Impact of visit density and magnetic resonance imaging monitoring on progression independent of relapse activity in relapsing multiple sclerosis

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INTRODUCTION

- Progression independent of relapse activity (PIRA) is the most important contributor of disability accrual in relapsing multiple sclerosis (MS).
- The identification of PIRA events can be affected by visit frequency, granularity of assessment tools and availability of imaging and fluid biomarkers of disease activity.

AIM

- To assess the impact of visit frequency and regular magnetic resonance imaging (MRI) monitoring on the identification of Expanded Disability Status Scale (EDSS)-based PIRA in patients with relapsing MS.

METHODS

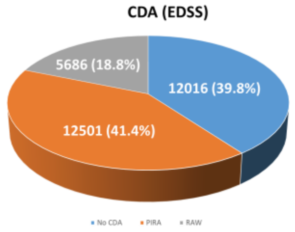
- This is a multicentric, retrospective, cohort study based on prospectively acquired data from the Italian Multiple Sclerosis Register
- Inclusion criteria: diagnosis of Clinically Isolated Syndrome or relapsing-remitting MS; first visit on or after January 1, 2000; at least 3 EDSS evaluations; at least 5 years of follow-up.
- PIRA was defined as a 24-week confirmed disability accrual (CDA: EDSS increase of 1.5 points if baseline EDSS=0; 1.0 point if EDSS>1.0 and < 5.5; 0.5 point if EDSS>5.5) with roving baseline and absence of relapses < 90 days before and < 30 days after the onset of both CDA and confirmation visit.
- The same definition was applied in the whole sample, in the subgroup of patients with at least 1 visit every year and in the subgroup of patients with at least 1 brain and/or spinal cord MRI every year

RESULTS

Whole sample (n=30203)

Characteristics of study sample

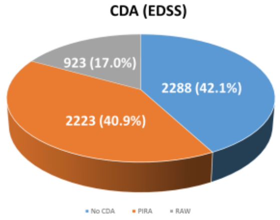
	Whole sample (n=30203)
Age at baseline, mean, SD, years	36.7 ± 11.1
Sex, female, n (%)	20739 (68.7)
Disease duration at baseline, mean, SD, years	5.5 ± 7.2
EDSS at baseline, mean, SD	2.0 ± 1.4
DMT at baseline, n (%) Total Platform-DMT HE-DMT	 28156 (93.2) 26047 (86.2) 2109 (7.0)
Follow-up duration, mean, SD, years	11.3 ± 4.6
EDSS at follow-up, mean, SD	2.9 ± 2.2



Patients with ≥ 1 visit every year (n=5434)

Characteristics of study sample

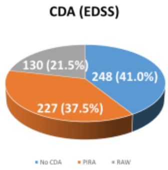
	Patients with > 1 visit every year (n=5434)
Age at baseline, mean, SD, years	36.6 ± 11.1
Sex, female, n (%)	3646 (67.1)
Disease duration at baseline, mean, SD, years	5.0 ± 6.8
EDSS at baseline, mean, SD	2.0 ± 1.43
DMT at baseline, n (%) Total Platform-DMT HE-DMT	 5310 (97.7) 4854 (89.3) 456 (8.4)
Follow-up duration, mean, SD, years	9.5 ± 3.9
EDSS at follow-up, mean, SD	2.7 ± 1.9

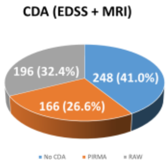


Patients with ≥ 1 brain/spinal cord MRI every year (n=605)

Characteristics of study sample

	Patients with > 1 brain/spinal cord MRI every year (n=605)
Age at baseline, mean, SD, years	35.1 ± 11.1
Sex, female, n (%)	393 (65.0)
Disease duration at baseline, mean, SD, years	4.3 ± 6.3
EDSS at baseline, mean, SD	2.1 ± 1.5
DMT at baseline, n (%) Total Platform-DMT HE-DMT	 589 (97.4) 497 (82.1) 92 (15.2)
Follow-up duration, mean, SD, years	8.7 ± 3.7
EDSS at follow-up, mean, SD	2.9 ± 2.1





Legend to Tables and Figures
SD: Standard Deviation; EDSS: Expanded Disability Status Scale; DMT: Disease Modifying Therapy; HE: Highly-Effective; CDA: Confirmed Disability Accrual; PIRA: Progression Independent of Relapse Activity, RAW: Relapse Associated Worsening; MRI: Magnetic Resonance Imaging; PIRMA: Progression Independent of Relapse and Magnetic Resonance Imaging Activity
Platform DMT: interferons, glatrramer acetate, dimethylfumarate, teriflunomide, azathioprine; HE-DMT: natalizumab, cladribine, S1PM modulators, antiCD20, alemtuzumab, mitoxantrone, cyclophosphamide,

CONCLUSIONS

- While visit frequency does not affect PIRA detection, the availability of regular MRI monitoring significantly impacts on the classification of disability accumulation phenotype.
- One third of EDSS-based PIRA events were underpinned by traditional focal inflammatory activity at brain/spinal cord MRI.
- Further studies are needed to clarify whether smoldering MS has been overestimated or should be unveiled through more granular assessments.

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DISCLOSURES

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