Secondary Progressive MS (SPMS): Terminology and Definitions

SPMS[1]

- Typically diagnosed retrospectively
- History of gradual worsening after an initial relapsing disease course
- No clear criteria to determine the transition point when RRMS converts to SPMS

Disability worsening vs progression[2]

Worsening:
Any increase in impairment/disability, including residual deficits following a relapse ("relapse-associated worsening")

Progression:
Clinical evidence of disease progression,* independent of relapses, over a given period of time, determined annually ("progression independent of relapse activity")

*Defined by EDSS changes from baseline[3] or composite measures (eg, a change in EDSS score or ≥20% change in T25FW or ≥20% change in 9HPT)[4] with change confirmed after at least 3 months

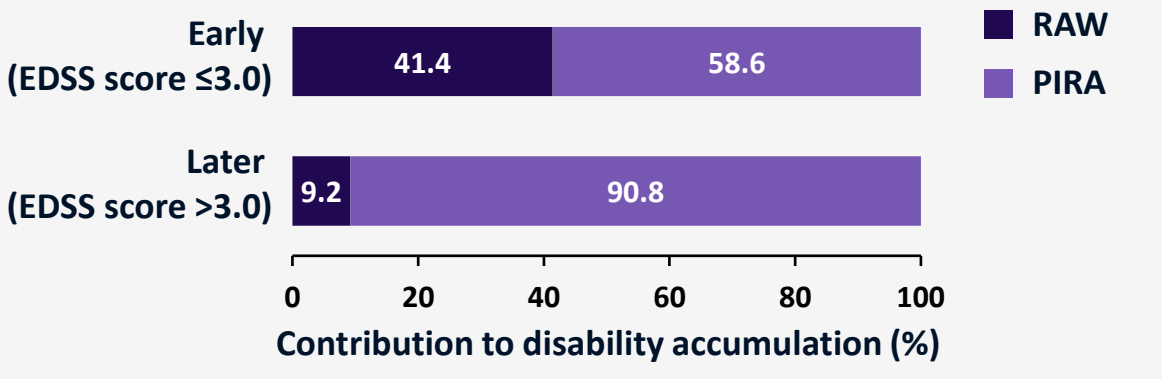
EDSS, Expanded Disability Status Scale; T25FW, Timed 25-Foot Walk; 9HPT, 9-Hole Peg Test.

1. Lublin FD et al. *Neurology*. 2014;83:278-286; 2. Lublin FD et al. *Neurology*. 2020;94:1088-1092; 3. Lublin FD et al. *Brain.* 2022 Feb 1 [Epub ahead of print] doi: 10.1093/brain/awac016; 4. Kappos L et al. *JAMA Neurol.* 2020;77:1132-1140.

Disability Progression Independent of Relapse Activity (PIRA)

- "Silent progression" appears to occur early in relapsing phase of disease, even at low levels of disability[1]
- May account for as much as 80% to 90% of overall disability accumulation in patients treated with DMT
  - Analyses of data from long-term observational studies[2] and clinical trials[3,4,5]
- Associated with accelerated brain atrophy[1,6] and retinal thinning[7]

Relative contribution of relapse-associated worsening (RAW) and PIRA to disability accumulation appears to differ in early vs later phases of disease[8]



EDSS=Expanded Disability Status.

1. UCSF MS-EPIC Team. *Ann Neurol.* 2019;85:653-666; 2. Kappos L et al. *Mult Scler*. 2018;24:963-973; 3. Kappos L et al. *JAMA Neurol.* 2020;77:1132-1140;
4. Gärtner J et al. *Mult Scler.* 2022;28:1562-1575; 5. Lublin FD et al. *Brain.* 2022 Feb 1 [Epub ahead of print] doi: 10.1093/brain/awac016;
6. Cagol A et al. *JAMA Neurol.* 2022;79:682-692; 7. Bsteh G et al. *Mult Scler J Exp Transl Clin*. 2020;6:2055217320966344; 8. Chen B et al. *Mult Scler Relat Disord*. 2022;59:103555.

Treatment of Secondary Progressive MS (SPMS)

All available **DMTs are approved to treat relapsing SPMS**[1]

- One FDA approval (ocrelizumab) for primary progressive MS, regardless of relapse activity

None approved specifically for **non-relapsing or inactive SPMS**[1]

Reliance on **symptomatic therapies** and **nonpharmacologic interventions**[2]

Unmet need for therapies that address ongoing treatment-resistant **pathology** and **progression independent of acute inflammation**[2,3]

1. FDA. https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed October 8, 2022; 2. Ontaneda D et al. *Lancet.* 2017;389:1357-1366;
3. Lublin FD et al. *Brain.* 2022 Feb 1 [Epub ahead of print] doi: 10.1093/brain/awac016.