RELAPSING REMITTING MS: CURRENT DISEASE MODIFYING THERAPIES, CONSIDERATIONS IN CHOOSING TREATMENT AND ACUTE RELAPSE MANAGEMENT

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Disclosures

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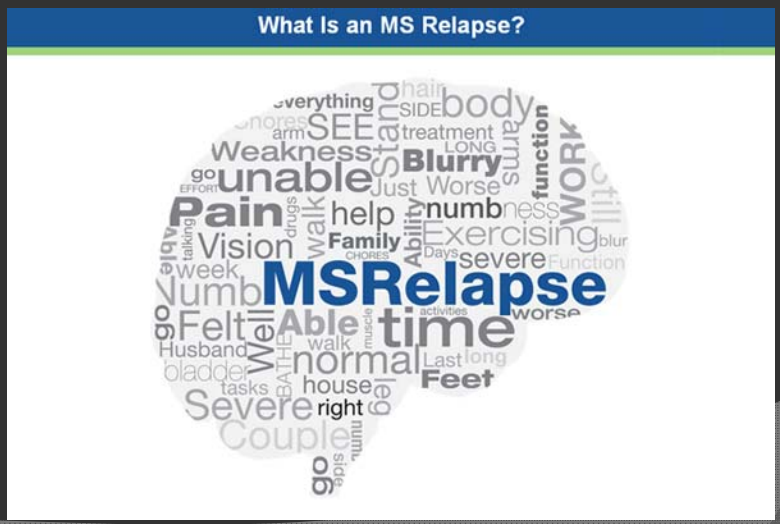
Therapy

- Four Tiered Approach
  - **Acute Therapy for Exacerbations**
  - Disease Modifying Therapy
  - Symptomatic Management
  - Rehabilitation

What is an MS Relapse?



What is not a relapse?

- Symptoms of MS can worsen under certain conditions including:
  - Fever
  - Infection
  - Increased Body temperature
  - Extreme Fatigue
  - Emotional Stress

Relapse Treatment: Corticosteroids

- Oral Prednisone
  - 500mg – 1200mg po q daily x 3-5 days
- IV Methylprednisolone
  - 1 gram IV q daily x 3-5 days
- ACTH
  - 80 units sc or im q daily x 5 days

Relapse Treatment: Corticosteroids

- Side effects include:
  - Insomnia
  - GI upset
  - Irritability
  - Swelling
  - Increased Appetite

Off-Label Treatments for Acute Relapse

- Plasma exchange
  - life threatening relapse
  - No response to high dose IV steroids
- IVIG 0.4mg/kg
  - Severe DM
  - Poor tolerance of steroid therapy

Case 1

- 30 y.o. woman with a 5 year history of MS presents with new onset left leg weakness. She has a history of recurrent optic neuritis in the past. This has been present for the past 2 days. She has not had a fever or any other signs of infection.
- WOULD YOU TREAT THIS PATIENT FOR AN MS RELAPSE?

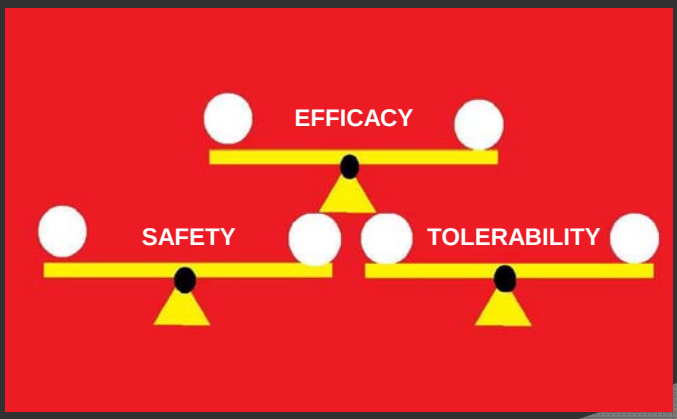
Therapy

- Four Tiered Approach
  - Acute Therapy for Exacerbations
  - **Disease Modifying Therapy**
  - Symptomatic Management
  - Rehabilitation

Our Current State of Affairs

- The 11 Distinct FDA Approved Treatments for MS are indicated for:
  - Clinically Isolated Syndrome
    AND/OR
  - Relapsing Forms of Multiple Sclerosis

Considerations when starting Disease Modifying Therapies



Other Considerations

- Non-neurologic Side Effects
- Sequencing of therapies
- Compliance with Monitoring

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Newly Approved Therapies!

Newly Approved Therapies: Alemtuzumab

- Dosing: 12mg/day IV for 3-5 days once a year
- Indications: Relapsing forms of MS
- MOA: monoclonal antibody to CD 52
- Prior Uses: Chronic Lymphocytic Leukemia

Newly Approved Therapies: Alemtuzumab

- Adverse Effects
  - Profound Lymphopenia
  - Autoimmune thyroid disease
  - Immune Thrombocytopenic Purpura
  - Infusion Reaction (Cytokine release)
  - Increased Susceptibility to Infections

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Newly Approved Therapies: Pegylated Interferon Beta 1-a

- Dosing: 125mcg SC every 2 weeks
- Relapsing MS
  - MOA: reduces pro-inflammatory cytokines
  - Inhibits T cell migration
  - Pegylation process allows the medication to have a prolonged effect

Newly Approved Therapies: Pegylated Interferon Beta 1-a

Common Adverse Events:

- Flu-like symptoms
- Injection Site Reactions
- Fever
- Headache

Case 2

- 51 yo man
- 20 year history of MS
- Therapy: Interferon SC every other day for 10 years
- EDSS 2.0
- Clinical status and MRI's stable
- Pt is having some injection fatigue, but feels he is doing well on his current therapy…

Case 2

- Which therapy may be a good choice for this patient?

Around the Corner

- One therapy is currently submitted for FDA approval

  Daclizumab

Daclizumab

- Dosing: 150mg every 4 weeks
- MOA: Binds to CD25 decreasing activated T cells
- Relapsing MS
- Prior Uses: Rheumatoid Arthritis, Kidney Transplant

PHASE II STUDIES - DACLIZUMAB

- SELECT:
  - ARR: 50-54% decrease
  - Confirmed Disability: 43-57% decrease
  - New Gd+ lesions: 79-86% reduction
  - New or enlarging T2 lesions: 70-79% reduction
- SELECTION (extension study)
  - ARR: 59% decrease
  - Confirmed Disability: 54% decrease
  - New T2 MRI lesions: 74% decrease
  - Gd+ lesions: 86% decrease

Daclizumab

- Adverse Events
  - Increased risk of infection
  - Abnormal liver function tests
  - Diarrhea
  - Constipation
  - Swelling of the extremities
  - Cutaneous skin reaction

Further Down the Road

Ocrelizumab

- Dosing: 600mg or 2,000mg
- Study Population: RRMS, PPMS
- MOA: Anti Cd20 (more humanized antibody)
- Also being studied in Rheumatoid Arthritis

Ocrelizumab

- Phase II studies showed ARR decreased by 73% (2,000mg) and 80% (600mg)
- Phase II studies showed 89% (600mg) and 96% (2000mg) decrease in Gd+ enhancing lesions compared to placebo
- Adverse Events
  - Infusion related reactions
  - Possible Increased risk of infection
  - One death from systemic inflammatory response of unknown cause

Kappos, Ludwig, et al. "Ocrelizumab in relapsing-remitting multiple sclerosis: a phase 2, randomised, placebo-controlled, multicentre trial." *The Lancet* (2011).

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Case 3

- 45 yo woman
- 3 year history of MS
- Previous therapies: injection therapy
- Recently diagnosed with Rheumatoid Arthritis
- EDSS of 3.5
- Pt is clinically stable but has 2 new small lesions on MRI

Case 3

- Which therapy would be most appropriate for this patient?

What's on the Horizon?

Other Drugs in earlier phases of Research

- Ofatumumab
- S1P Receptor Modulators
- Tcelna
- Statins
- Antibiotics
- Vitamin D3

Relapsing MS

- S1P Receptor Modulators
- Mastinib
- Ibudilast

Progressive MS

Potential Future Therapies

- Continued studies of drugs and mechanisms for myelin repair
  - ANTI- LINGO 1
  - Stem Cell Therapy
- Hormone Therapy
  - Estrogens
  - Testosterone

Other Avenues of Research

- Stem Cell Therapy
- Gene and DNA studies
- Personalized medicine and biomarkers
- Monitoring progression of disease

Any Questions?