Part I: Advances in Early Diagnosis and DMD Initiation in MS

- MS phenotypes and disease activity
- 2010 diagnostic criteria
- RIS/CIS update
- Rationale for early treatment
- Current DMTs (MOA, efficacy, safety)
- Emerging DMTs (ocrelizumab/ofatumumab, 2nd-generation S1Ps)
- What patients need to hear

MS Phenotypes

- Radiologically isolated syndrome (RIS)
  (Not officially recognized)
- Clinically isolated syndrome (CIS)
  (Categorized as high/low risk for MS based on brain MRI)
- Relapsing MS
- Primary progressive MS
- Secondary progressive MS

Lublin F et al. *Neurology*. 2014;83:278-286.

MS Disease Activity

- Two modifiers; defined time frame
- Active or not active
  - covers all phenotypes; determined by clinical relapse or new/enlarging T2 or contrast + MRI lesion
- Progressing or not progressing
  - covers progressive phenotypes; determined by presence/absence of gradual clinical worsening independent of relapses

Lublin F et al. *Neurology*. 2014;83:278-286.

MS Diagnosis

- Clinical supported by laboratory data
- Blood work (to r/o confounding diagnoses)
- MRI
  - brain MRI ± contrast
  - cervical/thoracic MRI
- CSF
  - oligoclonal bands
  - IgG index/intrathecal IgG antibody production
  - cell count, protein

2010 Diagnostic Criteria

Dissemination in Space
• ≥1 T2 lesion in at least 2/4 areas (periventricular; juxtacortical; infratentorial; spinal cord)
• Symptomatic brain stem/cord lesions excluded
Dissemination in Time
• Asymptomatic enhancing plus non-enhancing lesions
• New T2 and/or enhancing lesion on follow-up MRI

Polman C et al. *Ann Neurol*. 2011;69:292-302.

2010 Diagnostic Criteria

Progressive From Onset MS

≥1 year progression (retrospective; prospective)

2/3 criteria
- ≥1 T2 lesion in 1 area (periventricular, juxtacortical, infratentorial)
- ≥2 T2 cord lesions
- Positive CSF

Polman C et al. *Ann Neurol.* 2011;69:292-302.

RIS: Update

- Five-year risk for clinical event is 34%
  - 9.6% PPMS
- Cognitive deficits, thalamic atrophy present vs controls
- Predictors for clinical events
  - demographics (age ≤37 years, male)
  - clinical (pregnancy)
  - MRI (spinal cord/brainstem lesions; ↑ T2 lesions; contrast lesions)
  - laboratory (+CSF OCBs/↑ IL-8; abnormal VEP; abnormal OCT)

Lebrun C. *Rev Neurol.* 2015;171:698-706.
Azevedo et al. *Neurol Neuroimmunol Neuroinflamm.* 2015;2:e102.
Rossi et al. *Mult Scler.* 2015;21:1443-1452.

CIS and Single Symptomatic Lesion

- n=954 eligible CIS patients from 1995 to 2014
  - CIS with single symptomatic brainstem or spinal-cord lesion vs normal MRI, single asymptomatic lesion
  - these patients were more likely to have CSF +OCBs, and develop further clinical/MRI disease activity
  - these patients were more likely to reach EDSS 3 than CIS with ≥2 MRI lesions

Tintore M. Presented at: ECTRIMS 2015; Barcelona, Spain.

CIS: Update

- ↑ Risk of conversion for females, nonwhites, younger age, multifocal syndrome, incomplete recovery, low vitamin D, smoking, abnormal OCT, CSF OCBs, ↑ T2 lesions/contrast lesions/T1 black holes, spinal cord lesions
- ↑ Risk for disability with ↑ age, lack of DMT therapy, ↑ ARR, baseline pyramidal/gait issues, ↑ T2 lesion load

Jokubaitis VG et al. *Ann Clin Transl Neurol.* 2015;2:479-491.
Mitjana R et al. *Mult Scler.* 2014;20:1471-1477.
Thouvenot E. *Presse Med.* 2015;44:e121-e136.

Rationale for Early Treatment

- Prevent epitope spread
- Best strategy for organ specific immune diseases (learned from RA, SLE)
- MS involves accumulation of permanent CNS damage, loss of reserve (clinically silent for prolonged period)
- Anti-inflammatory strategies benefit axonal injury (at least early)

Rationale for Early Treatment

- Most untreated MS patients become disabled
- Benign MS is unusual (≤5%), and only identified retrospectively
- DMTs are effective (multiple phase III trials)
- Better long-term outcomes with early therapy
- Early treatment is within 3 months (at most 6 months) of CIS

Current DMTs

- 14 distinct DMTs
- 9 mechanisms of action (MOAs)
- Approved for relapsing forms of MS; they ↓ disease damage process, ↓ relapses/disability/MRI lesions
- Choice considers disease, drug, and patient factors
  - drug factors involve MOA, efficacy, safety/tolerability

Individual Agents

- First-line parenterals
  - interferon betas (IFNβs)
  - glatiramer acetate (GA)
- Orals
  - fingolimod (0.5 mg daily)
  - teriflunomide (14 mg/7 mg daily)
  - dimethyl fumarate (240 mg twice daily)

Individual Agents

- Second/third-line parenterals
  - natalizumab (300 mg IV Q4 weeks)
  - alemtuzumab (12 mg IV daily x5 days in year 1, daily for 3 days in year 2)
  - daclizumab
  - mitoxantrone (12 mg/m^2 IV Q3 months)

Interferon βs (IFNβs)

- Five distinct products
  - IFNβ-1b SC 250 mcg every other day (Betaseron, Extavia)
  - IFNβ-1a SC 44 (or 22) mcg 3x weekly (Rebif), IM 30 mcg weekly (Avonex), PEG IFNβ-1a 125 mcg every 14 days (Plegridy)

IFNβs

MOA

- Anti-inflammatory regulatory cytokine (shifts cytokine network); ↑ suppressor cells activity
- ↓ matrix metalloproteinases, adhesion molecule expression; ↑ soluble adhesion molecules
- ↓ monocyte activation; ↓ MHC class II on APCs
- Anti-viral (anti-infectious), antineoplastic

Cocco E, Marrosu MG. *Ther Clin Risk Manag.* 2015;11:759-766.

IFNβs

Efficacy

- Effective in relapsing forms of MS and first attack

Safety

- Good safety (no major issues), with long-term data
- CBC+diff, hepatic panel, TSH monitored Q3-4 months in year 1, then Q6 months (IM IFNβ-1a annually): very unusual to stop due to laboratory abnormality
- Minimal/no pregnancy safety issues (? smaller babies)
- Rare cases of thrombotic microangiopathy (hypertension, renal disease early clues)
- Neutralizing antibodies (NAbs) are basically nonfactor (may test to try to support suboptimal response)

Cocco E, Marrosu MG. *Ther Clin Risk Manag.* 2015;11:759-766.

Glatiramer Acetate (GA)

- Two distinct products
  - GA 40 mg SC 3x weekly, or 20 mg SC daily (Copaxone)
  - generic GA 20 mg SC daily (Glatopa)

MOA

- Random polymers of 4 AA; biophysical analog of MBP
- Binds HLA class II; induces regulatory T cells
- Affects monocytes, dendritic cells, microglia; ↑ BDNF

Caporro M et al. *Patient Prefer Adherence.* 2014;8:1123-1134.

Glatiramer Acetate

Efficacy

- Effective in relapsing forms of MS including first attack

Safety

- Excellent safety, with long-term data
- No discernable pregnancy issues
- No blood monitoring required

Caporro M et al. *Patient Prefer Adherence.* 2014;8:1123-1134.

Fingolimod

MOA

- Sphingosine 1 phosphate (S1P)-1 receptor modulator; also binds S1P receptors 3, 4, 5)
- Phosphorylated to active form
- Prevents homing receptor CCR7+ lymphocyte egress from lymphoid tissue (naïve, central memory T cells)
  - effector T cells spared
- Penetrates into CNS; may have direct effects on neurons and glia

Sanford M. *Drugs.* 2014;74:1411-1433.

Fingolimod

Efficacy

- Effective in relapsing forms of MS
- Consistent reduction in brain volume loss

Safety

- Concerns with regard to significant cardiac disease (especially bradycardia, conduction/AV block issues); pulmonary disease (PFT deterioration); diabetes/cataract/inflammatory eye disease (macular edema)
  - First-dose observation; ophthalmological evaluation at baseline, 4 months
  - must consider drugs with QT interval implications

Sanford M. *Drugs.* 2014;74:1411-1433.

Fingolimod

Safety

- Concerns about infection: immunity to VZV; HSV and VZV infections; cryptococcal infections; PML (9 cases thus far)
- Low lymphocyte count concerns; vaccines less effective; possible pregnancy concern; rare hypertension; rebound issue
- Rebound issues

Sanford M. *Drugs.* 2014;74:1411-1433.

Teriflunomide

MOA

- Selective, reversible inhibition of dihydroorotate dehydrogenase (mitochondrial enzyme)
- Blocks de novo (but not salvage) pyrimidine pathway; cytostatic for rapidly dividing lymphocytes

Efficacy

- Effective in relapsing forms of MS and first attack MS

Miller A. *Clin Ther.* 2015;37:2366-2380.

Teriflunomide

Safety

- Pregnancy exposure concerns (animal model data); drug enters semen
- Hepatic monitoring (esp ALT monthly for first 6 months)
- TB reactivation (limited)
- Rare hypertension, peripheral neuropathy concerns
- Drug can be removed with cholestyramine washout

Miller A. *Clin Ther.* 2015;37:2366-2380.

Dimethyl Fumarate

MOA

- Fumaric acid ester which may activate Nrf2 pathway; ↓ circulating lymphocytes with shift from Th1→Th2
- Restricts cell migration by ↓ ICAM-1, VCAM-1, E-selectin

Efficacy

- Effective in relapsing forms of MS

English C, Aloi JJ. *Clin Ther.* 2015;37:691-715.

Dimethyl Fumarate

Safety

- Minority develop sustained lymphopenia
- Four cases of PML [sustained lymphopenia (≤800 lymphocytes) age >50, may be risk factor]
- Pregnancy risk unclear
- Some GI upset – initial, self-limiting

English C, Aloi JJ. *Clin Ther.* 2015;37:691-715.

Natalizumab

MOA

- Humanized monoclonal antibody directed against α4 integrin adhesion molecule on lymphocytes
- Blocks lymphocyte penetration into CNS

Efficacy

- High efficacy for relapsing forms of MS
  - may see confirmed improvement in some patients

Kornek B. *Patient Prefer Adherence.* 2015;9:675-684.

Natalizumab

Safety

- Risk of PML (risk mitigation factors involve JCV antibody status and index, duration of natalizumab therapy, prior immunosuppression)
- Rare HSV/VZV meningitis, encephalitis
- Persistent NAbs (loss of efficacy; indication to change therapy)
- Hypersensitivity
- Unclear pregnancy issues
- Rebound issues

Kornek B. *Patient Prefer Adherence.* 2015;9:675-684.

Alemtuzumab

MOA

- Humanized monoclonal antibody directed against CD52
- Produces rapid, long lasting depletion of mobile T cells (CD4+ > CD8+) for several years; B cells, monocytes for several months
- Induction agent/prolonged effects
  - restored cells enriched for T regs

Ruck T et al. *Int J Mol Sci.* 2015;16:16414-16439.

Alemtuzumab

Efficacy

- High efficacy for relapsing forms of MS
  - excellent brain volume loss data
  - may see confirmed improvement in some patients

Safety

- Mandated monthly blood and urine screenings for 48 months to detect secondary/immune mediated complications (thyroid disease 40%, ITP 2%, glomerular kidney disease <1%)

Ruck T et al. *Int J Mol Sci.* 2015;16:16414-16439.

Daclizumab

- Humanized IgG1 monoclonal antibody to CD25 (IL2Rα)
  - selective blockade of high-affinity receptor
- MOA involves T cells and innate immunity (↑ regulatory CD56 bright NK cells, blocks activated T cells)
- Daclizumab high-yield process (Dac-HYP) given SC

Plender N, Martin R. *Exp Neurol.* 2014;262(Pt A):44-51.
Kappos L et al. *N Engl J Med.* 2015;373:1418-1428.

Daclizumab: DECIDE Trial in RRMS

- Phase III study (n=1841; up to 144 wks)
- 150 mg daclizumab-HYP Q4W vs 30 mcg IFN β-1a Q1W

	Dac-HYP	IFN β-1a	*P*
Annualized relapse rate Relapse-free	0.22 67%	0.39 51%	<0.0001 (↓ 45%) ↓ 41%
3-mo disability progression	16%	20%	0.16 (↓ 16%)
New/newly enlarged T2 hyperint. lesions at wk 96	4.3	9.4	<0.001 (↓ 54%)

- Dac-HYP: ↓ 65% of new contrast lesions; ↓ 52% of new T1 lesions vs IFN β-1a (*P*<0.0001)
- Incidence of AEs: similar in 2 arms (serious AEs: increased in Dac-HYP)
  - cutaneous (37% vs 19%; serious 2% vs <1%), hepatic (ALT/AST >5x ULN: 6% vs 3%), infectious (65% vs 57%; serious 2% vs <1%)

Kappos L et al. *N Engl J Med.* 2015;373:1418-1428.

Anti-CD20 Monoclonal Antibodies

- Depletes B cells through ADCC, CDC, apoptosis mechanisms
- Rituximab (chimeric anti-CD20 IgG1): IV
- Ocrelizumab (humanized IgG1): IV
  - >90% epitope overlap with rituximab
  - ↑ ADCC vs CDC
- Ofatumumab (human IgG1): SC or IV
  - distinct CD20 epitope
  - binds more tightly, slower dissociation rate
  - ↑ CDC vs ADCC

Rommer PS et al. *Clin Exp Immunol.* 2014;175:373-384.

Ocrelizumab

- OPERA I (n=821) and OPERA II (n=835)
  - relapsing MS, 96 weeks, ocrelizumab 600 mg IV Q6 months vs SC IFNβ-1a 44 mcg 3x weekly
  - ARR 0.156 vs 0.292 (↓ 46%); ARR 0.155 vs 0.290 (↓ 47%), *P*<0.0001
  - pooled confirmed disability 12 weeks 9.8% vs 15.2% (↓ 40%, *P*=0.0006)
  - pooled confirmed disability 24 weeks 7.6% vs 12% (↓ 40%, *P*=0.0025)
  - contrast lesion number 0.016 vs 0.286 (↓ 94%), 0.021 vs 0.416 (↓ 95%) (*P*<0.0001)
  - new/enlarging T2 lesions 0.323 vs 1.413 (↓77%), 0.325 vs 1.904 (↓ 83%) (*P*<0.0001); most at week 24

Hauser SL et al. *N Engl J Med.* 2016 Dec 21. [Epub ahead of print].

Ocrelizumab

- ORATORIO (n=732)
  - PPMS, +CSF, age 18-55, randomized 2:1 to ocrelizumab 600 mg IV vs placebo
  - confirmed 12 week EDSS progression ↓ 24% (*P*=0.0321); 24 weeks ↓ 25% (*P*=0.0365)
  - benefits on 25 FTW change ↓ 29% (p=0.04), ΔT2 lesion volume (-3.4% vs +7.4%, *P*<0.0001), brain volume loss (-0.9% vs -1.1%, ↓ 17.5%, *P*=0.02)

Hauser SL et al. *N Engl J Med.* 2016 Dec 21. [Epub ahead of print].

Ofatumumab

- Two positive phase II relapsing MS trials
- n=38 evaluated 100, 300, 700 mg IV ofatumumab (over 2 infusions) vs placebo in two 24 week alternate treatment periods
  - new brain MRI lesions ↓ >99% in first 8-24 weeks by all ofatumumab doses; no safety issues; no HAHA antibodies

Sorensen PS et al. *Neurology.* 2014;82:573-581; *Neurology.* 2014;82(S17):1.007.

Ofatumumab

- MIRROR trial n=232 evaluated 3 mg Q12W, 30 mg Q12W, 60 mg Q12W, 60 mg Q4W SC ofatumumab vs placebo (half of 30/60 mg groups received initial 3 mg at week 0)
  - week 0-12 showed 65% contrast lesion reduction; week 4-12 showed ≥90% ↓ (for cumulative doses ≥30 mg)
  - linear B cell suppression: 32-64 cells/mcL associated with 1 new lesion/year (vs 16 new lesions with placebo)
  - defines lowest dose giving maximal benefit

Sorensen PS et al. *Neurology.* 2014;82:573-581; *Neurology.* 2014;82(S17):1.007.

Second-generation S1P Receptors Modulators

- Fingolimod (1>5>4>3)
  - phosphorylated in vivo
  - might want to spare S1P-2,3 (cardiovascular receptors), maintain S1P-1 (lymphocytes and astrocytes), and possibly S1P-5 (oligos)
- Siponimod (BAF-312) (1=5>4)
  - positive phase II relapsing trial; positive phase III (EXPAND) SPMS trial (n=1,530; 0.25 → 2 mg vs placebo)
- Ponesimod (ACT-12880) (1>5>3)
  - positive phase II relapsing trial; current phase III (OPTIMUM) relapsing trial vs teriflunomide (n=1,100; 20 mg)
- Ceralifimod (ONO-4641) (1=5>4)
  - positive phase II data in relapsing MS; abandoned

Available at: Clinicaltrials.gov.

Second-generation S1P Receptors Modulators

- Ozanimod (RPC-1063) (1>5>4)
  - positive phase II relapsing trial; phase III 2 yr RADIANCE (enrolled) and 1 yr SUNBEAM relapsing trial (n=1,200 each; 0.5, 1 mg vs IM IFNβ-1a)
- Amiselimod (MT-1303)
  - positive phase II (MOMENTUM) relapsing trial (n=415) 0.1, 0.2, 0.4 mg vs placebo over 24 weeks; higher dose efficacy on MRI lesions, relapses, GM atrophy
- CS-0777 (1>5>3)
  - phosphorylated in vivo
  - positive phase I trial in relapsing forms of MS

Available at: Clinicaltrials.gov.

Repair Strategies

- Anti-LINGO-1 monoclonal antibody
- Recombinant human IgM22
- High-dose biotin (vitamin H)

What Patients Need to Hear

- MS DMTs are "invisible therapy"
  - patients have to buy into their value
    - must understand intellectual rationale for therapy
    - must be able to tolerate it
    - should be partners in therapy selection
- MS DMTs are, overall, safe, well-tolerated, and effective
  - most side effects can be managed

Part I: Bottom Line

- Start using "active vs not active," "progressing vs not progressing"
- Start using the 2010 diagnostic criteria
- Treat within 3 months of CIS
- Be open to all the DMTs; have a good idea of risk/benefit ratio
- Let patients know there are advances in progressive MS therapy/repair strategies

Part II: Emerging Concepts in MS Management

- Important environmental/comorbidity factors
- Quality measures and implementation
- Surveillance MRI
- Steroid protocols
- Proactive strategies for side effects
- Clues to personalize therapy

Modifiable MS Factors

- Smoking
  - ↑ risk for MS; ↑ transition to SPMS (by 4.7% annually); may have genetic component
- Vit D deficiency
  - ↑ risk for MS; may treat disease activity; significance may be limited to Caucasians vs Blacks, Hispanics
- Diet
  - dietary salt linked to immune-mediated disease (affects T regs, Mϕ); anti-inflammatory diet preferred; anti-inflammatory gut microbiome
- Physical/mental exercise, body weight, stress, socialization

MS and Psychiatric Comorbidity

- Depression, anxiety are recognized to ↓ QOL; depression ↓ DMT adherence/compliance
- Canadian study used population based health data to compare n=44,452 MS vs n=220,849 matched controls
- Incidence/prevalence of anxiety, bipolar disorder, depression, schizophrenia ↑ in MS
  - MS depression prevalence 20.1% vs 11.9%, anxiety disorder 8.7% vs 5.1%, bipolar disorder 4.7% vs 2.3%, schizophrenia 1.28% vs 1.03%
- Conclusion: psychiatric comorbidity common in MS; males face greater risk of depression

Marrie RA et al. *Neurology*. 2015;85:1972-1979.

Psychiatric Comorbidities and Adverse Health Behaviors

- Evaluated n=949 consecutive MS patients from 4 centers
- Alcohol dependence and smoking were independent risk factors for anxiety and depression
- Alcohol dependence associated with ↑ incidence of depression (not anxiety); depression associated with ↑ incidence of alcohol dependence
- Conclusion: alcohol/smoking associated with anxiety/depression in MS; treating these issues might ↓ anxiety/depression

McKay KA et al. *Mult Scler*. 2015 Aug 5. pii: 1352458515599073.

Vascular Risk Factors

- n=489 MS vs n=175 healthy controls
- Evaluated hypertension, heart disease, smoking, obesity, type I diabetes
- Hypertension, smoking ↑ in MS
- MS more likely to have ≥3 (18.8% vs 8.6%) and ≥2 (49.9% vs 36%) risk factors
- MS with hypertension and heart disease showed ↓ GM and cortical volume; MS with obesity showed ↑ T1 lesion volume; MS smokers showed ↓ brain volume

Kappus N et al. *J Neurol Neurosurg Psychiatry*. 2016;87:181-187.

Disease-Specific Quality Measures

- Reportable/repeatable measures that can document quality care/identify gaps in care
- Most applicable to chronic diseases
- AAN has proposed 11 such measures for MS
  - first two not recommended for accountability programs

Rae-Grant A et al. *Neurology*. 2015;85:1904-1908.

AAN 2015: MS Quality Measurement Set

1. MS diagnosis (% diagnosed in past year who met international criteria)
2. Comparison MRI within 2 years of diagnosis (% with repeat MRI ± contrast)
3. Current MS disability scale score (11 options)
4. Annual fall risk screening

Rae-Grant A et al. *Neurology*. 2015;85:1904-1908.

AAN 2015: MS Quality Measurement Set

5. Percentage of patients with UTI
6. Exercise/physical activity counseling
7. Fatigue score stable/improved
8. Cognitive impairment testing
9. Depression screening
10. Depression score stable/improved
11. QOL score stable/improved

Rae-Grant A et al. *Neurology*. 2015;85:1904-1908.

Representative Measures for Patient Use

- Patient determined disease steps (PDDS) (disability score, self-administered at least once a year)
- Fall risk via patient interview/validated instrument
- MS modified fatigue impact scale (MS-MFIS) (21 items, 5 to 10 minutes)

Rae-Grant A et al. *Neurology*. 2015;85:1904-1908.

Representative Measures for Patient Use

- Cognitive assessment (symbol digit modalities test, SDMT)
- Depression screen (Beck depression inventory, BDI; two question screen)
- QOL tool (MS QOL: 54 items, 11-18 minutes)

Rae-Grant A et al. *Neurology*. 2015;85:1904-1908.

New MS MRI Protocol Recommendation

- Brain MRI 6 months after starting/switching DMT (new baseline), then every 1-2 years on DMT
- Do orbit MRI for severe optic neuritis
- MS MRI protocol emphasizes 3D sequences, slice thickness ≤3 mm, no gap
  - brain MRI: 3D T1, 3D sagittal T2-FLAIR, 3D T2, 3D FLASH post-contrast, 2D axial DWI
  - spinal MRI: sagittal T1 and PD, STIR, phase sensitive inversion recovery (PSIR); axial T2 or T2 through suspicious lesions; in some cases: T1 post-contrast
  - PML protocol: 3D sagittal T2 FLAIR, 2D axial DWI (5 mm, no gap); annual MRI for JCV antibody negative; Q3 to 6 months for JCV antibody positives on natalizumab >18 months

Traboulsee A et al. *AJNR Am J Neuroradiol*. 2015; doi: 10.3174/ajnr.A4539. PMID: 26564433.

New MS MRI Protocol Recommendation

- MRI requisition should specify: diagnostic study (date of onset), treatment monitoring, PML surveillance (high or low risk), unexpected decline/reassessment of diagnosis
- MRI report should indicate: findings are typical, atypical, not consistent with MS
  - should provide appropriate differential diagnosis

Traboulsee A et al. *AJNR Am J Neuroradiol.* 2015; doi: 10.3174/ajnr.A4539. PMID: 26564433.

Steroid Therapy

- COPOUSEP trial involved 13 French MS centers
- MS patients with acute relapse (≤15 days) randomized to oral (n=100) or IV methylprednisolone (n=99) 1,000 mg daily x3 days
- Proportion of improved patients at 28 days 81% (n=66) vs 80% (n=72)
  - similar adverse events; ↑ insomnia in oral group (77% vs 64%)
- Conclusion: oral steroids gave equivalent results to IV steroids for treating acute MS attacks

Le Page E et al. *Lancet.* 2015;386:974-981.

Proactive Strategies

Bottom Line

- Awareness and education; be pre-emptive/ institute early
- Patient buy-in
- Use available help/resources (e.g. REMS program)
- Be accessible/provide written materials

Clues to Personalize Therapy

- Consider disease, drug, and patient factors
- Take into account disease activity and prognostic profile
- Partner with patient
- Give your best advise clearly
- Follow closely and don't be afraid to switch

Part II: Bottom Line

- Convey/address modifiable MS factors
- Implement the MS quality measures, MRI protocols
- High-dose oral steroids are acceptable to treat MS relapses

Patient Assessment Tools

Information for patients on the Quality Assessment Measures for MS discussed in this activity can be found on the MS Society's website: www.nationalmssociety.org.

A direct link to the full listing of assessment measures can be found at: http://www.nationalmssociety.org/For-Professionals/Clinical-Care/Managing-MS/Rehabilitation/Rehabilitation-Paradigm/Assessment-Measures

Direct links to the Quality Assessment Tools for Patient Use can be found at the following links:

- Cognitive assessment (symbol digit modalities test, SDMT) can be found at: http://fliphtml5.com/lkxp/yhep/basic
- Depression screen (Beck depression inventory, BDI; two question screen) can be found at: http://www.bmc.org/Documents/Beck-Depression-Inventory-BDI.pdf
- QOL tool (MS QOL: 54 items, 11-18 minutes) can be found at: http://www.nationalmssociety.org/For-Professionals/Researchers/Resources-for-Researchers/Clinical-Study-Measures/Multiple-Sclerosis-Quality-of-Life-Inventory-(MSQL