Progress in the field: therapeutic improvements for all patients?

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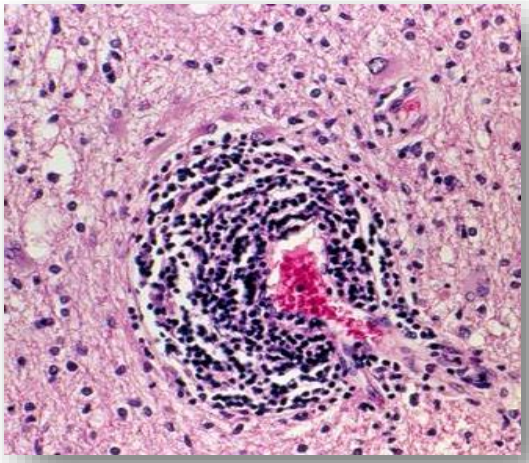
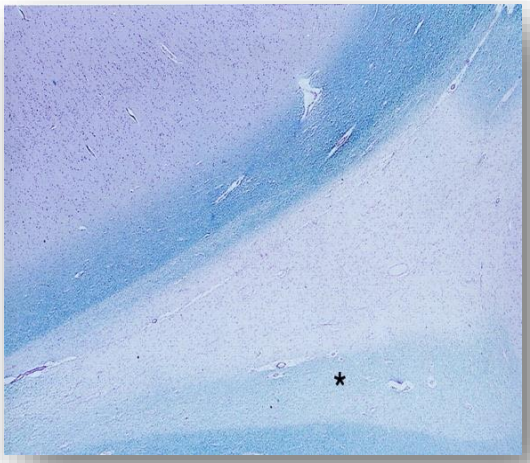
Main features of MS

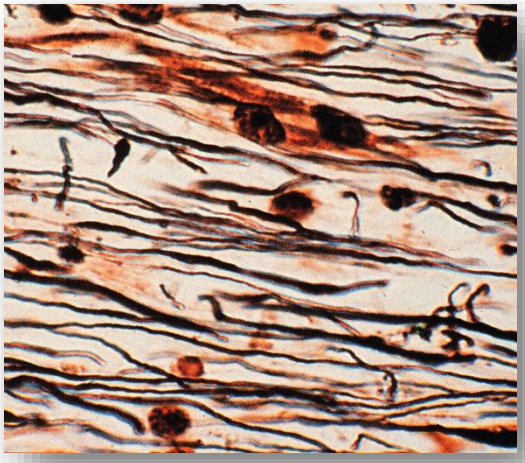
Inflammation



Demyelination

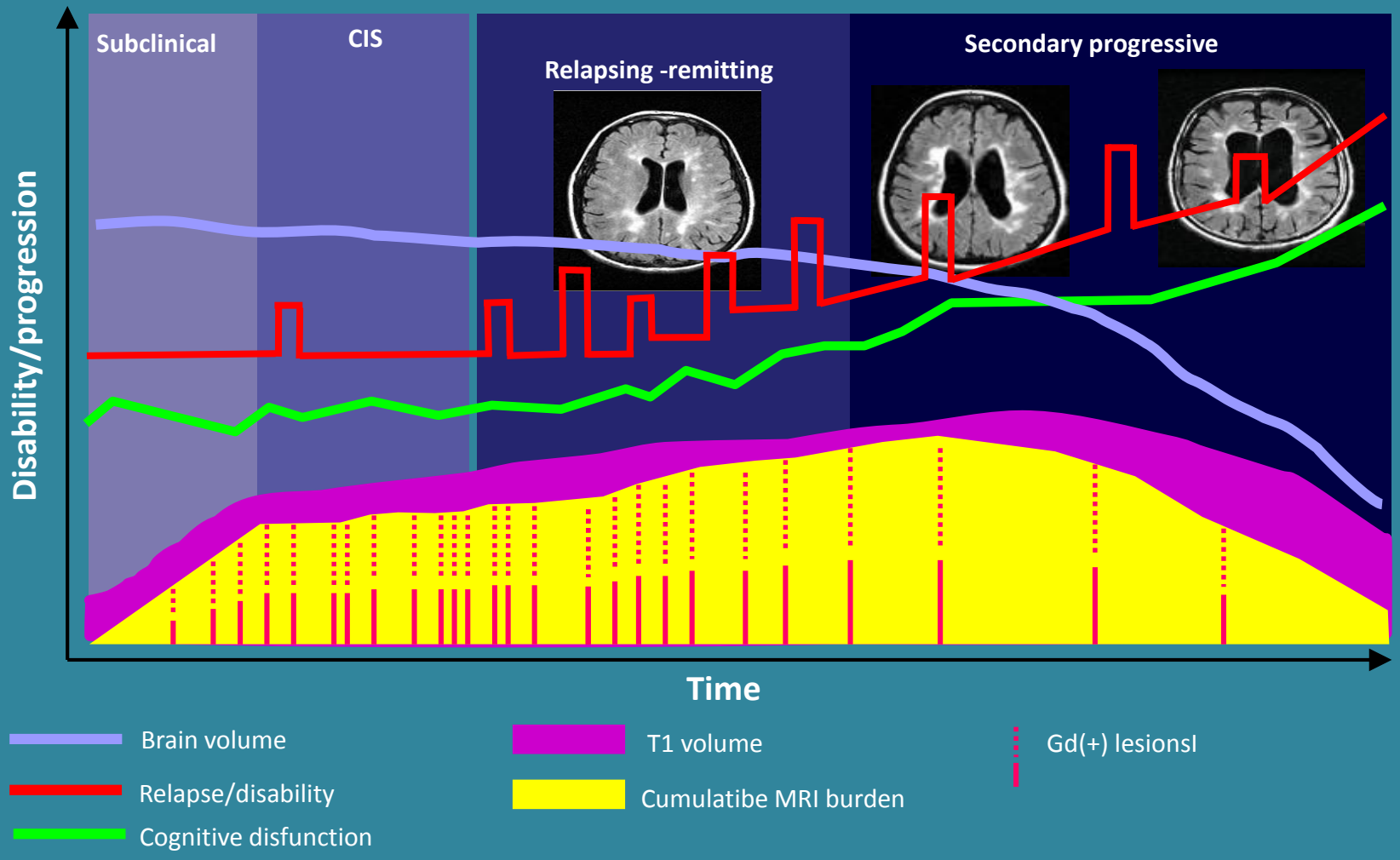


Axonal loss



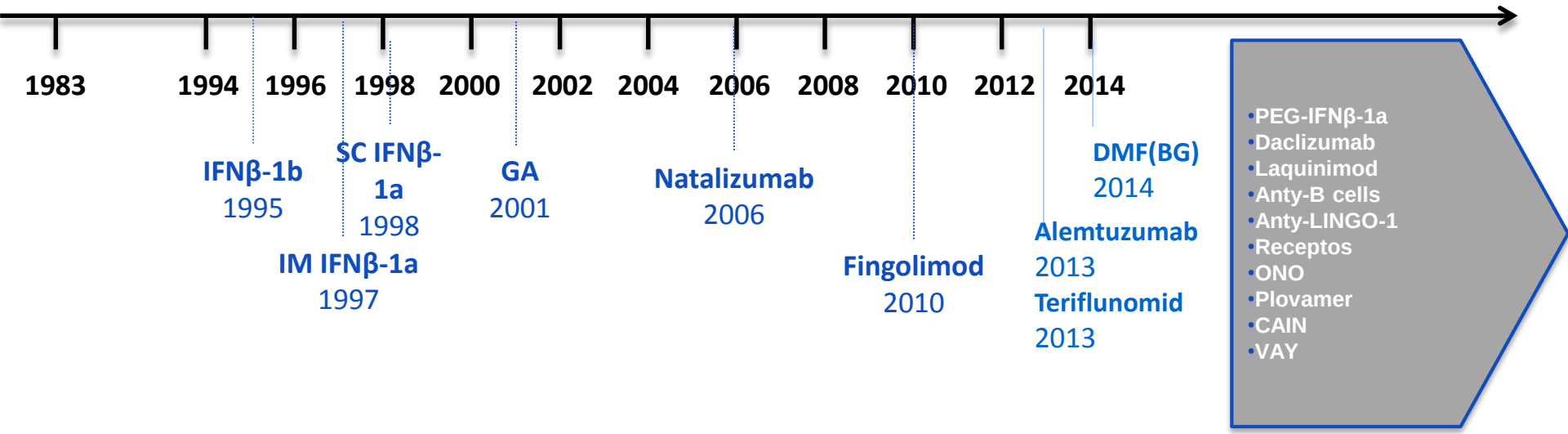
MS=multiple sclerosis

Natural course of multiple sclerosis



Trapp BD, et al. *Neuroscientist*. 1999;5:48-57.

Development of MS therapy



MSFC = złożona skala oceny stanu sprawności w stwardnieniu rozsianym; IFNβ = interferon beta; IM = domięśniowo; SC = podskórnie; GA = octan glatirameru; BG-12 = fumaran dimetylu; PEG = PEGylowany; UE = Unia Europejska.

1. Kurtzke J. *Neurology.* 1983; 33: 1444-1452; 2. Whitaker J et al. *Mult Scler.* 1995; 1: 37-47; 3. Havrdova E et al. *Lancet Neurol*. 2009; 8: 254-260; 4. Phillips J et al. *Mult Scler.* 2011; 17: 970-979.

Platform therapies

Interferon beta i glatiramer

Rebif® (Interferon beta-1a)	**22/44 mcg s.c. 3 x tydzień**
Avonex® (Interferon beta-1a)	**30 mcg i.m. 1 x tydzień**
Betaferon® (Interferon beta-1b)	**250 mcg s.c. co 2 dzień**
Extavia® (Interferon beta-1b)	**250 mcg s.c. co 2 dzień**
Copaxone (glatiramer)	**20 mg s.c. codziennie**

New MS therapies 2013/2015

- Monoclonal Abs
  - Natalizumab
  - Alemtuzumab
  - Rituximab
  - Ocrelizumab
  - Daclizumab
- Oral drugs
  - Fingolimod
  - Teriflunomid
  - DM Fumarate (BG-12)
  - Laquinimod
- New platform drugs
  - Peg-IFNb
  - Cop 3xweek

Current MS landscape

- Treatments can be separated along multiple categories:
  - Immunomodulators vs. Immunosuppressants

Not always clearly separated, MoA/clinical profile can combine both (e.g. Tecfidera, Aubagio).

  - First line vs. second line

Distinction differs between countries, payors/insurances, e.g. not made by FDA.

  - Platform vs. novel

Distinction mostly reflects history and experience collected with specific treatments.

  - Injectables vs. orals

Route of administration – helpful when preferences for convenience are relevant.

  - Moderate vs. high efficacy

Important distinction, but limited direct comparison is an important caveat.

- Categorizations serve different purposes and have limitations.

Increasing spending for MS drugs

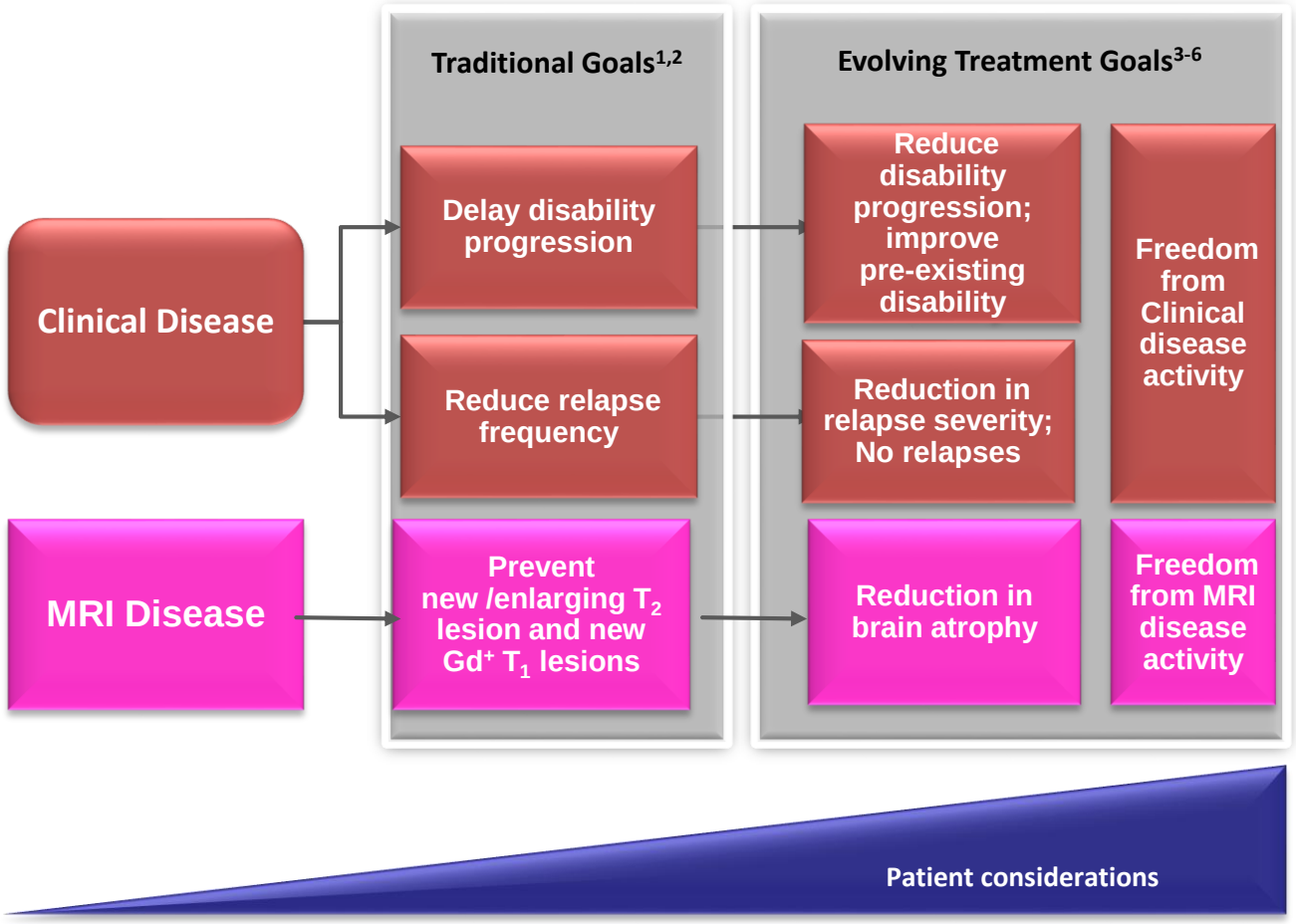
- Drug costs account for up to 75% of the total cost of MS care
- MS drugs account for 3.1% of total US drug costs
- MS pricing has increased more than any other therapeutic area over the last several years

			TREND		
RANK	THERAPY CLASS	PMPY SPEND	UTILIZATION	UNIT COST	TOTAL
1	Inflammatory Conditions	$80.03	8.5%	15.7%	**24.3%**
2	Multiple Sclerosis	$52.36	3.2%	9.7%	**12.9%**
3	Oncology	$41.64	8.9%	11.7%	**20.7%**
4	Hepatitis C	$37.95	76.1%	666.6%	**742.6%**
5	HIV	$27.24	4.5%	10.3%	**14.8%**
6	Miscellaneous Specialty Conditions	$11.10	27.3%	8.2%	**35.6%**
7	Growth Deficiency	$9.98	-0.9%	7.5%	**6.6%**
8	Hemophilia	$5.49	-0.8%	17.6%	**16.9%**
9	Pulmonary Arterial Hypertension	$5.41	7.6%	6.2%	**13.8%**
10	Transplant	$5.13	0.8%	-3.1%	**-2.3%**
	TOTAL SPECIALTY	**$311.11**	**5.8%**	**25.2%**	**30.9%**

Current MS landscape

- Common features across the spectrum of treatment choices in MS:
  - All treatments address the inflammatory component of the disease.
  - Benefit to Risk profile: higher efficacy is traded for less safety.
- Predicting future course of disease in individual patients is difficult.
  - Currently mostly based on clinical phenotype (age, gender, weight, smoking).
  - Limited accuracy.
  - More useful to predict course of disease, less useful in predicting response to treatment.
- Challenge lies in making the best trade-off at the right time in the right patient.

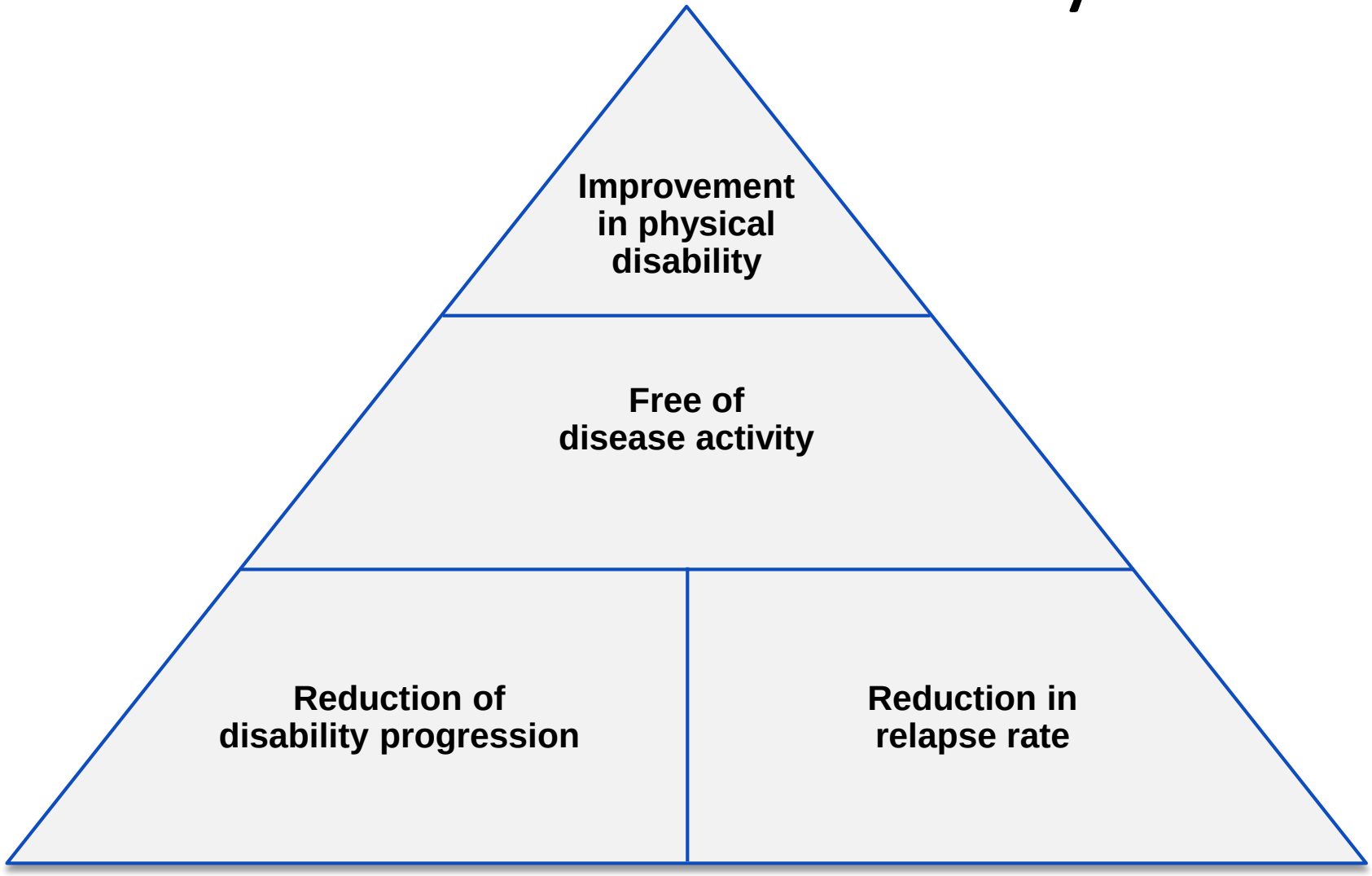
New Therapies Allow Us to Re-evaluate Our Treatment Goals



Gd=gadolinium

1. IFNB MS Study Group. *Neurology* 1993;43:655-61; 2. PRISMS Study Group. *Lancet* 1998;352:1498-504; 3. Kappos L et al. *N Engl J Med* 2010;362:387-401; 4. Cohen JA et al. *Lancet* 2012;380:1819-28; 5. Coles AJ et al. *Lancet* 2012;380:1829-39; 6. O'Connor P et al. *N Engl J Med* 2011;365:1293-303.

How To Define Efficacy?

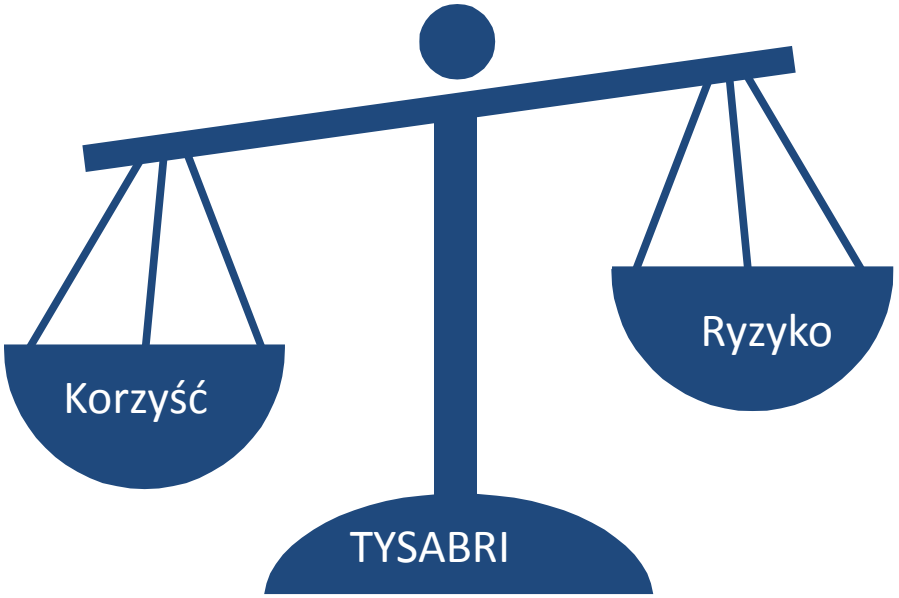


Benefit/risk

68%relapse reduction

42-54%reduced risk for disability

5,3- increase in disease-free paatients



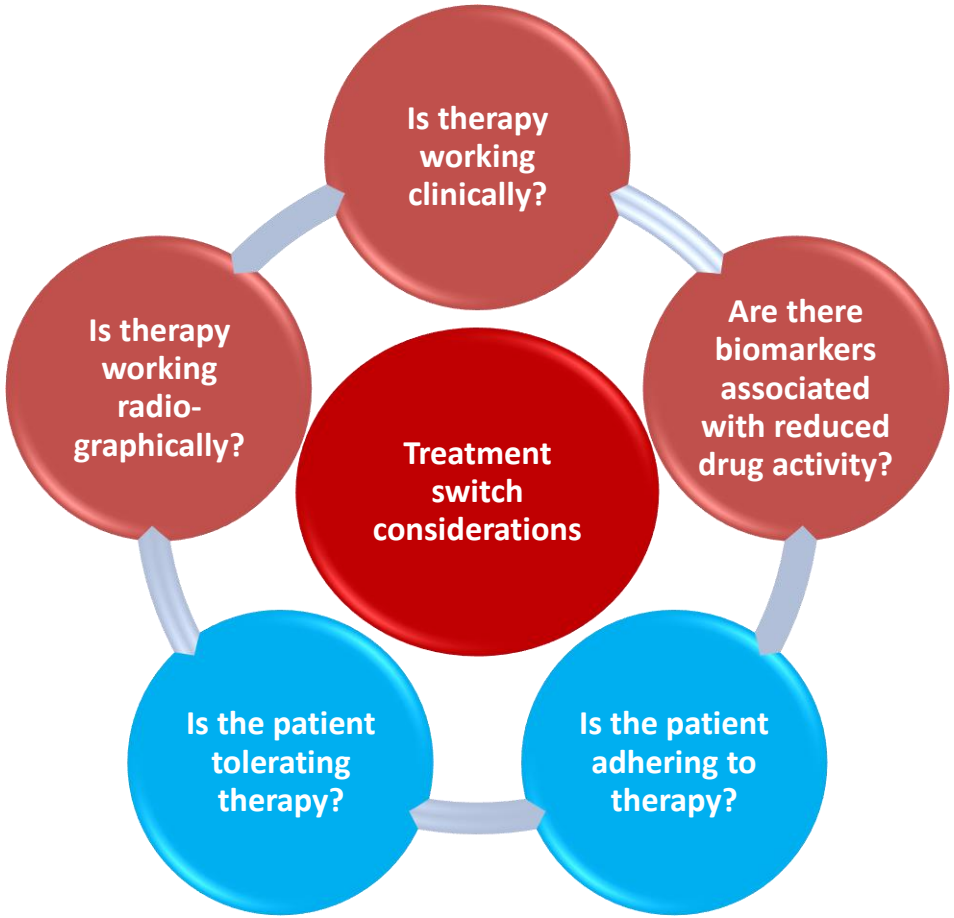
Risk of PML ≈ 1,31 u 1000[3]
Any other adverse event

Risk stratification plan?

1. Polman C et al. N Engl J Med 2006; 354 (9): 899-910.
2. Havrdova E et al. Lancet Neurol 2009; 8 (3): 254-60.
3. Biogen Idec. Data on file as of April 1st

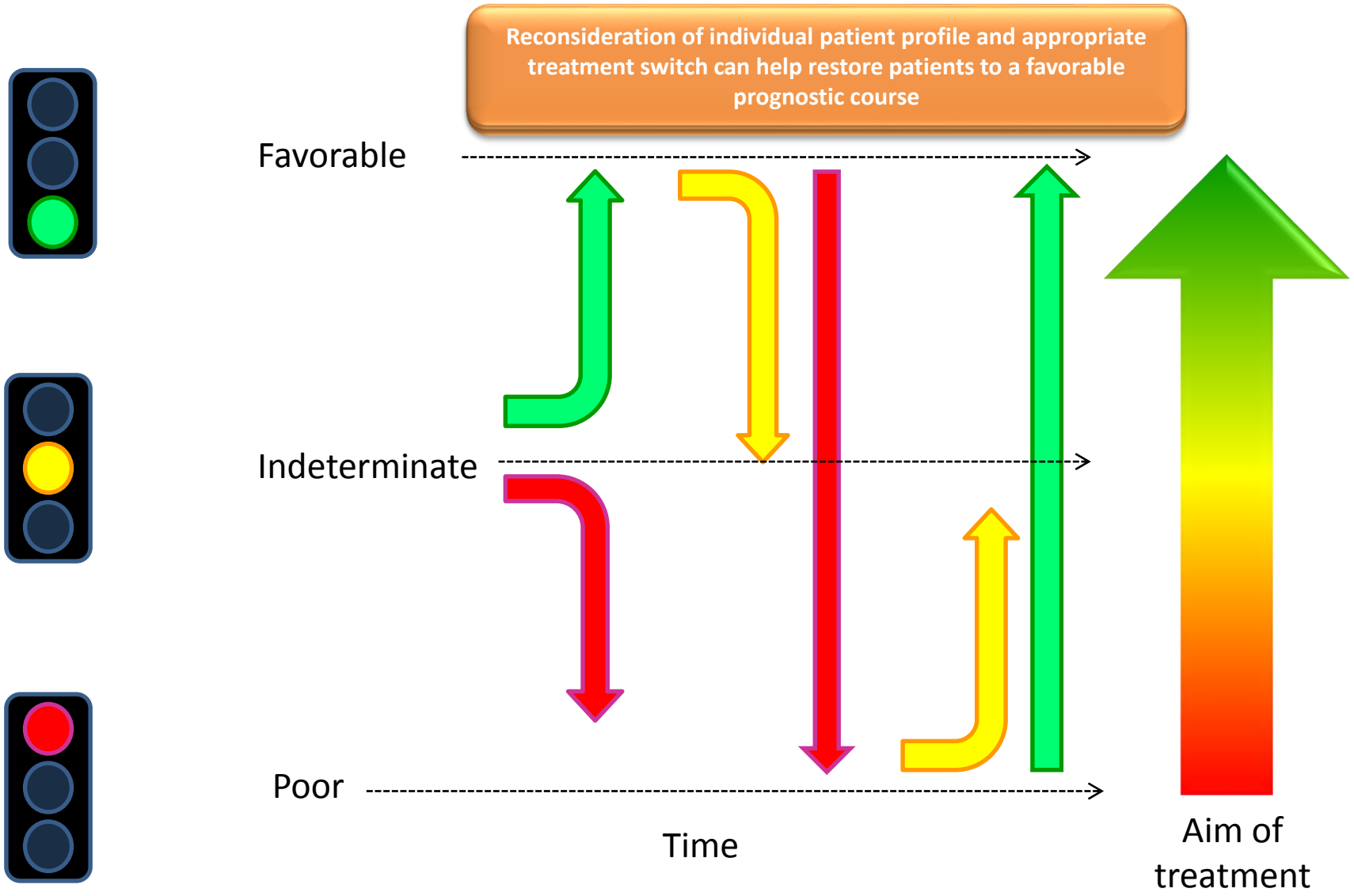
Ongoing Assessment of Treatment Outcomes Is Important for Optimal Disease Management

- Monitor for ongoing relapse and MRI disease activity
  - Consider prognostic factors and switch quickly if patient is having an inadequate response
- Regularly assess adherence to therapy to optimize treatment outcomes
  - Route/frequency of administration and treatment tolerability may impact patient adherence



Coyle PK. *CNS Drugs* 2013;27:239-47.

Treatment Decisions Should Be Driven by the Individual Patient Profile



Freedman MS et al. *Curr Res Med Opin* 2009;25:2459-70.

Disease Activity in the First 2 Years Is Predictive of Long-term Disability

Activity During 2-Year Trial	Odds of Severe Disability* 15 Years Later
≥2 Gd lesions	8.96
≥2 Relapses	4.44
≥3 New T_2 lesions	2.90

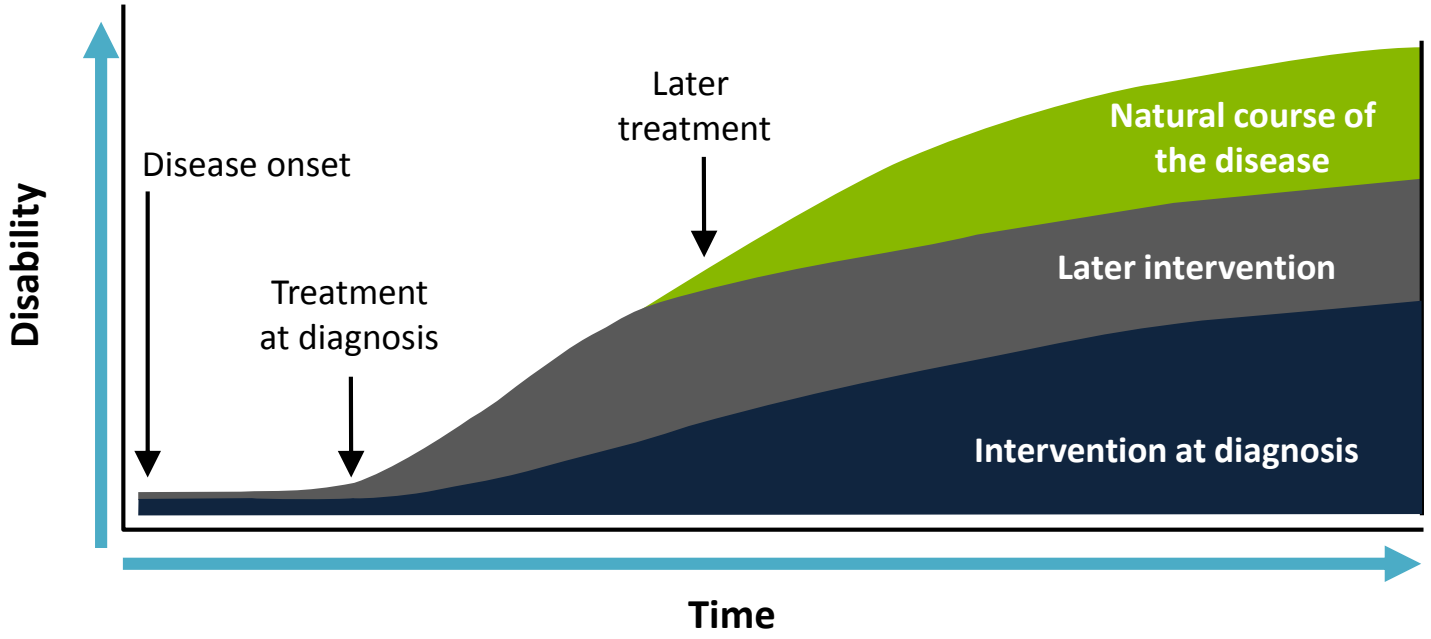
*Odds of being in worst vs. best quartile

- Ongoing clinical or MRI disease activity during interferon treatment in a 2-year trial was predictive of disability progression 15 years later

*EDSS>4.5.

Bermel RA et al. *Ann Neurol.* 2013;73:95-103.

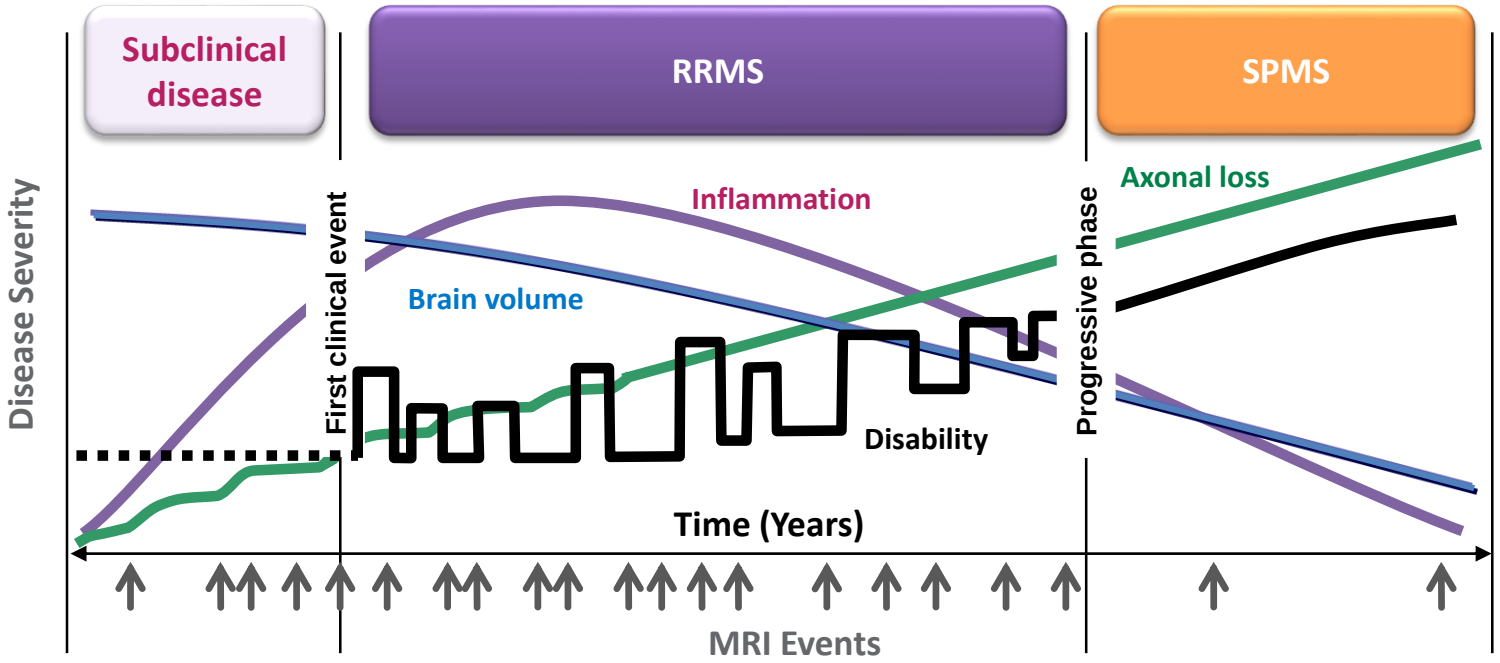
Early Treatment Provides the Greatest Chance for Modifying Disease Prognosis



- There appears to be a therapeutic window in MS when greatest benefit can be obtained from the most effective intervention as early as possible

Miller JR. *J Manag Care Pharm* 2004;10(suppl S-b):S4-11.

Early Subclinical Axonal and Brain Volume Loss Predicts Disability Progression

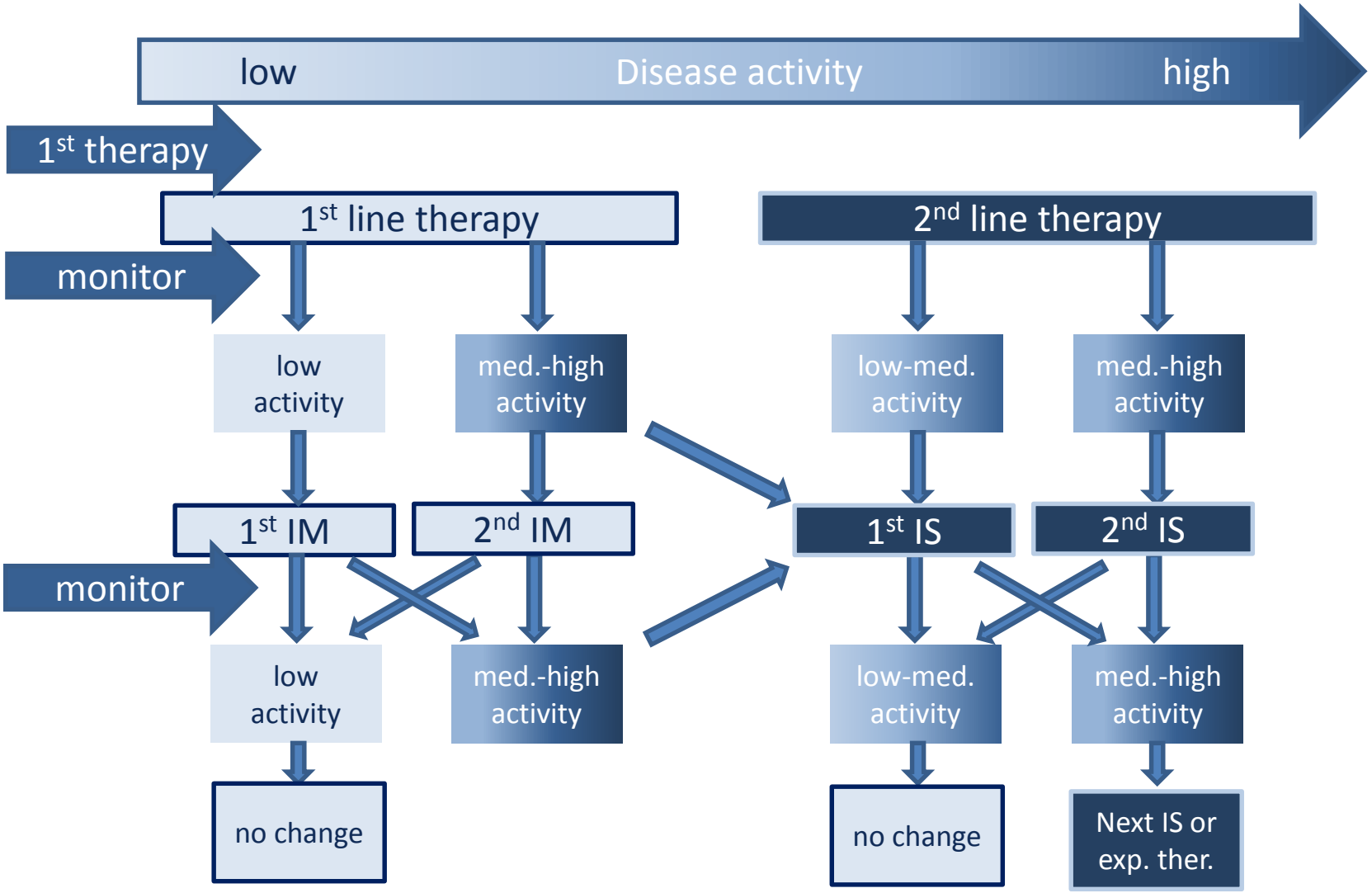


- Subclinical inflammation, demyelination, and neurodegeneration may be present for months, or even years, before a patient experiences clinical symptoms[1]
- Inflammatory activity early in the disease, including MRI and clinical events, is predictive of long-term disability progression[2-4]

MRI=magnetic resonance imaging; RRMS=relapsing remitting multiple sclerosis; SPMS=secondary progressive multiple sclerosis

1. Stüve O et al. *Drugs* 2008;68:73-83; 2. Brex PA et al. *N Engl J Med* 2002;346:158-64; 3. O'Riordan JI et al. *Brain* 1998;121:495-503; 4. Confavreux C et al. *Brain* 2003;126:770-82. Image adapted from Compston A, Coles AJ. *Lancet* 2008;372:1502-17.

Treatment strategies in MS



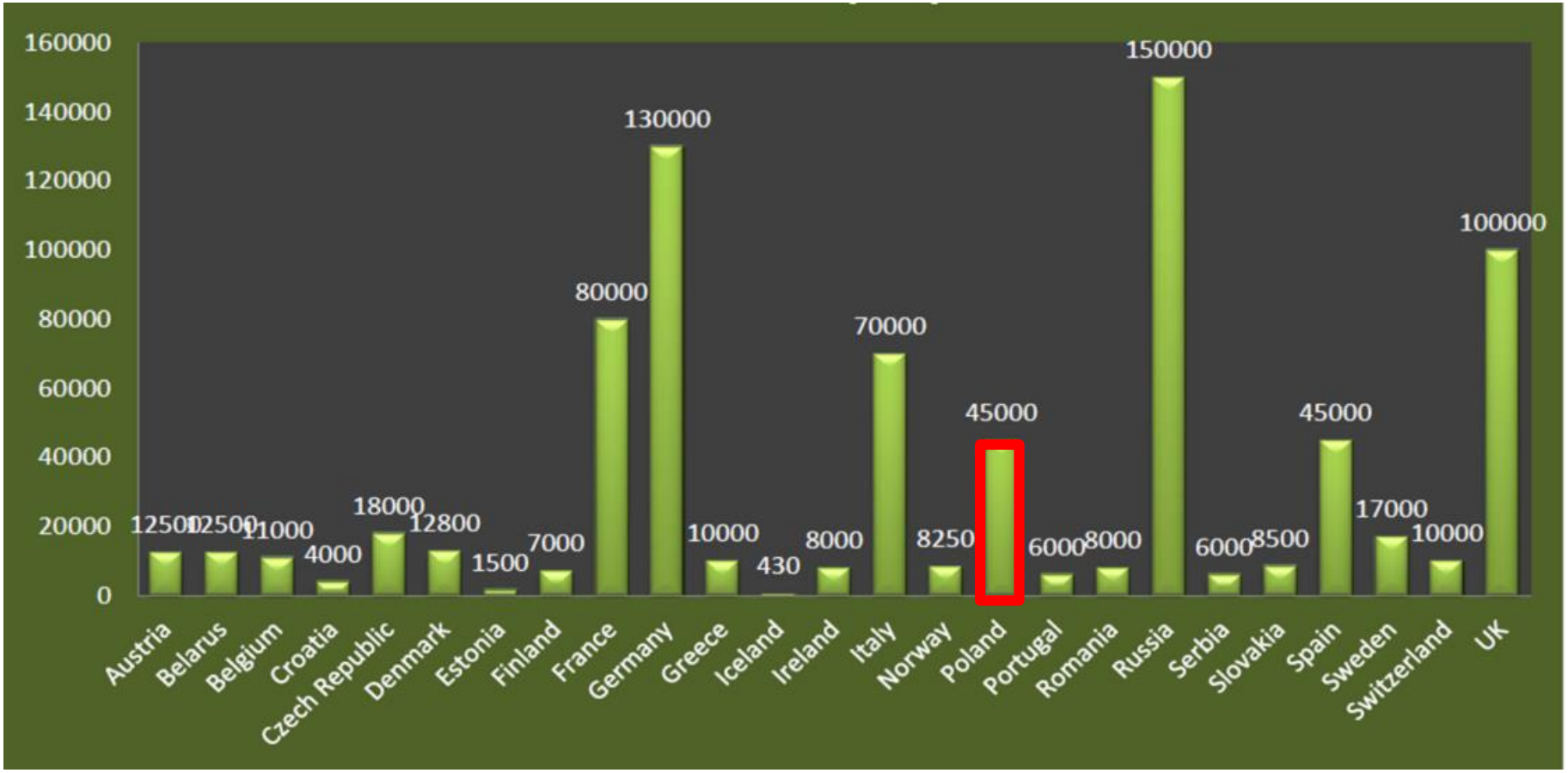
Current MS landscape

- Choice of therapy depends on:
  - Features and preferences of the individual patient
  - Experience and preferences of the neurologist

- Remaining unmet needs:
  - Benefit/Risk: Treatments with long-term high efficacy, safety, and convenience
  - Predictive markers to find the right drug for the right patient
  - Treatments for progressive MS

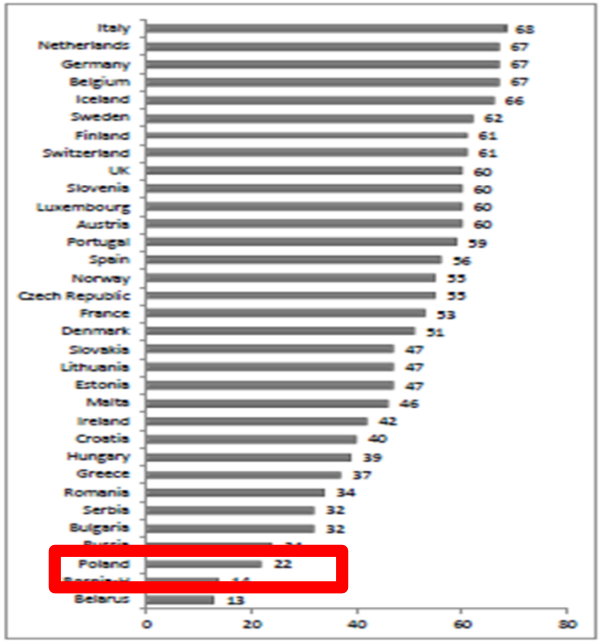
Access to second line treatments and therapies for multiple sclerosis - for all patients ???

Poland vs. Europe (Estimated number of people with MS)

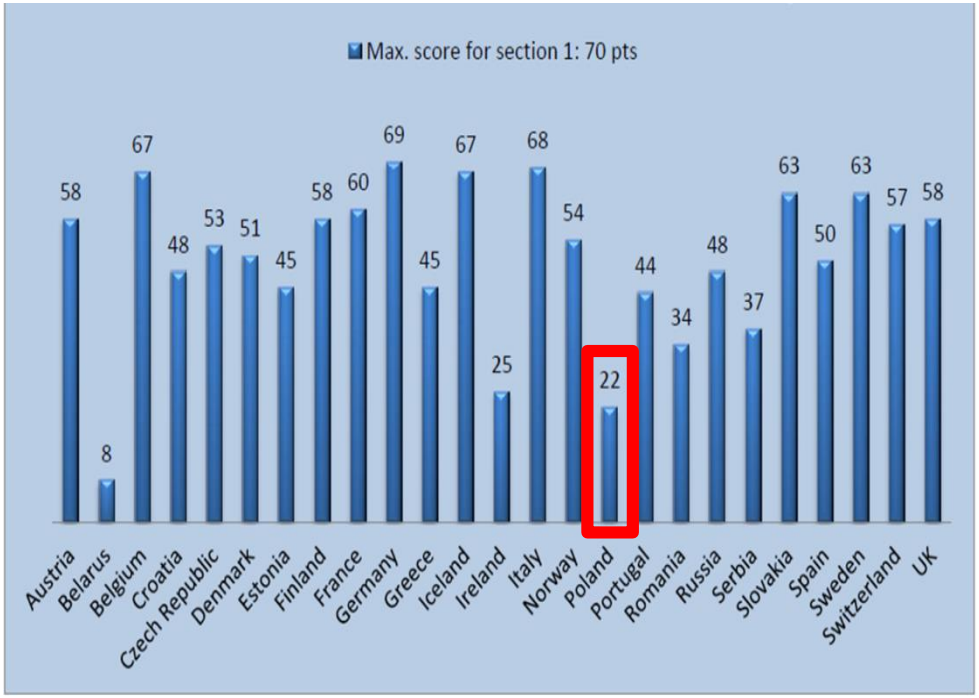


Poland vs. Europe (Slow progress in access to treatment and therapies)

2011*



2013**



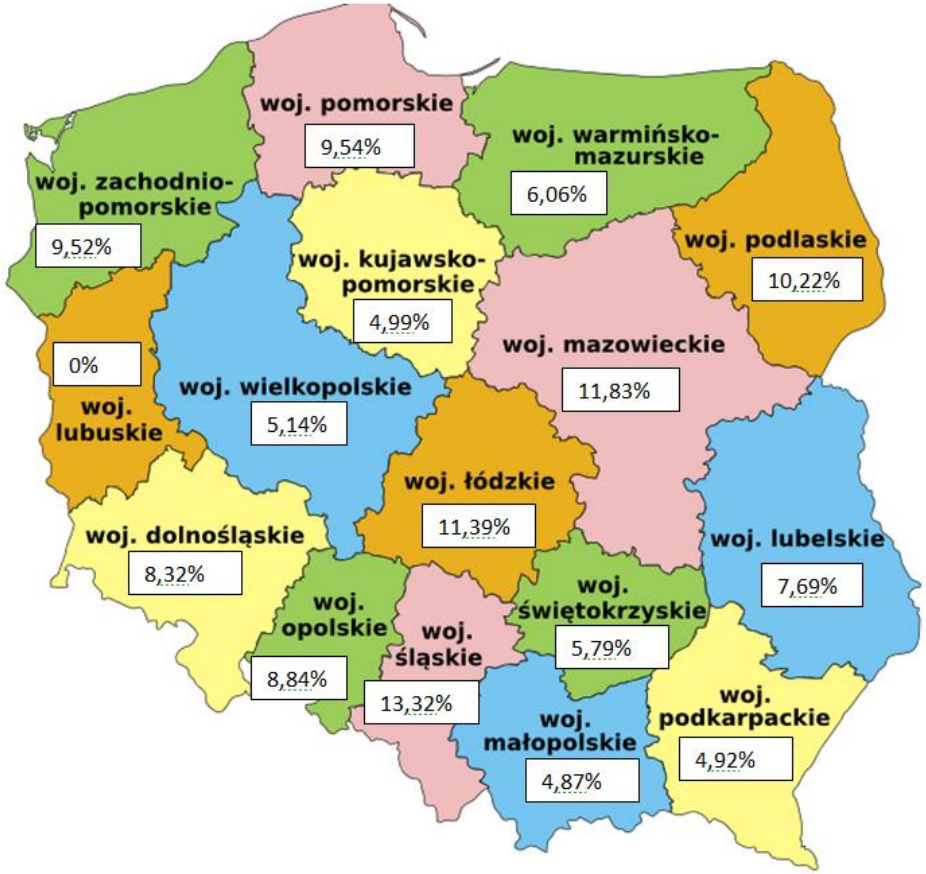
The current situation of MS in Poland

- Poland is the 6th country in Europe:
  - with the **highest incidence of MS** (45,000*)
  - but with the **lowest availability of** MS **treatment**.

- **One of the most significant problems is limitation of access to 2nd-line therapy:**
  - only 12,000** patients with MS are treated in total,
  - 1st-line patients: 6,700 **
  - 2nd-line patients: only 493** (7,4% vs. global average rate of 20%)

Number and geographical spread of 2nd-line clinics

Percentage of 2nd-line patients in each voivodship*



** 02.2015 Data*

Main limitations of the drug programme

Criteria

1. The inclusion criteria to 2nd-line is more restrictive vs label, which is an additional hurdle for patients
2. Evaluation of 1st-line treatment effectiveness includees MRI, which is conducted one year after treatment start
3. The 2nd-line program is limited in time (5-years)

Main limitations of the drug programme

Bureaucracy

1. To meet administrative requirements for 2nd-line inclusion, the patient has to be treated for at least 1 year, although signs of failure appear much earlier
2. Disproportional distribution of funds among the 2nd-line clinics
3. Uneven geographical spread of 2nd-line clinics
4. Restrictive bureaucratic criteria for clinics willing to start 2nd-line treatment (blockade on regional level)

Main limitations of the drug programme

Awareness

Still insufficient awareness of patients and doctors about the possibility of 2nd-line treatment

Unwillingness of 1st line clinic „to lose" the patient being send to 2nd line clinic.

Thank you!

EUROPEAN
MULTIPLE SCLEROSIS
PLATFORM