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-β1b) 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)
- (Plegridy)
- (Avonex)
- (Betaseron)
- (Copaxone)
- (Novantrone)
- (Rebif)
- (Tysabri)
- (Aubagio)
- (Lemtrada)
- (Ampyra)
- (Gilenya)
- (Tecfidera)

**US Daclizumab: RRMS**
Immunopathogenesis of MS in the Periphery for Available Disease Modifying Therapies

Immunopathogenesis of MS in the CNS for Available Disease Modifying Therapies

LIMIT THE DAMAGE
Previously Used Simplified Algorithm for the Treatment of MS

Initiate Therapy for MS with IFNβ or GA

- Poor tolerance, inadequate treatment response
  - Switch to GA if IFNβ used
  - Switch to IFNβ if GA used

- Good tolerance, adequate treatment response
  - Continue IFNβ or GA
BARTS-MS TREAT-2-TARGET-NEDA ALGORITHM

NEDA = no evident disease activity

Define the individual’s MS & risk

Choose a therapeutic strategy

Maintenance-escalation

Choose therapy

A

B

C

Initiate or Switch or Escalate Rx

Rebaseline

Monitoring

Suboptimal response?

Yes

No

Induction

Choose therapy

X

Z

Y

Complete course / Re-treat

Rebaseline

Monitoring

Breakthrough disease?

Yes

No

Induction

Your choice?

Patient’s preferences?

Only one licensed induction therapy at present

Rebaselining:

IFNβ, 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?

IFNβ= interferon-beta; NABs = neutralizing antibodies; Rx = treatment

Personalized Risk-Benefit Assessment of Newer Therapies

**Lower Burden with Treatment Frequency?**

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<th>Month</th>
<th>Total</th>
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*Not US approved as of 12/16*

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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

- Rebasing or retreat 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

- A patient-centered approach is critical in the treatment and management of MS
References and Resources


