# Age-Stratified Real-World Outcomes in People with Relapsing Multiple Sclerosis over 50 Years of Age After Switching to Cladribine Tablets from High Efficacy Disease-Modifying Therapies

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## RESEARCH IN CONTEXT

1. **This study adds to the growing body of real-world evidence (RWE) demonstrating the sustained effectiveness of cladribine tablets (CladT) in people with relapsing multiple sclerosis (PwRMS) aged ≥50 years after switching from other high-efficacy disease-modifying therapies (HE DMTs).**
2. **These data support CladT as a valuable option in older PwRMS for whom other HE DMTs are becoming less suitable, but who still require effective MS therapy.**

## OBJECTIVE

**To report on the clinical and radiological impact of CladT over 3 years in a USA real-world cohort of PwRMS aged under and over 50 years, following their switch from another HE DMT to CladT**

## INTRODUCTION

CladT (3.5 mg/kg cumulative dose over 2 years) are approved in the United States for the treatment of PwRMS due to sustained impact on radiological and clinical outcomes[1]

There is a paucity of RWE on the efficacy of DMTs, including CladT, after switching from other HE DMTs in PwRMS aged 50 years and older

## METHODS

- This is a single-centre, retrospective study of medical records of PwRMS (age ≥18 years) treated with ≥1 course of CladT from April 2019 to April 2023 at The University of Texas Southwestern Medical Center, Dallas, TX, USA
- Data were descriptively analysed in PwRMS aged under and over 50 years for the year prior to CladT initiation (Baseline) through the 3 years after CladT initiation for:
  - Whole cohort; N=164
  - Prior HE cohort (subgroup); N=81
- Prior treatments identified for inclusion in the prior HE cohort include non-oral DMTs namely natalizumab, ocrelizumab, alemtuzumab, rituximab, and ofatumumab

### Key endpoints

- **Annualised relapse rate (ARR)**
- **Magnetic resonance imaging (MRI) activity**
- **Hospitalisations and urgent care/ emergency department (ED) visits**

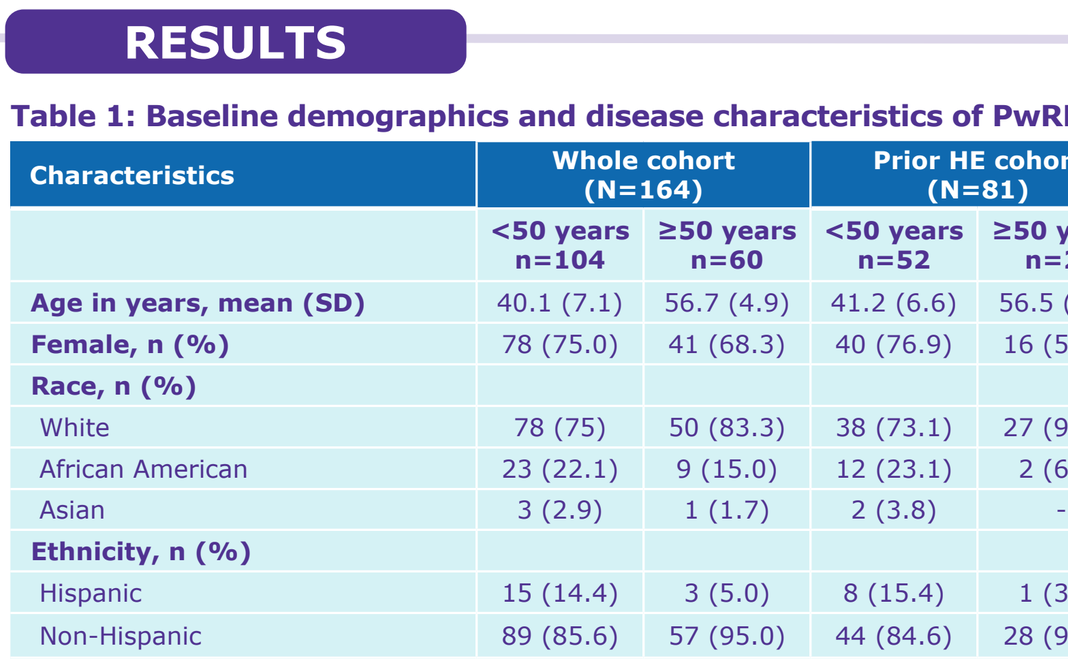
## RESULTS

### Table 1: Baseline demographics and disease characteristics of PwRMS

| Characteristics | Whole cohort (N=164) | | Prior HE cohort (N=81) | |
|---|---|---|---|---|
| | <50 years n=104 | ≥50 years n=60 | <50 years n=52 | ≥50 years n=29 |
| **Age in years, mean (SD)** | 40.1 (7.1) | 56.7 (4.9) | 41.2 (6.6) | 56.5 (4.9) |
| **Female, n (%)** | 78 (75.0) | 41 (68.3) | 40 (76.9) | 16 (55.2) |
| **Race, n (%)** | | | | |
| White | 78 (75) | 50 (83.3) | 38 (73.1) | 27 (93.1) |
| African American | 23 (22.1) | 9 (15.0) | 12 (23.1) | 2 (6.9) |
| Asian | 3 (2.9) | 1 (1.7) | 2 (3.8) | - |
| **Ethnicity, n (%)** | | | | |
| Hispanic | 15 (14.4) | 3 (5.0) | 8 (15.4) | 1 (3.4) |
| Non-Hispanic | 89 (85.6) | 57 (95.0) | 44 (84.6) | 28 (96.6) |
| **Mean disease duration, years (SD)** | 10.1 (5.8) | 15.7 (7.8) | 12.4 (5.7) | 16.0 (8.4) |
| **Median number of prior treatments, n, (SD) [Range]** | 2.6 (1.6) [1,8] | 3.1 (1.8) [1,9] | 3.1 (1.6) [1,8] | 3.7 (2.0) [1,9] |

HE, high-efficacy; PwRMS, people with relapsing multiple sclerosis; SD, standard deviation.

### Figure 1: Most common recent DMT prior to initiating CladT (whole cohort)

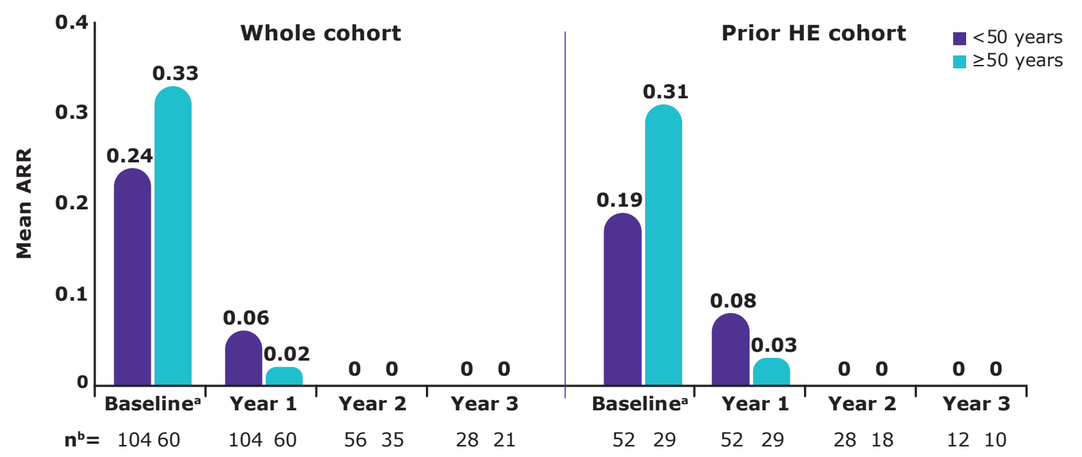



CladT, cladribine tablets; DMT, disease-modifying therapy; PwRMS, people with relapsing multiple sclerosis.

Natalizumab and ocrelizumab were the most common HE DMTs prior to initiating CladT, across both age groups. The most common reasons for discontinuing HE DMTs were tolerability (<50 years) and suboptimal efficacy (≥50 years)

Please refer to **Supplementary Figure 1** and **2** for more details on reasons for discontinuing HE DMTs and for delay in initiating the second dose of CladT.

### Figure 2: ARR through 3 years after initiating CladT

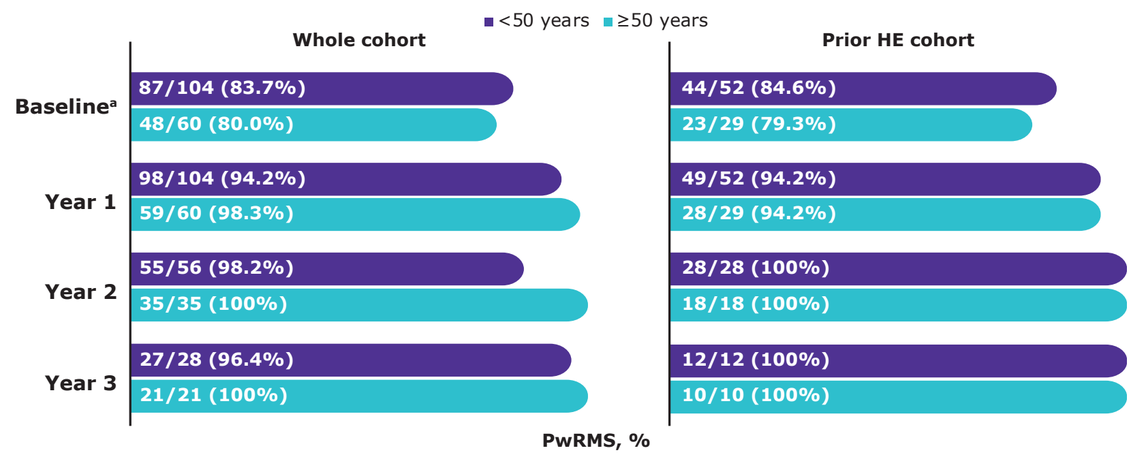



[a]One patient on HE DMT had 6 relapses during baseline period. [b]Number of PwRMS at the time of present analysis. Remaining PwRMS are yet to reach this timepoint.

ARR, annualised relapse rate; CladT, cladribine tablets; DMT, disease-modifying therapy; HE, high-efficacy; PwRMS, people with relapsing multiple sclerosis.

A reduction in ARR (≥50 years - whole cohort: 93.9%; prior HE cohort: 90.3%; <50 years – 75%; 57.9%) was observed between baseline and year 1 after initiating CladT, which was sustained through 3 years with no relapses in PwRMS who have reached Year 2 and 3 across both age groups and in the whole and prior HE cohorts

### Figure 3: Percentage of PwRMS free from MRI activity through 3 years after initiating CladT




[a]One patient on HE DMT had 6 relapses during baseline period. CladT, cladribine tablets; DMT, disease-modifying therapy; HE, high-efficacy; MS, multiple sclerosis; MRI, magnetic resonance imaging; PwRMS, people with relapsing multiple sclerosis.

Among the PwRMS included in this analysis, there was an overall increase in the percentage of PwRMS free from MRI activity through 3 years after initiating CladT, across both age groups and in the whole and prior HE cohorts

### Table 2: Hospitalisation and urgent care/ED visits prior to/after CladT initiation

| | Whole cohort (N=164) | | | | Prior HE cohort (N=81) | | | |
|---|---|---|---|---|---|---|---|---|
| | <50 years (n=104) | | ≥50 years (n=60) | | <50 years (n=52) | | ≥50 years (n=29) | |
| **CladT initiation** | **Year prior** | **Year after** | **Year prior** | **Year after** | **Year prior** | **Year after** | **Year prior** | **Year after** |
| Hospitalisations due to MS relapse/symptoms, n | 6 | 3 | 5 | 1 | 2 | 2 | 2 | 1 |
| Urgent care/ED due to MS relapse/symptoms, n | 6 | 1 | 3 | 0 | 1 | 0 | 0 | 0 |

CladT, cladribine tablets; ED, emergency department; HE, high-efficacy; MS, multiple sclerosis.

MS-related hospitalisations and ED visits were reduced after CladT initiation, across both age groups and in the whole cohort and prior HE cohort

## CONCLUSIONS

- **Overall, there was a reduction in ARR from baseline to year 3 (≥50 years - whole cohort: 0.33 to 0.00; prior HE cohort: 0.31 to 0.00; <50 years - 0.24 to 0.00; 0.19 to 0.00) in PwRMS who switched from other HE DMTs to CladT**
- **An increase in the percentage of PwRMS free from MRI activity and a decrease in MS-related hospitalisations were observed after CladT initiation, across both age groups (<50 and ≥50 years) and in the whole and prior HE cohorts**

**SCAN FOR AFFILIATIONS, DISCLOSURES AND SUPPLEMENTARY MATERIALS**

**Reference:** 1. MAVENCLAD (cladribine) tablets [package insert]. EMD Serono, Inc.; 2024.

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# Supplementary Materials


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**Author Disclosures**

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**KBl** has received research support from UCB and NeuroNEXT. He has served as an advisor to TG Therapeutics.

**SM** reports personal compensation for consulting services from Horizon Therapeutics, Bristol Myers Squibb, Novartis, and TG Therapeutics and research support from Genentech.

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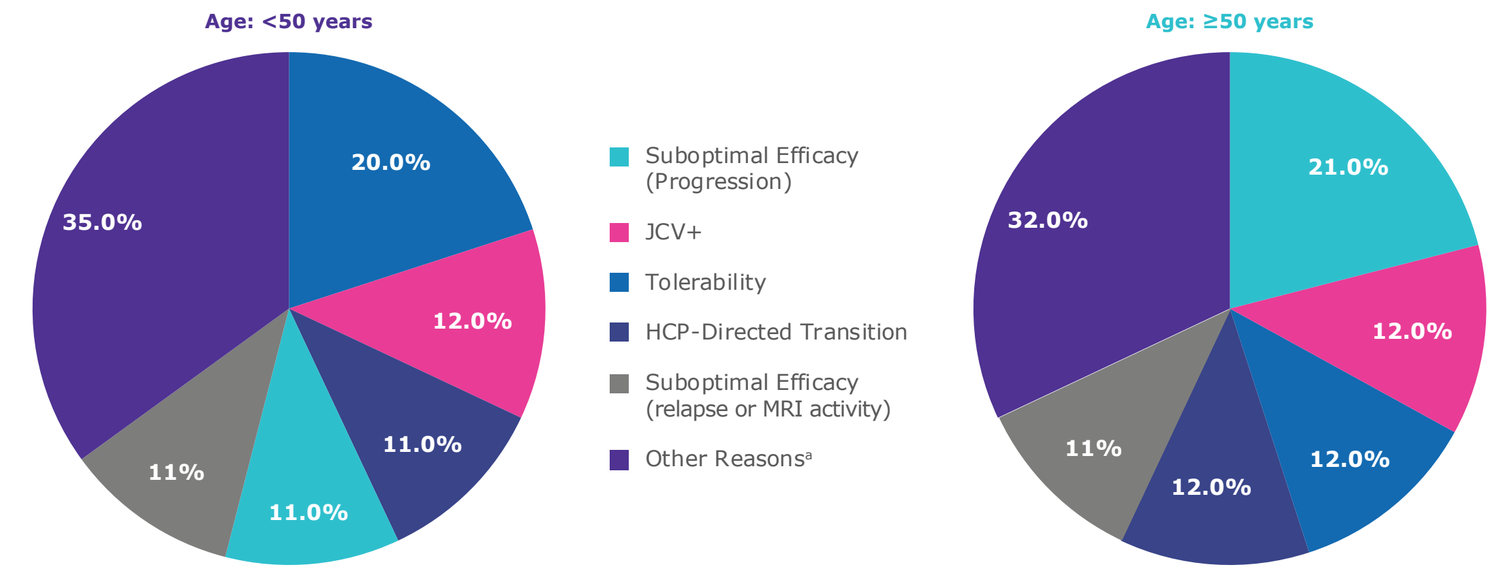
# Supplementary Materials

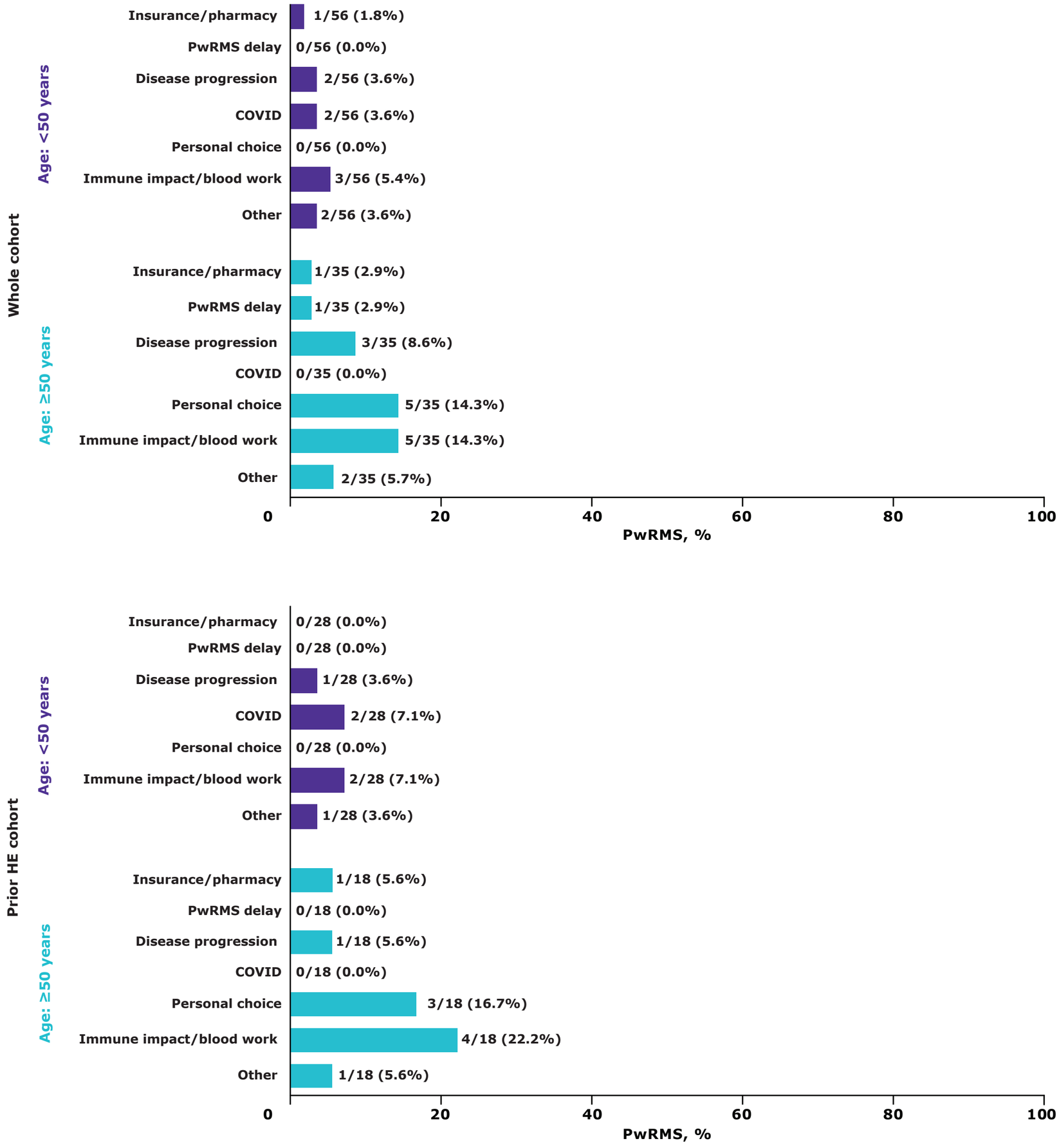
## Supplementary Figure 1: Reasons for discontinuing most recent DMTs prior to initiating CladT




[a]For the <50 year age cohort, other reasons include safety concerns, immune impact, cost/access, route/frequency of administration, pregnancy, PwRMS who felt MS therapy was not helping them, adherence/persistence and other. For the ≥50 year age cohort, other reasons include cost/access, immune impact, safety concerns, route/frequency of administration, intolerance, and other.

CladT, cladribine tablets; DMT, disease-modifying therapy; JCV, John Cunningham virus; MRI, magnetic resonance imaging.

## Supplementary Figure 2: Reasons for delay in initiating second CladT course (n=27/91 [29.7%])




CladT, cladribine tablets; COVID-19, coronavirus disease 2019; PwRMS, people with replasping multiple sclerosis.