Evaluating the effectiveness of cladribine in secondary progressive multiple sclerosis: a study of the Italian MS Register

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INTRODUCTION

Cladribine is a disease-modifying immune reconstitution oral therapy approved for adult patients with relapsing multiple sclerosis (RMS) and currently also refundable in Italy for secondary progressive (SPMS) patients. A decrease in relapse activity and progression phenomena were observed in RMS patients treated with cladribine. Assessing whether similar effects occur in SPMS patients is crucial to further unravel the complexity of MS progression pathways.

AIM

To assess the effect of cladribine on the annualized relapse rate (ARR) and progression independent of relapse activity (PIRA) phenomena in a cladribine-treated cohort in the Italian MS Register (RISM) of SPMS patients identified with a data driven definition.

METHOD

A retrospective cohort study was conducted considering SPMS patients identified with a data driven definition based on a version of Lorscheider's algorithm and treated with at least one cicle of cladribine recorded in RISM after January 1, 2018, at least 5 years of follow-up and annual neurological evaluations. Adjusted ARR was calculated in the overall cohort in the two years before and after cladribine initiation. PIRA was considered as a recurrent event through the follow-up and defined as a sustained progression of disability, confirmed at 6 months, in the absence of a relapse since 90 days prior the Expanded Disability Status Scale (EDSS) with documented increase. Ghosh-Lin Cox type regression for the marginal mean was used to assess PIRA.

RESULTS

After applying the inclusion criteria, we retrieved a cohort of 48 data driven-defined SPMS patients, of whom 36 (75%) were female. The median (IQR) follow-up was 8.86 (5.08-16.60) years. The median (IQR) disease duration at cladribine start was 7.77 (4.93-16.18) years and the median age at treatment start was 46.58 (38.81-53.87) years. ARR decreased (p<0.0001) from 0.33 (95% CI 0.23-0.47) in the two years preceding cladribine start to 0.16 (0.09-0.29) two years after in the overall cohort. The risk of PIRA resulted similar before (40 events in 24/48 patients) and after (25 events in 19/48 patients) cladribine treatment initiation (HR=1.07, 95%CI=0.63-1.83, p=0.80).

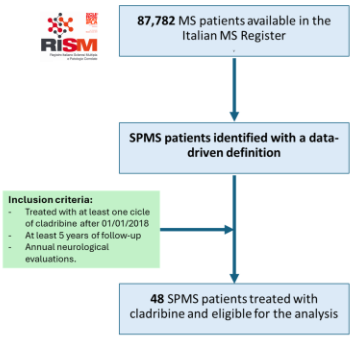
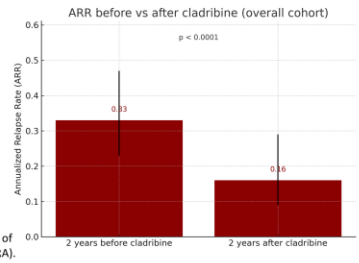


Figure 1. Flowchart of the patient selection procedure.

	Overall population (n=48)
Female sex, n (%)	36 (75.0%)
Age at onset (median, IQR), years	36.83 (26.60-45.64)
Disease duration at cladribine start (mean±SD), years	10.85 ± 8.05
Time from onset to first visit (median, IQR), years	0.65 (0.29-1.10)
Follow-up (median, IQR), years	8.86 (5.08-16.60)
Age at cladribine initiation (median, IQR), years	46.58 (38.81-53.87)
First EDSS recorded (median, IQR)	2.50 (1.50-3.12)
EDSS at SPMS conversion (median, IQR)	4.50 (4.00-5.50)

Table 1. Baseline clinical and demographic characteristics.



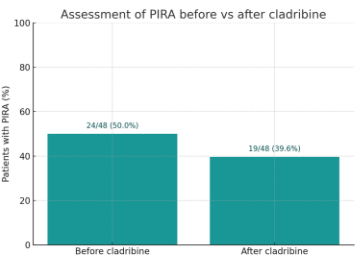


Figure 2. Graphical representation of the outcome analysis (ARR and PIRA).

CONCLUSIONS

In this cohort of SPMS patients from the RISM database, cladribine proved to be effective in reducing the ARR. The risk of PIRA was not influenced by cladribine treatment.

A larger cohort and longer follow-up will be essential to further investigate these findings.

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