



A Glimpse at Immunomodulators in MS

An Interview with

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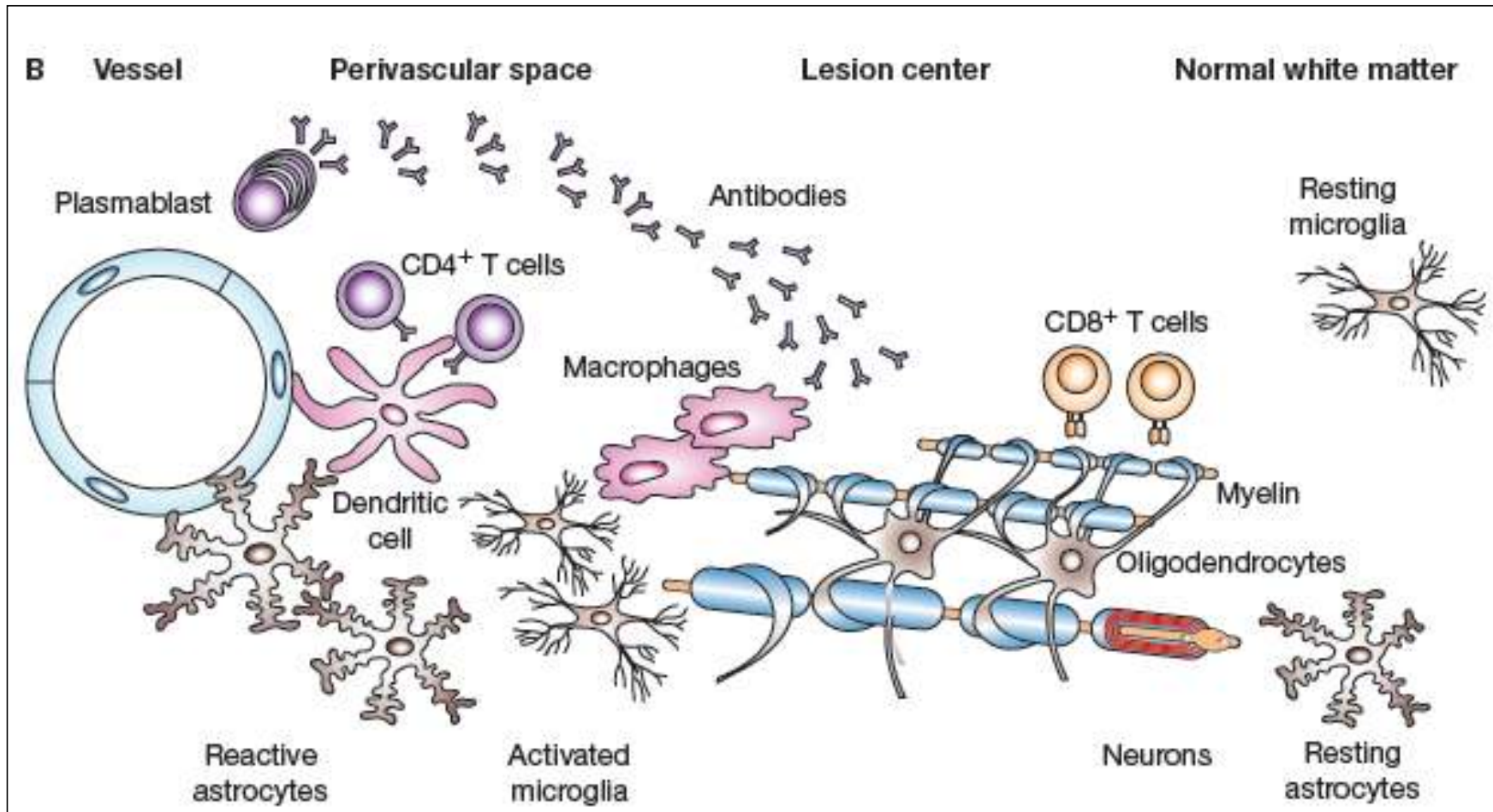
Introduction

- This interview with Dr Freedman will discuss:
 - History of immunomodulators in the treatment of relapsing-remitting MS (RRMS)
 - The central role of immunomodulators in MS treatment
 - Personalizing treatment algorithms for MS including co-morbidities and lifestyle of the patient
 - Considerations and future directions in the treatment of MS

History of Immunomodulators in RRMS

- Disease-modifying drugs or immunomodulators
 - Target the pathogenic processes of MS
 - Can alter the course of MS
- Interferon-beta-1b (IFN- β 1b) was the first treatment approved for relapsing-remitting MS (RRMS)

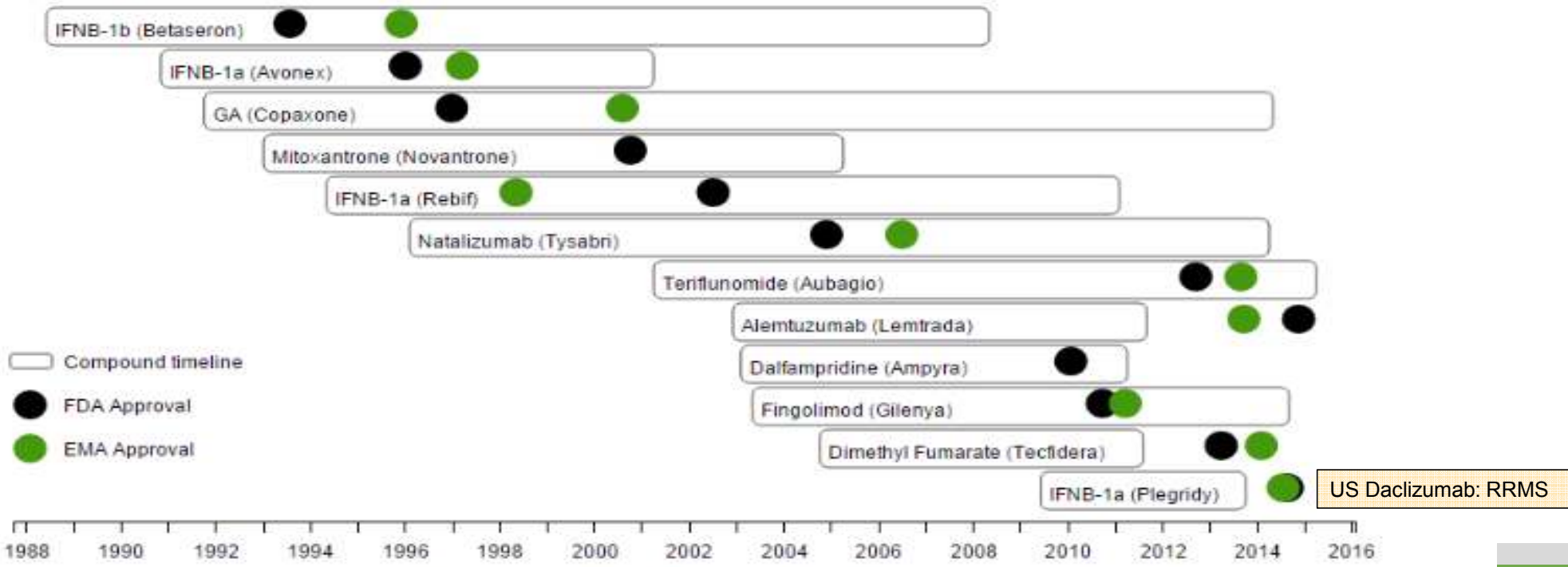
Immunopathogenesis of Multiple Sclerosis (MS)



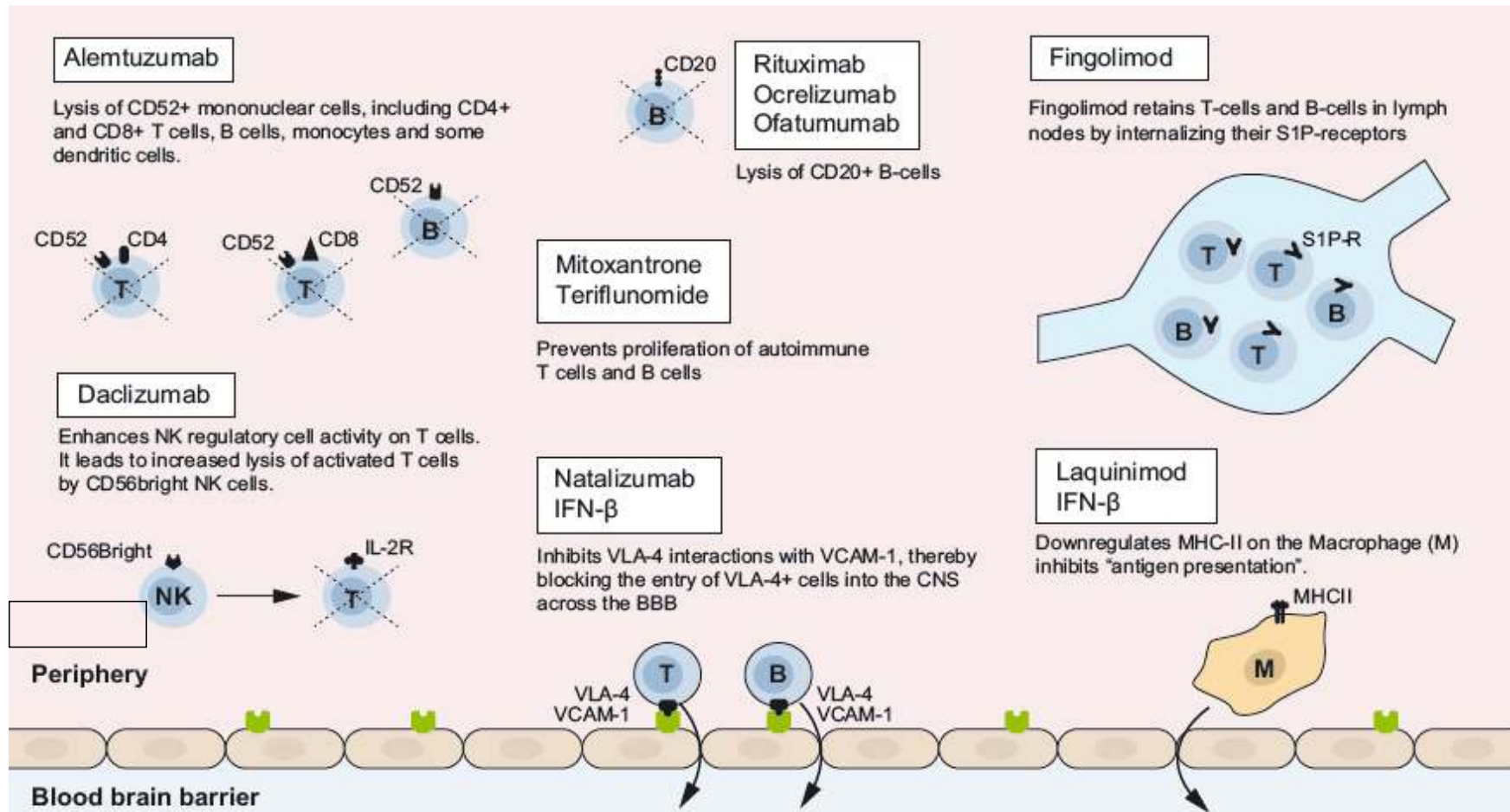
Timeline of MS Treatment Approvals

CIS N=554, 3 trials RRMS N=32405, 65 trials PPMS N=2574, 5 trials SPMS N=2856, 7 trials Mixed N=17369, 62 trials

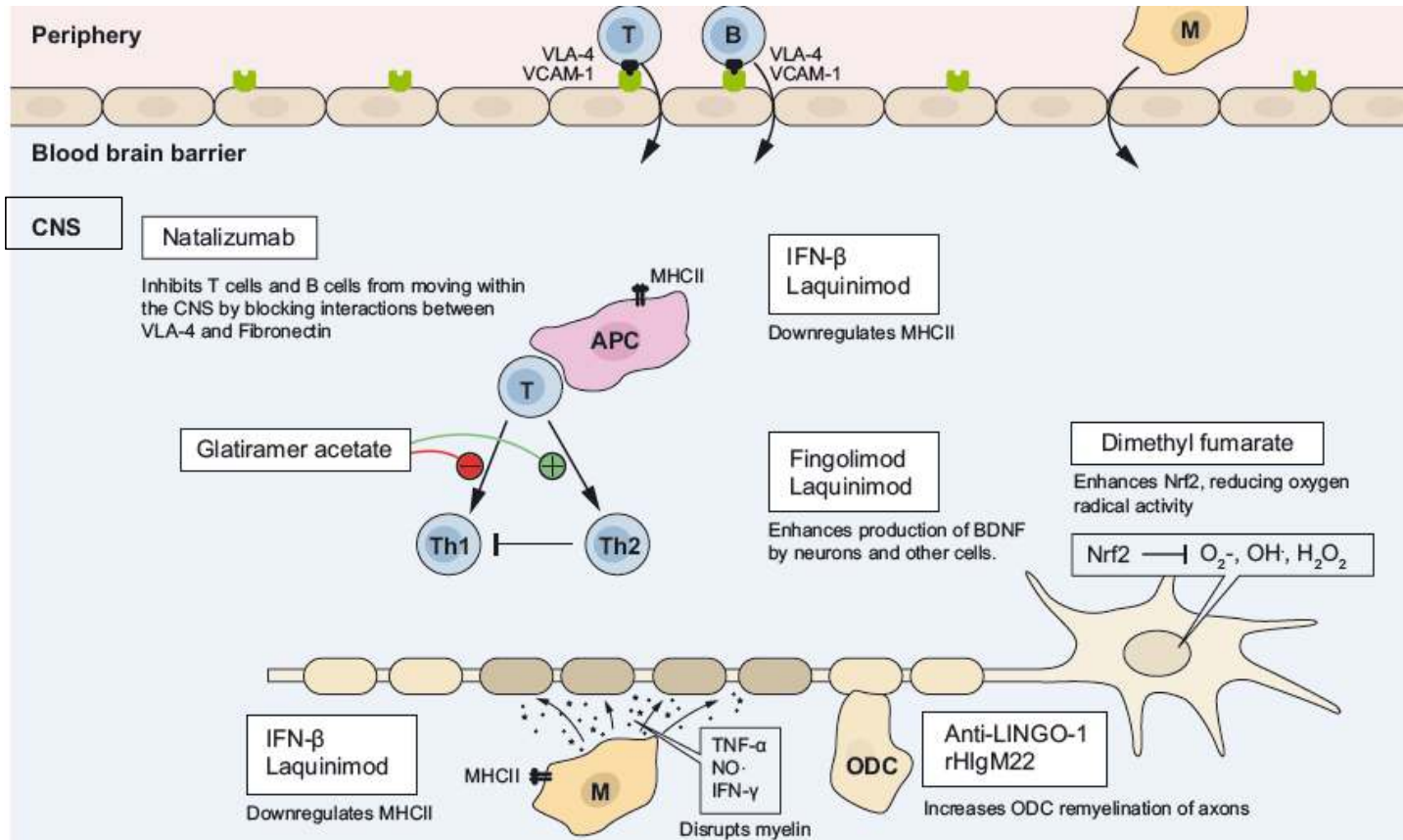
- Overview
- Alemtuzumab
- Dalfampridine
- Dimethyl Fumarate
- Fingolimod
- Glatiramer Acetate
- IFNB-1b
- IFNB-1a (Rebif)
- IFNB-1a (Plegridy)
- IFNB-1a (Avonex)
- Mitoxantrone
- Natalizumab
- Teriflunomide



Immunopathogenesis of MS in the Periphery for Available Disease Modifying Therapies



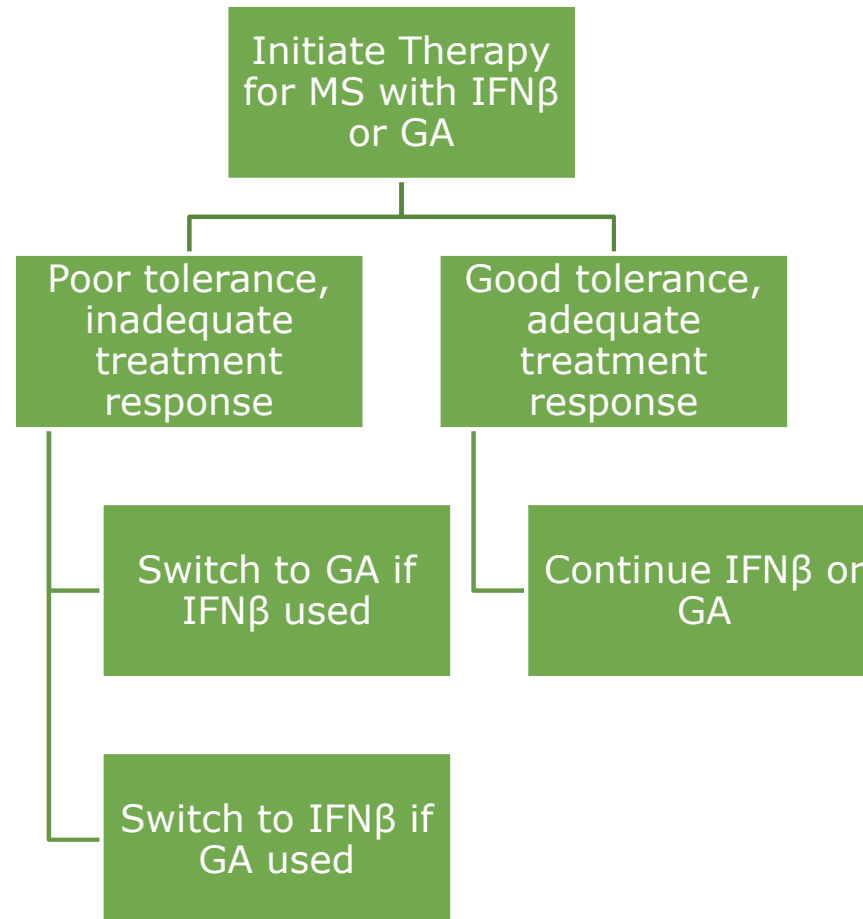
Immunopathogenesis of MS in the CNS for Available Disease Modifying Therapies



Cross AH, Naismith RT. *J Intern Med* 2014;275(4):350–363

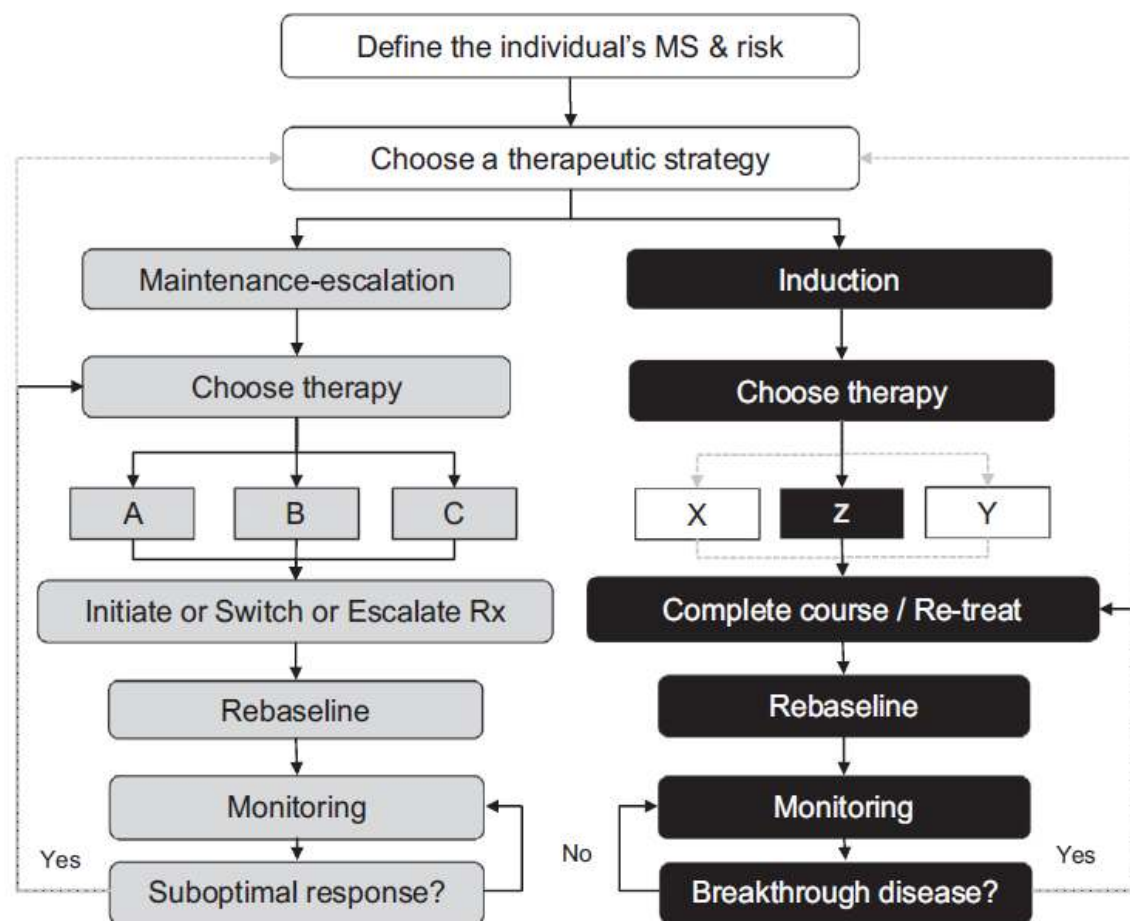
LIMIT THE DAMAGE

Previously Used Simplified Algorithm for the Treatment of MS



BARTS-MS TREAT-2-TARGET-NEDA ALGORITHM

NEDA = no evident disease activity



- MS prognosis based on clinical and MRI indices
- Life style and goals
- Shared goals for therapy

- Patient's preferences?
- Your choice?

- Patient's preferences?
- Your choice?

- Only one licensed induction therapy at present

Rebasing:

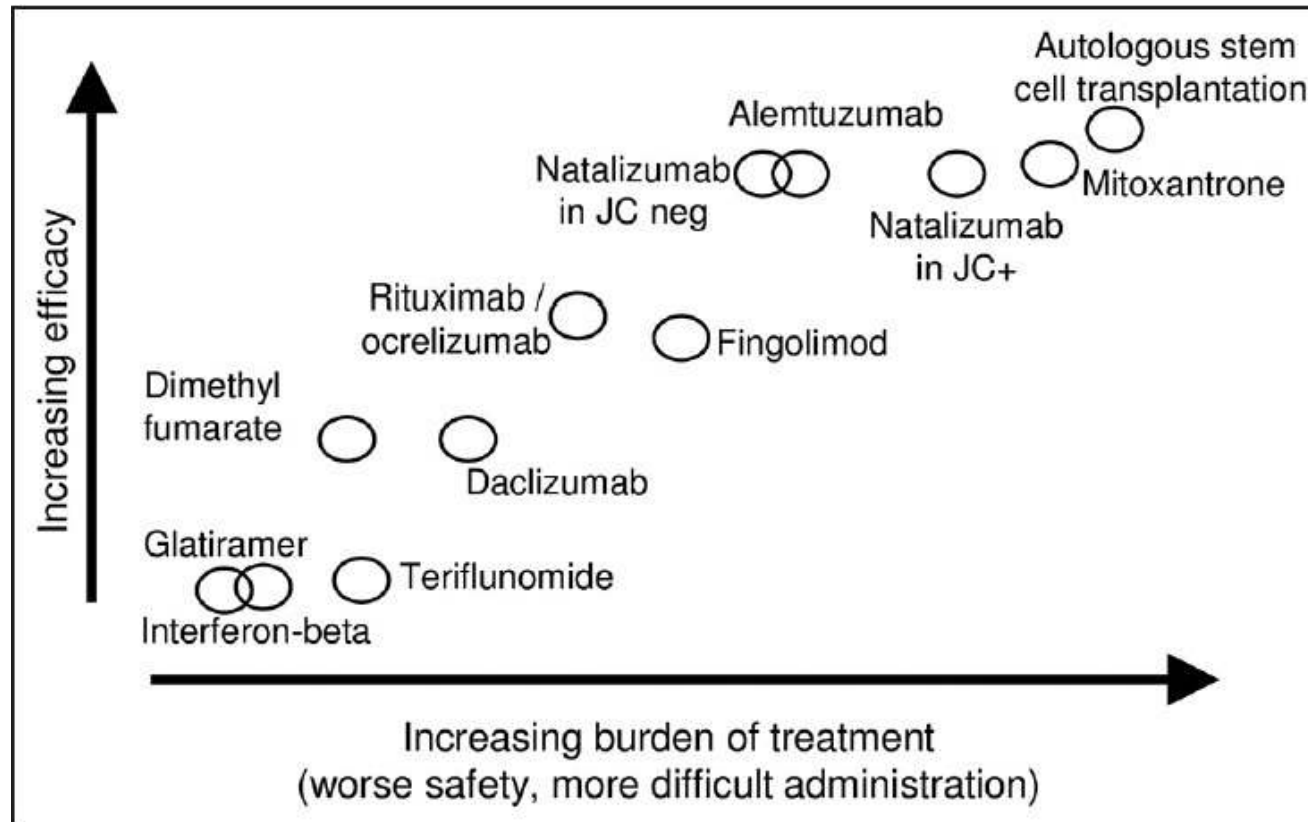
- IFN β , natalizumab, fingolimod, teriflunomide, Dimethyl-Fumarate=3-6 months
- Glatiramer acetate=9 months
- Alemtuzumab=24 months

Individual measures:

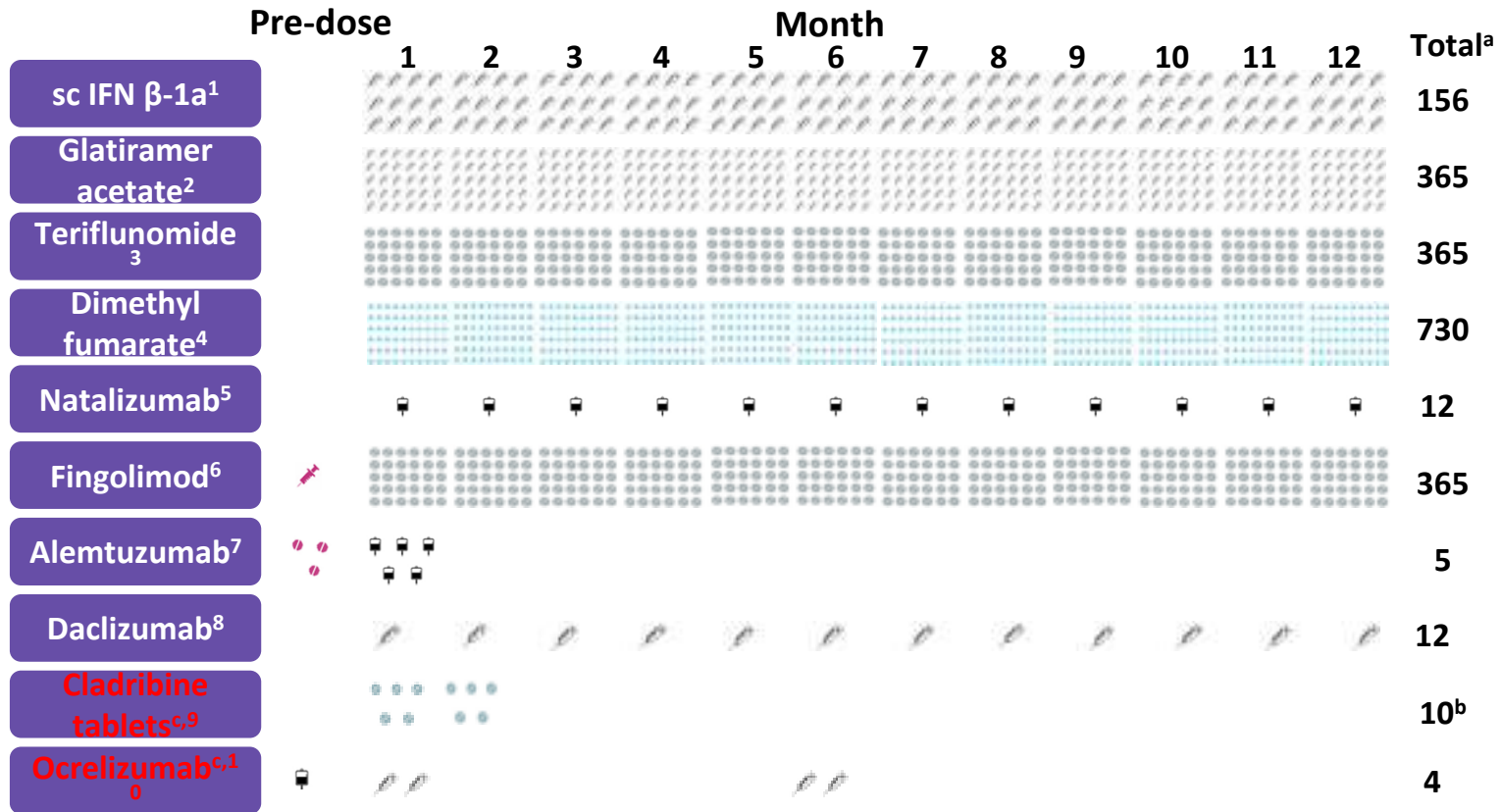
- Evidence of disease activity?
- Tolerability/safety?
- Adherence?
- Drug or inhibitory markers, e.g. NABs?

IFN β = interferon-beta; NABs = neutralizing antibodies; Rx = treatment

Personalized Risk-Benefit Assessment of Newer Therapies



Lower Burden with Treatment Frequency?



Not US approved as of 12/16

^aTotal number of administrations over the first 12 months of treatment. ^b3.5 mg/kg. 5 days of treatment separated by 1 month; total number of tablets dependent on weight. ^c These agents are under clinical investigation and have not been proven to be safe and effective. There is no guarantee they will be approved in the sought-after indication. IFN, interferon; sc, subcutaneous; SmPC, Summary of Product Characteristics. 1. Rebif® EU SmPC; 2. Copaxone® SPC; 3. Aubagio® EU SmPC; 4. Tecfidera® EU SmPC; 5. Tysabri® EU SmPC; 6. Gilenya® EU SmPC; 7. Lemtrada® EU SmPC; 8. Zinbryta® EU SmPC; 9. Giovannoni G, et al. N Engl J Med 2010;362:416–26; 10. Kappos L et al. Lancet 2011;378:1779–87; 11. Katsarava Z et al. BMC Neurol 2015;15:170; 12. Kruk ME, Schwalbe N. Clin Ther 2006;28:1989–95; 13. Devonshire V et al. Eur J Neurol 2011;18:69–77

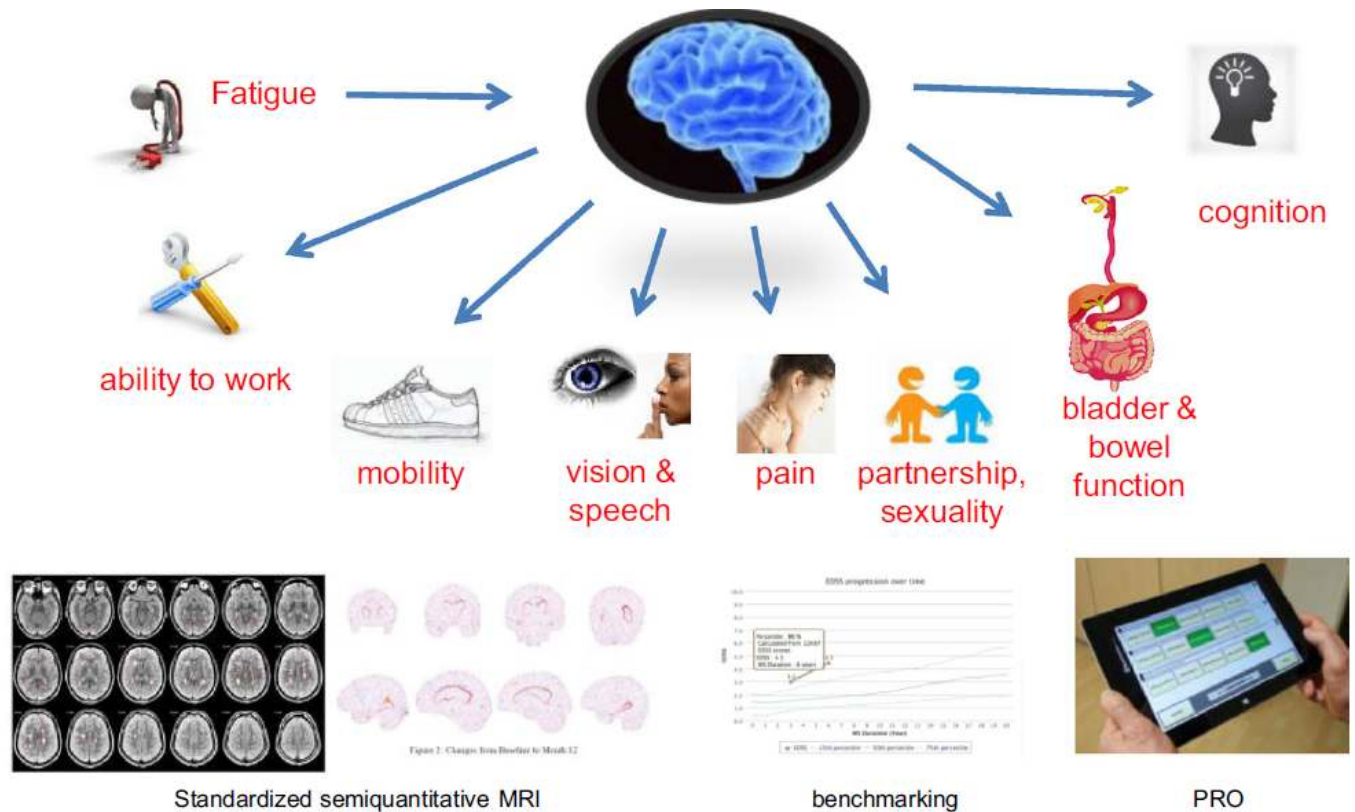
THINK AHEAD TO IMPROVE OUTCOMES

Considerations and Future Directions in MS Therapy

- A future-focused management plan that optimizes treatment and minimizes adverse effects
- Limiting exposure time of agents
- Combining and sequencing agents to achieve improved outcomes
- Rebaselining or retreating with safest immunomodulators or in combination with other therapies may be helpful in certain situations to maintain the desired response

Considerations for Lifestyle and Non-Pharmacologic therapy and Assessment of MS Treatment

- Lifestyle changes
 - Stop smoking
 - Exercise is helpful – small bouts are good
 - Rehabilitation programs help
- Address Comorbidities
 - Obesity, Hypertension
 - Uncontrolled diabetes
 - Cardiovascular disease
- Traditional Outcome Measures
 - Benchmarking, relapses and disability
- Newer Measures of Outcome
 - MRI assessments
- Patient Reported Outcomes (PRO)



Ziemssen T et al., *J Neurol* 2016;263(6):1053-1065

Conclusions and Perspectives in MS

- Risk-benefit profiles of each agent should be considered in individual patients
 - Personalized treatment algorithms should include optimal choice, sequences and combinations of currently available agents
 - Lifestyle modifications and management of comorbidities should be incorporated in MS treatment approaches
 - Immunomodulators are efficacious and safe for the treatment of MS
 - MRI can be used to monitor disease, but can be misinterpreted
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- A patient-centered approach is critical in the treatment and management of MS

References and Resources

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