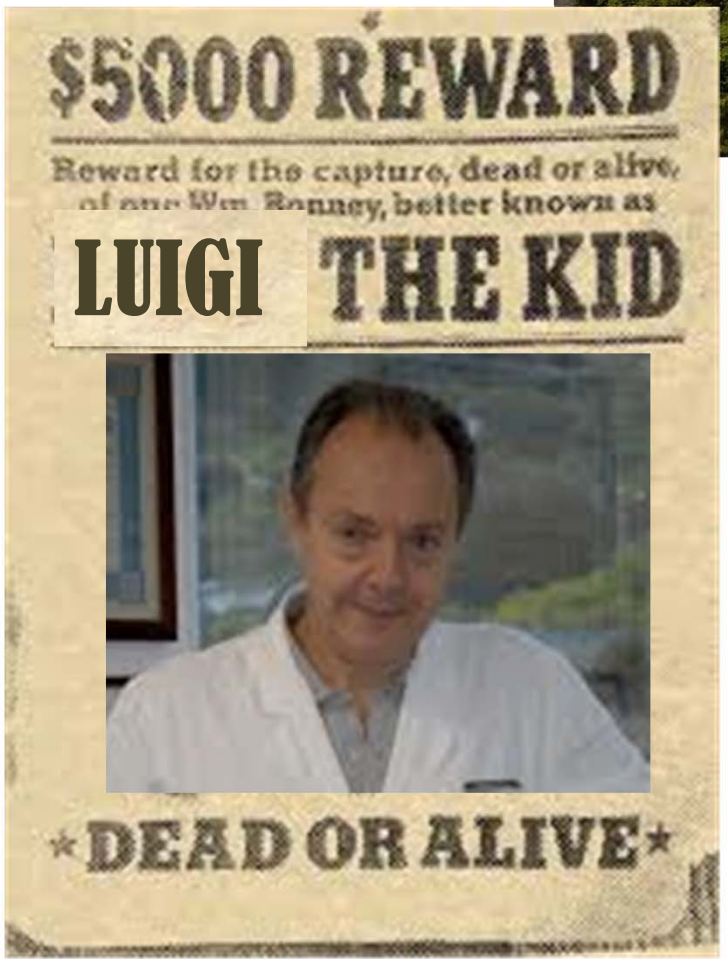
Costo sanitario diretto pazienti afferenti al Centro SM di Cefalù – anno 2015

Farmaco	Medicinale	Costo sanitario	n° pazienti	Costo sanitario diretto
II linea	natalizumab	€ 23.476	117	€ 2.746.692
	fingolimod	€ 21.004	67	€ 1.407.268
I linea	IFN beta 1A (Rebif 44)	€ 14.248	154	€ 2.194.192
	IFN beta 1A (Rebif 22)	€ 10.706	48	€ 513.888
	glatiramer acetato	€ 9.950	136	€ 1.353.200
	IFN beta 1A (Avonex)	€ 10.291	39	€ 401.349
	IFN beta 1b (Betaferon)	€ 6.327	18	€ 113.886
	IFN beta 1B (Extavia)	€ 6.327	1	€ 6.327
	teriflunomide	€ 10.406	0	€ 0
	dimetil fumarato	€ 12.646	0	€ 0
	alemtuzumab	€ 29.301	0	€ 0
				€ 8.736.802

Attuale visione economica di un Centro SM

Direttore Generale

Farmacista



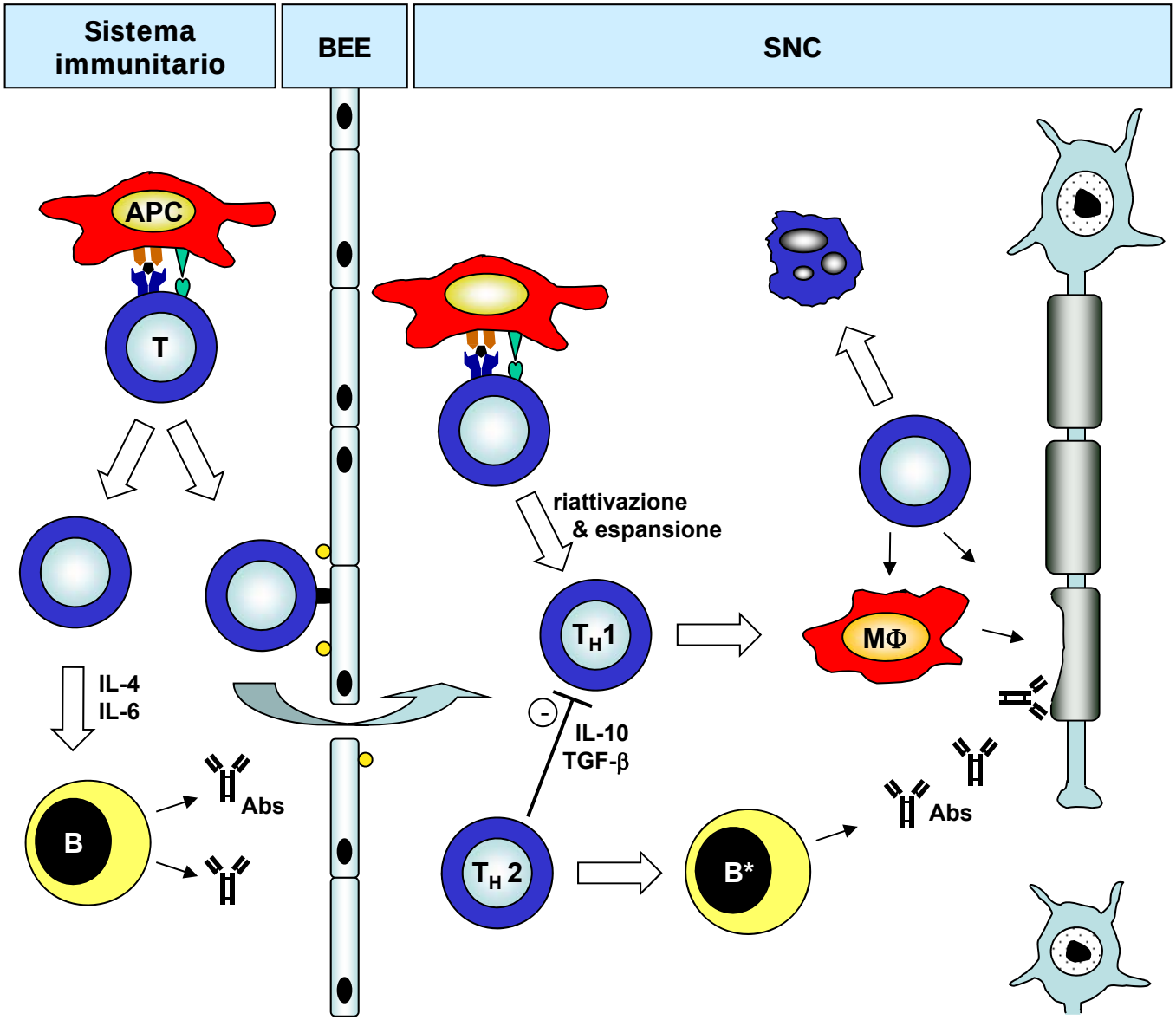
Neurologo

Risparmio SSR Sicilia per pazienti in sperimentazioni farmacologiche (2014)

PAZIENTI IN SPERIMENTAZIONE (Cefalù)			
	Spesa SSR	Nr. pazienti	Totale Risparmio annuo per la Regione
	€		€
Visite ambulatoriali (x 6)	13.5	200	16.200
Esami diagnostici (RMN, ematochimica, etc)	700	200	140.000
Terapie immunomodulanti	11.000	200	2.200.000

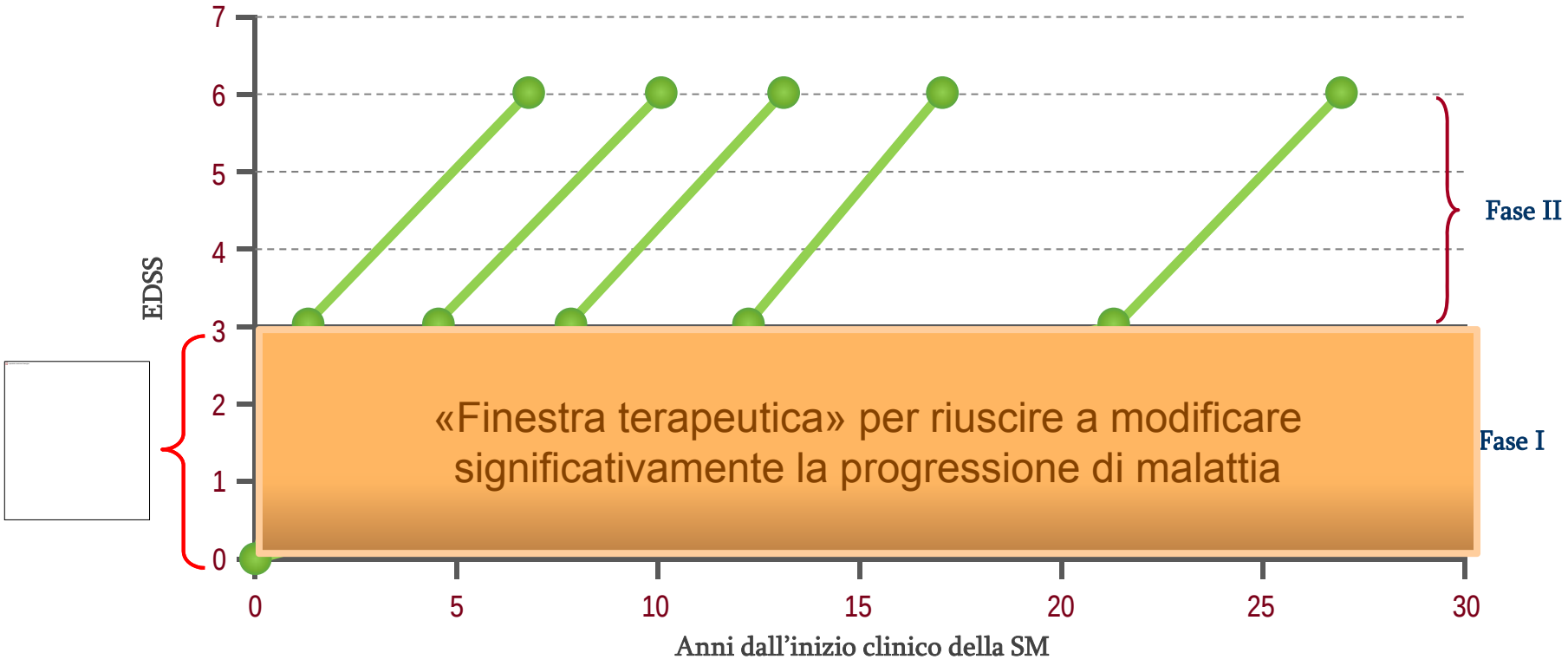
Sperimentazioni nei 17 Centri SM Regione Siciliana			
	Spesa SSR	Nr. pazienti	Totale Risparmio annuo per la Regione
	€		€
Visite ambulatoriali (x4)	13.5	400	21.600
Esami diagnostici (RMN, ematochimica, etc)	700	400	280.000
Terapie immunomodulanti	11.000	400	4.400.000

La SM è una malattia immunomediata cronica



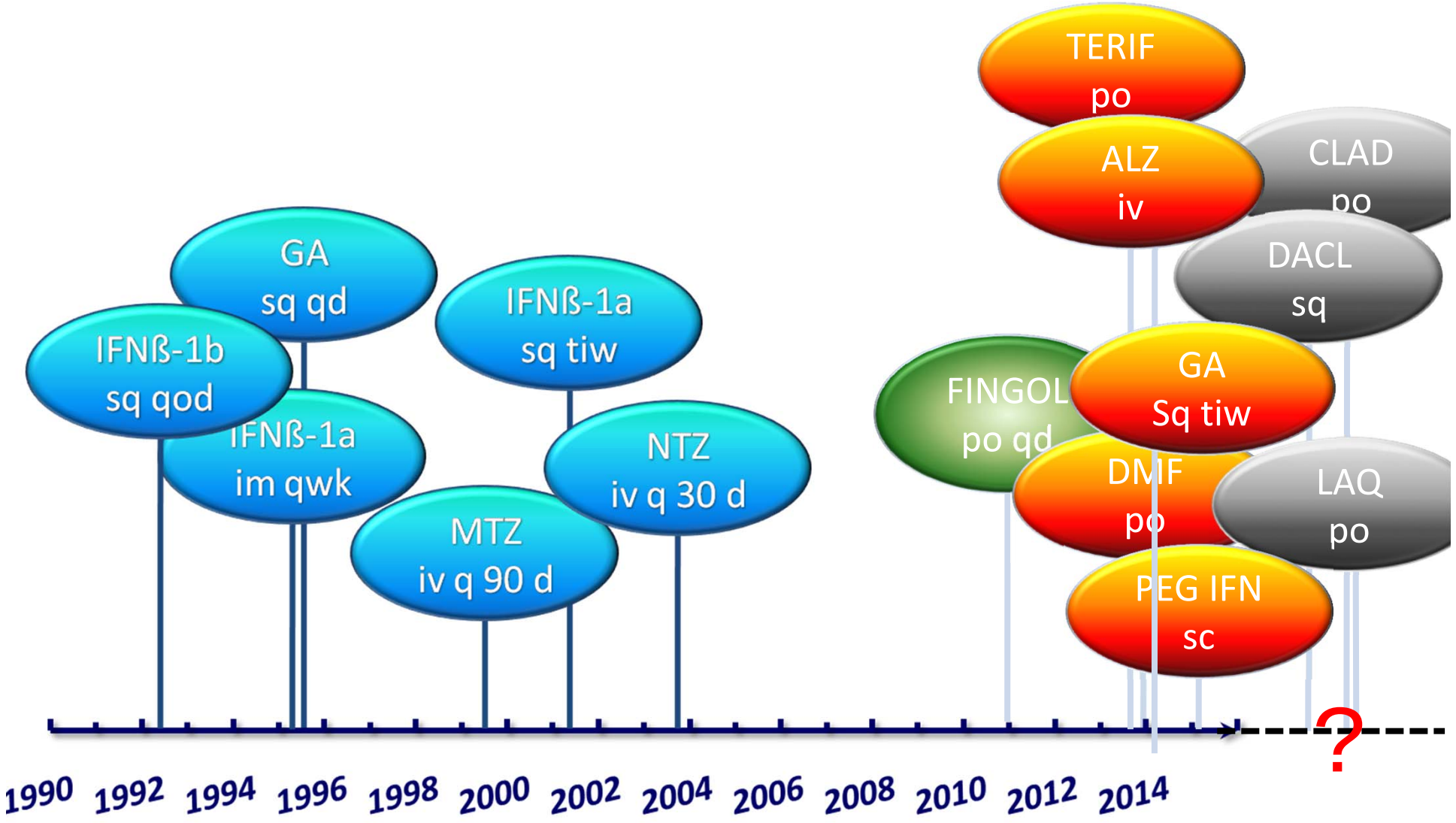
Kieseier e Wiendl, 2007

Perché è così importante trattare il più precocemente ed efficacemente possibile?

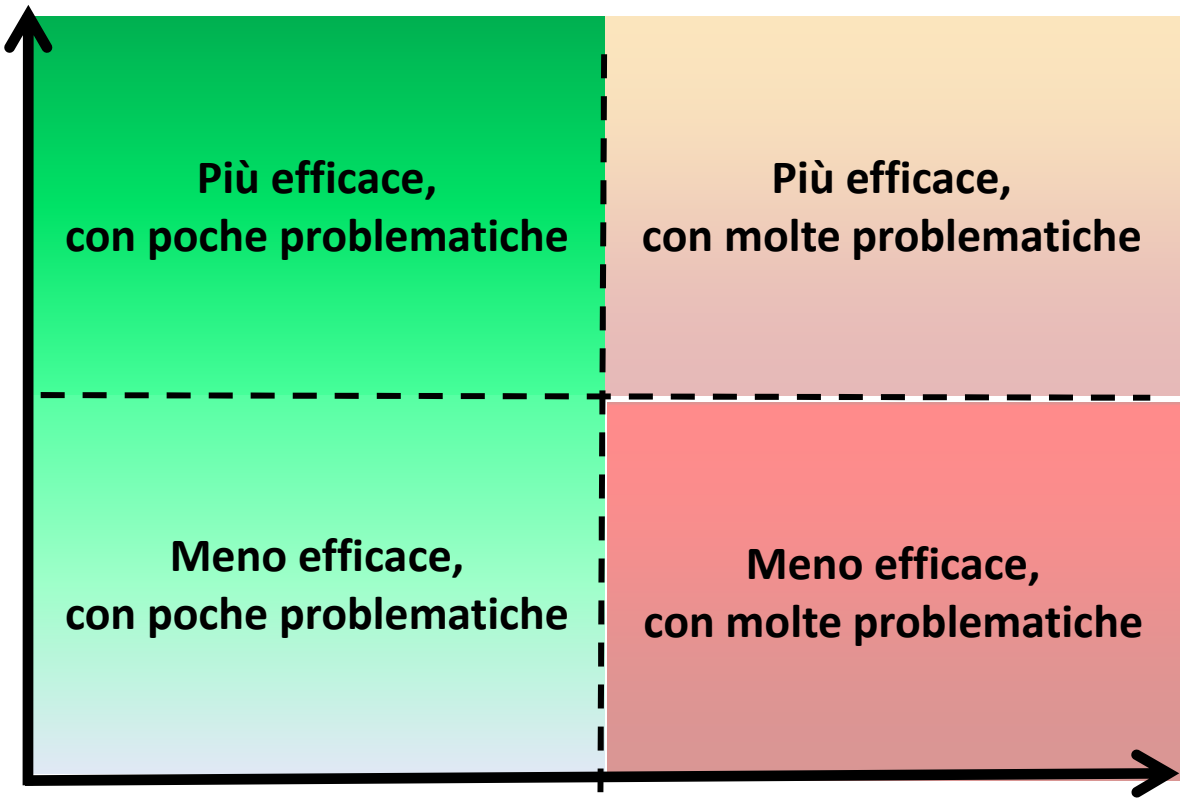


Leray E. et al. Brain. 2010 Jul;133(Pt 7):1900-13.

Presente e “futuro prossimo” delle DMT per la SM



La terapia ottimale per la SM RR: un buon bilancio tra efficacia e problematiche



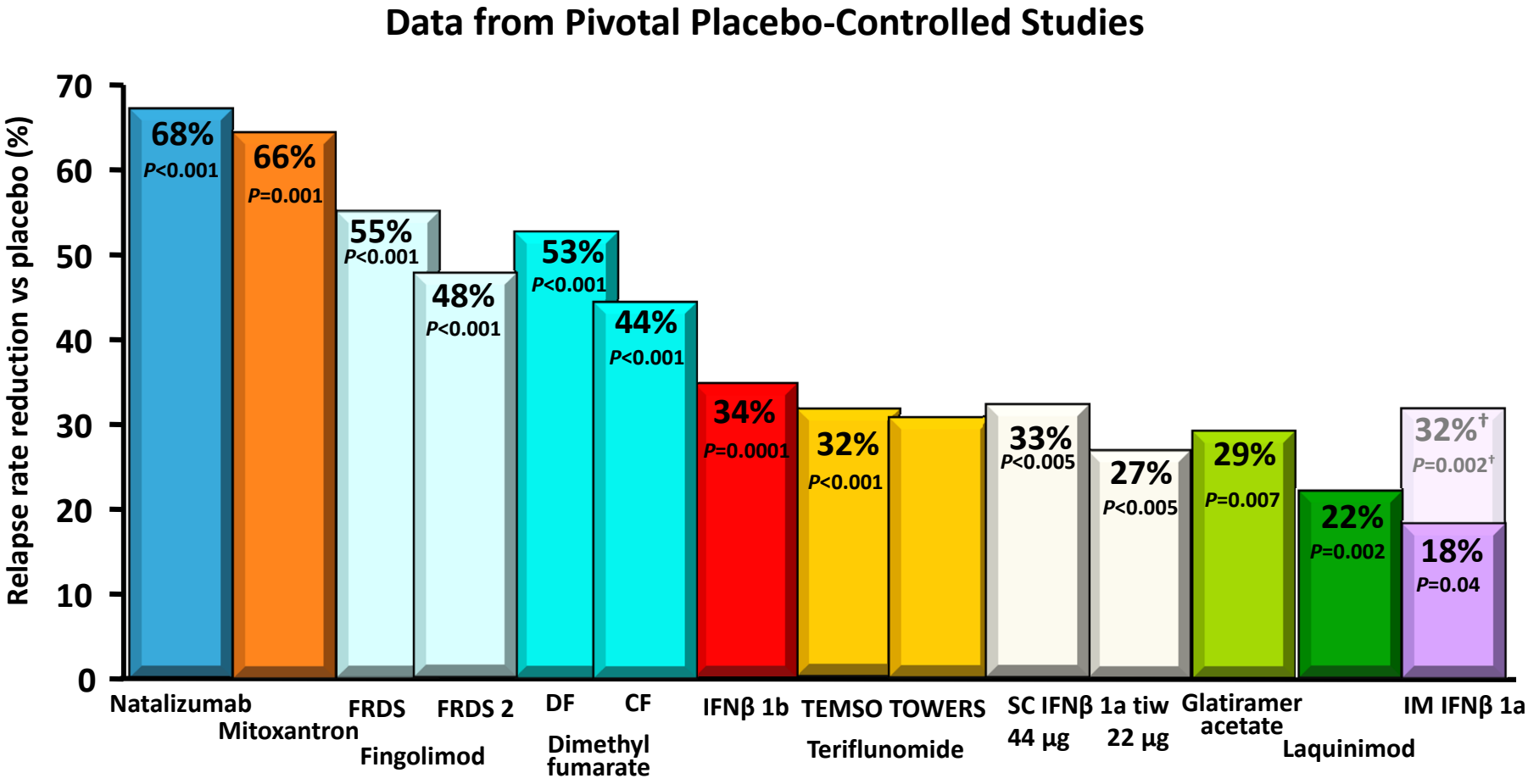
Efficacia:

Ricadute
Disabilità
Attività RMN
Atrofia RMN

Problematiche:

Tolerabilità
Safety
Costi
Monitoraggio

Efficacy of First- and second-line drugs on annualized relapse rate



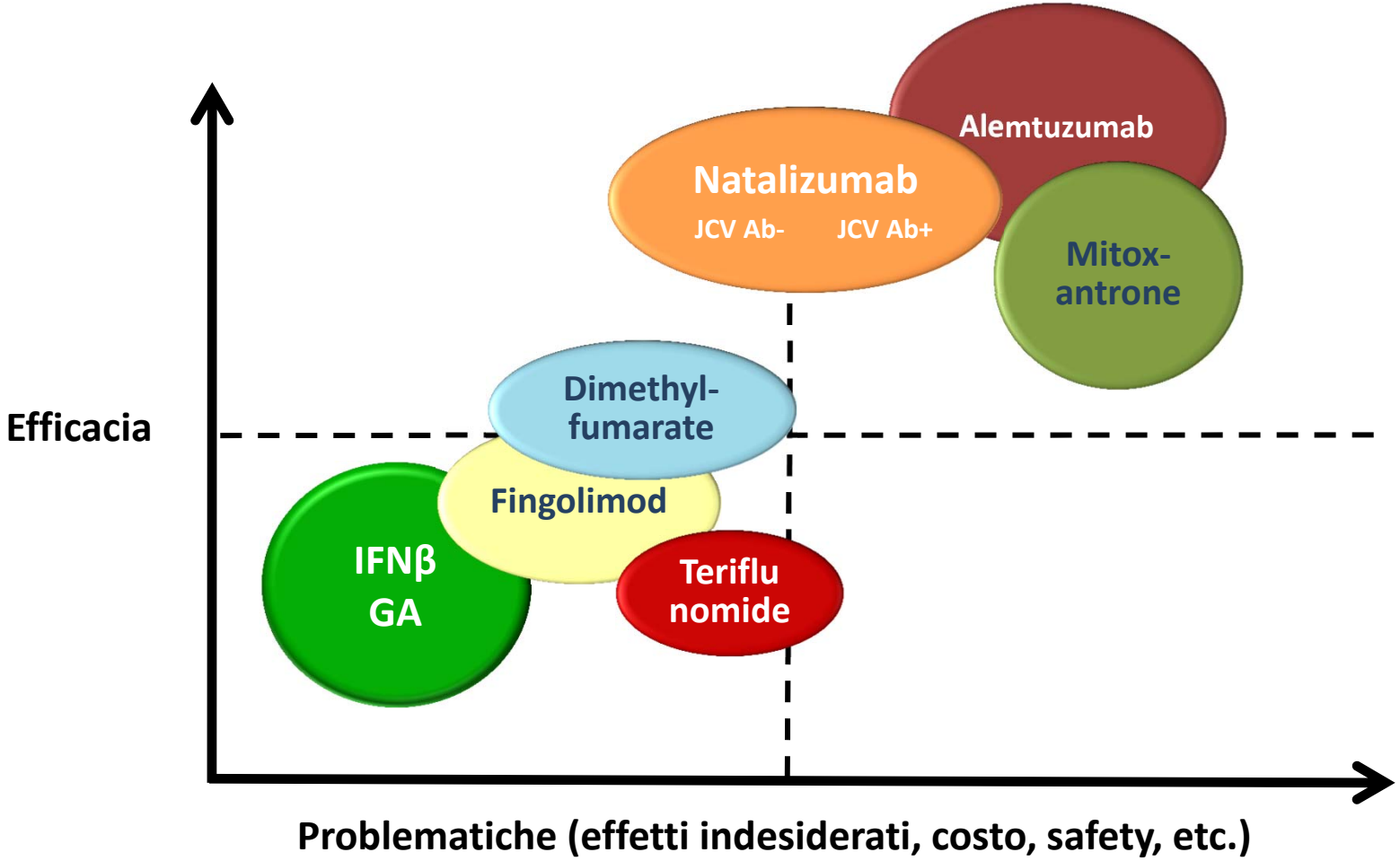
*Results (intent to treat) from separate clinical studies cannot be directly compared; †for patients completing 2 years in the study.

FRDS: FREEDOMS; DF: DEFINE; CF: CONFIRM;

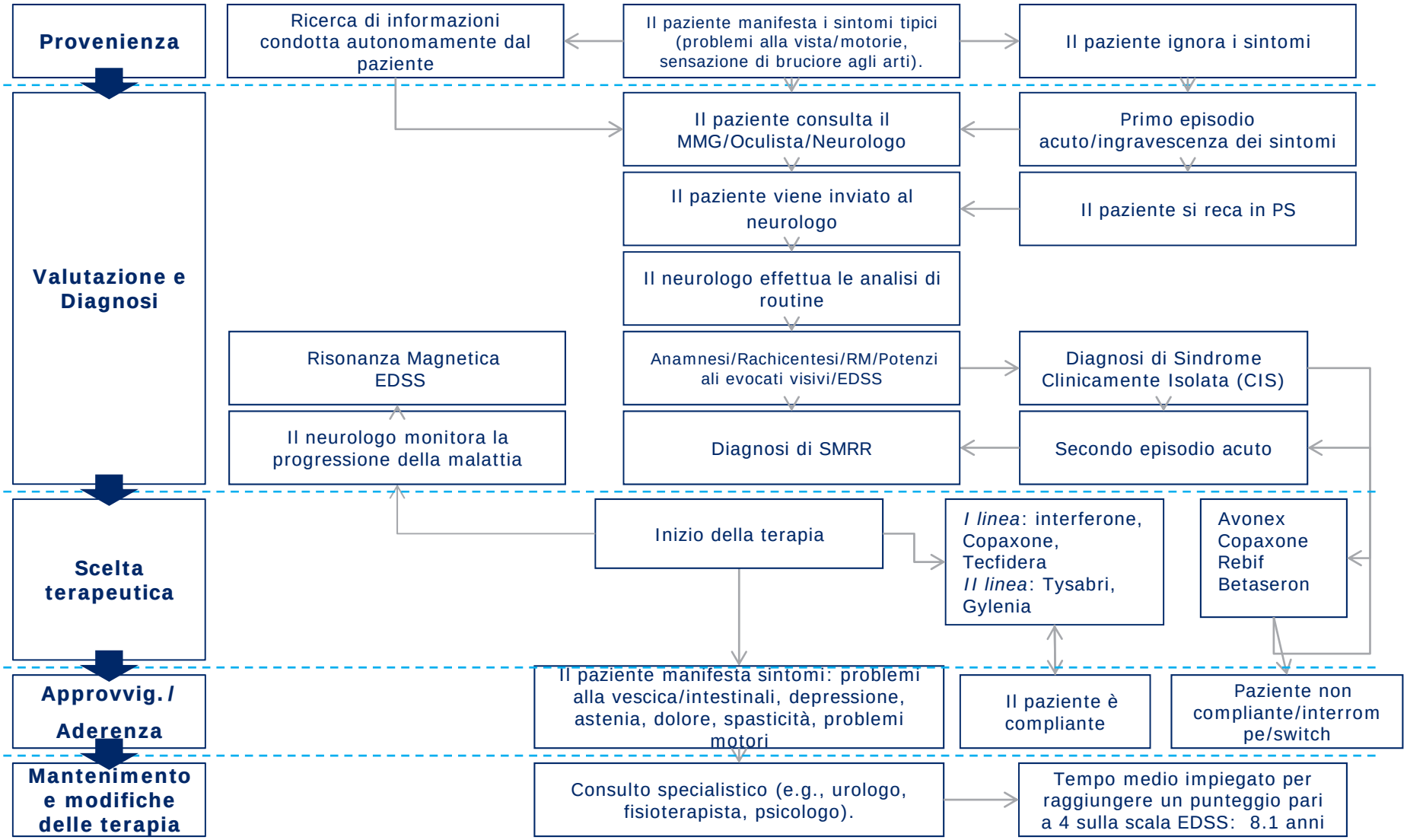
Effetti comparativi terapie SM

	Relapses	Disability	Active lesions	Brain atrophy	**Safety & tolerability**
IFN/GA	+	+/-	++	-	+++
Natalizumab	+++	+++	+++	+	+/-
Alemtuzumab	+++	+++	+++	+++	+/-
Fingolimod	++	++	++	+++	+
Teriflunomide	+	++	++	?	++
Fumarate	++	+	+++	+/-	++
Laquinimod	+	+++	+	+++	+++

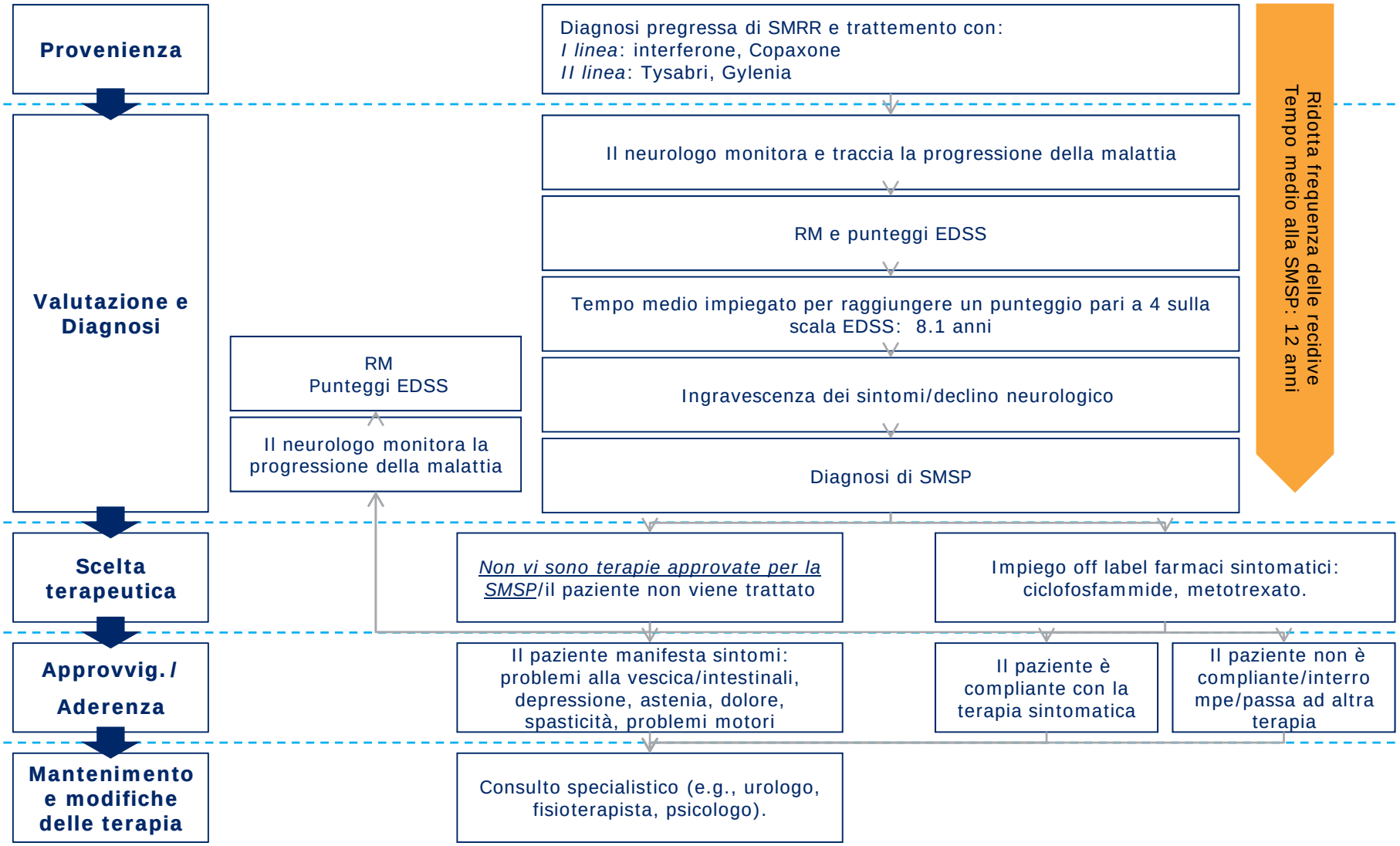
La terapia ottimale per la SM RR: effetto sul tasso di ricaduta



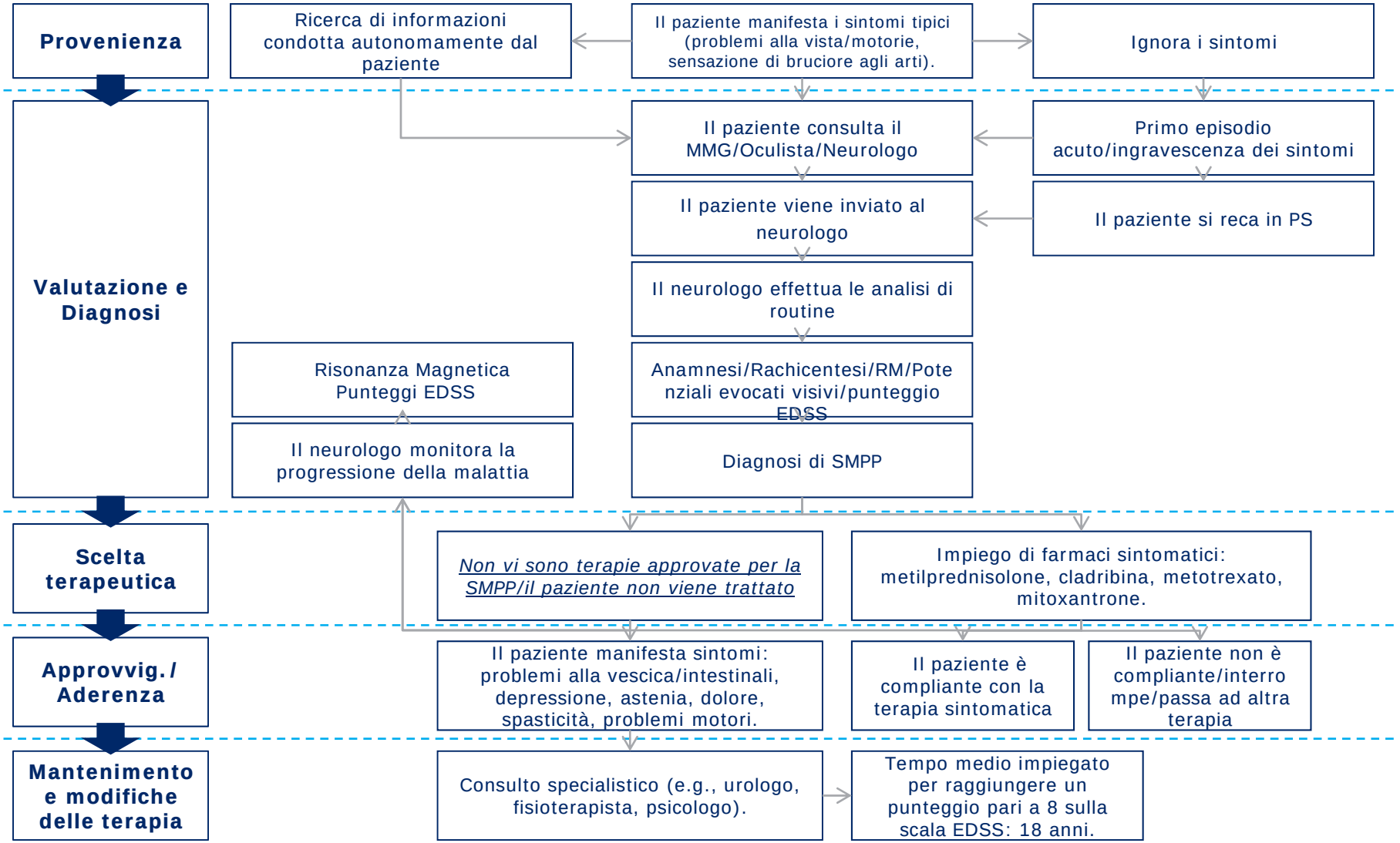
Percorso paziente con SM recidivante remittente **(SMRR)**



Percorso paziente con SM secondaria progressiva (**SMSP**)



Percorso paziente con SM Primaria Progressiva **(SMPP)**



Nuovi paradigmi assistenziali nell'ambito della SM

Players	Punti chiave

Paziente / rete	• Diagnosi precoce (incluso assetto cognitivo)
	• Definizione tipologia del paziente (età, sesso, gravità, compliance, genetica)
	• Trattamento precoce
	• Algoritmi terapeutici "sequenziali"
	• Impatto economico
	• Follow up stringente all'inizio per rapidi switch (obiettivo: NEDA)
	  • Risonanza Magnetica (carico lesionale, attività, atrofia)
	  • Biomarcatori
	  • Valutazione EDSS
	  • Test cognitivi
	  • Compliance
	• Post-marketing (registri, farmacovigilanza)

Medico / infermiere	
Istituzioni / Pharma	

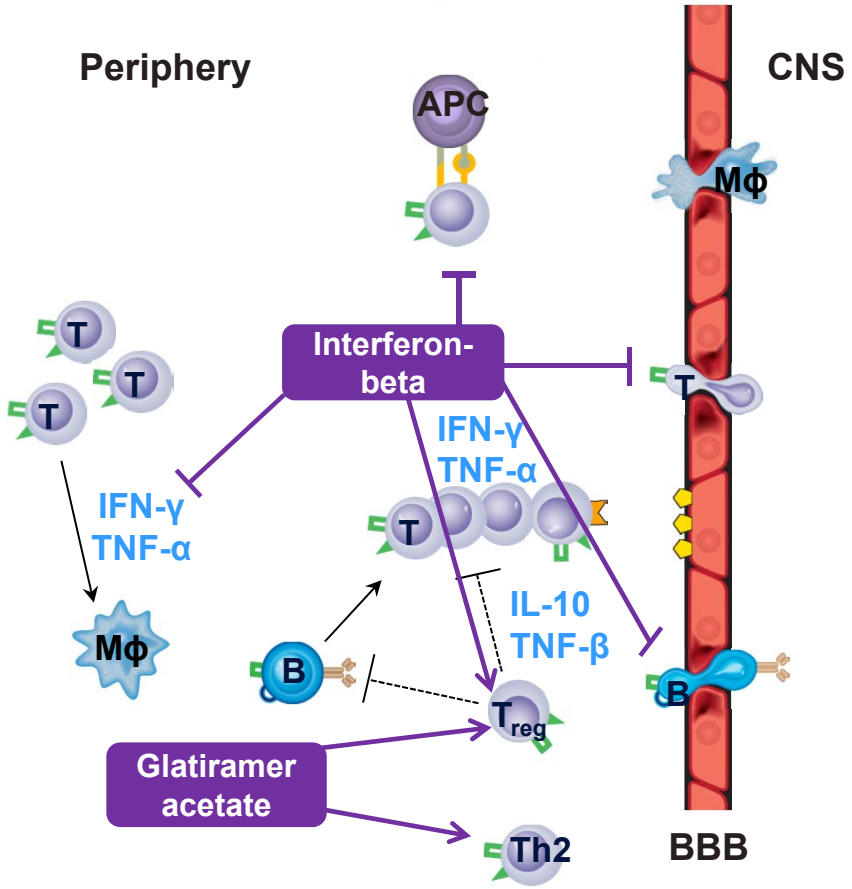
Traditional Therapies for RRMS Have Generalized Effects on the Immune System

Proposed effects of IFNB-1b[1]

- Enhancement of suppressor T-cell activity
- Reduction of pro-inflammatory cytokine production
- Down-regulation of antigen presentation
- Inhibition of lymphocyte trafficking to the CNS
- It is not known if these effects play an important role in the observed clinical activity of IFNB-1b in MS

Proposed effects of glatiramer acetate[2]

- Modulation of immune processes believed to be responsible for MS pathogenesis
- Potential activation of suppressor T cells in the periphery (based on animal and in vitro systems)
- The mechanisms by which GA exerts its effects in patients with MS are not fully understood



Exact mechanisms of action have not been fully elucidated

American Academy of Neurology
65th Annual Meeting
San Diego, California

Clinical Efficacy and Safety of Peginterferon Beta-1a in Relapsing Multiple Sclerosis: Data from the Pivotal Phase 3 ADVANCE Study

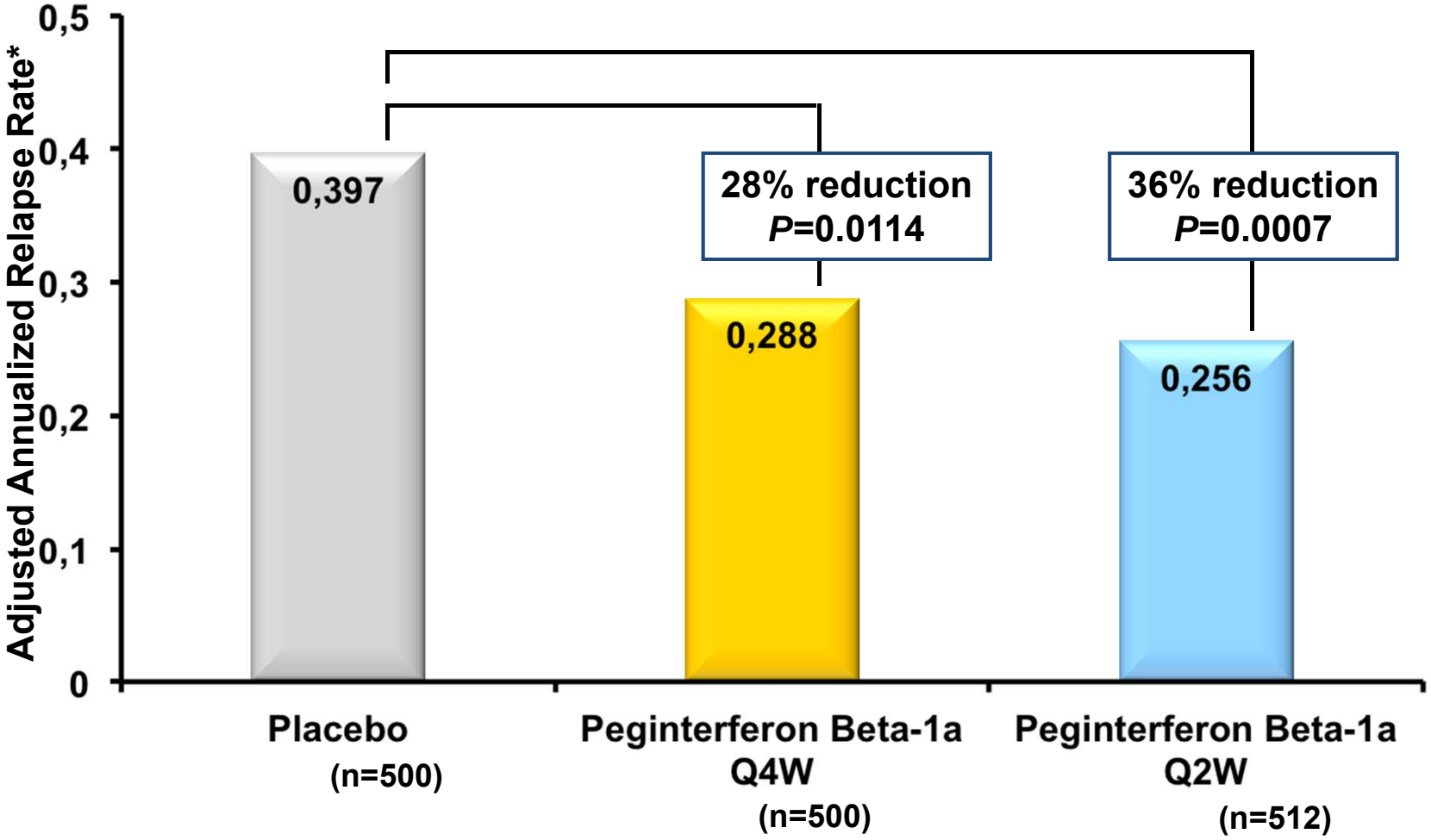
Prof Peter A. Calabresi, MD

March 20, 2013

Peter A. Calabresi[1], Bernd Kieseier[2], Douglas L Arnold[3], Laura Balcer[4], Jean Pelletier[5], Shifang Liu[6], Ying Zhu[6], Ali Seddighzadeh[6], Bjorn Sperling[6], Serena Hung[6], Aaron Deykin[6]

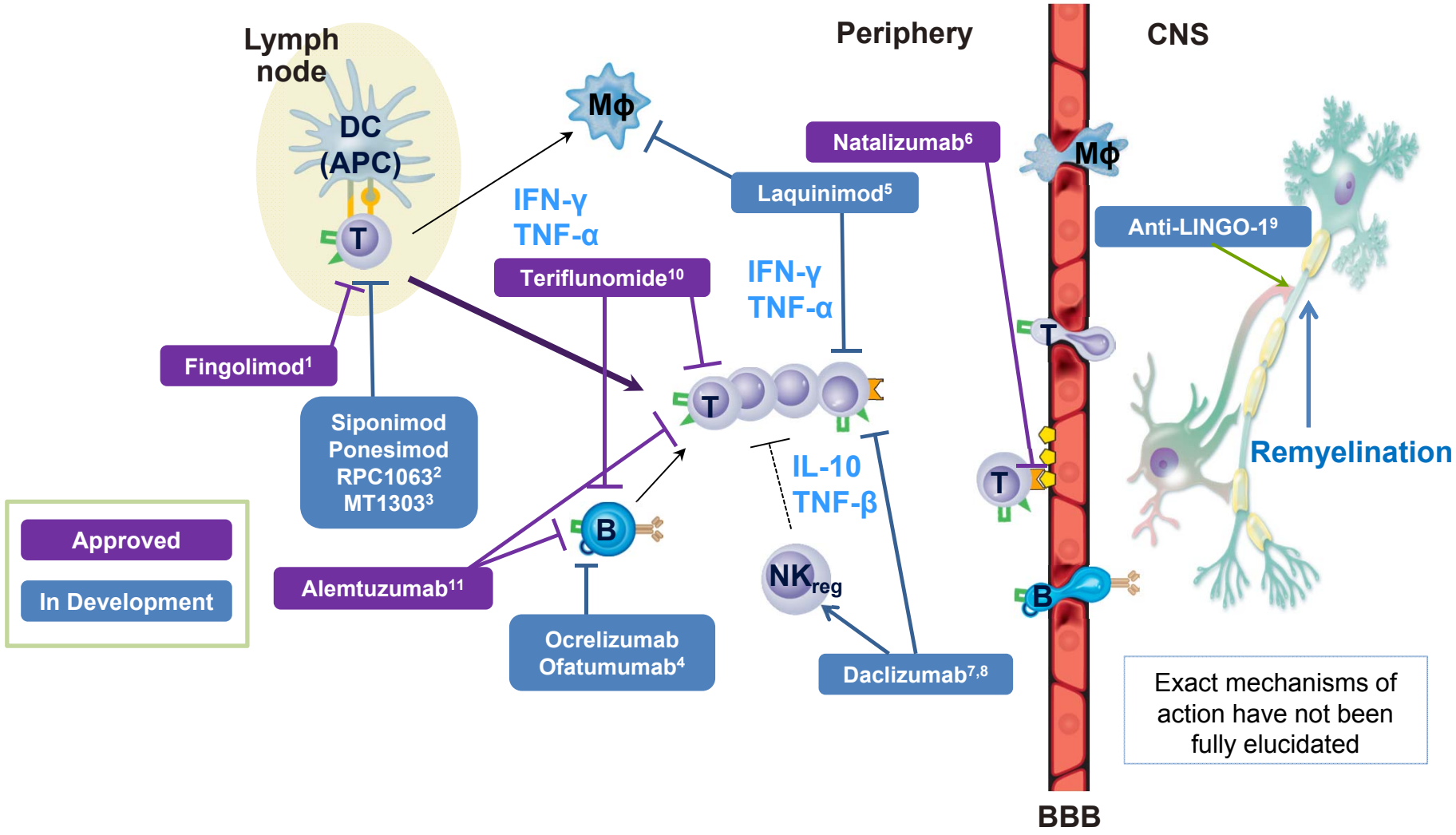
[1]Johns Hopkins University, Baltimore, MD, USA; [2]Heinrich-Heine University, Düsseldorf, Germany; [3]Montreal Neurological Institute, McGill University, and NeuroRx Research, Montreal, Quebec, Canada; [4]Department of Neurology, New York University, Langone Medical Center, New York, NY, USA; [5]Departments of Neurology and Research (CRMBM), CHU Timone, Marseille, France; [6]Biogen Idec Inc., Cambridge, MA, USA.

Phase 3 ADVANCE: Primary Endpoint Annualized Relapse Rate



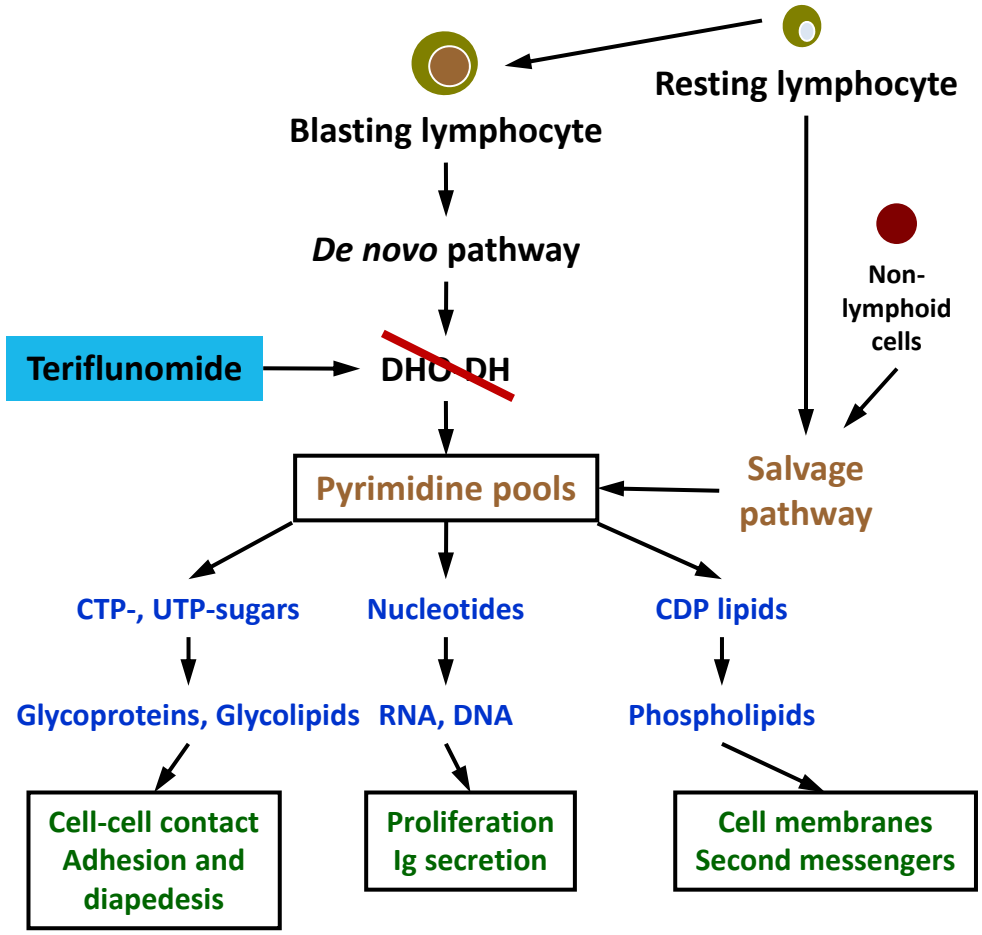
*Based on negative binomial regression; adjusted for baseline EDSS score (<4, ≥4), baseline relapse rate, age (<40 years, ≥40 years).
Calabresi PA et al. ECTRIMS 2013.

Newer Agents (Approved and in Development) Have Specific Targets



Teriflunomide

- A selective dihydro-orotate dehydrogenase inhibitor
- Blocks de novo pyrimidine synthesis, thus reducing the proliferation of autoreactive T- and B-cells
- Preserves replication and function of cells (e.g. haemopoietic cells, memory T-cells) living on the existing pyrimidine pool (salvage pathway)
- Administered orally as 14 mg tablet once daily

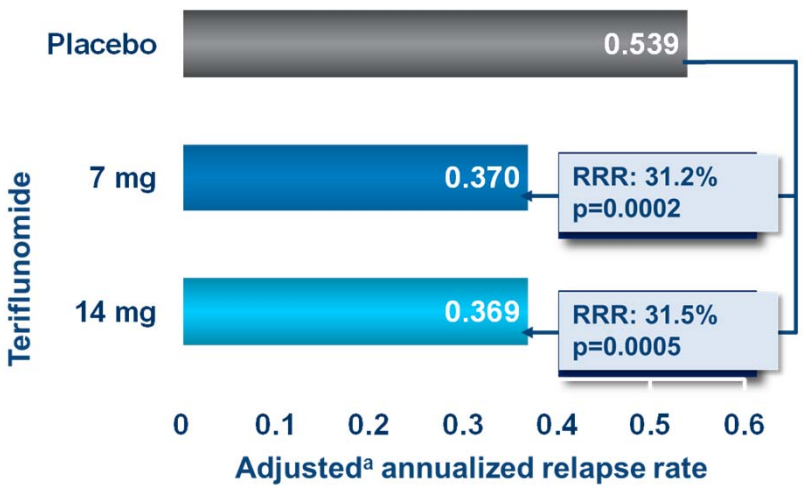


DHO-DH, dihydro-orotate dehydrogenase

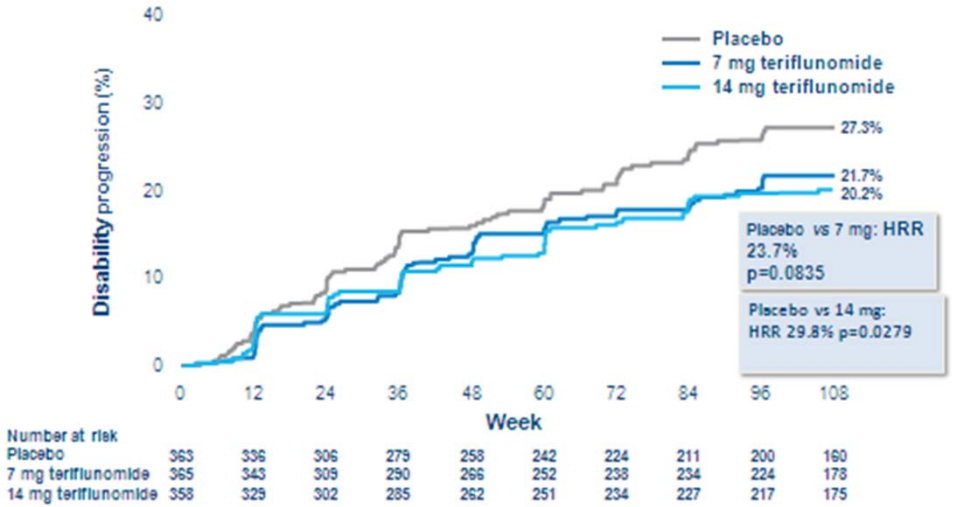
Teriflunomide: efficacia terapeutica

TEMSO

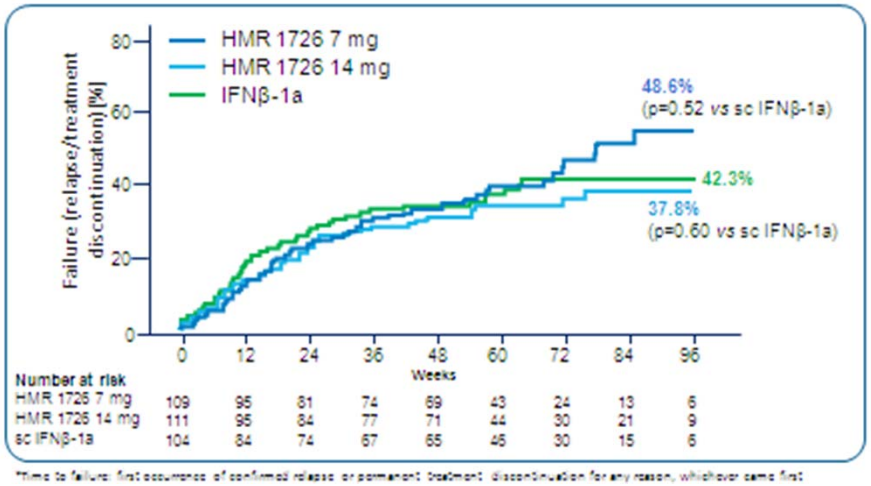
Annualized Relaps Rate



3-month Confirmed Progression



TENERE: Time to Failure



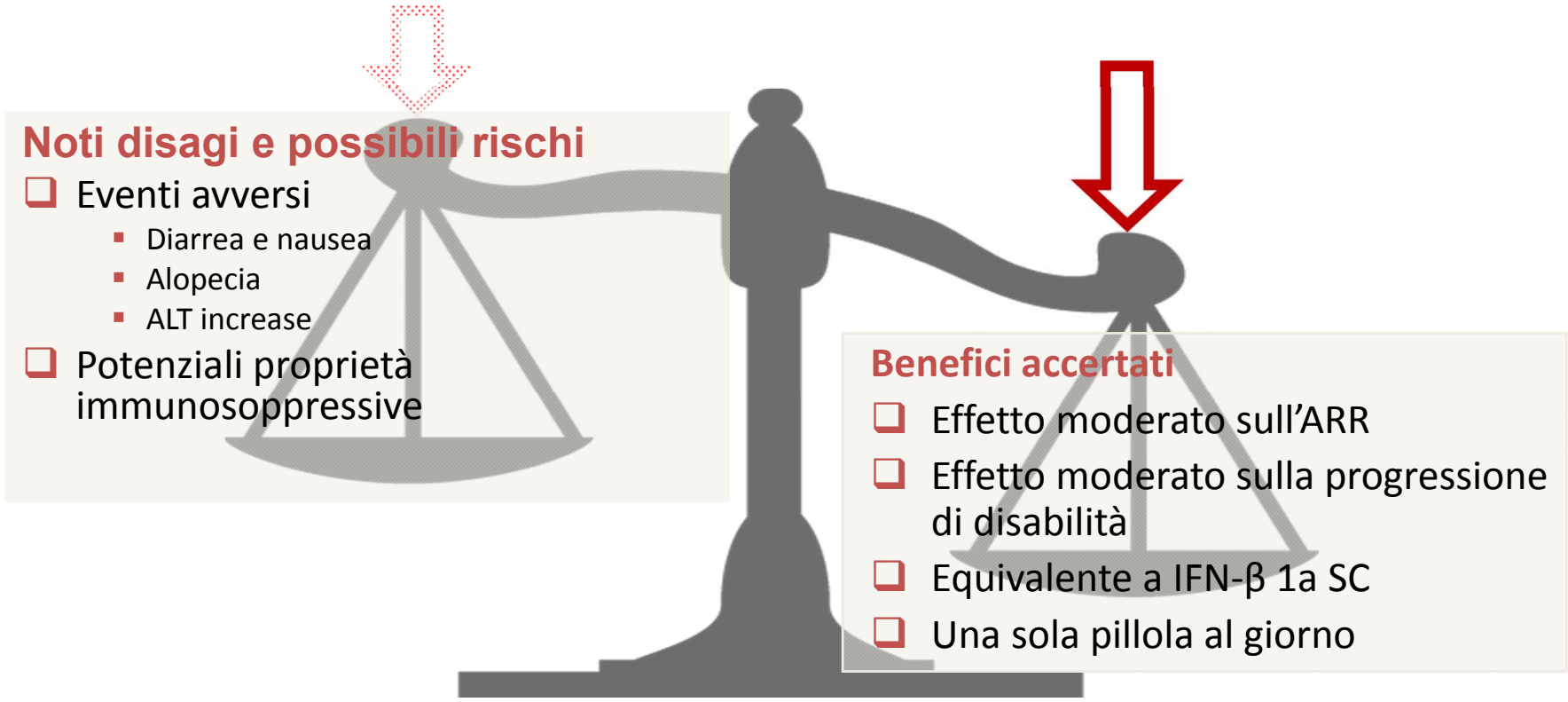
[a] Time to failure: first occurrence of confirmed relapse or permanent treatment discontinuation for any reason, whichever came first

Teriflunomide: profilo di safety (TEMSO)

Patients (%)	**Placebo (n=360)**	**Teriflunomide 7 mg (n=368)**	**Teriflunomide 14 mg (n=358)**
Nasopharyngitis	27.2	25.5	26.0
Headache	17.8	22.0	18.7
Diarrhoea	***8.9***	***14.7***	***17.9***
Fatigue	14.2	12.8	14.5
ALT increased	***6.7***	***12.0***	***14.2***
Nausea	***7.2***	***9.0***	***13.7***
Hair thinning	***3.3***	***10.3***	***13.1***
Influenza	10.0	9.2	12.0
Back pain	13.1	10.6	11.5
Urinary tract infection	9.7	7.3	10.3
Pain in extremity	*13.1*	*7.1*	*9.2*

Teriflunomide is teratogenic and pregnancy is contraindicated in 2 years after discontinuation of teriflunomide, unless treatment with cholestyramine or active charcoal is undertaken.

Teriflunomide: valutazione rischi / benefici



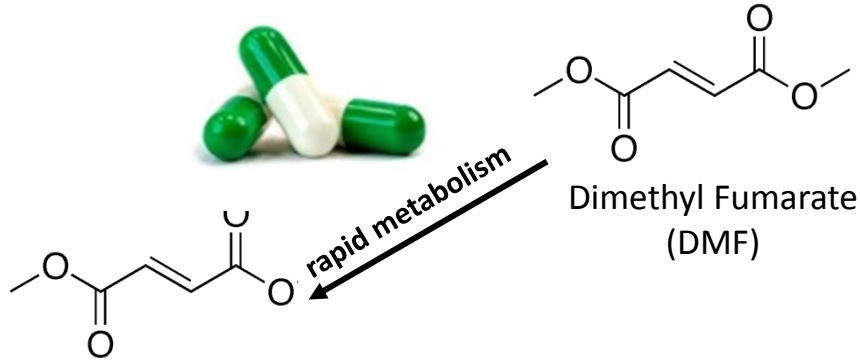
Noti disagi e possibili rischi

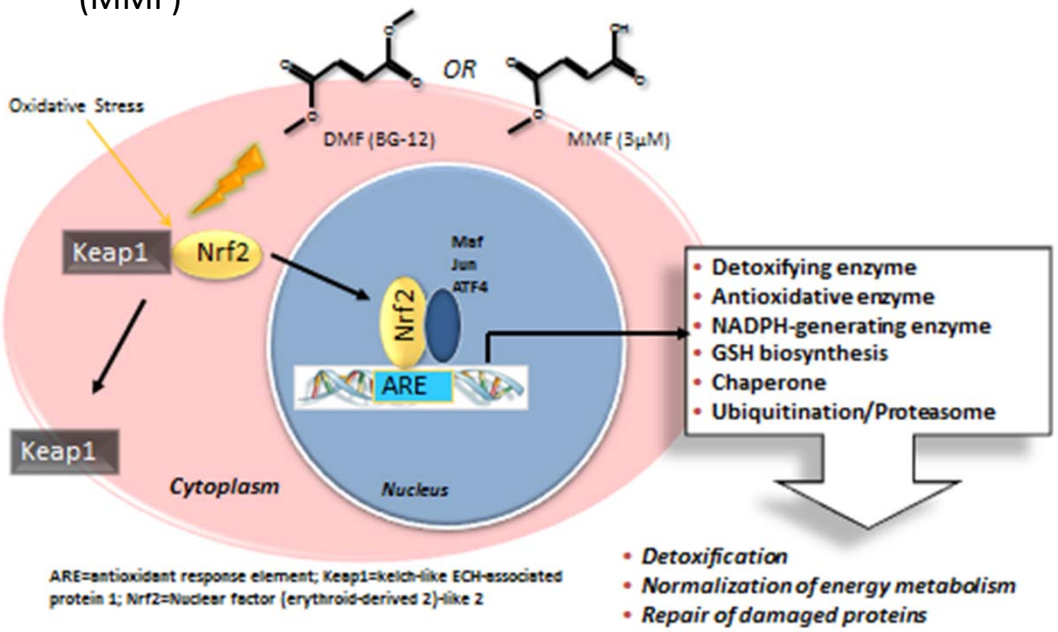
- Eventi avversi
  - Diarrea e nausea
  - Alopecia
  - ALT increase
- Potenziali proprietà immunosoppressive

Benefici accertati

- Effetto moderato sull'ARR
- Effetto moderato sulla progressione di disabilità
- Equivalente a IFN-β 1a SC
- Una sola pillola al giorno

Dimetilfumarato (BG 12)

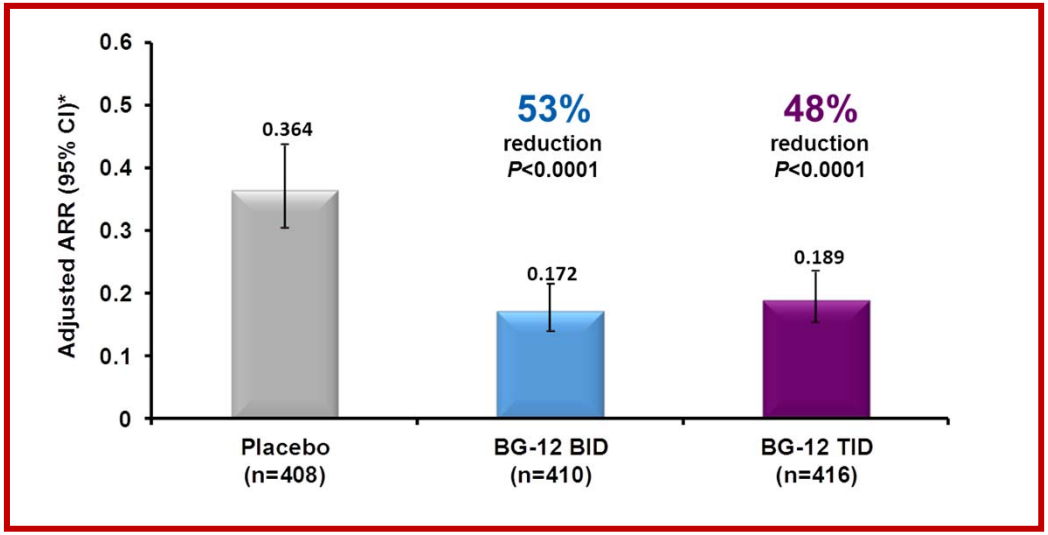




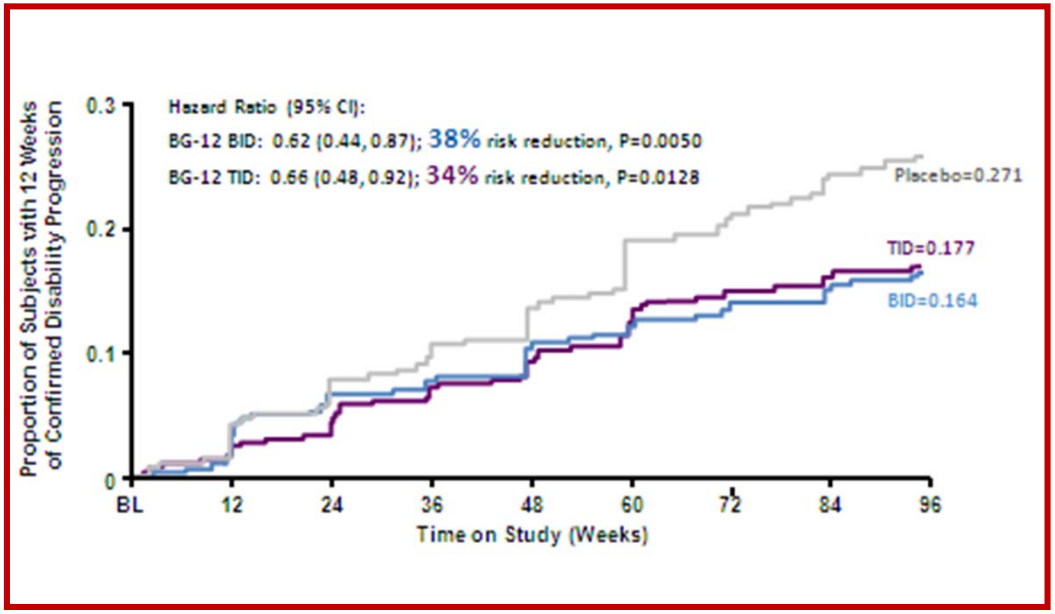
Linker et al., 2011; Lin et al., 2011; Baird and Dinkova-Kostova 2011

- Fumarate is a naturally occurring molecule that is essential for cellular oxidative respiration (Citric Acid Cycle)
- Dimethyl fumarate (DMF) 120 mg formulated into enteric-coated oral microtablets contained in a capsule
- Administration: 240 mg twice daily
- DMF is rapidly and quantitatively converted to monomethyl fumarate (MMF) after absorption

Dimetilfumarato: efficacia terapeutica (DEFINE)

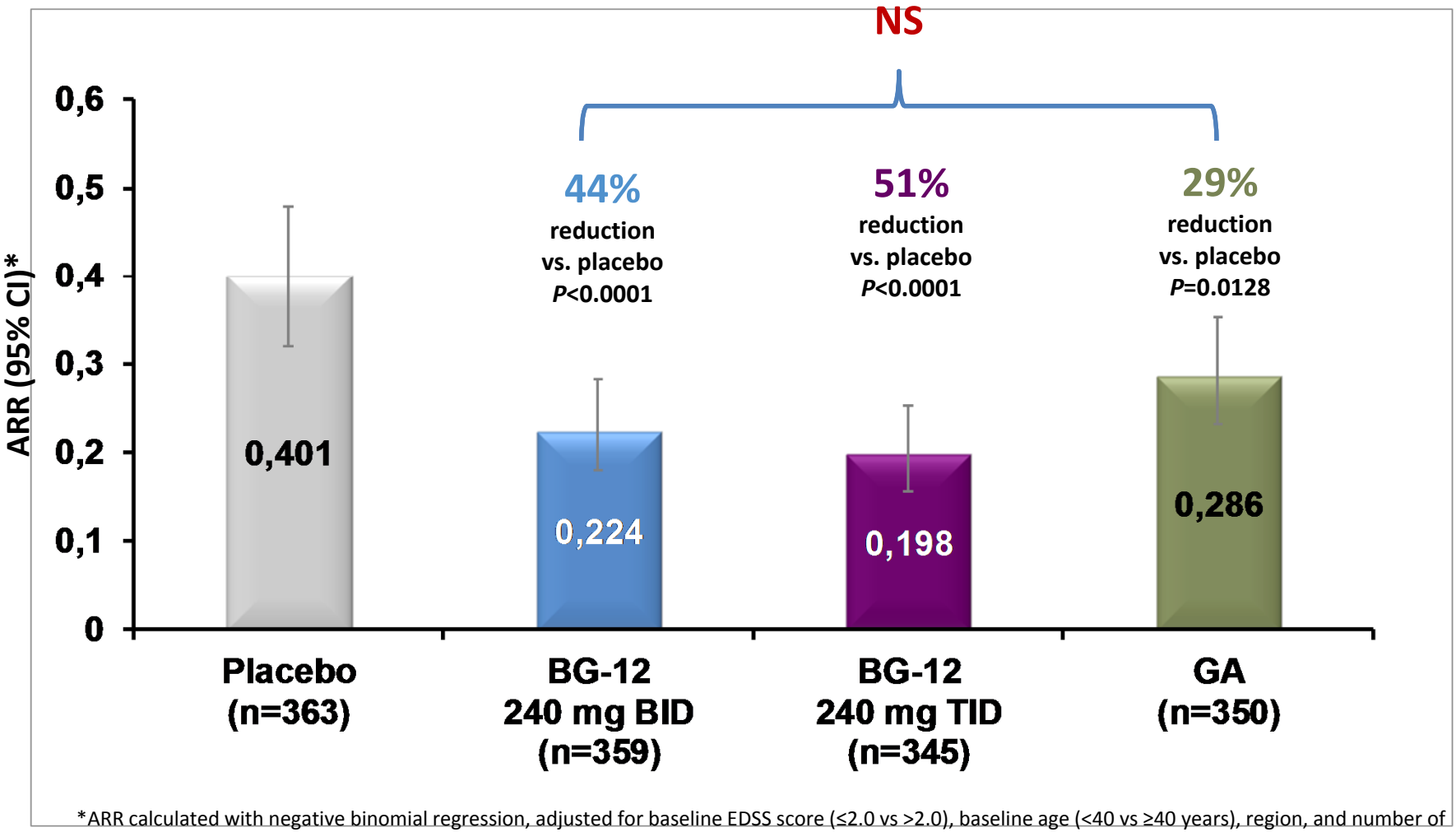


Annualized relapse rate



Confirmed (3 months) disability progression

Dimetilfumarato: efficacia terapeutica (CONFIRM)
Annualized relapse rate



*ARR calculated with negative binomial regression, adjusted for baseline EDSS score (≤2.0 vs >2.0), baseline age (<40 vs ≥40 years), region, and number of relapses in the year prior to study entry.

Profilo di safety del Dimetilfumerato

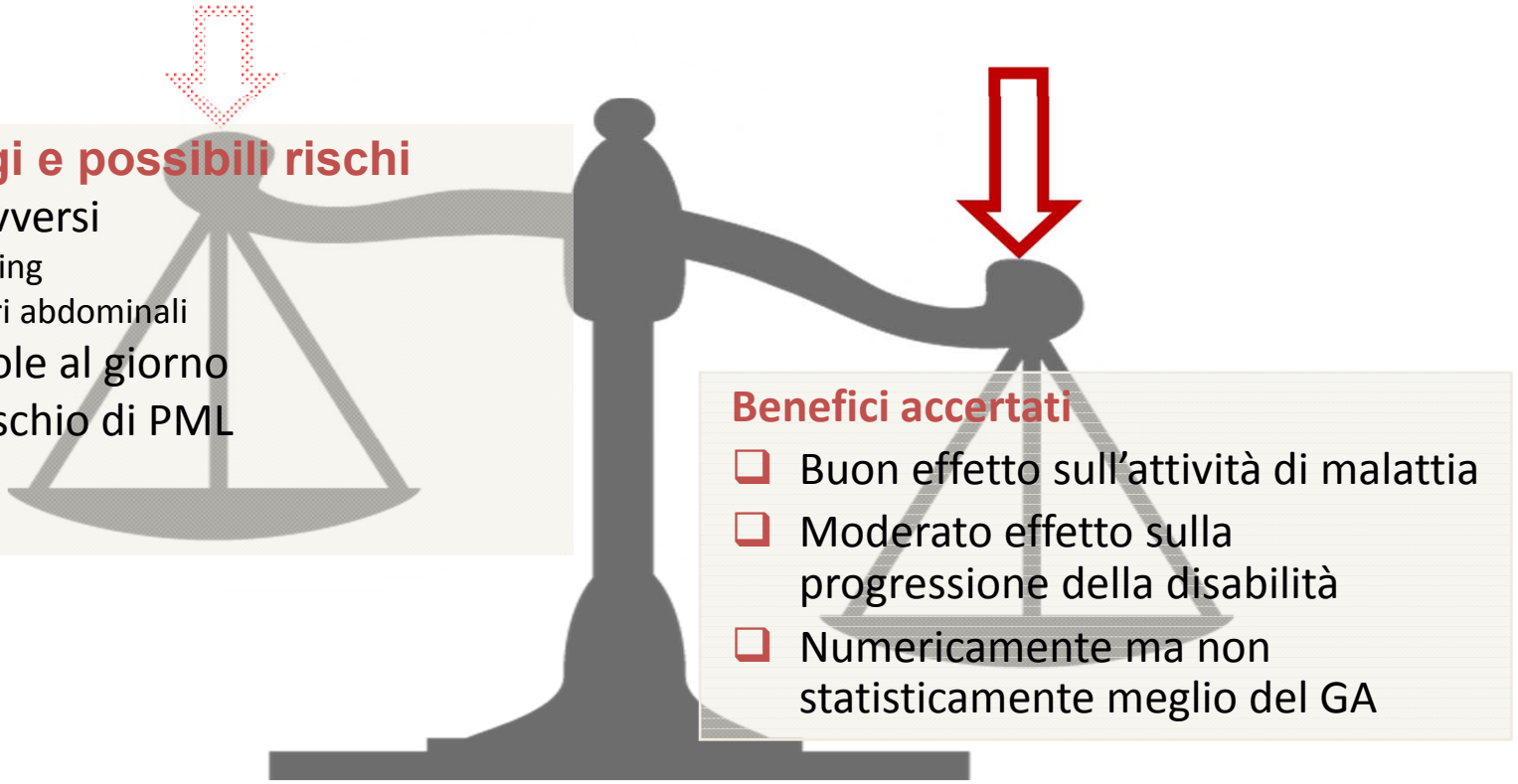
Adverse Events	
AEs with ≥ 5% difference in incidence *BG-12 Group vs. placebo*	
47% vs 9%	Flushing
9% vs 3%	Upper Abdominal Pain
6% vs 0%	Hot Flush
5% vs 0%	Severe upper Abdominal Pain
5% vs 0%	Paraesthesia

Safety Results
Discontinuations: 13% vs 9% (BG-12 vs placebo)
MS relapse was only SAE occurring in >1 pt/group. All others: PID, phlebitis, abdominal pain, urinary retention, MS only occurred in a single patient (*N=192*)
• Overall rate of Infection not different than Placebo (34%) • Nasopharyngitis was the most common infectious AE, more in placebo • No opportunistic infections reported

Few cases of PML in MS or psoriasis patients treated with dimethyl fumarate as monotherapy. Associated with low lymphocyte counts.

Kappos L et al. *Lancet* 2008; 372:1463–72

Dimetilfumarato: valutazione rischi / benefici



Noti disagi e possibili rischi

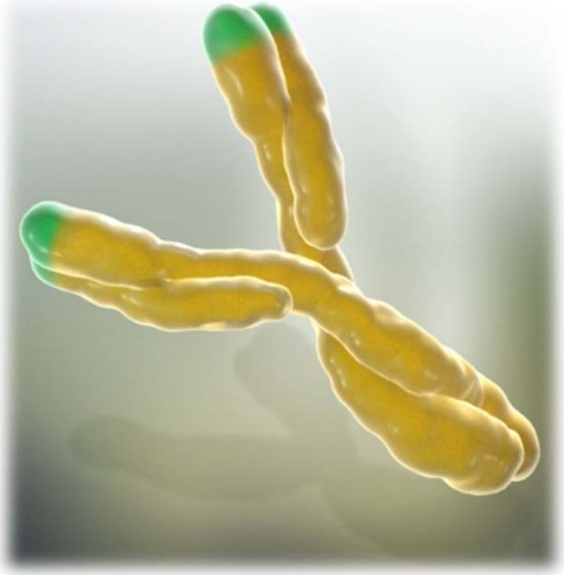
- Effetti avversi
  - Flushing
  - Dolori abdominali
- Due pillole al giorno
- Basso rischio di PML

Benefici accertati

- Buon effetto sull'attività di malattia
- Moderato effetto sulla progressione della disabilità
- Numericamente ma non statisticamente meglio del GA

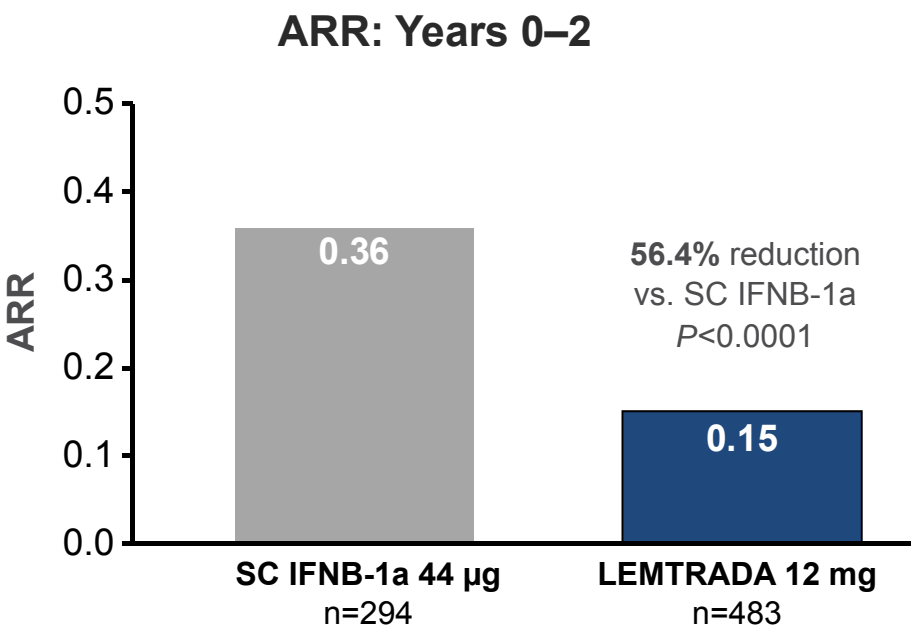
Alemtuzumab overview

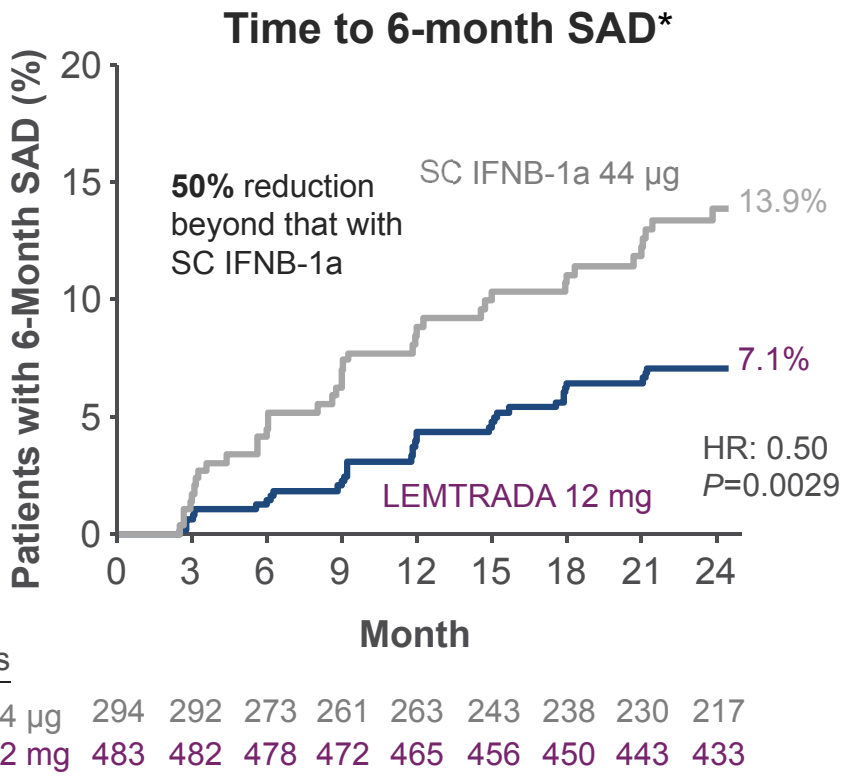
- **INDICAZIONE TERAPEUTICA:** indicato per i pazienti adulti con sclerosi multipla recidivante-remittente (SMRR) con malattia attiva definita clinicamente o attraverso le immagini di risonanza magnetica[1]
- **TIPOLOGIA:** anticorpo monoclonale umanizzato prodotto mediante DNA ricombinante[1]
- **TARGET:** glicoproteina CD52 di superficie presente ad alte concentrazioni sui linfociti B e T[1]
- **VIA DI SOMMINISTRAZIONE:** infusione endovenosa[1]
- **FREQUENZA DI SOMMINISTRAZIONE:** 2 cicli a distanza di 12 mesi[1]
- **POSOLOGIA:** I ciclo: 12 mg/die per 5 giorni consecutivi (dose totale di 60 mg)[1]
  II ciclo: 12 mg/die per 3 giorni consecutivi (dose totale di 36 mg)[1]



Alemtuzumab significantly reduced ARR and SAD[a] vs IFNB-1a SC in treatment naïve patients at year 2

Pooled CAMMS223/CARE-MS I data





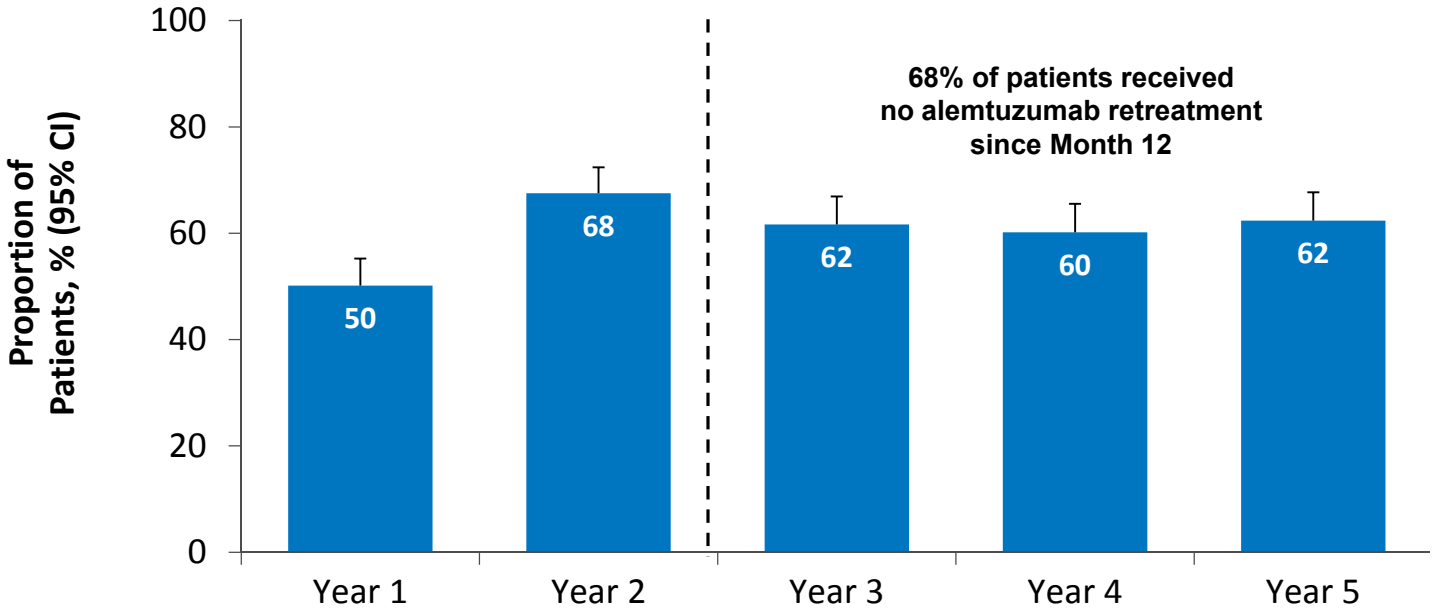
No. of Patients

SC IFNB-1a 44 µg	294	292	273	261	263	243	238	230	217
LEMTRADA 12 mg	483	482	478	472	465	456	450	443	433

[a]In the CARE-MS I study, there was no statistical significant in 6 month reduction of SAD.
ARR, annualized relapse rate; **HR**, hazard ratio; **SAD**, sustained accumulation of disability.
Kieseier BC et al. Presented at: American Academy of Neurology; 2014; Philadelphia. P2.209.

Proportion Achieving NEDA was Maintained Over 5 Years

Proportion of Patients With NEDA Over 5 Years



	Year 1	Year 2	Year 3	Year 4	Year 5
No. of Patients	369	354	326	324	319
Clinical disease activity-free	82%	85%	82%	84%	85%
MRI activity-free[1]	60%	77%	72%	70%	70%

1. Arnold DL, Traboulsee A, Cohen JA, et al. Presented at: ECTRIMS; October 7-10, 2015; Barcelona, Spain, P1100.

Risks identified during the ALEMTUZUMAB clinical development program

Identified Risk		Rate in LEMTRADA-Treated Patients	Notes
ITP	Autoimmune Events	~1% (1 fatality prior to implementation of monitoring program)[1]	• Onset generally occurred 14-36 mo after first exposure[1] • Most cases responded to first-line medical therapy[1]
Nephropathies	Autoimmune Events	0.3% (anti-GBM n=2)[1]	• Generally occurred within 39 mo after last administration[1] • Responded to timely medical treatment and did not develop permanent kidney failure[2]
Thyroid disorders (Hypo-/hyper-)	Autoimmune Events	~36%[a] (serious, 1%)[1]	• Onset occurred 6-61 mo after first LEMTRADA exposure; peaked in year 3 and declined thereafter[3] • Most mild to moderate, most managed with conventional medical therapy, however, some patients required surgical intervention[1] • Higher incidence in patients with history of thyroid disorders[1]
IARs		>90% (serious, 3%)[4,5]	• Occurred within 24 h of LEMTRADA administration[1] • Most mild to moderate; rarely led to treatment discontinuation[1] • May be caused by cytokine release following mAb-mediated cell lysis[1]
Infections		71% (serious, 2.7%)[1]	• Incidence highest during first mo after infusion; rate decreased over time[3] • More common with LEMTRADA; predominately mild to moderate in severity[1] • Generally of typical duration; resolved following conventional medical treatment[1]

[a]Through 48 mo after first exposure.

ITP, immune thrombocytopenia; **GBM**, glomerular basement membrane; **mAb,** monoclonal antibody.

1. LEMTRADA Summary of Product Characteristics. Genzyme Therapeutics Ltd, UK; September 2013; 2. Wynn D, et al. Presented at: European Committee for Treatment and Research in Multiple Sclerosis; 2013; Copenhagen; P597; 3. Coles AJ, et al. *Neurology.* 2012;78:1069-1078; 4. Coles AJ, et al. Lancet; 2012;380:1829-1839; 5. Cohen JA, et al. Lancet. 2012;380:1819-1828.

Efficacy and Safety of Ocrelizumab in Relapsing Multiple Sclerosis – Results of the Phase III Double-blind, Interferon beta-1a-controlled OPERA I and II Studies

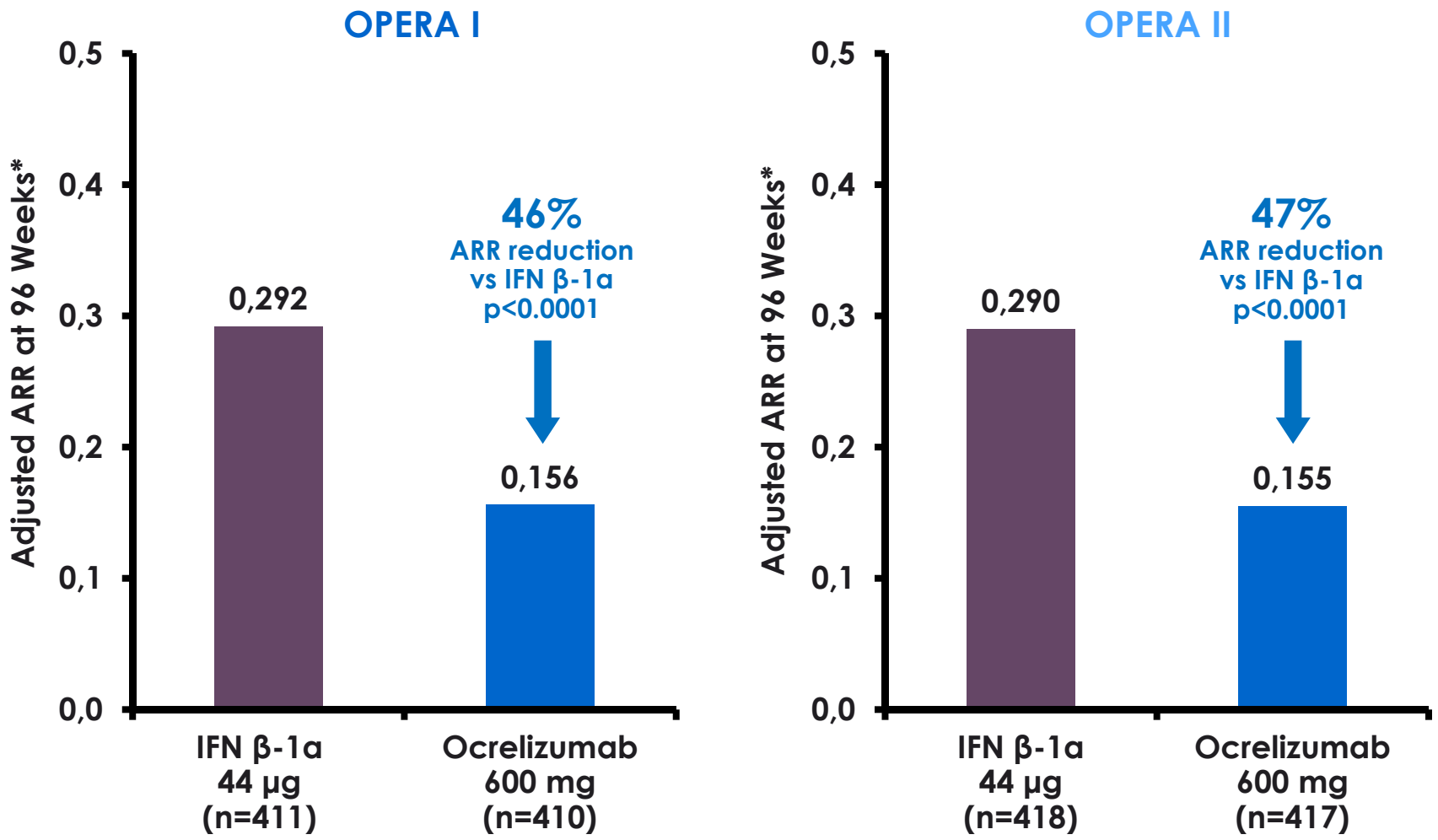
SL Hauser, GC Comi, H-P Hartung, K Selmaj, A Traboulsee, A Bar-Or, DL Arnold, G Klingelschmitt, F Lublin, H Garren, L Kappos, on behalf of the OPERA I and II clinical investigators

OPERA I, NCT01247324; OPERA II, NCT01412333

31st Congress of the European Committee for Treatment and Research in Multiple Sclerosis 2015

Platform presentation number 190

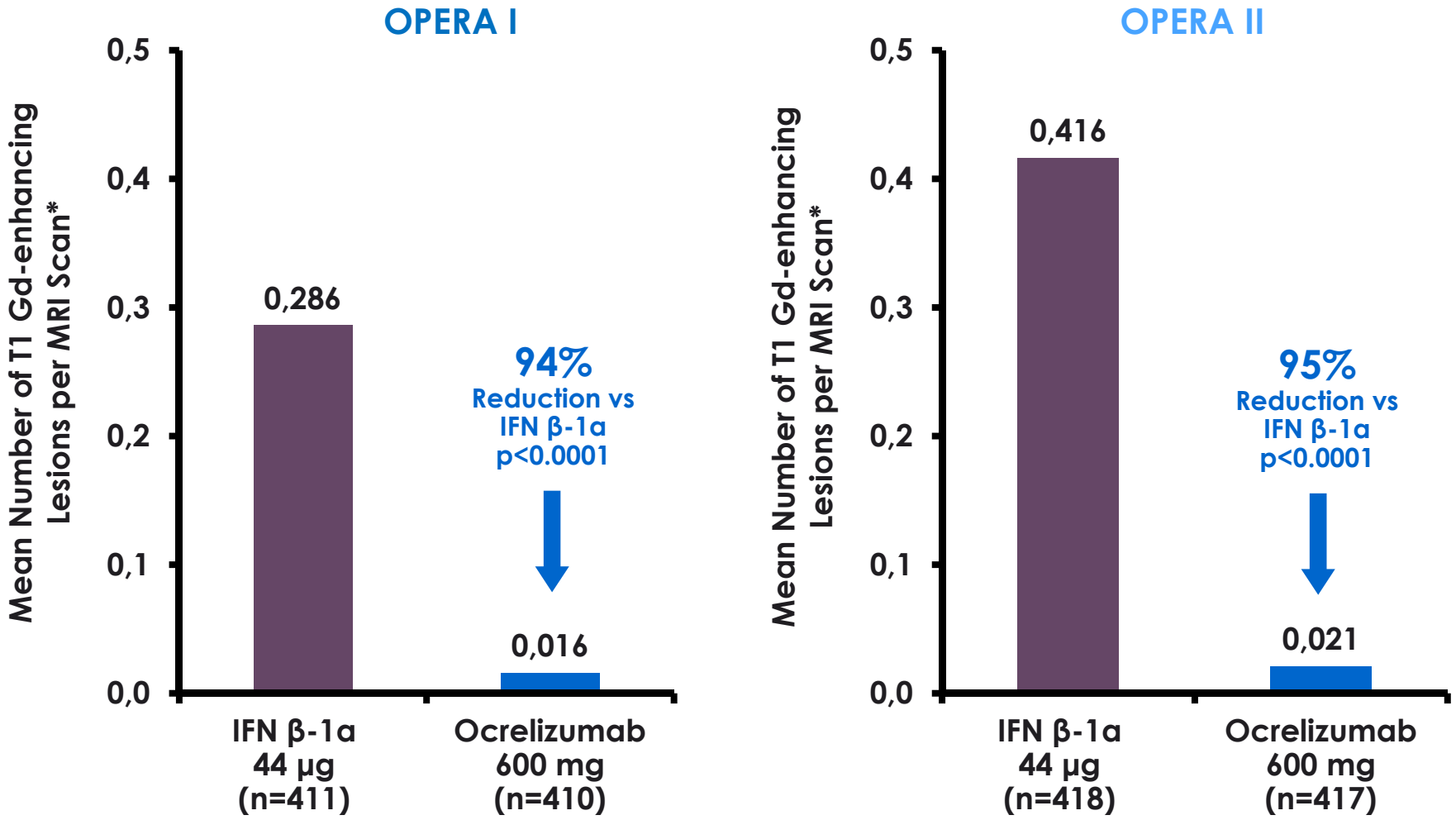
Primary endpoint:
Significant reduction in ARR compared with IFN β-1a



ITT

*Adjusted ARR calculated by negative binomial regression and adjusted for baseline EDSS score (<4.0 vs ≥4.0), and geographic region (US vs ROW).
ARR, annualised relapse rate; EDSS, Expanded Disability Status Scale; IFN, interferon; ROW, rest of the world.

Secondary endpoint: Significant reduction in number of T1 Gd⁺ lesions compared with IFN β-1a



ITT

*Adjusted by means calculated by negative binomial regression and adjusted for baseline T1 Gd lesion (present or not), baseline EDSS (<4.0 vs ≥4.0) and geographical region (US vs ROW).

EDSS, Expanded Disability Status Scale; Gd⁺, gadolinium enhancing; IFN, interferon; MRI, magnetic resonance imaging; ROW, rest of the world.

Efficacy and Safety of Ocrelizumab in Primary Progressive Multiple Sclerosis – Results of the Phase III, Double-blind, Placebo-controlled ORATORIO Study

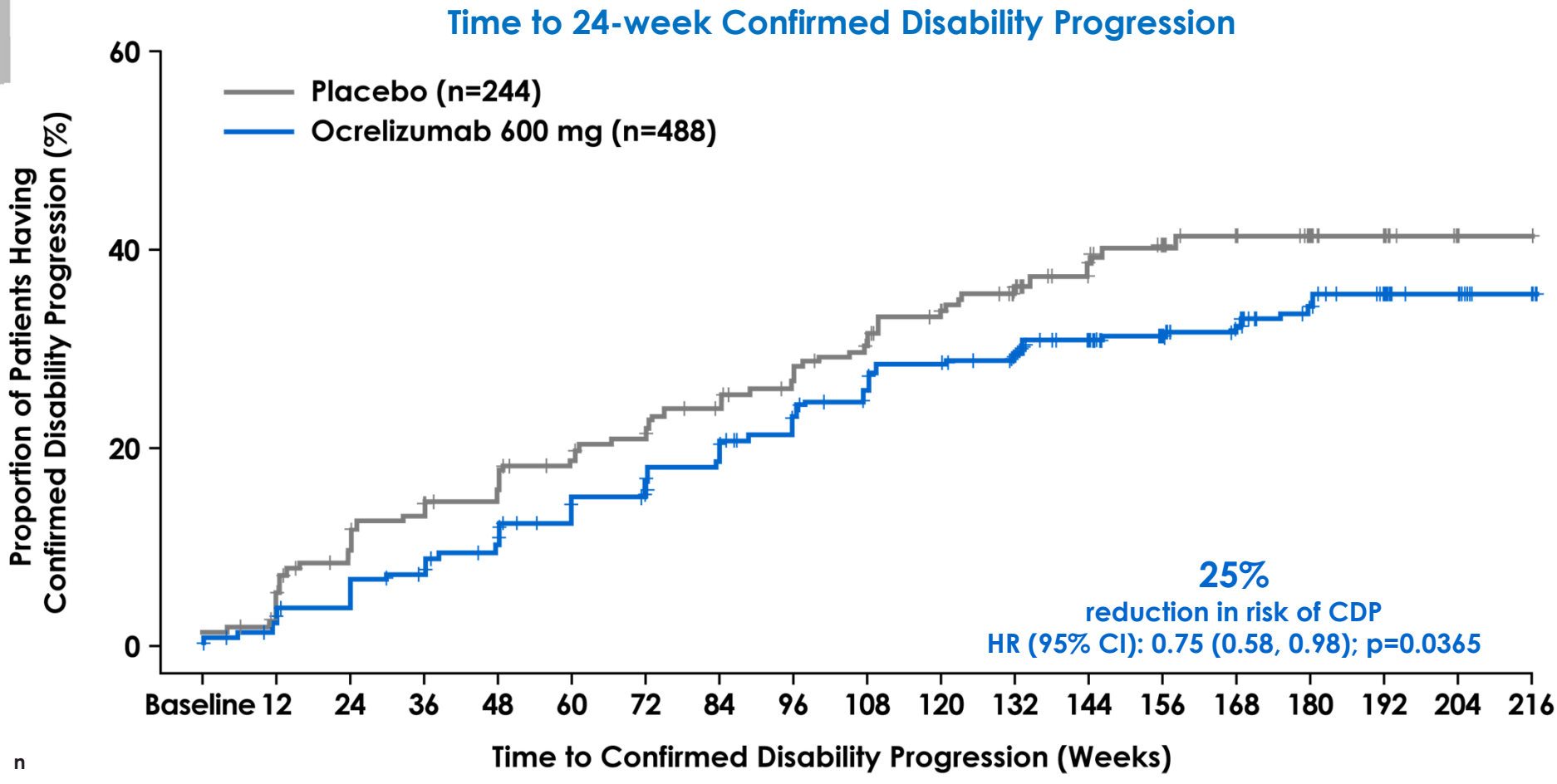
X Montalban, B Hemmer, K Rammohan, G Giovannoni, J de Seze, A Bar-Or, DL Arnold, A Sauter, D Masterman, P Chin, H Garren, J Wolinsky, on behalf of the ORATORIO clinical investigators

NCT01194570

31st Congress of the European Committee for Treatment and Research in Multiple Sclerosis 2015

Platform presentation number 228

Secondary endpoint: Significant reduction in 24-week CDP

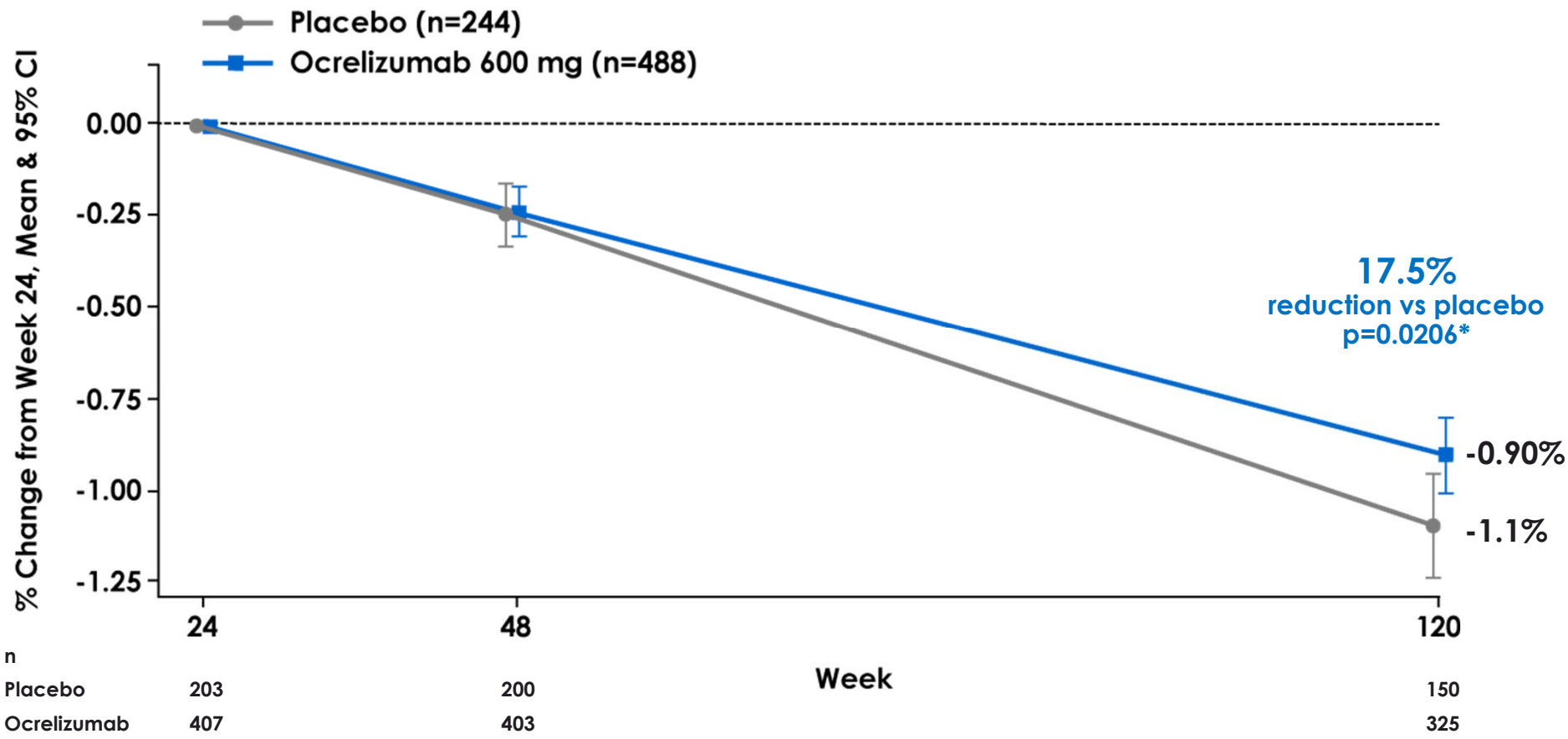


n																			
Placebo	244	234	214	202	193	183	176	166	157	148	139	125	89	70	50	33	22	7	2
Ocrelizumab	487	465	454	437	421	397	384	367	349	330	313	290	217	177	144	87	50	21	7

Analysis based on ITT population; p-value based on log-rank test stratified by geographic region and age.
Patients with initial disability progression who discontinued treatment early with no confirmatory EDSS assessment were considered as having confirmed disability progression.
CDP, confirmed disability progression; EDSS, Expanded Disability Status Scale; HR, hazard ratio; ITT, intent to treat.

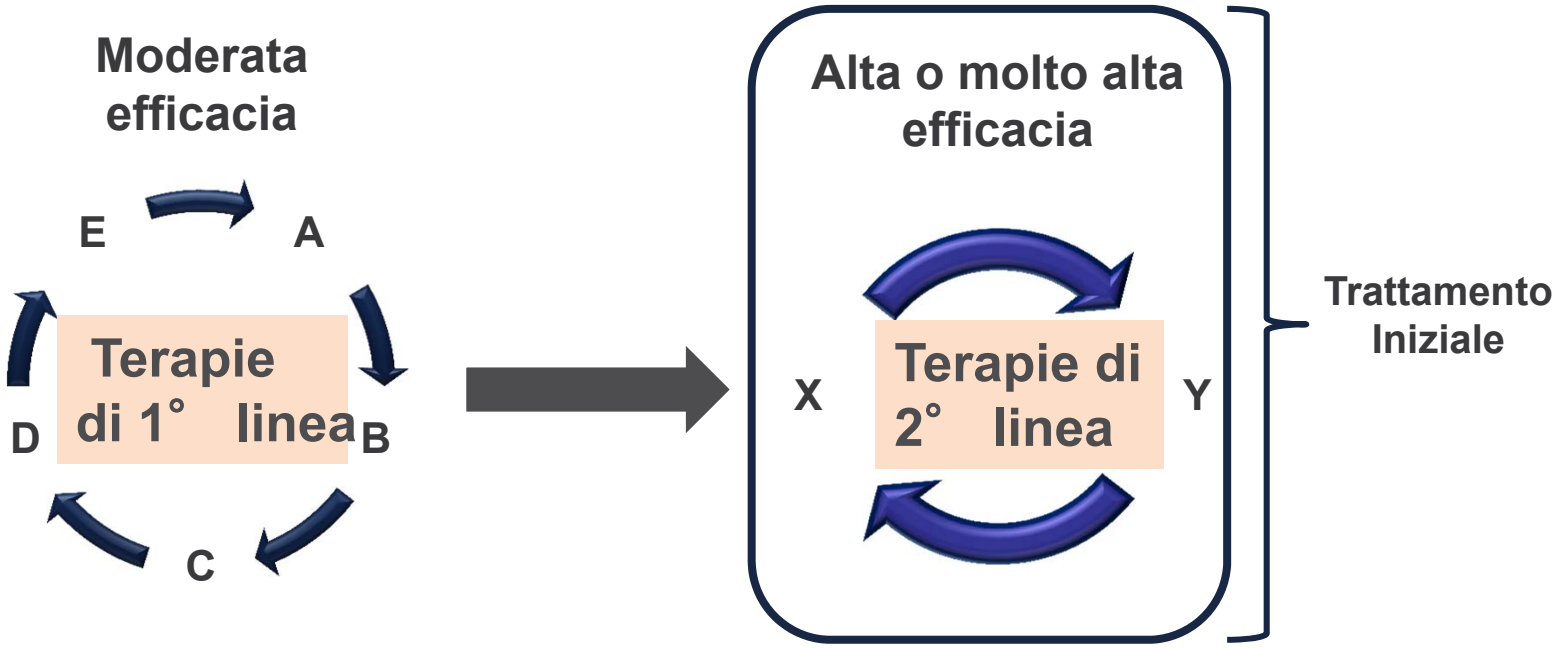
Secondary endpoint: Significant reduction in the rate of whole brain volume loss

Percent Change of Whole Brain Volume from Week 24 to Week 120



*Analysis based on ITT population with week 24 and at least one post-week 24 assessment; p-value based on MMRM at 120 week visit adjusted for week 24 brain volume, geographic region and age.
CI, confidence interval; ITT, intent to treat.

L’approccio tradizionale al trattamento della SM



- **Il decorso di malattia è molto eterogeneo tra I vari pazienti….e ciò nel tempo condiziona le scelte terapeutiche[1-3]**

1. Rio J et al. *Ann Neurol* 2006;59:344-52; 2. Miller A et al. *J Neurol Sci* 2008;274:68-75; 3. Rudick RA et al. *Lancet Neurol* 2009;8:545-59.
Figure adapted from Rio J et al. *Curr Opin Neurol* 2011; 24:230-7.

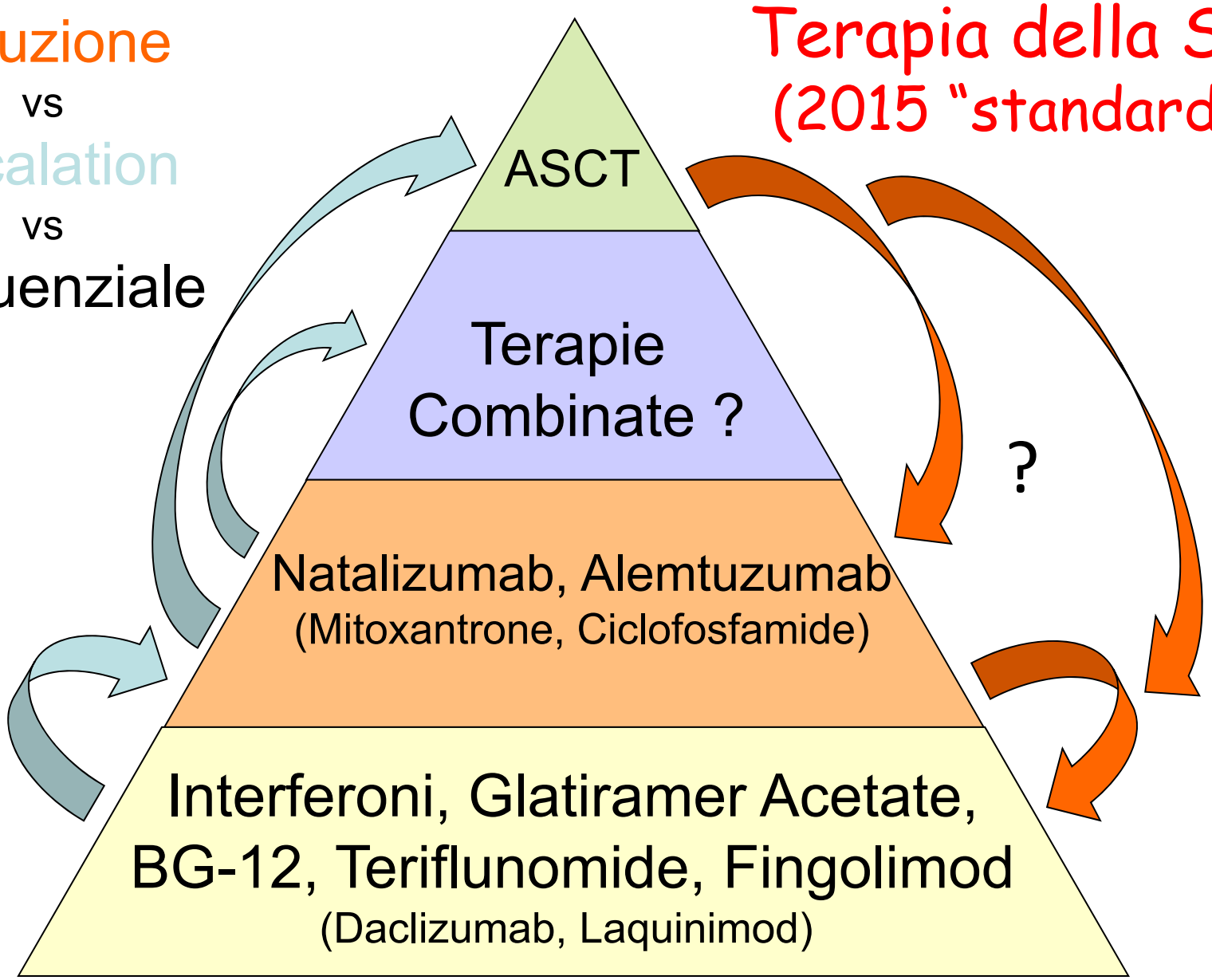
Induzione

vs

Escalation

vs

Sequenziale



A Proposed Treatment Algorithm

- **Treatment for Non-Aggressive Disease/First-line**
  - Injectables (GA/IFNβs)[1-4]
  - DMF[5]
  - Teriflunomide[6]
  - Fingolimod[7,a]

- **Treatment for Aggressive Disease/First-line**
  - Alemtuzumab[8]
  - Natalizumab[9] (especially JCV-negative patients)

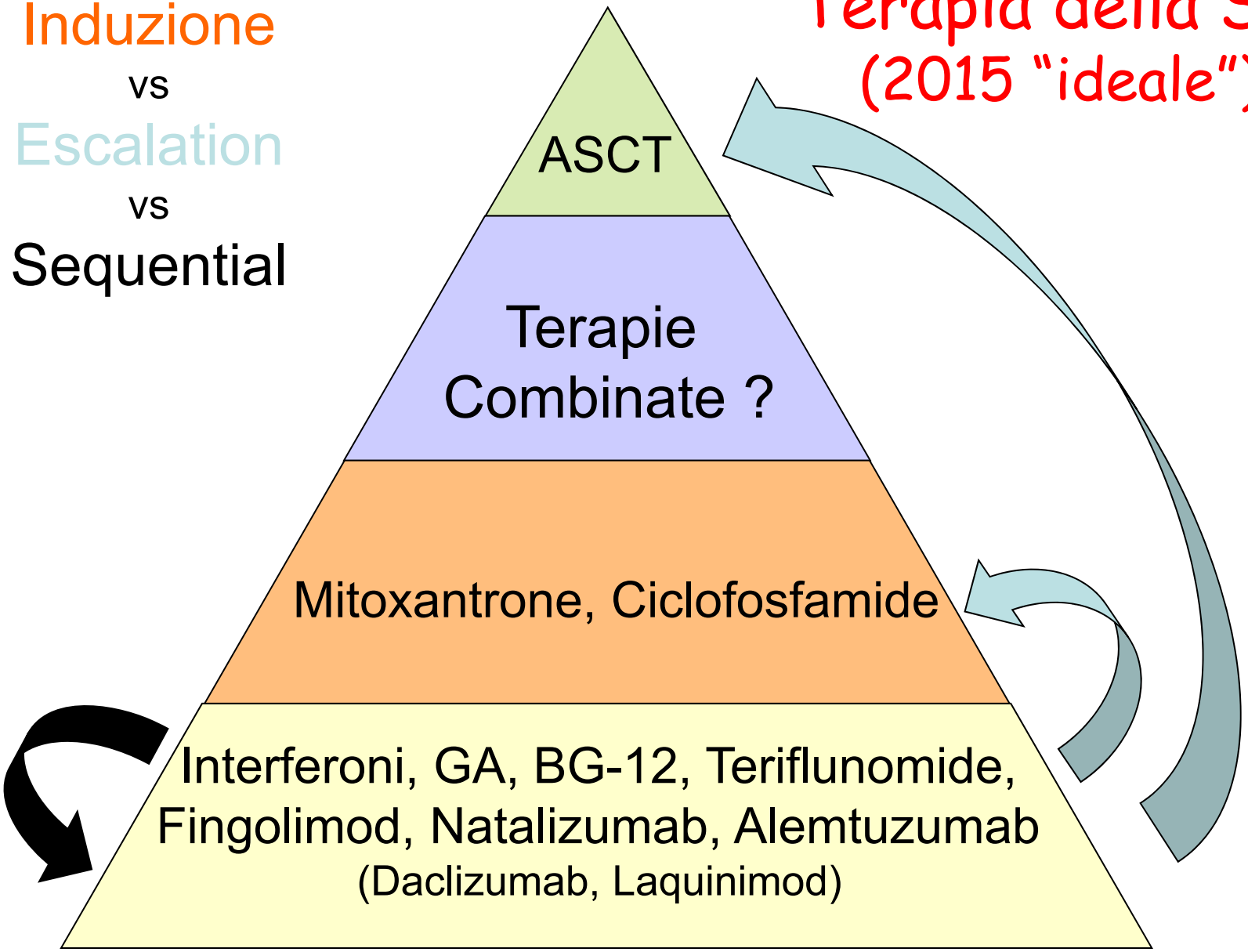
→

- **Escalation Treatment**
  - Fingolimod[7,a]
  - DMF[5]
  - Natalizumab[9,a]
    - » Option for escalation from fingolimod or DMF
  - Alemtuzumab[8,b]
    - » Option for escalation from any treatment

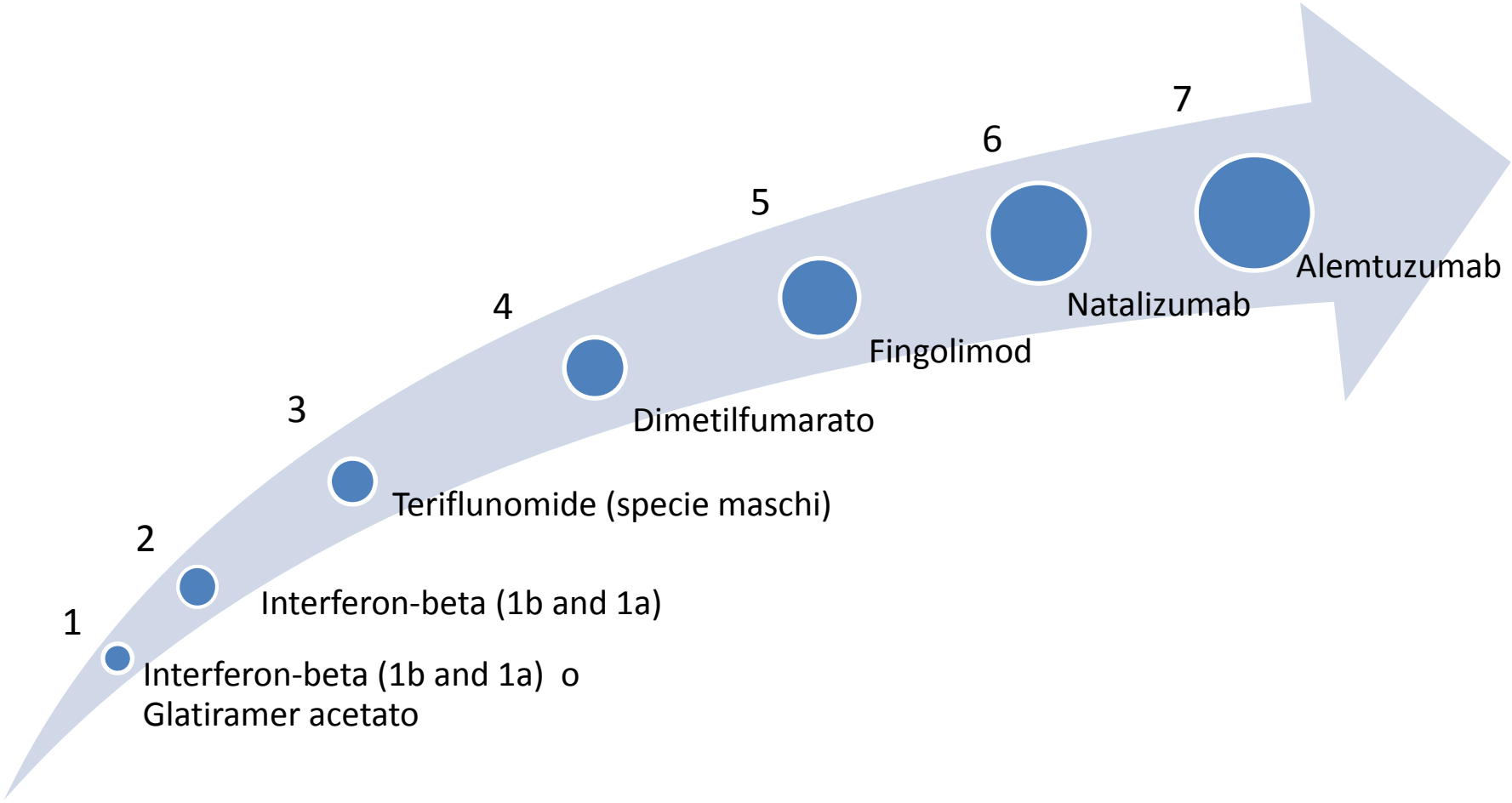
[a] Approved by the EMA for those with high disease activity despite treatment or in patients with rapidly evolving severe MS. [b] Approved by the EMA for those with active RRMS defined by clinical or imaging features.

Induzione
vs
Escalation
vs
Sequential

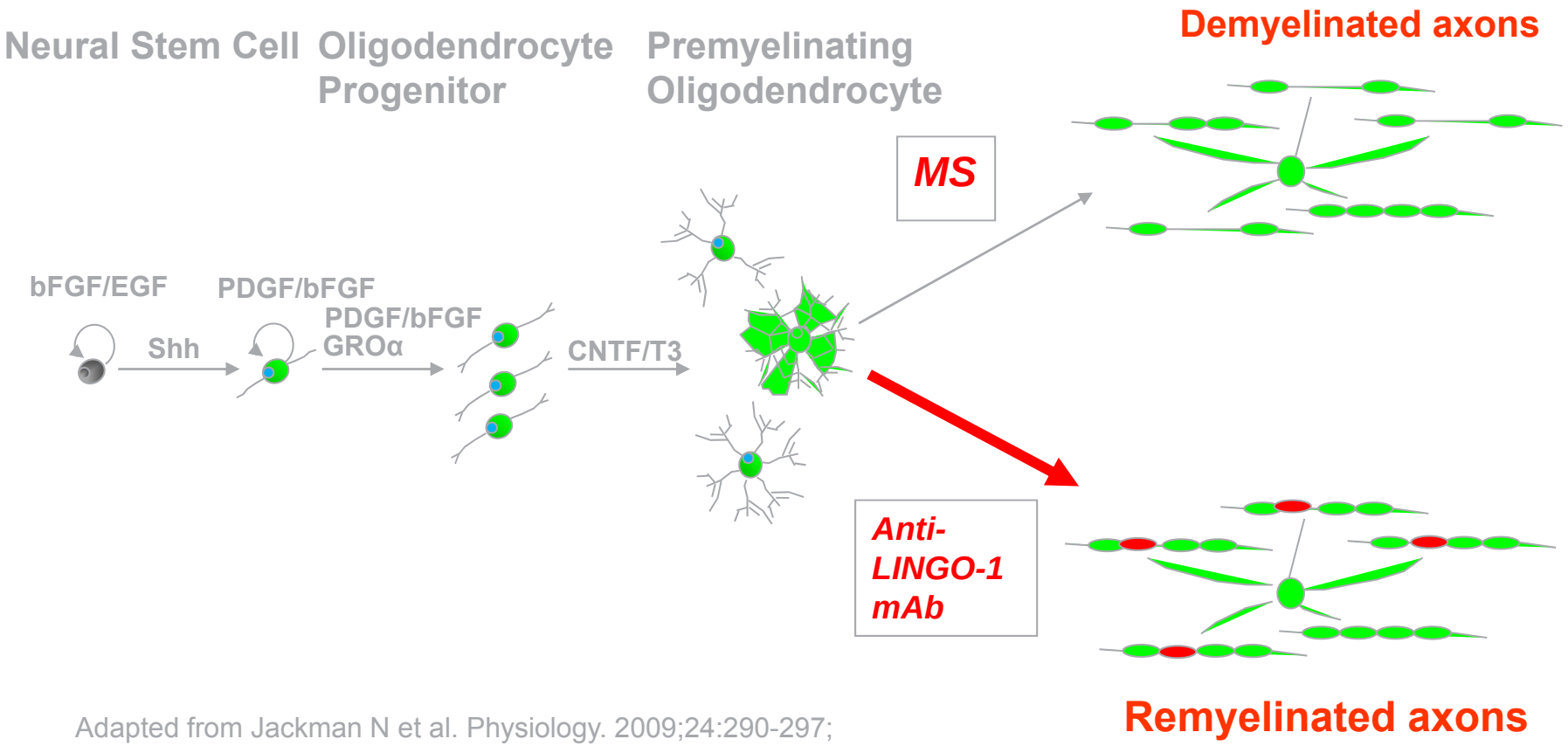
Terapia della SM (2015 "ideale")



Potenziale sequenza di inizio trattamento in pazienti con CIS o early active RR MS (2015)

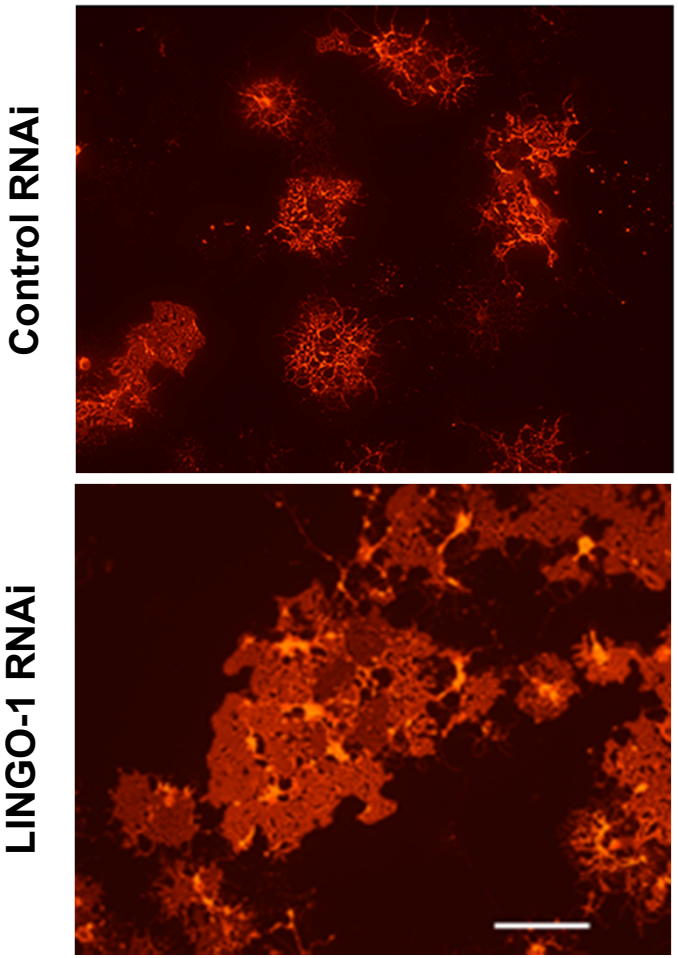


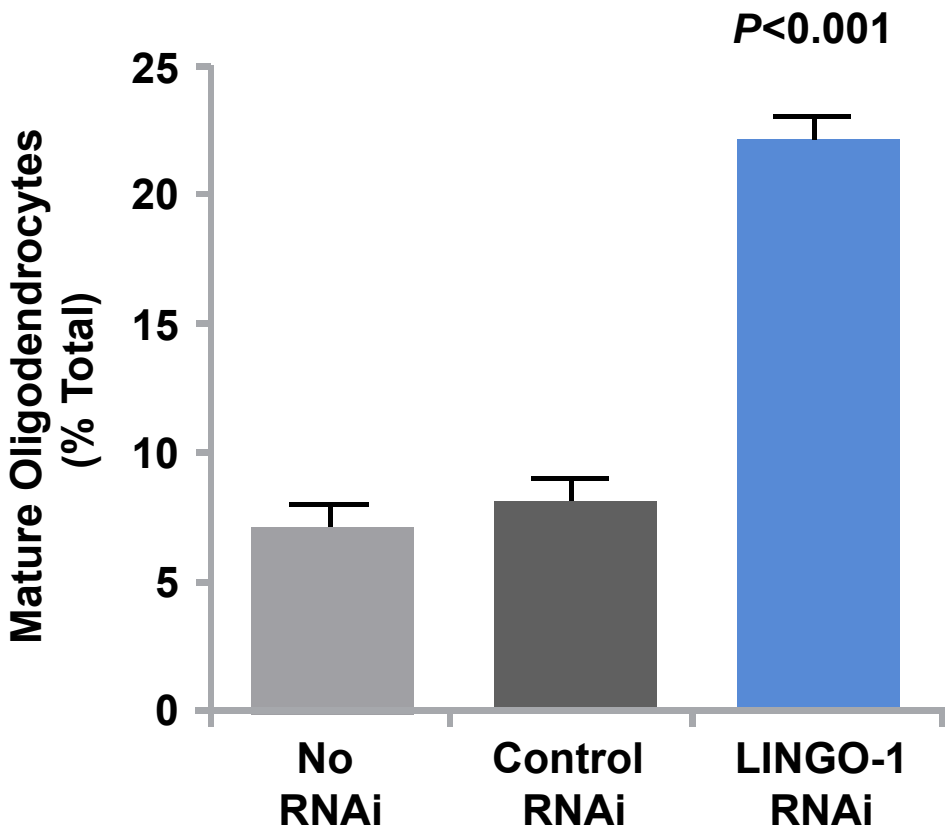
Anti-LINGO-1 Antagonist Antibodies Promote Remyelination



Adapted from Jackman N et al. Physiology. 2009;24:290-297;
Zhang SC. Nat Rev Neurosci. 2001;2:840-843

LINGO-1 Blockade Results in Oligodendrocyte Differentiation

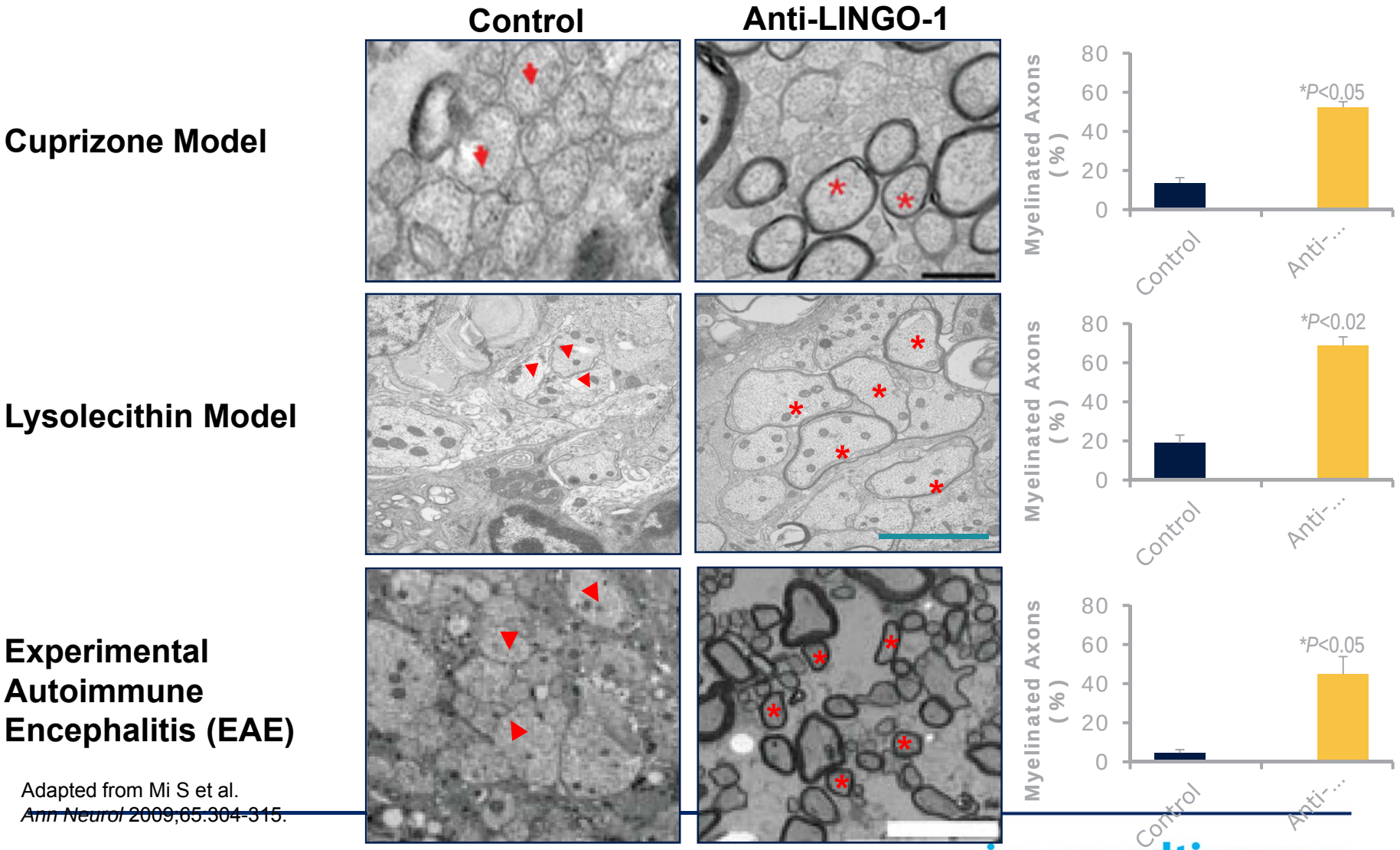




RNAi=ribonucleic acid interference.
Mi S et al. *Nat Neurosci.* 2005;8:745-751.

Anti-LINGO-1 is not approved for MS.

Anti-LINGO-1 Antibody Results in Remyelination in Animal Models of Demyelination



Adapted from Mi S et al. *Ann Neurol* 2009;65:304-315.

ims consulting group

Anti-LINGO-1 is not approved for MS.

Anti-LINGO-1 Phase II Clinical Development Plan

RENEW

Acute Optic Neuritis

- Placebo-controlled proof of concept
- Subjects with recent first episode of acute optic neuritis
- Dose: 100 mg/kg q4wks ×6
- Endpoints:
  - Visual evoked potential (VEP)/multifocal VEP (latency delay)
  - Optical coherence tomography (retinal nerve fiber and ganglion cell layer loss)
  - Visual function (low contrast letter acuity, visual quality of life)

SYNERGY

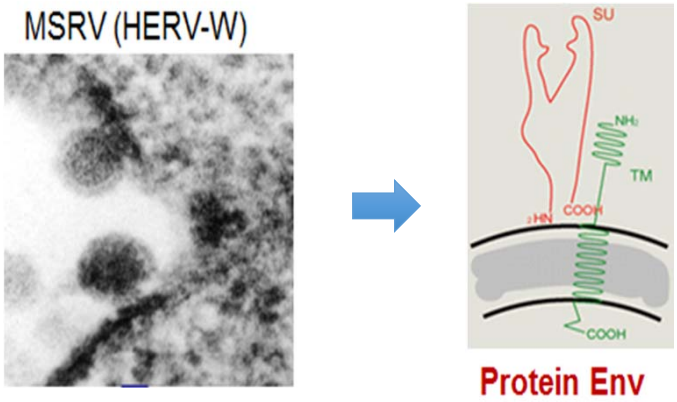
Relapsing Forms of MS

- Placebo-controlled proof of concept and dose ranging
- Subjects with RRMS and relapsing SPMS receiving IM IFNβ-1a
- Dose: 3, 10, 30, 100 mg/kg q4wks ×18
- Physical and cognitive endpoints:
  - EDSS/T25FW/9HPT/PASAT composite
  - Primary=improvement
  - Key secondary=delayed progression
  - MS-COG
  - MRI (MTR, DTI, black holes, atrophy)

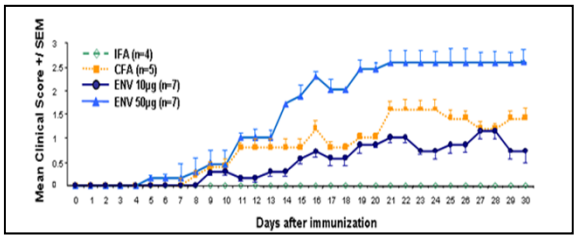
q4wks=every 4 weeks; IM=intramuscular; IFNβ=interferon beta; EDSS=Expanded Disability Status Scale; T25FW=Timed 25-Foot Walking Test; 9HPT=9-Hole Peg Test; PASAT=Paced Auditory Serial Addition Test; MRI=magnetic resonance imaging; MTR=magnetization transfer ratio; DTI=diffusion tensor imaging.
ClinicalTrials.gov Identifiers: RENEW: NCT01721161; SYNERGY: NCT01864148.

BIIB033 (Anti-LINGO-1) is not approved for MS.

MSRV-Env appears as a critical target for MS pathogeny

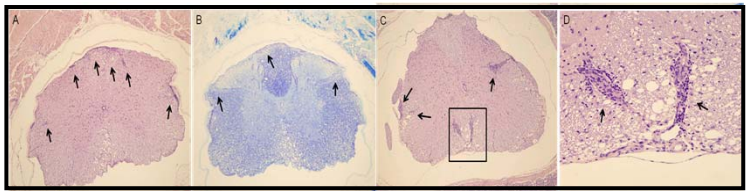


- Env induces MS-like symptoms in mice



C57/Bl6 mouse EAE with MOG antigen

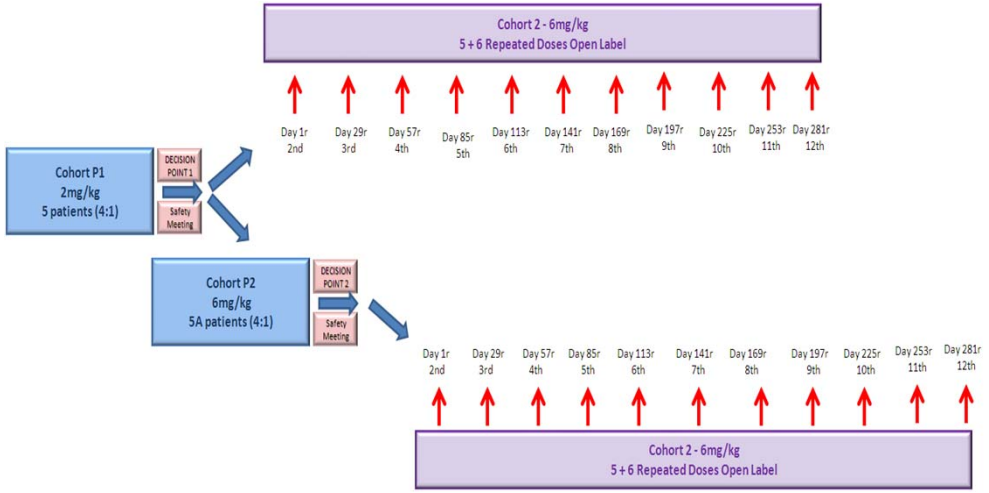
- Env induces demyelination in mice



- In vitro toxicity shown on different cells

Perron et al. PlosOne 2013

Phase IIa study design and patient characteristics

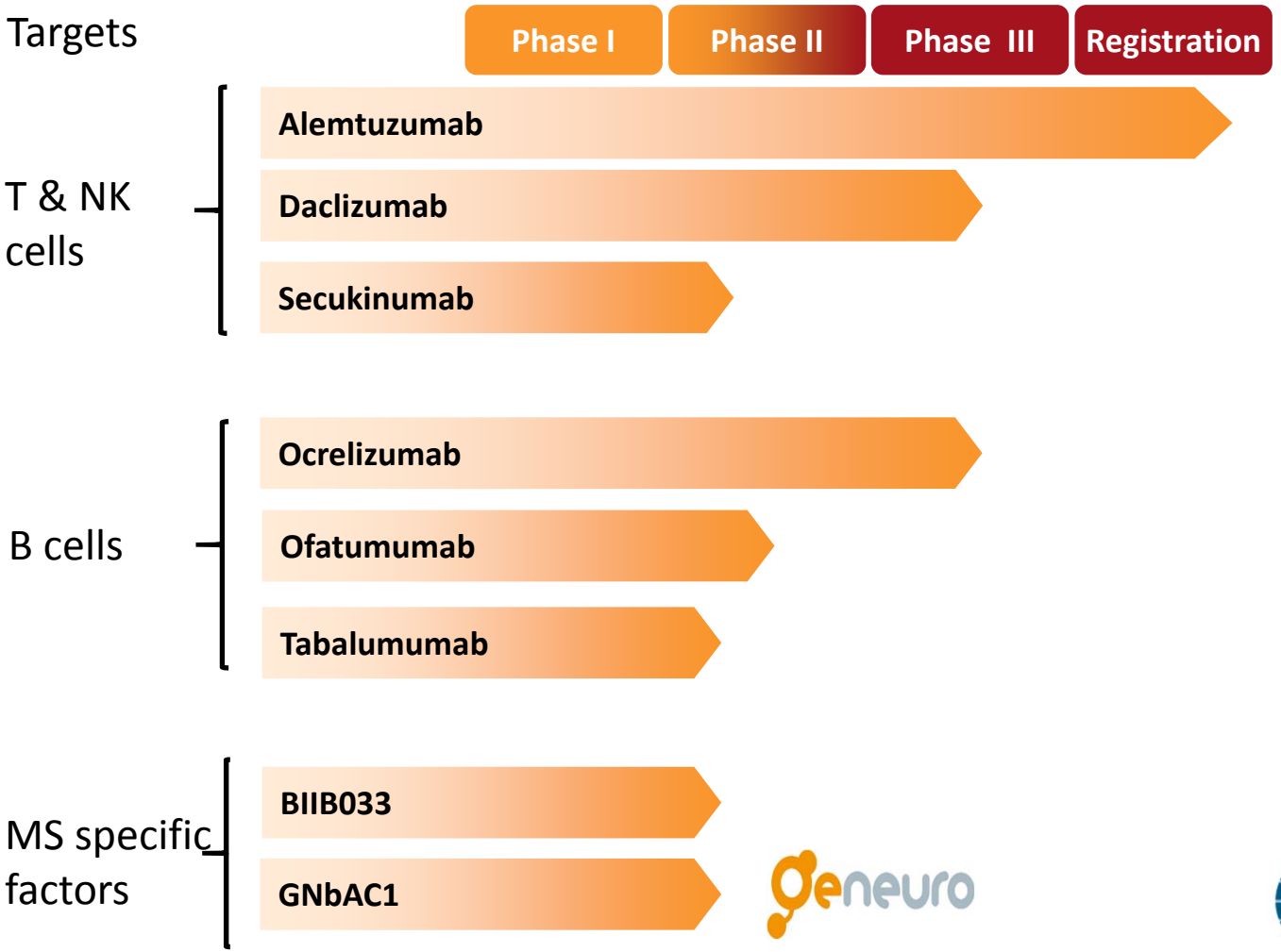


Single-blind, placebo-controlled dose-escalating randomised study, followed by a 12 month open-label extension

- IV administration of GNbAC1 every 4 weeks
- 10 patients recruited in Basel and Geneva, allocated in 2 cohorts of 2 mg/kg and 6 mg/kg
- Inclusion criteria: EDSS up to 6.5; exclusion of patients with any other treatment; no MSRV-Env level requirements
- 9 out of 10 patients had progressive MS

	EDSS (mean)
RRMS (n=1)	2.5
PPMS (n=3)	5.0
SPMS (n=6)	5.2

Pipeline of mAbs in MS clinical development



WORLDWIDE CLINICAL TRIALS
SCIENTIFICALLY MINDED · MEDICALLY DRIVEN


Grazie

Marika: hai lasciato il rubinetto della farmacia aperto…

XXXVI
CONGRESSO NAZIONALE
SIFO

Catania,
Centro Congressuale Fieristico
Culturale "Le Ciminiere"
22-25 OTTOBRE 2015