Progress in MS: Current and Emerging Therapies

Presented by:
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Cambridge, Ontario, Canada
Today’s Discussion

- Natural History and Classification of MS
- Treating MS
- Management of the Disease
- Community Support and Services
- Questions & Answers
NATURAL HISTORY AND CLASSIFICATION OF MS
Standard Teaching About MS

• Chronic demyelinating disease of the CNS (i.e. brain, spinal cord and optic nerve)
  – Does not affect peripheral nerves
• Recurrent episodes of reversible (+/-) neurologic dysfunction
• Inflammatory pathology
• Immune-mediated “autoimmune characteristics”
MS is a Neurodegenerative Disease

- MS causes irreversible axonal damage / transection, resulting in neuronal death
- MS patients develop brain atrophy

Neural Function is Severely Disrupted by Myelin Damage Caused by Inflammation\textsuperscript{1,2}

Areas where myelin has been damaged, interrupt communication
Exposed nerve fibers are severed, causing permanent damage

Healthy nerve cell

Nerve impulse moves quickly
\~10.1 \text{ m/sec}\textsuperscript{*}

Nerve impulse moves slowly
\~0.9 \text{ m/sec}\textsuperscript{*}

Nerve impulse blocked

\textsuperscript{*} As measured in dorsal root ganglia in mice\textsuperscript{2}
Neuronal Damage Begins Prior to Clinical Presentation

<table>
<thead>
<tr>
<th>Time (Years)</th>
<th>Clinical Symptoms</th>
<th>Clinical Threshold</th>
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- Clinically Isolated Syndrome
- Relapsing Remitting
- Secondary Progressive

First Clinical Attack

Axonal Loss

Demyelination
MS: Brain Volume and MRI Changes

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<th>Preclinical</th>
<th>C. I. S.</th>
<th>Relapsing Remitting</th>
<th>Secondary Progressive</th>
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**Brain volume**

**Relapses and Impairment**

**MRI Burden of Disease**

**New lesions**

C.I.S., clinical isolated syndrome

Adapted from Goodkin DE. UCSF MS Curriculum. January 1999
**Clinically Isolated Symptom**
The first neurologic episode that lasts at least 24 hours, and is caused by inflammation/demyelination in one or more sites in the CNS.

**Relapse Remitting**
Most frequent form (85%)  
Most commonly preceded by CIS  
Unpredictable attacks which may or may not leave permanent deficits followed by periods of remission

**Secondary Progressive**
Onset of gradual neurological progression after prolonged RRMS  
Relapses become less frequent and may cease altogether

**Primary Progressive**
Uncommon (10-15%)  
Steady increase in disability without relapses
Disease Progression

• Over 20-25 years, 80-85% of MS will progress from CIS to relapsing-remitting MS to secondary progressive MS

• IT IS IMPORTANT TO TREAT EARLY
MRI Evidence of Dissemination of Lesions in the CNS

Image from Dr. Marc Girard.
MRI Evidence of Black Holes and Atrophy

TREATING MS
MS Treatment Requires a 3-Pronged Approach

1. Management of acute attacks
2. Management of symptoms
3. Management of underlying disease
Management Options for Acute Attacks

Steroids

- I.V. (methylprednisolone 1 g daily x 3-5 days)
- High-dose Oral (prednisone 1250 mg daily x 3-4 days)

Either is acceptable\(^1\) – Choice depends on regional facility and physician preference

Steroids do not alter course of MS; only the duration and severity of that attack

Management of Symptoms

- Depression
- Spasticity
- Bladder and bowel
- Pain
- Fatigue
- Mobility
- Sexual dysfunction
MANAGEMENT OF THE DISEASE
Management of Disease

• Goals of First Line MS Therapy
• Aubagio, Avonex, Betaseron, Copaxone, Extavia, Rebif, Tecfidera
  – Reduce the frequency, severity and duration of relapses
  – Preserve cognitive function
  – Slow or delay accumulation of disability due to disease progression
  – Prevent development of new lesions as seen on MRI scans
  – Keep people with MS functioning normally
Injectable First Line Therapy

- Avonex, Betaseron, Copaxone, Extavia and Rebif
  - Comparable effectiveness (30% reduction in relapse frequency and severity; 80% reduction in MRI activity; modest slowing of disability progression)
  - Differences in side effects and injection frequency
  - Choose according to lifestyle, and patient choice
  - Safe and years of experience
Side Effects of First Line Therapies

- Interferons: Avonex, Betaseron, Extavia, Rebif
  - Flu-like symptoms
  - Injection site reactions
  - Liver/thyroid/CBC abnormalities
  - Easily manageable

- Copaxone
  - Lipoatrophy
  - Injection hypersensitivity reactions
Tecfidera: New Oral First Line Therapy

Tecfidera (BG-12)

• Oral – Two pills, twice-daily
• Side effects in first month of treatment include flushing, diarrhea, abdominal cramping, nausea
• Minimal monitoring
• Excellent early safety data
• Likely as or more effective than standard injectable drugs (49% relapse rate reduction; 90% reduction in MRI activity; slows disability progression over two years; reduction in brain atrophy; comparator arm with Copaxone in EXTEND)
Just Approved: Aubagio (teriflunomide)

- Daily oral agent, two doses available (dose decision made by neurologist)
- Has recently obtained first line approval
- Three large clinical trials
- Easy to use, easy to monitor and well tolerated
- Hair thinning, nausea, diarrhea
- Possible effect on the developing fetus – women and men must use contraceptives
- Effective (approximately equal to injectable DMT; 31% ARR reduction; 20% disability progression)
- Immunosuppressant – but able to reverse over days
- Limited safety data
Second Line Therapies

Tysabri

- Monthly infusion
- $$$$$$, limited access
- PML (new JC virus testing and now titre testing) – we can now manage risks
- Effective (68% relapse rate reduction; 90% MRI activity reduction; slows disability progression)
- Well-tolerated
Second Line Therapies

Gilenya

- Daily oral agent
- $$$$, limited access
- Significant need for monitoring – macular edema, cardiac, dermatologic
- Effective (54% ARR reduction; 30% progression; robust MRI effect)
- Immunosuppressant
- Limited safety data (varicella, zoster, macular edema, cardiac effects, PML, malignancies)
Coming Soon: Alemtuzumab

- IV – human monoclonal antibody
- Likely will only get second line approval
- Very easy to give – (five days in year 1 then two days in year 2 – may repeat in year 3)
- Three large clinical trials
- Highly effective c/w Rebif 44 (68% reduction in relapse rate; decreased MRI activity and brain atrophy; trend to decreased disability)
- Seems to have sustained benefit at three years in extension trials
- Immunosuppressant – don’t know how long effects last – no way to reverse
- Long-term monitoring required – ITP, serious infection, thyroid, kidney
Pipeline: 1-3 Years

- Monoclonal Antibodies (Daclizumab)
  - Infrequent IV
  - Highly effective in clinical trials
  - Unknown cost and coverage
  - Unknown risks long term, thyroid and autoimmune

- Laquinimod
- Pegalated Interferon
- Lingo
Comparing Available Therapies

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<th>Drug</th>
<th>Reduction ARR</th>
<th>Progression</th>
<th>MRI</th>
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<tbody>
<tr>
<td>Avonex</td>
<td>37%</td>
<td>32%</td>
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<tr>
<td>Copaxone</td>
<td>29%</td>
<td>12% (NS)</td>
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<tr>
<td>Betaseron</td>
<td>34%</td>
<td>48% (relapse free)</td>
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<tr>
<td>Rebif 44</td>
<td>32%</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Tysabri</td>
<td>68%</td>
<td>54%</td>
<td></td>
</tr>
<tr>
<td>Gilenya</td>
<td>54%</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Tecfidera</td>
<td>49%</td>
<td>53%</td>
<td>90%</td>
</tr>
<tr>
<td>Teriflunomide</td>
<td>31%</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>68%</td>
<td>30%</td>
<td>42%(atrophy)</td>
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<tr>
<td>(vs. Rebif)</td>
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This Neurologist’s Approach to DMT: Old and New

- **Disease Factors**
  - Severity of clinical disease (number and severity of attacks, EDSS score, cognitive function)
  - Appearance of MRI
  - Risk factors (age, gender)
  - Failure of first line DMT

- **Patient Factors**
  - Age, gender, other health issues
  - Preference, lifestyle
  - Extended health plan, employment issues
  - Risk tolerance
This Neurologist’s Approach to DMT: Old and New

• Older DMT as First Line Therapy
  — Young
  — Female, wanting to have children
  — Mild disease, and relatively inactive MRI
  — No extended health benefits
  — Risk averse

• New Orals as First Line Therapy
  — Older, Males
  — More severe disease – Tecfidera over teriflunomide
  — Preference, lifestyle, injection phobia
  — Extended health plan, employment issues
  — Risk tolerant
Realistic Treatment Expectations for All DMT, Both Old and New

• DMTs may:
  — Delay progression to CDMS
  — Reduce the number and severity of acute attacks
  — Preserve ability to work, drive, and maintain and enjoy social relationships, leading to an improved quality of life
  — Slow down disease progression

• DMTs will not:
  — Cure MS
  — Eliminate MS symptoms
  — Reverse existing damage to the CNS
  — Completely eliminate future disease
In the Past, What We Knew About MS Represented “The Tip of the Iceberg”
Today, We Understand Much More…

Better Known
- MRI
- Pathophysiology
- Natural history
- DMT

Still Unknown
- Etiology
- Definitive treatments
MS SOCIETY OF CANADA
BRANT COUNTY CHAPTER CLIENT SERVICES

Presented by:
Colleen Armstrong
Office Administrator, Brant County Chapter
MS Society of Canada

Mission:
To be a leader in finding a cure for multiple sclerosis and enabling people affected by MS to enhance their quality of life
Who Do We Serve?

• Our primary clients are people who are:
  – Living with a diagnosis of MS & allied diseases
  – Waiting for a diagnosis with respect to MS & allied diseases
  – Close to a person with MS & allied diseases, such as family and friends
  – Caregivers to a person with MS & allied diseases, who may also include family and friends
Goal of Client Services

• To provide programs and services to those affected by multiple sclerosis to achieve the highest possible quality of life while living with daily challenges that MS presents
How We Help

Programs and services available:

- Fundraising
- Bedolfe Grant Program
- Monthly Support Group
- Information and Referral
- Education events
- Funding assistance, equipment and SAP
- Volunteer Opportunities
  - Board Members
  - Fundraising
  - Support Group Facilitator
QUESTIONS & ANSWERS