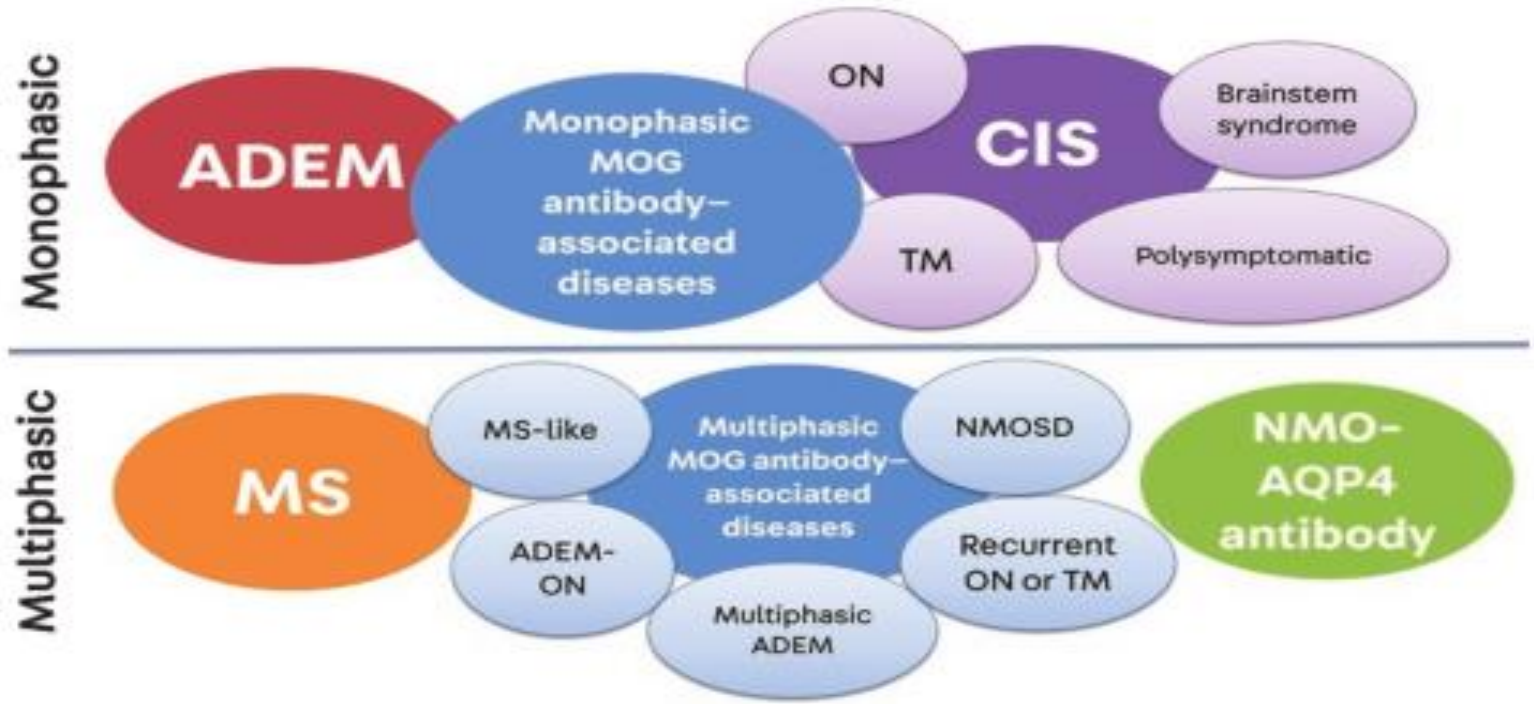
PAEDIATRIC MULTIPLE SCLEROSIS

Dr. Tiny Mazhani

AQUIRED DEMYELINATING SYNDROMES

- Acute illnesses characterised by neurological deficits persisting for at least 24 hours
- Involving the optic nerve, brain or spinal cord
- Associated with regional area of increased T2 signal on conventional MRI



Chitnis 2019

MULTIPLE SCLEROSIS DEFINITION

Autoimmune, inflammatory and neurodegenerative disorder

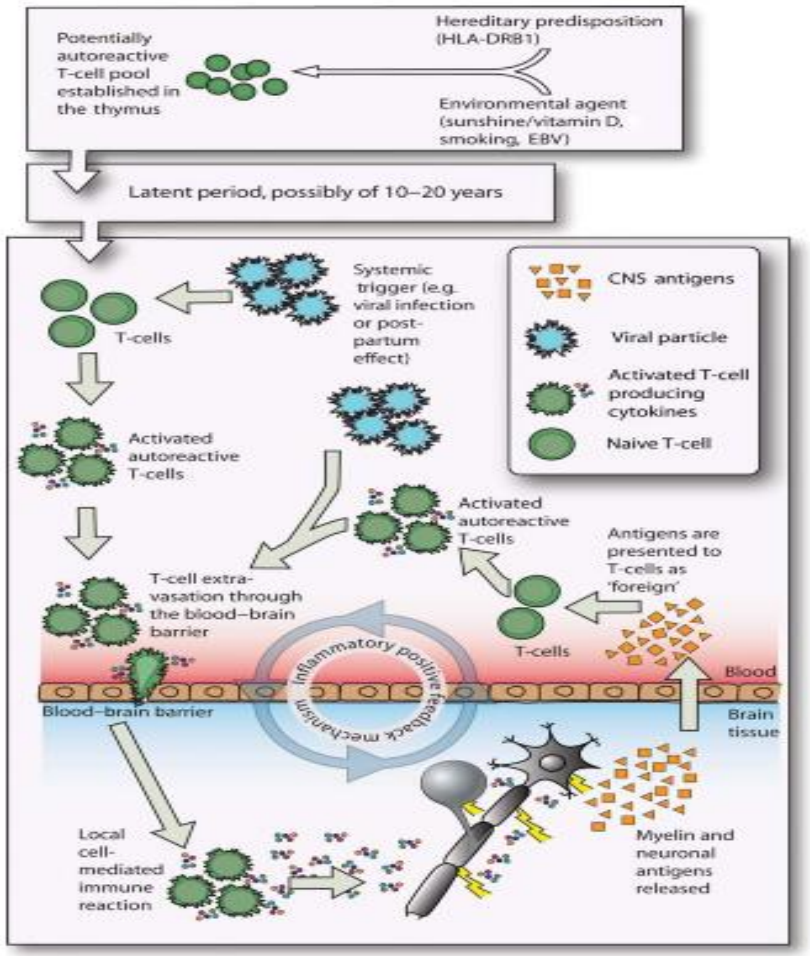
Requires evidence of dissemination of CNS inflammatory activity

- Distributed in more than one CNS location –DIS
- Distributed over time – DIT

MS CLINICAL PHENOTYPES

- Radiologically isolated syndrome (RIS)
- Clinically isolated syndrome (CIS)
- Relapsing remitting MS (RRMS)
- Primary progressive MS (PPMS)
- Secondary progressive MS (SPMS)

PATHOGENESIS



Rejdak 2010

MS is characterised by:

- CNS inflammation
- Formation of plaques
- Demyelination
- Axonal injury
- Axonal loss

Inflammation	Axonal degeneration	Microglial activation	Mitochondrial injury	Oxidation byproducts	Glutamate excitotoxicity
					
• Compartmentalized inflammation • T cells, B cells • Lymphoid follicles • Relatively intact blood-brain barrier	• Demyelination • Loss of trophic support • Anterograde degeneration • Retrograde degeneration • Transsynaptic degeneration • Histotoxic hypoxia	• Surrounding chronic active lesions • Clustering preactive lesions • Tracking along axons (repair versus degeneration) • Oxidation products	• Nuclear/ mitochondrial DNA mutations • Clonal expansion and amplification • Decreased energy production and axonal degeneration • Amplification of oxidation	• Accumulation of reactive oxygen species (ROS) • Poor clearance with defective mitochondria • Microglial oxidative burst	• Direct demyelinating effects • Dysregulation of calcium homeostasis in axons and oligodendrocytes

Ontaneda 2019

INCIDENCE

- 15 to 46% of children presenting with ADS will be diagnosed with MS after 5 year follow-up
- 0.13 to 0.66 per 100 000 children per year
- Up to 10% of all MS patients have their first demyelinating attack before the age of 18 years

EPIDEMIOLOGY

- F>M after age of 10 years
- Childhood spent in temperate climates – inadequate exposure to sunlight
- Clusters in some families – FHx present in 20%
- Large ethnic diversity: African and Hispanic

RISK FACTORS

1. Low Vit D
2. Infections
3. Parental smoking
4. Genetic susceptibility: HLA-DRB *15:01
5. Obesity
6. Earlier onset of puberty
7. Lack of breastfeeding
8. Dietary intake: salt intake, iron deficiency
9. Gut microbiota – trigger, actinobacteria

MS in Africa

Heine 2020

- 49000 cases in SSA (2800 new cases per year). 19.5% increase in the last 5 years – Heine 2020

Bhigjee Al, KZN 2007:

- Prevalence per 100 000: whites 25.63, Indians 7.59, Mixed ancestry 1.94, Blacks 0.22
- Similar clinical features: motor disability – 50%, ON – 25.1%
- MRI abn - 69.1%, Oligoclonal bands – 82%

MS in African Children

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism Reports

journal homepage: www.elsevier.com/locate/ymgmr

Identification of an iron-responsive subtype in two children diagnosed with relapsing-remitting multiple sclerosis using whole exome sequencing

Susan J. van Rensburg[a,*], Armand V. Peeters[b], Ronald van Toorn[c], Johan Schoeman[c], Kelebogile E. Moremi[a], Carel J. van Heerden[d], Maritha J. Kotze[e]

- 2 children, mixed ancestry with RRMS
- WES: gene variants in iron absorption and transport
- *TMPRSS6, TF, CUBN, SLC25A32, CD163, COQ3*
- No HLA DR1*1501
- Iron is an essential co-factor in myelin synthesis
- Long term remission on regular iron supplementation

2012 IPMSSG definition for Paediatric CIS

Pediatric clinically isolated syndrome (CIS) (all are required)
A clinical CNS event with presumed inflammatory demyelinating cause
Absence of a clinical history of CNS demyelinating disease (if any, see pediatric MS)
No encephalopathy except as readily explained by fever
Criteria for MS diagnosis on baseline MRI are not met

2012 IPMSSG definition for Paediatric Multiple Sclerosis

Two or more CIS separated by more than 30 days involving more than one area of CNS

One CIS associated with MRI findings consistent with criteria of DIS and in which follow-up MRI shows at least one new lesion consistent with DIT criteria

One ADEM attack followed by 1 CIS 3 or more months after symptom onset that is associated with new MRI findings consistent with criteria for DIS

A CIS whose MRI findings are consistent with criteria for DIS and DIT (at least 1 T2 lesion in at least 2 of 4 areas: spinal cord, infratentorial, juxtacortical, and periventricular [DIS] associated with a simulataneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions [DIT] if the patient is >12 years old

DISSEMINATION IN SPACE (DIS)

- 1/more T2 lesions that are characteristic for MS
- In at least 2 of the following areas:
- Periventicular
- Juxtacortical/cortical
- Infratentorial
- Spinal cord

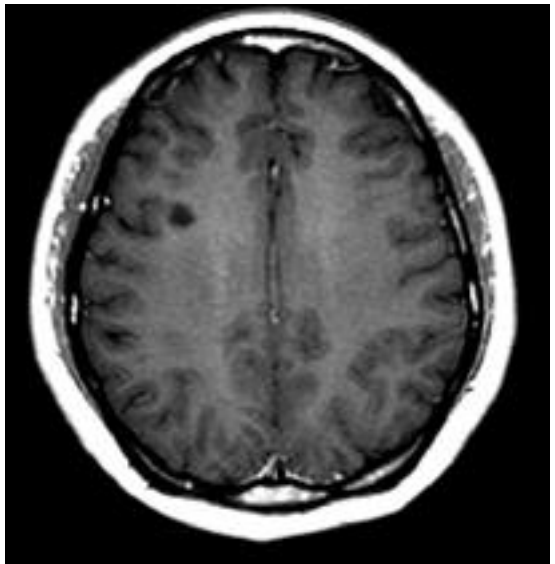
DISSEMINATION IN TIME

- Presence of gadolinium enhancing and non-enhancing lesions on single MRI scan

or

- By a new T2 and/or gadolinium enhancing lesion on follow up scan

- T1 hypointense lesions (black holes): complete tissue loss from a previous inflammatory event



2010 McDONALD CRITERIA

- Enabled diagnosis of MS in a child > 11 years:

  Presenting with CIS

  +

  evidence of DIS and DIT on MRI

❖Provided that the clinical presentation did not meet the criteria for ADEM

2017 McDONALD CRITERIA

Changes include:

1. OCB to substitute for DIT
   in a patient with typical CIS who fulfil requirement for DIS

2. The inclusion of a symptomatic lesion as evidence of DIS or DIT

3. Inclusion of cortical grey matter lesions in DIS
   (now considered in combination of juxtacortical lesions)

2017 McDONALD CRITERIA

- ❖Highlights the exclusion of an alternative diagnosis
- ❖Highlight that criteria should only be applied to patients with typical CIS
- MRI spine cord:

  Part of routine MS workup

  Lead to higher sensitivity

  Lesions > in cervical region, diagnostic yield

CLINICAL FEATURES AND COURSE

- MS before 18 years: Relapsing Remitting
- Progressive MS: exclude alternative diagnosis
- Important considerations:

    Inability to articulate sensory or visual deficits

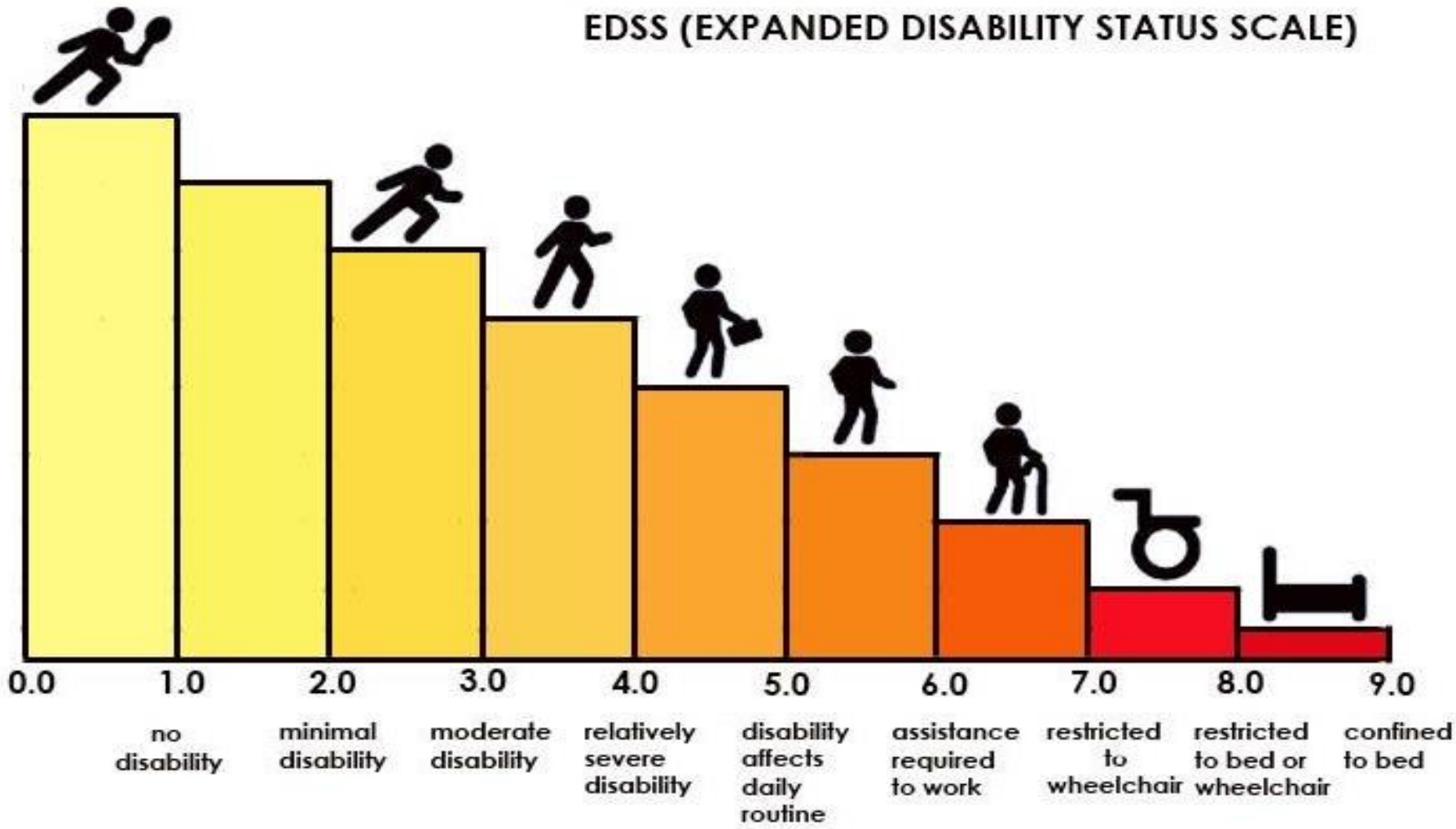
    Previous studies included MOG-Ab-positive conditions

CLINICAL FEATURES AND COURSE

- Clinical features similar to adults
- 2/3 poly-symptomatic presentation:

  sensory, cerebellar, visual, brainstem, pyramidal
- Younger children: encephalopathy, motor, co-ordination
- Older children: sensory deficits
- Fatigue and depression

(Rostasty et al)


EDSS (EXPANDED DISABILITY STATUS SCALE)
0.0
1.0
no disability
2.0
minimal disability
3.0
moderate disability
4.0
relatively severe disability
5.0
disability affects daily routine
6.0
assistance required to work
7.0
restricted to wheelchair
8.0
restricted to bed or wheelchair
9.0
confined to bed

ADEM

- Second demyelinating episode - 10% (MDEM)
- ADEM presentation later diagnosed as MS – 20%
- Risk Factors for developing MS:
  - Periventricular lesions
  - T1 hypointense lesions
  - Lesion distribution that was not diffusely bilateral

❖ADEM is not a harbinger for MS

(Krupp et al)

CIS and MS

Increased MS risk

- High IgG index
- OCB
- Older children

Low risk of MS

- ADEM like presentation
- Lesions in BG
- Polyfocal event

Predictors of Evolution Into Multiple Sclerosis After a First Acute Demyelinating Syndrome in Children and Adolescents

Laura Papetti[1], Lorenzo Figà Talamanca[2], Alberto Spalice[3], Federico Vigevano[1], Diego Centonze[4] and Massimiliano Valeriani[1,5]

Best predictors of evolution to MS

- OCB
- Past EBV infection
- Periventricular lesions
- Hypointense lesions
- Lesions in the corpus callosum

DISEASE COURSE

- Relapse rate higher in earlier years
- Shorter interval between attack and 2nd demyelinating event

- Lesions load at 1st MRI + disease activity in 1st year

  suggests

  Highly active disease in children

- Slower rate of accrual of disability compared with adult onset MS

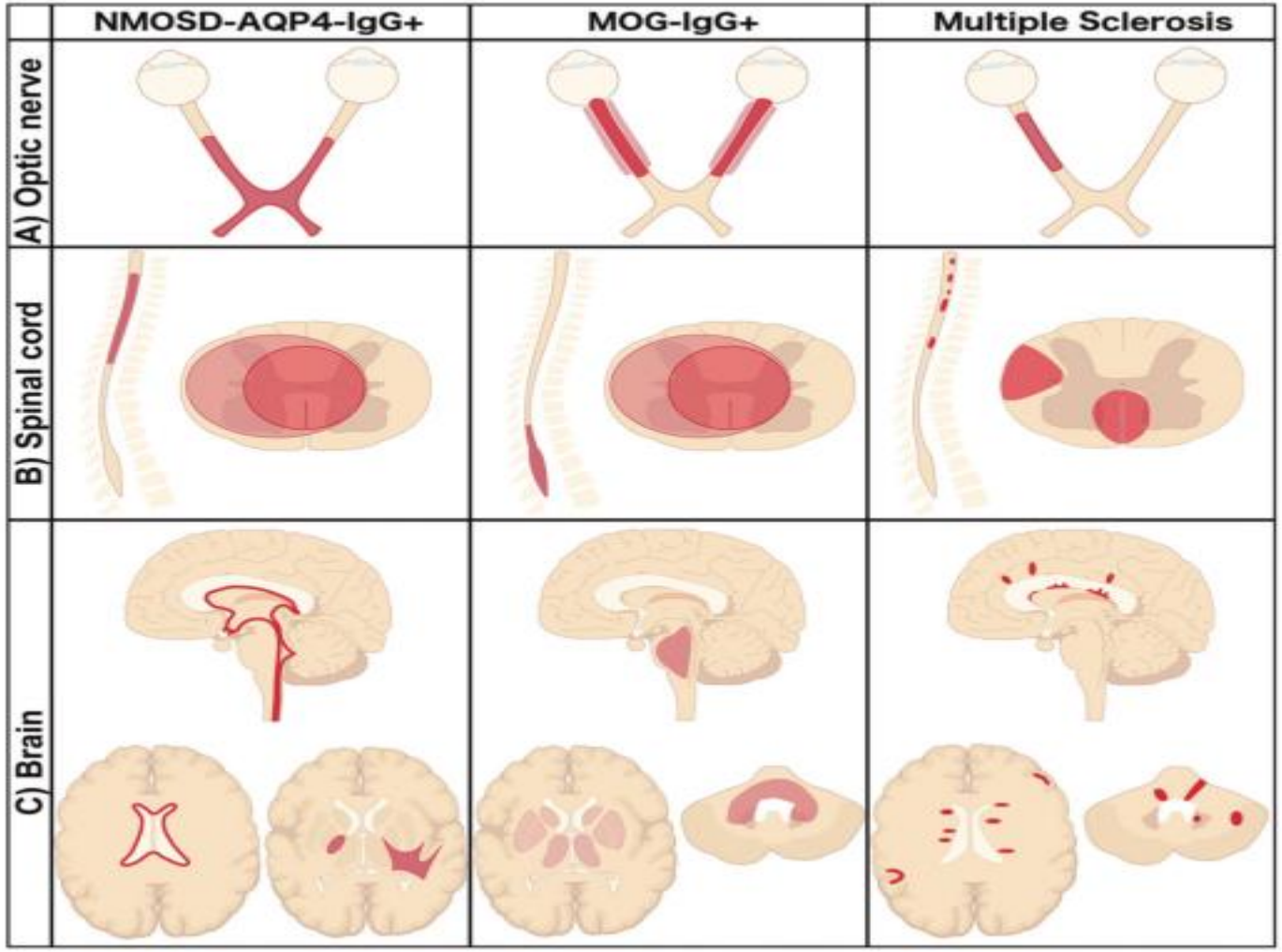
COGNITIVE IMPAIRMENT

- Cognitive development and mood affected in MS
- Impairment in: executive function, processing speed, visuo-motor integration, attention and memory
- Linked to a younger age at onset
- Present at early stages of disease including CIS
- Vulnerability of the developing brain to a single episode of demyelination
- Neurodegenerative component of MS

MIMICS

1. Antibody-mediated disorders
   MOG, AQP4
2. Acute infections of the CNS
   EBV, mycoplasma, enterovirus
3. Inherited leukodystrophies
   Alexander ds, mitochondrial cytopathies, MTCL
4. Inflammatory vasculopathies
   SLE, vasculitis, n.sarcoidosis
5. Genetic disorders

MS vs antibody mediated disorders



Dutra 2018

	NMOSD – AQP4	MOG-AD	MS
Optic nerve	Long length, bilateral Posterior ON invol. Chiasmatic extention	Long length, bilateral Anterior ON involve Intraorbital ON swelling Perineural gad-enhance	Unilateral Short length
Spinal cord	Cervico-thoracic LETM Central or both c&p >50% cord area	Medullary conus Thoraco-lumbar Central or both c&p Atypical on axial views	Cervical Longitudinal Peripheral Short length
Brain	Periventricular Circumventricular Cortico-spinal tracts Vasogenic edema	Basal ganglia Thalamic Infra-tentorial	Oviod Periventricular, callosal, juxta-cortical, infratentorial, intrapontine

doi:10.1093/brain/awz144 BRAIN 2019: 142; 1858–1875 | 1858

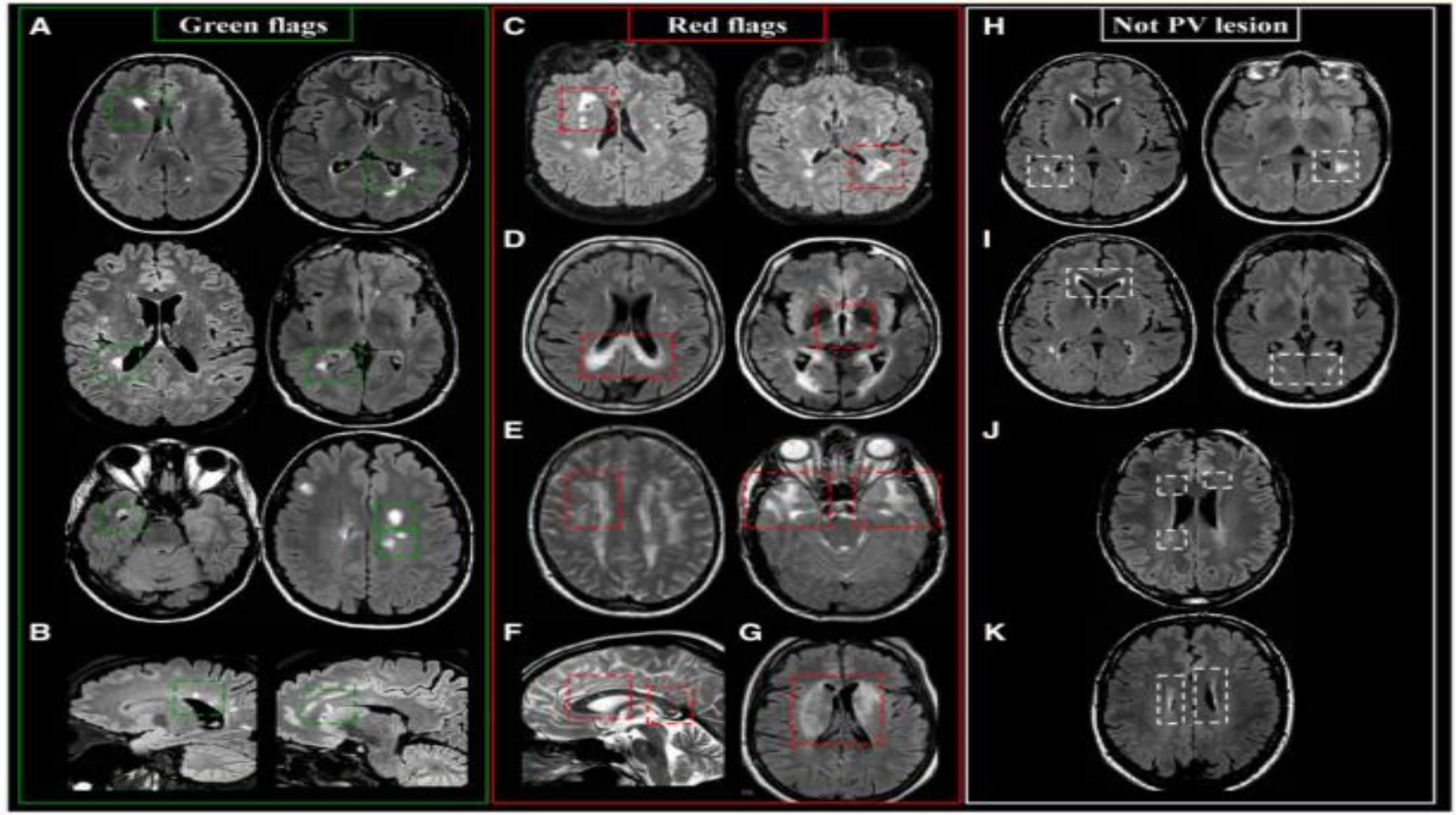
BRAIN
A JOURNAL OF NEUROLOGY

REVIEW

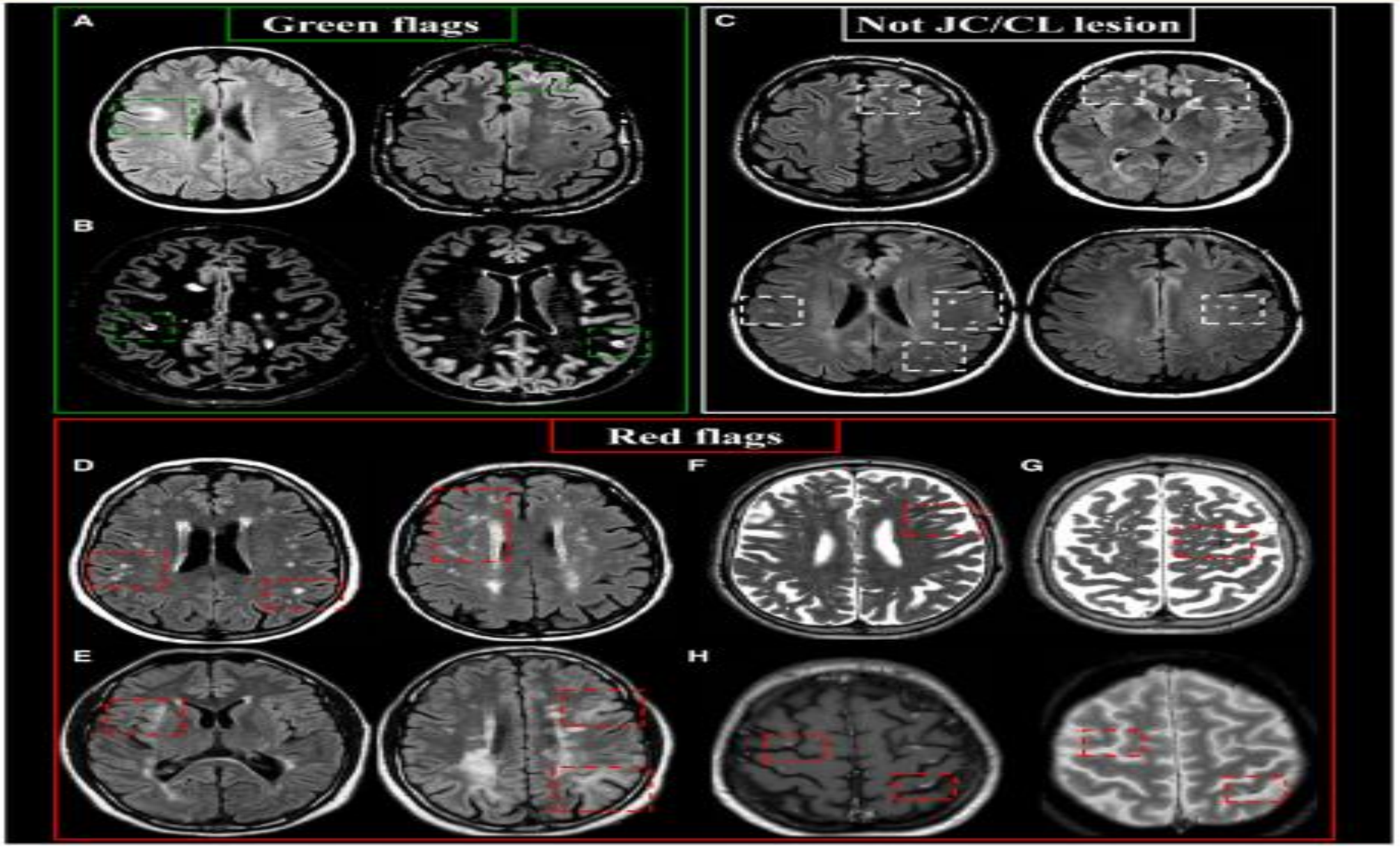
Assessment of lesions on magnetic resonance imaging in multiple sclerosis: practical guidelines

Massimo Filippi,[1,2,3] Paolo Preziosa,[1,3] Brenda L. Banwell,[4] Frederik Barkhof,[5,6] Olga Ciccarelli,[7,8] Nicola De Stefano,[9] Jeroen J.G. Geurts,[10] Friedemann Paul,[11] Daniel S. Reich,[12] Ahmed T. Toosy,[7] Anthony Traboulsee,[13,14] Mike P. Wattjes,[15] Tarek A. Yousry,[16,17] Achim Gass,[18] Catherine Lubetzki,[19] Brian G. Weinshenker[20] and Maria A. Rocca[1,2]

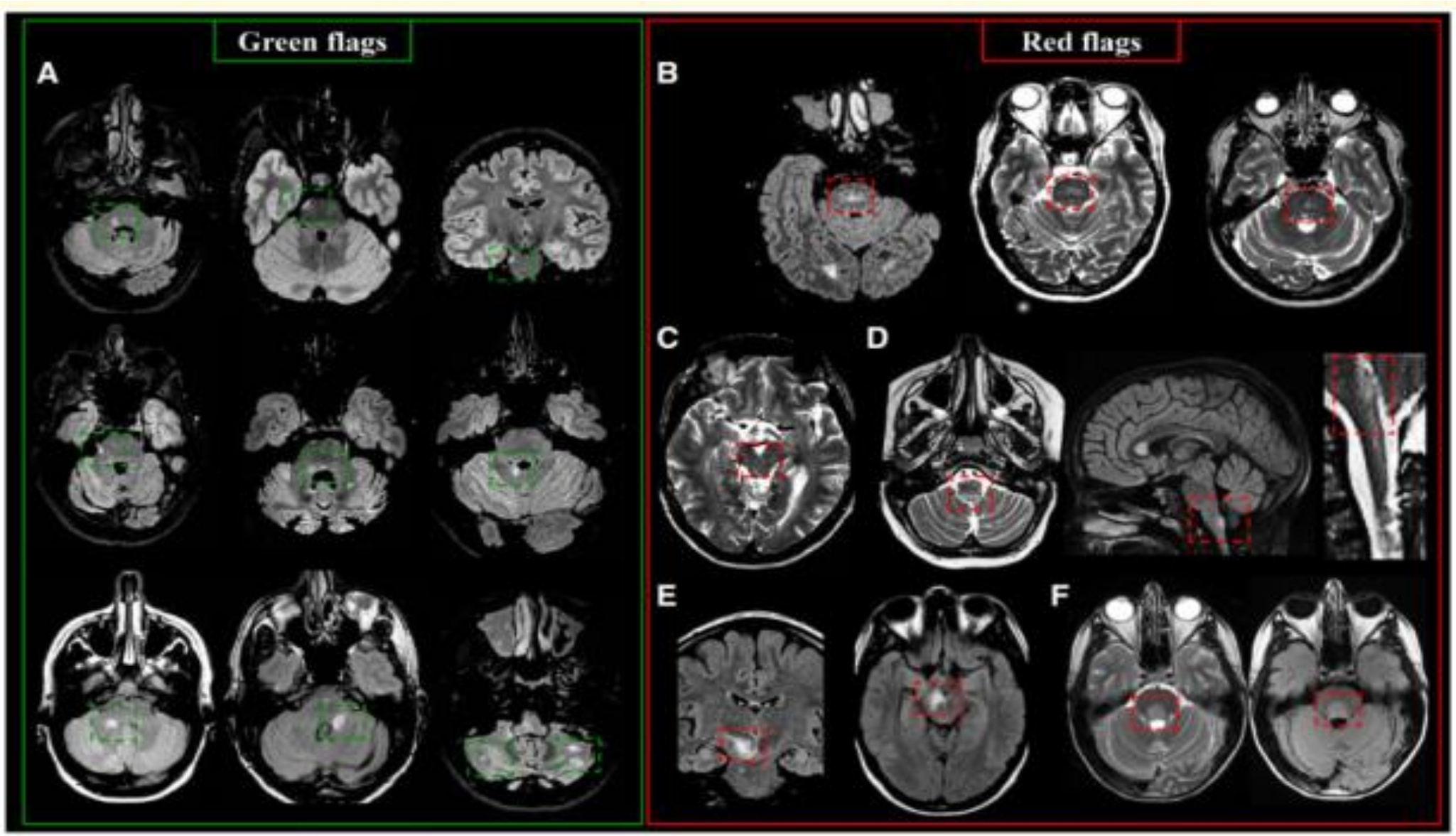
Periventricular lesions



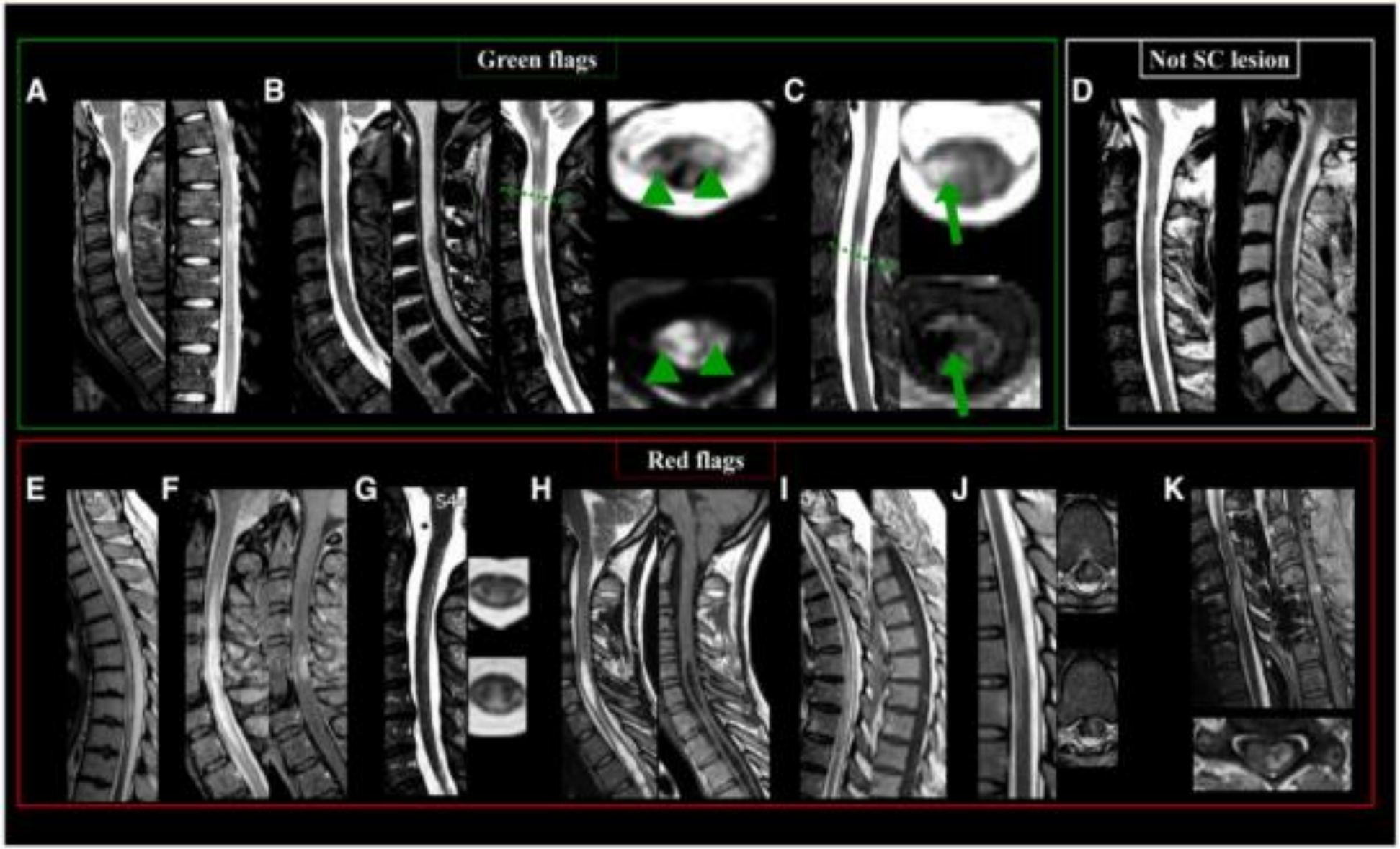
Cortical/juxtacortical lesions



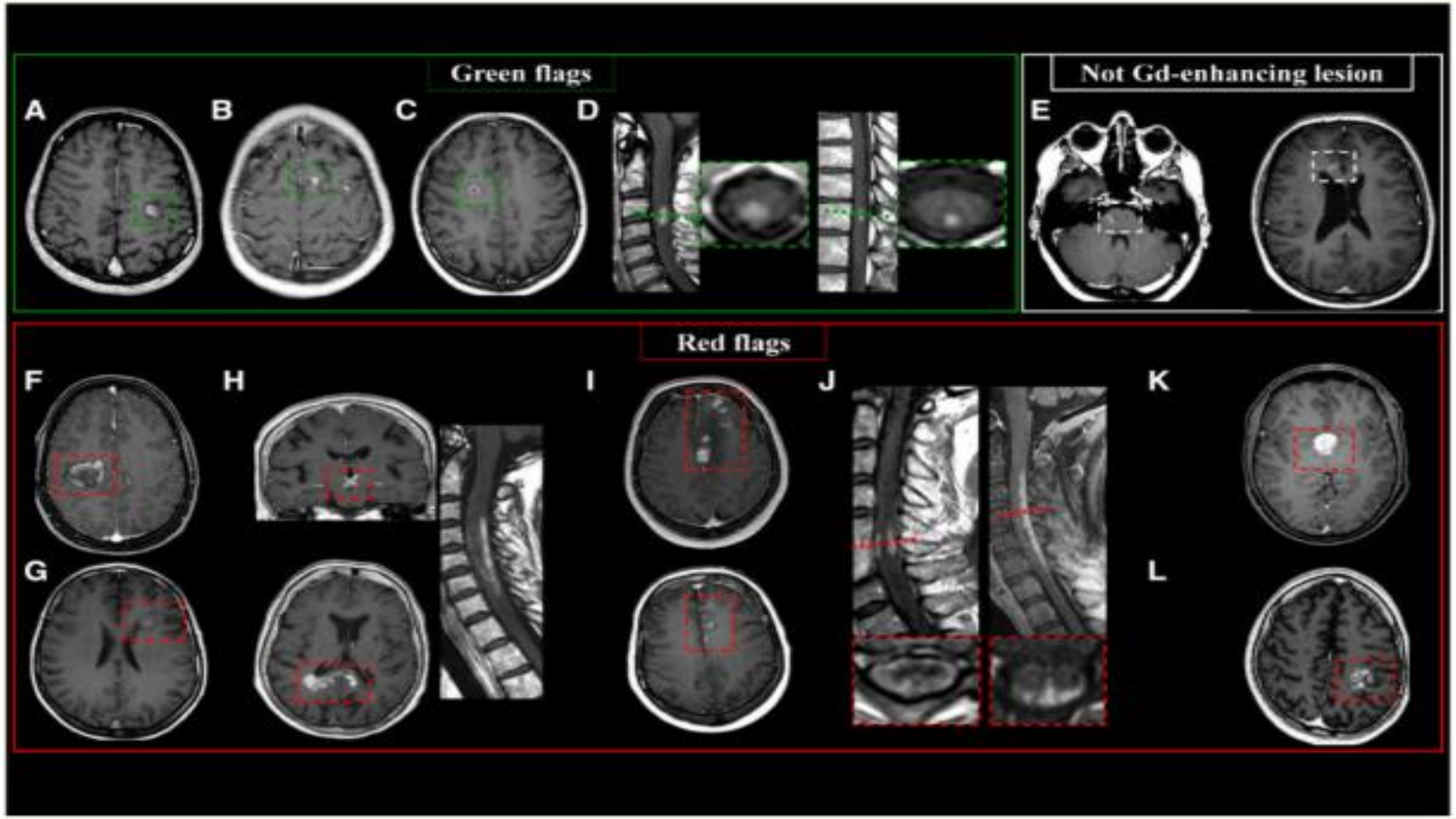
Infratentorial lesions



Spinal cord lesions

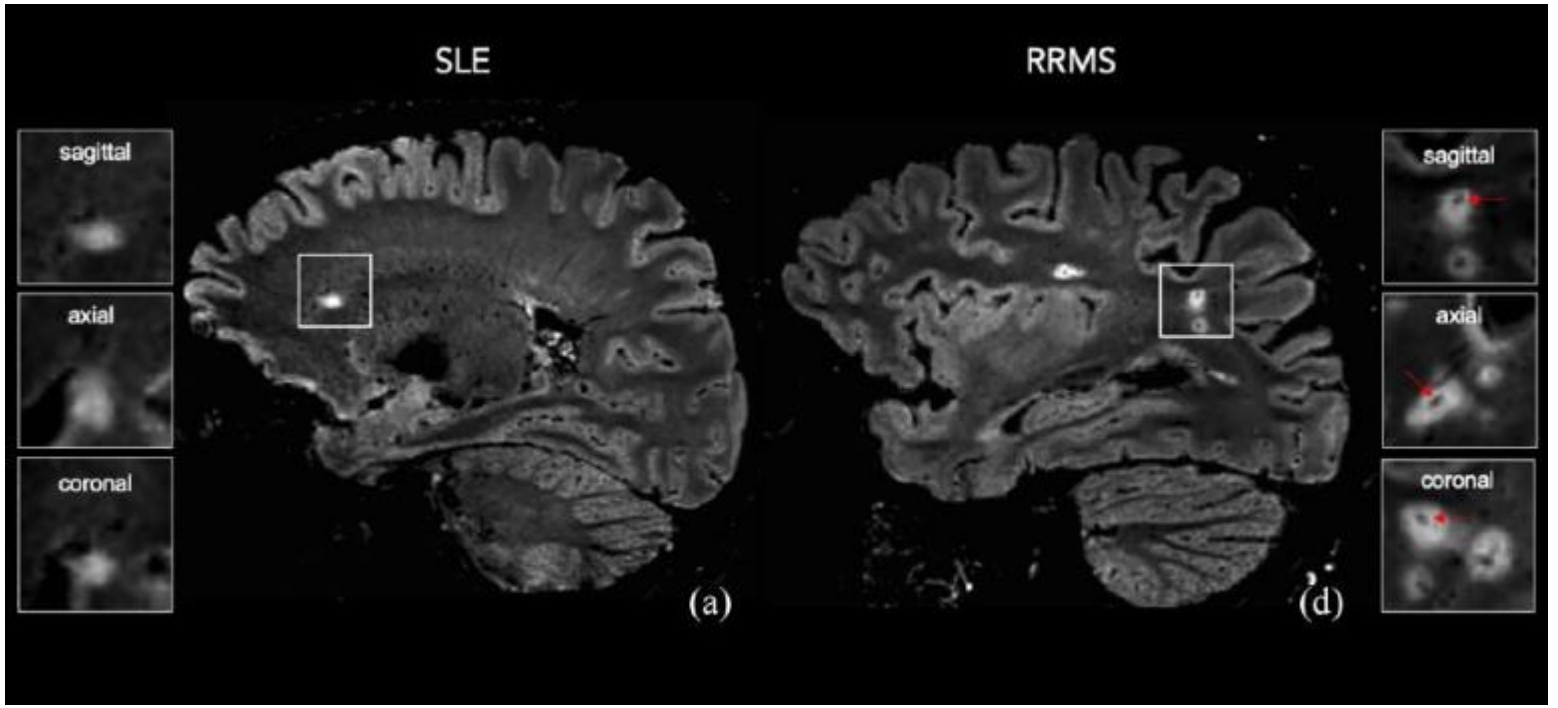


Gadolinium-enhancing lesions

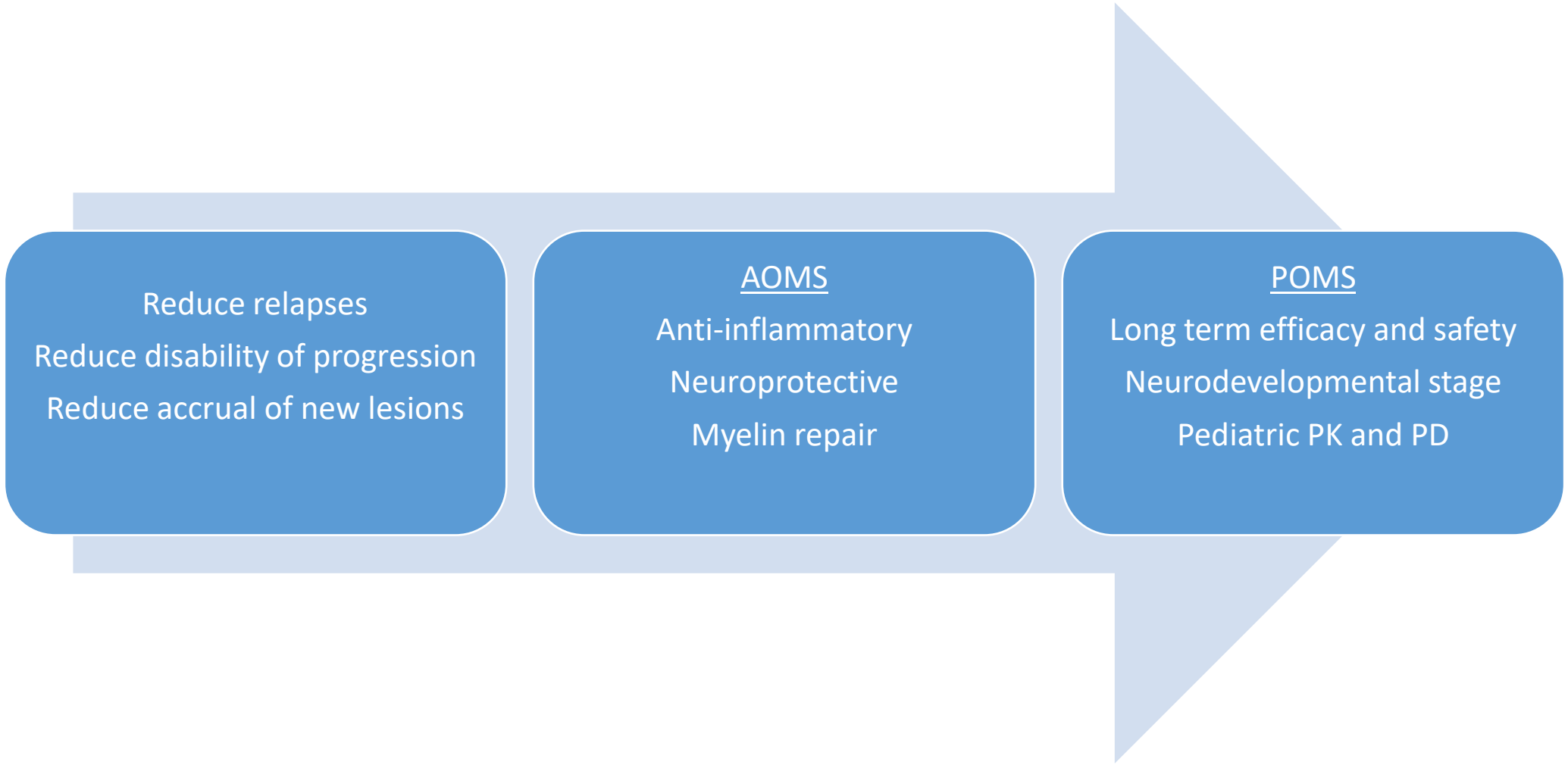


Central vein sign

- Presence of a vein at the center of brain white matter lesions
- Differentiates MS from other disorders – NMO, vasculitis, migraine
- 3D FLAIR MRI (3T) CVS can accurately predict MS – 97% accuracy



GOALS OF TREATMENT



Comprehensive approach addressing need of patient and family

- Long term use of DMT
- Social and school support
- Cognitive assessment
- Lifestyle assessment and modification
- Symptom management
- Mental health assessment and treatment

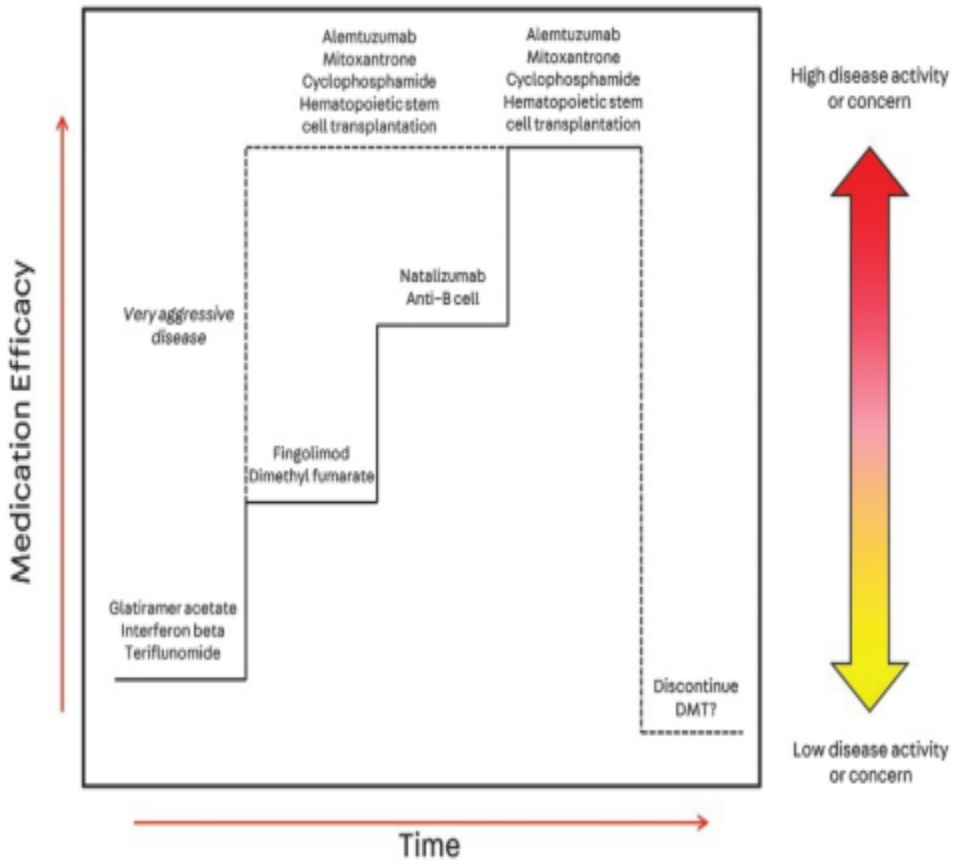
DECISION ON WHICH TREATMENT TO START

I. Severity and frequency of relapses
II. Route and MOA
III. Side effect profile
IV. Collaboration with patient and families

TREATMENT CHALLENGES

- Adherence and tolerability
- Onset during adolescence
- Injectable 1st line agents

ESCALATION THERAPY

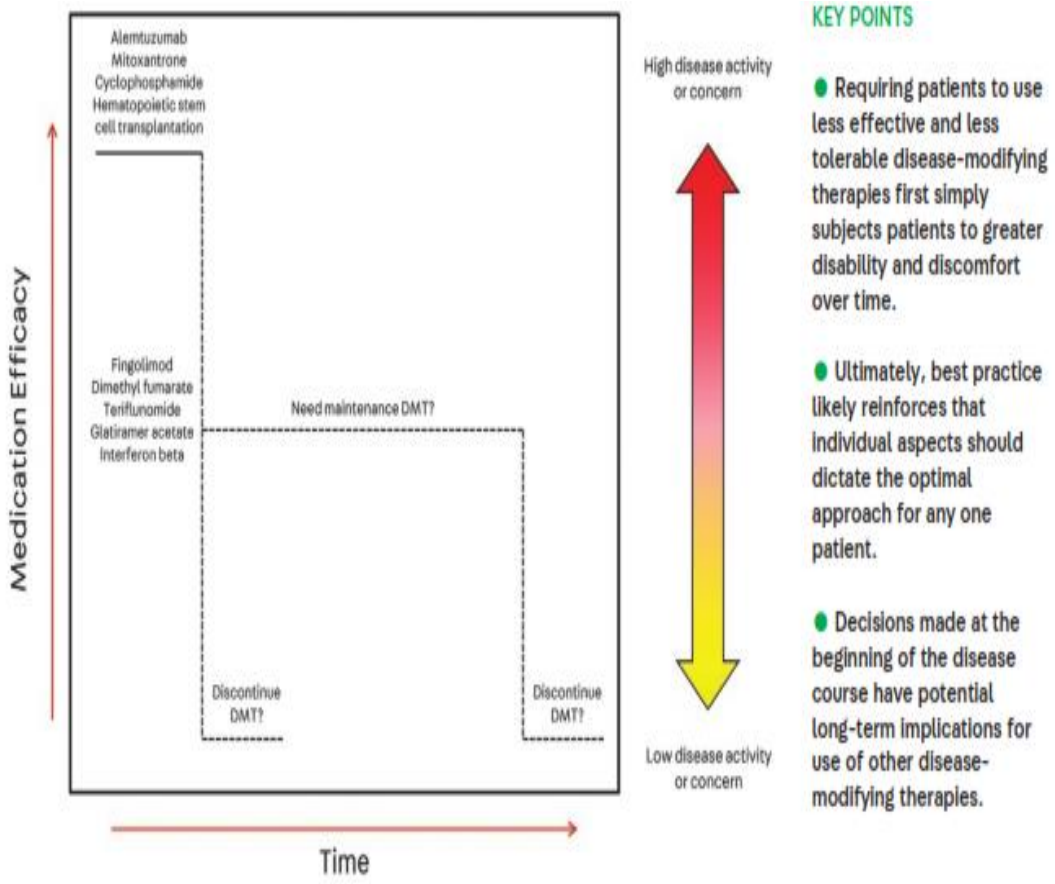


Gross 2019

- Conventional targets
- Relapses and progression of disability used to direct DMT

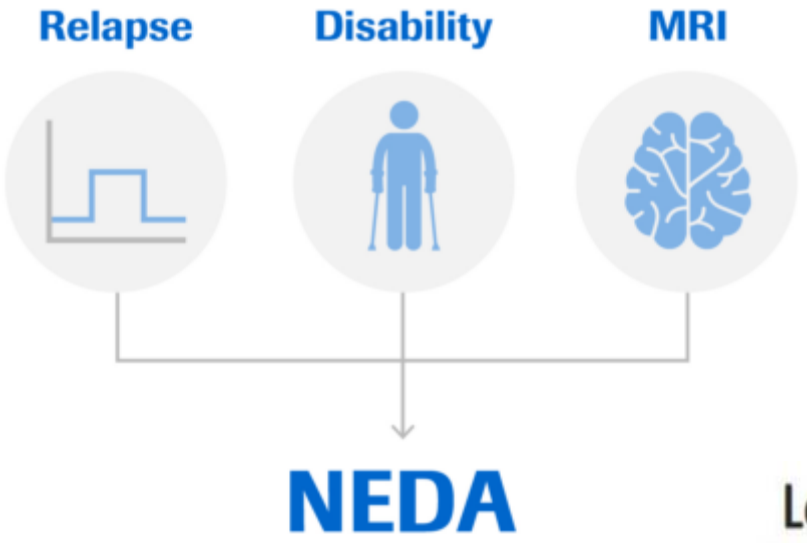
INDUCTION THERAPY

- New therapeutic aim: No Evidence of Disease Activity (NEDA)
- Disease Modifying Treatment (DMT) given after 1st attack decreases risk of further attacks
- Early DMT exposure was the only protective factor against EDSS increase
- More realistic: ? Minimal Evidence of Disease Activity



Gross 2019

- Absence of clinical relapses - ARR
- Absence of new, enlarging or enhancing MRI lesions –neT2
- Absence of confirmed disability progression



Level	Criteria
NEDA-1	No relapses
NEDA-2	+ Disability progression
NEDA-3	+ MRI activity
NEDA-4	+ Brain atrophy
NEDA-5	+ Cognition
NEDA-6	+ CSF neurofilament levels
NEDA-7	+ Patient-related outcomes
NEDA-8	+ Oligoclonal bands

IPMSSG GUIDELINES

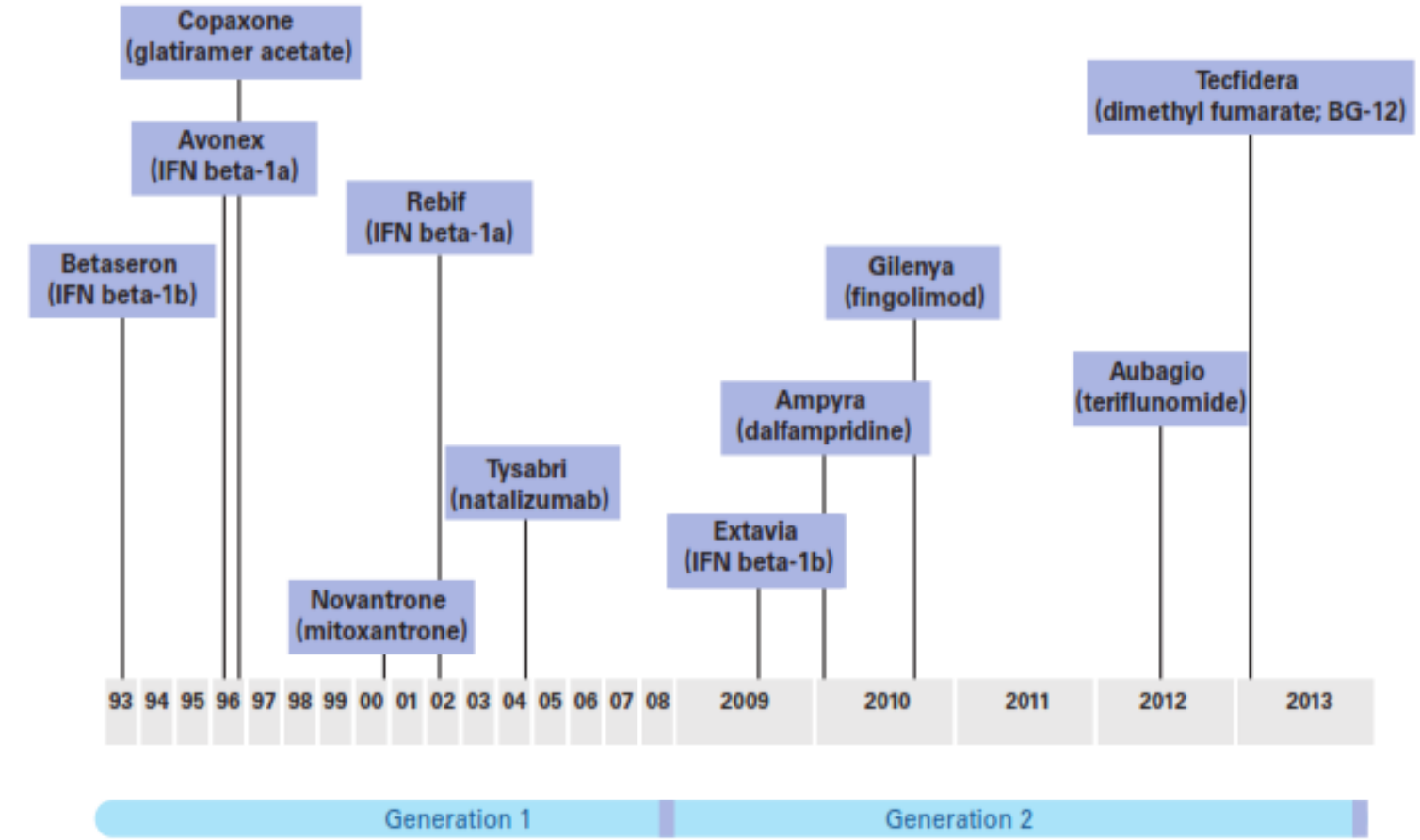
- Recommendation: prompt initiation of 1st line DMT after diagnosis
- Rationale: high rate of cognitive dysfunction

  single demyelinating attack affects age-expected brain growth

MS Disease Modifying Therapies

injectable	oral	infusion
• Interferon B 1a, 1b • Glatiramer acetate • Daclizumab	• Fingolimod • Dimethyl fumarate • Teriflunomide	• Natalizumab • Alemtuzumab • Ocrelizumab • Rituximab

Figure 1. Timeline Depicting the FDA Approval of DMDs and Other Agents for the Management of MS[20-30]



Owens 2013

INJECTABLES

Interferon Beta – 1a, 1b

Reduces BBB permeability

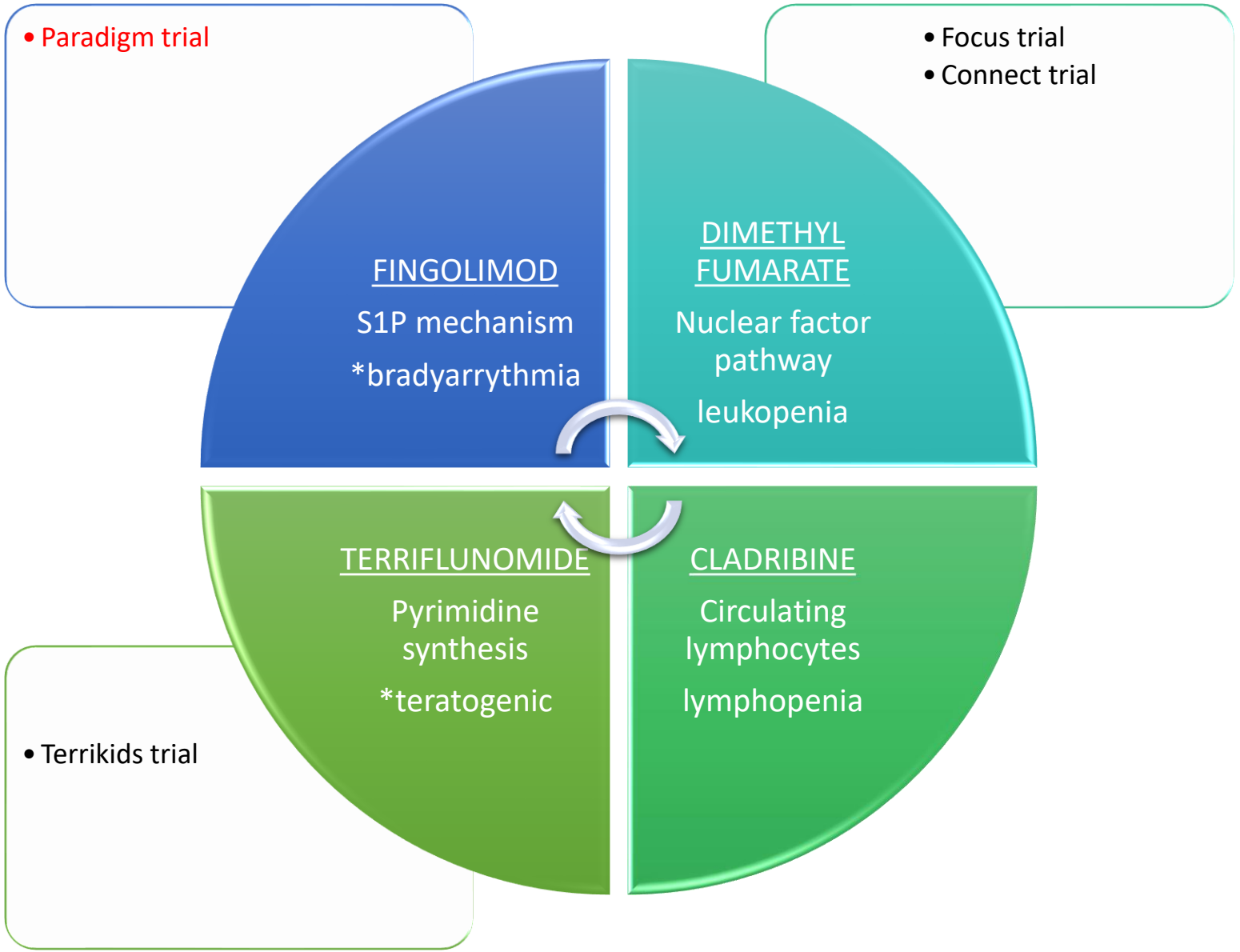
* Liver dysfunction

Glutiramer acetate

Regulatory T-cells

Hypersensitivity

Oral Drugs


• Paradigm trial
• Focus trial
• Connect trial
FINGOLIMOD
S1P mechanism
*bradyarrythmia
DIMETHYL FUMARATE
Nuclear factor pathway
leukopenia
TERRIFLUNOMIDE
Pyrimidine synthesis
*teratogenic
CLADRIBINE
Circulating lymphocytes
lymphopenia
• Terrikids trial

PARADIGMS TRIAL

POMS outcomes Age 10–17 [2]	Interferon β-1a	Fingolimod
n	108	107
Dosing	interferon β-1a at a dose of 30 µg per week	0.5 mg per day (0.25 mg per day for patients with a body weight of ≤40 kg
Adverse events	95.3% serious AE *n* = 7 (infection, supraventricular tachycardia) Convulsions *n* = 1, 0.9% AE > 10% Nervous system disorder 42% Psychiatric 10.3 Headache 29% Skin disorders 16.8%	88%serious AE *n* = 18, 16.8% (infection, leukopenia) Convulsions *n* = 6, (5.6%) AE > 10% Leukopenia Eye disorder Gastrointestinal disorders 34% Infection and infestation 59% Influenza 11% Respiratory tract upper 15.9% Nervous system disorder 43% Headache 31.8% Psychiatric 18.7% Skin disorders 18.7%
Completed trial 87.4%	88 (81.5%)	100 [93.5%]
Primary End Point, Adjusted Annualized Relapse Rate	0.67	0.12, 82% decrease compared with IFN B-1a, $P < 0.0001$
MRI		New T2 lesion, 53% absolute difference
Secondary End Point Annualized Rate of New or Newly Enlarging T2 Lesions	9.27	4.39 relative difference, 53%; $P < 0.001$
Reasons for Permanent Discontinuation of Medication	N = 11, lack of treatment effect	Elevated liver aminotransferase levels, macular edema, cardiac arrhythmias or electrocardiographic (ECG) abnormalities, and pregnancy

Duignan 2019

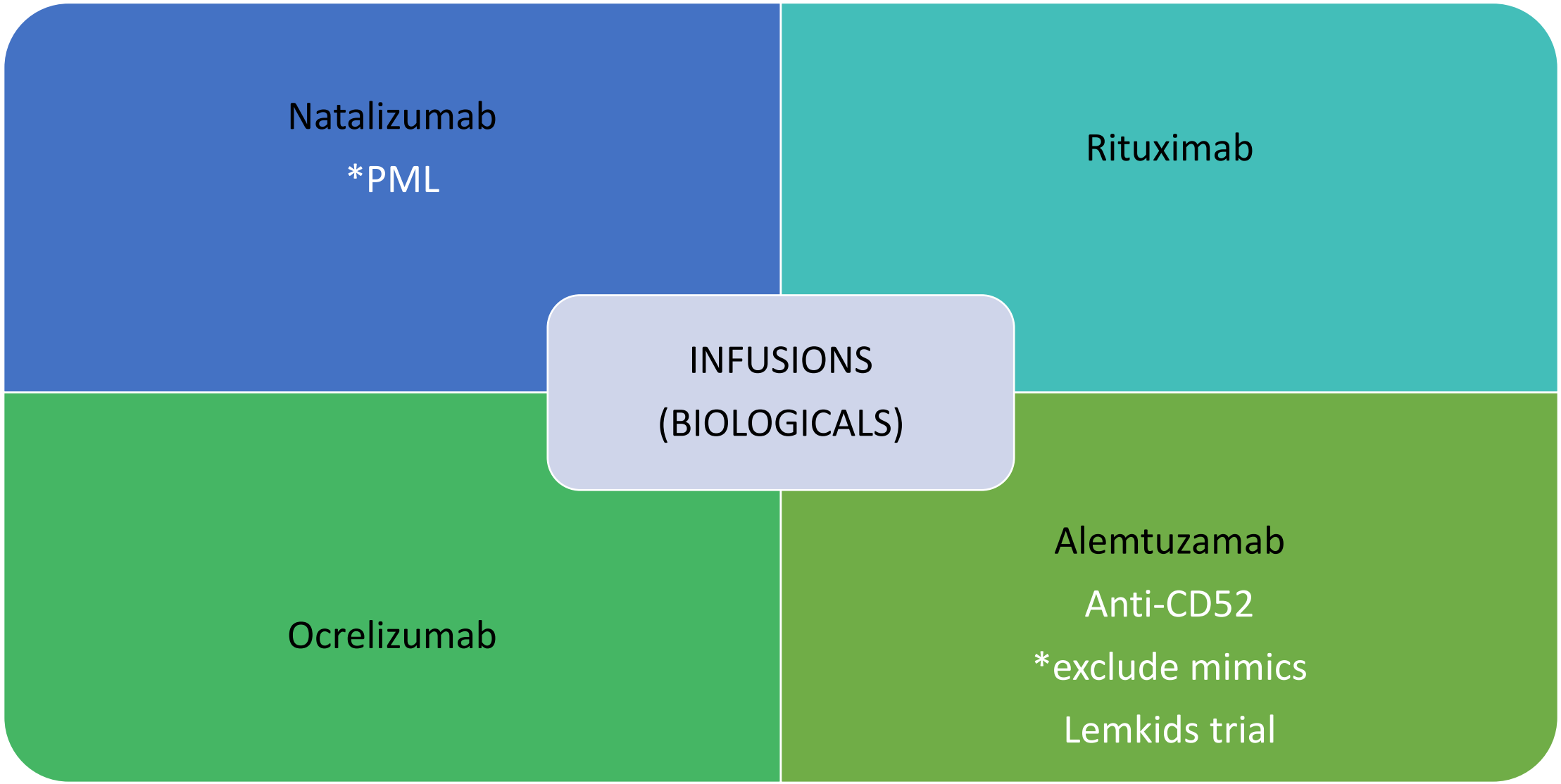

Natalizumab
*PML
Rituximab
INFUSIONS
(BIOLOGICALS)
Ocrelizumab
Alemtuzamab
Anti-CD52
*exclude mimics
Lemkids trial

Table II: Disease-modifying drugs

Drug	Brand name and dose	Presumed mechanism of action	Adverse events	Paediatric consideration
Interferon-β1a Interferon-β1b	Betaferon 250μg alternate days, SC Rebif 22μg or 44μg three times weekly, SC Avonex 30μg weekly intramuscularly Plegridy 125μg pegylated every 2wks, SC	Reduces blood–brain barrier permeability and modulates T-cell, B-cell, and cytokine functions	Injection site reaction, flu-like symptoms, liver function test elevation, leukopenia, (depression)	In younger children, alanine transaminase/ aspartate transaminase elevation more prominent Titrate more slowly
Glatiramer acetate	Copaxone 20mg daily Or 40mg three times a week	Stimulates regulatory T cells	Injection site reaction, hypersensitivity reaction	
Natalizumab	Tysabri 3–5mg/kg (maximum dose 300mg) monthly	Prevents lymphocytes from entering into the central nervous system	Infusion reaction, progressive multifocal leukoencephalopathy	Children more likely to be negative to John Cunningham virus Risk of seroconversion
Fingolimod	Gylenia 0.5mg tablet daily	Interferes with S1P mechanism and prevents lymphocytes exiting the lymph nodes	Bradyarrhythmia, macular oedema, herpes viruses infection (varicella-zoster virus)	Thymic maturation Adherence
Terifunomide	Aubagio 7mg or 14mg daily	Inhibits pyrimidine synthesis (general immunosuppression)	Hepatotoxicity (potential need for gastronintestinal washout), teratogenic risk	Teratogenicity
Dimethyl fumarate	Tecfidera 240mg tablet twice a day	Activates the nuclear-related factor 2 transcriptional pathway, modulates nuclear factor κB, which could have anti-inflammatory effects	Flushing, gastrointestinal symptoms, leukopenia	
Alemtuzamab	Lemtrada 5d intravenous infusion in year 1 followed by 3d infusion year 2	Anti-CD52^{+}-Ab; depletes mature circulating B and T cells	Infusion reactions, infection, secondary malignancies, autoimmune disorders, thrombocytopenia	Exclude other mimics such as MOG-Ab and AQP4-Ab before treatment
Cladribine	Mavenclad 3.75mg/kg tablets, up to 20d/y	Selective depletion of lymphocytes	Lymphopenia, infection	

Ab, antibody; AQP4-Ab, aquaporin-A antibodies; MOG-Ab, myelin oligodendrocyte glycoprotein antibodies; SC, subcutaneously.

Duignan 2019

Table 6. FDA Black Box warning and contraindications.

Natalizumab	Progressive Multifocal Encephalopathy (PML) Contraindicated if history of PML.
Teriflunomide	Contraindicated in patients with pre-existing acute or chronic liver disease
	contraindicated in women of childbearing potential Hepatotoxicity and risk of teratogenicity
Alemtuzumab	Risks of serious and sometimes fatal autoimmune conditions, infusion reactions, and various malignancies. It is contraindicated in human immunodeficiency virus due to CD4 + lymphocyte count reductions
Daclizumab	Daclizumab is contraindicated in Hepatitis B and C or liver impairment Removed from US market due to Autoimmune encephalitis Risk of severe liver injury and immune-mediated disorders, such as skin reactions, lymphadenopathy, and noninfectious colitis
Fingolimod	Fingolimod is contraindicated: if there is a cardiac event or vascular event like a stroke or TIA, irregular heart rate in the past 6 months and or medication that slows the QTc
Siponimod	Patients with a CYP2C9*3/*3 genotype (4) In the last 6 months, experienced myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization, or Class III/IV heart failure (4) Presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker (4)

Duignan 20019

MONITORING

- For tolerability and efficacy of treatment
- Clinical review: 3-6 monthly
- MRI: 6-12 monthly

<u>IPMSSG MRI recommendations:</u>

- 6 monthly
- Monitor response to treatment
- Asses accrual of asymptomatic lesions
- 6 months after initiation to avoid premature definitions of treatment failure
- Should ideally include brain and spine

IPMSSG MRI recommendations

Controversies

- ❖Duration of MRI spine
- ❖Gad-enhancement in all scans?
- Temporary phenomenon – lasting for 3 weeks
- Accumulation in the CNS
- New or enlarging T2 lesions is a more robust measure of disease activity
- Gad limited to specific clinical questions

TREATMENT FAILURE

Definition:

1. Ongoing clinical activity (relapses)

and

2. MRI activity (new T2 lesions)

- ❖ Patients fully compliant and on full dosages
- ❖ Period of time for drug to be effective

PROGNOSTIC FACTORS

- Highly active disease in 40% of children
- Long term prognosis less favourable
- Irreversible deficits at a younger age, longer disease duration
- Highly active patients more likely to require 2nd line therapy
- Improvement in prognosis compared to pre-treatment era
- Marked reduction in relapse rates and MRI parameters in patients who received natalizumab and rituximab

TRIALS

❖IPMSSG vision to advance care in paediatric MS

❖Consensus IPMSSG recommendations for future clinical trials in POMS

<u>Challenges in POMS clinical trails</u>

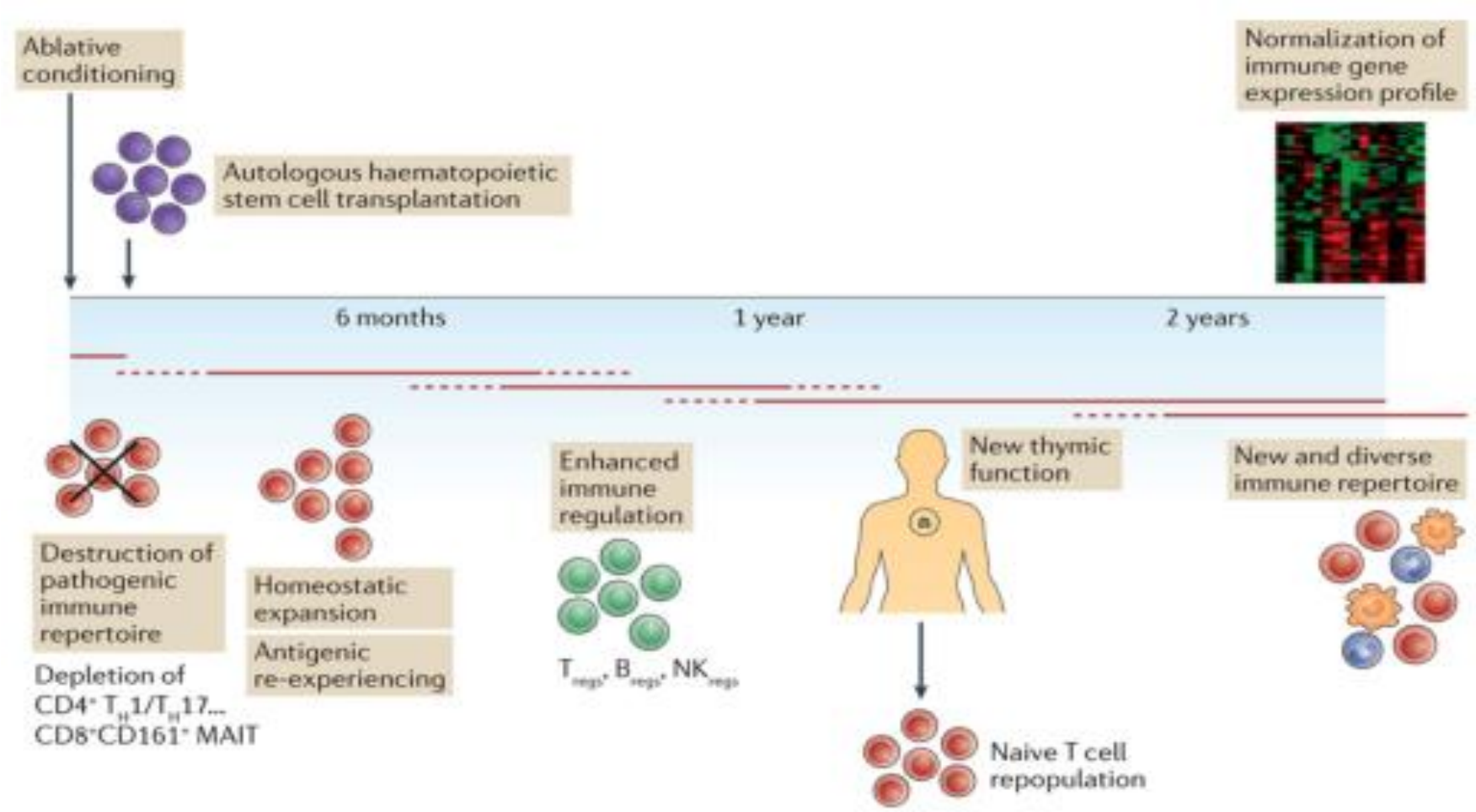
- Time to complete study enrolment
- Risk of incomplete enrolment
- Limited pool of possible clinical trial candidates
- Site specific challenges
- Financial risk
- Patient and family endorsement

Table III: Therapeutic trials

Name	Study population	Design	Primary objective	ClinicalTrials.gov identifier
PARADIGMS: safety and efficacy of fingolimod in paediatric patients with multiple sclerosis	215 participants with paediatric RRMS	A 2y, double-blind, randomized, multicentre, active-controlled core phase to evaluate safety and efficacy of daily fingolimod vs weekly interferon-β1a intramuscularly in paediatric patients with multiple sclerosis and 5y fingolimod extension phase	To evaluate the safety and efficacy of fingolimod vs interferon-β1a intramuscularly in paediatric patients	NCT01892722
CONNECT: phase 3 efficacy and safety study of dimethyl fumarate in paediatric patients with RRMS	142 participants with RRMS, aged 10–17y	Open-label, randomized, multicentre, multiple-dose, active-controlled, parallel-group, efficacy and safety study of dimethyl fumarate in children with RRMS, with optional open-label extension	To evaluate the safety, tolerability, and efficacy of BG00012 in paediatric patients with RRMS, compared with a disease-modifying treatment and to assess health outcomes and evolution of disability	NCT02283853
TERIKIDS: efficacy, safety, and pharmacokinetics of teriflunomide in paediatric patients with relapsing forms of multiple sclerosis	166 participants with RRMS, aged 10–17y	A 2y, multicentre, randomized, double-blind, placebo-controlled, parallel group trial to evaluate efficacy, safety, tolerability, and pharmacokinetics of teriflunomide administered orally once daily in paediatric patients with relapsing forms of multiple sclerosis followed by an open-label extension	To assess the effect of teriflunomide compared with placebo on disease activity measured by time to first clinical relapse	NCT02201108
FOCUS: study of the effect of dimethyl fumarate on MRI lesions and pharmacokinetics in paediatric patients with RRMS	22 participants with RRMS, aged 10–17y	Open-label, multicentre, multiple-dose study of the effect of BG00012 on MRI lesions and pharmacokinetics in paediatric patients with RRMS	Evaluate the effect of BG00012 (dimethyl fumarate) on brain MRI lesions in paediatric participants with RRMS	NCT02410200
LemKids: a study to evaluate efficacy, safety, and tolerability of alemtuzumab in paediatric patients with RRMS with disease activity on previous disease-modifying therapies	50 participants with RRMS, aged 10–17y	A multicentre, open-label, single-arm, before-and-after switch study to evaluate the efficacy, safety, and tolerability of alemtuzumab in paediatric patients with RRMS with disease activity on previous disease-modifying therapy	To evaluate the efficacy, safety, and tolerability of alemtuzumab (intravenously) in paediatric patients aged 10–<18y with RRMS who have disease activity on previous disease-modifying therapy	NCT03368664

Duignan 2019

STEM CELL THERAPY IN MS



Muraro 2017

JAMA Neurology | Original Investigation

Long-term Outcomes After Autologous Hematopoietic Stem Cell Transplantation for Multiple Sclerosis

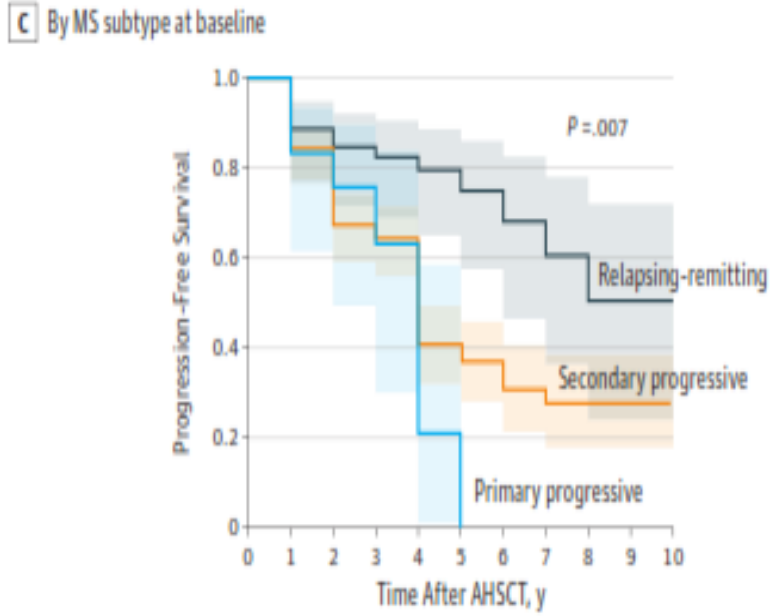
Muraro 2017

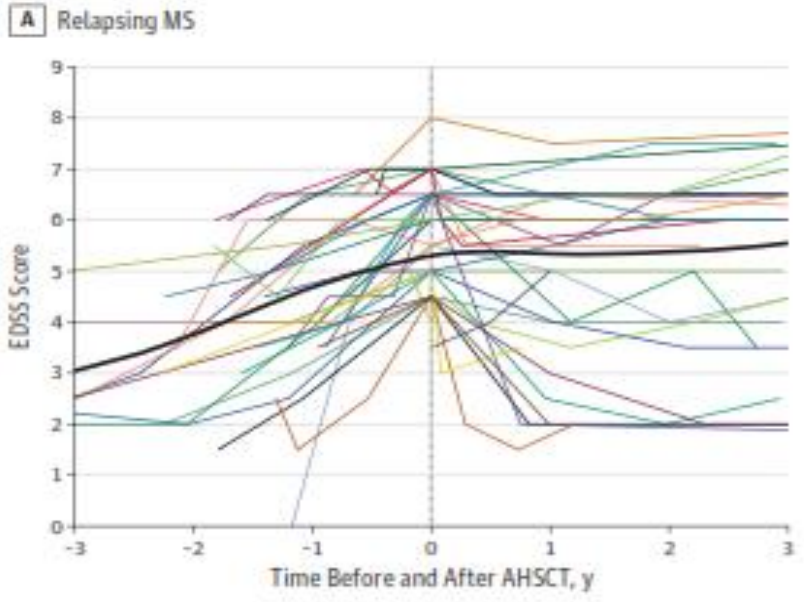
Objective:

- To evaluate long term outcomes of AHSCT in MS patients

Conclusions:

- 46% remained free from neurological progression for 5 years after transplant
- Factors associated with better outcomes: younger age, relapsing forms of MS, fewer prior immunotherapies, and lower baseline EDSS score





Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Position Statement

Autologous Hematopoietic Cell Transplantation for Treatment-Refractory Relapsing Multiple Sclerosis: Position Statement from the American Society for Blood and Marrow Transplantation

Jeffrey A. Cohen[1,*], Laura E. Baldassari[1], Harold L. Atkins[2], James D. Bowen[3], Christopher Bredeson[2], Paul A. Carpenter[4], John R. Corboy[5], Mark S. Freedman[6], Linda M. Griffith[7], Robert Lowsky[8], Navneet S. Majhail[9], Paolo A. Muraro[10], Richard A. Nash[11], Marcelo C. Pasquini[12], Stefanie Sarantopoulos[13], Bipin N. Savani[14], Jan Storek[15], Keith M. Sullivan[13], George E. Georges[4]

CONCLUSION

In summary, the ASBMT endorses AHCT as a "standard of care, clinical evidence available" for treatment-refractory relapsing MS. This document is not a treatment guideline, but is intended to provide guidance to physicians, patients, payers, policy makers, and other stakeholders on coverage decisions and the appropriate use of this procedure for MS.

beat-ms

BEst Available Therapy

vs.

Autologous Hematopoietic Stem Cell Transplant for MS

STEM CELL THERAPIES IN CHILDREN

Hematopoietic stem cells: I/AHSCT

- No RCT in POMS
- Observational studies in 21 patients: no worsening of EDSS, 16 improvement in EDSS, 19 relapse free, 15 MRI stability.
- No adverse events

Mesenchymal Stem Cells

- No reports in POMS

FUTURE PERSPECTIVES

Key to improving outcomes in MS

1. Early recognition and the ability to make an early accurate diagnosis in children – e.g. revised criteria / use of antibodies to differentiate, new biomarkers (CVS)
2. Effective and safe drugs to eliminate the ongoing inflammation
3. Prevent relapse
4. Minimize disability

❖Future research should be based on these goals

THANK YOU

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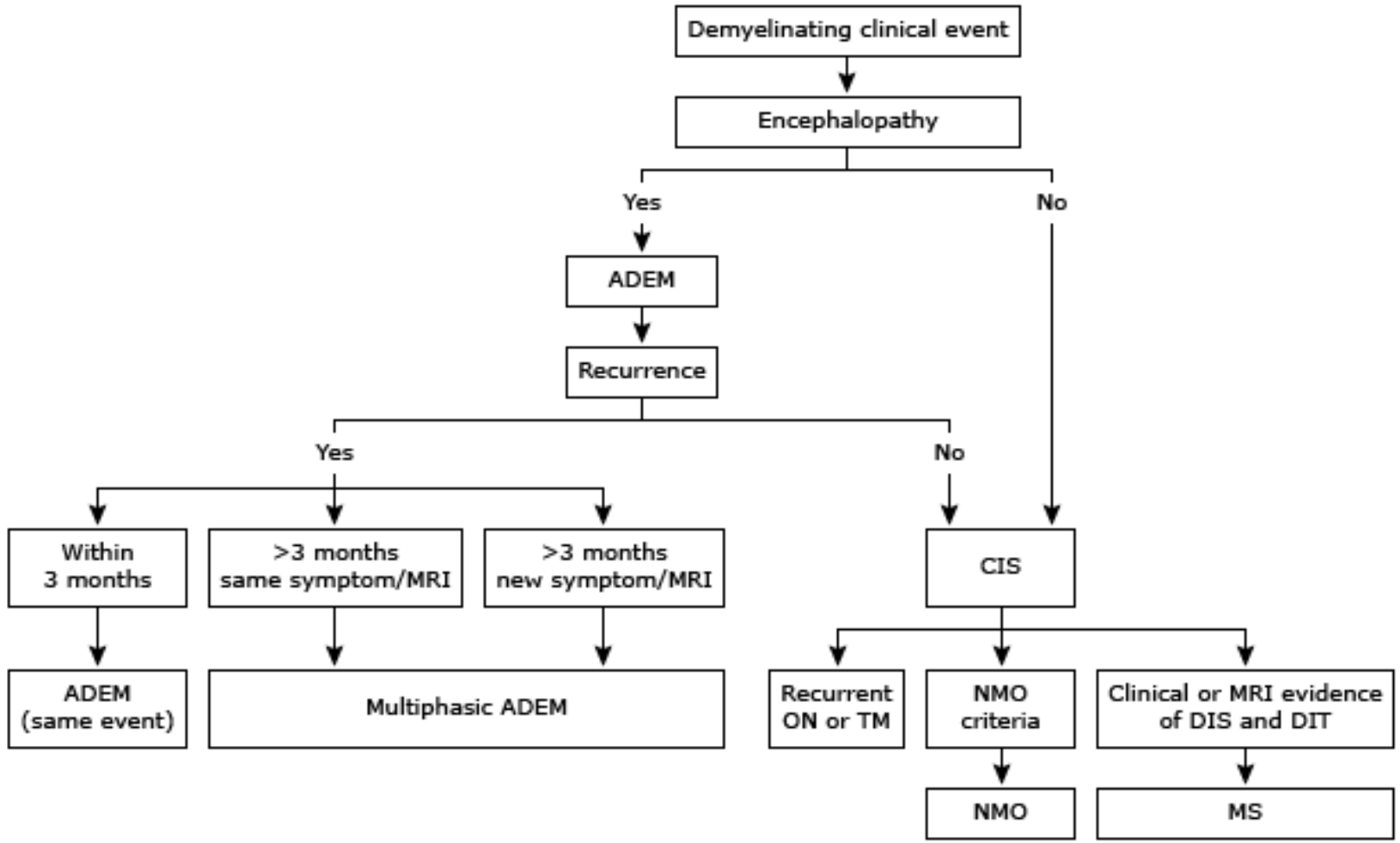
Diagnosis of demyelinating clinical event



ADEM: acute disseminated encephalomyelitis; CIS: clinically isolated syndrome; ON: optic neuritis; TM: transverse myelitis; NMO: neuromyelitis optica; DIS: dissemination in space; DIT: dissemination in time; MS: multiple sclerosis.

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