Considerations for Discontinuing DMT:

Does the Risk-Benefit Ratio of DMT Change with Time and/or Age?



Comi G et al. Lancet. 2017;389:1347-1356; Grebenciucova E, Berger JR. Curr Neurol Neurosci Rep. 2017;17:61.

Discontinuing DMT in Stable or Progressive Disease: Summary of Evidence

- Numerous retrospective, observational, nonblinded studies with mixed results¹
 - Heterogeneous in size, population, types of DMTs, and reasons for discontinuation
 - Most included adults of any age

Predictors of disease reactivation after discontinuation of DMT
Younger age ^{2,3}
Female sex ²
Shorter duration without relapses ^{2,3}
MRI activity at discontinuation ³ (defined as three or more new/enlarged T2 lesions or one or more Gd+ lesion)
 Degree of disability (moderate vs severe or progressive phase)² Moderate disability associated with greater risk of disease activity

• Severe disability or progressive disease associated with greater risk of disability progression

DMT Discontinuation in Older People with MS

498 MS patients older than 50 years with no disease activity for ≥3 years in a French registry¹
132 discontinuers; 366 continuers

Discontinuers²

100% were on older injectable DMTs

34.9% restarted over a mean follow-up of 7 years (mean time to restart 1.6 years)

Continuers vs discontinuers³

No difference in risk of relapse or disability progression Higher risk of reaching EDSS score 6.0 in discontinuers Excluding patients with EDSS scores >6.0 at baseline (7% of continuers and 36% of discontinuers) 600 MS patients older than 60 years treated with DMT for ≥2 years at 3 US centers^{2,3} 178 patients (29.7%) discontinued

Discontinuers²

Most common reasons: side effects (49%), stable disease (28%), age (23%)

1 relapse occurred

10.7% restarted (patient-initiated discontinuers restarted more often than provider-initiated)

Continuers vs discontinuers³

No difference in PS, T25FW, or 9HPT

Staying on treatment associated with reduced quality of life (EQ-5D index) over follow-up period of 5.3 years

EDSS, Expanded Disability Status Scale; EQ-5D, EuroQol- 5 Dimension; PS, processing speed; T25FW, Timed 25-Foot Walk; 9HPT, 9-Hole Peg Test. 1. Kaminsky AL et al. *J Neurol*. 2020;267:3518-3527; 2. Hua LH et al. *Mult Scler*. 2019;25:699-708; 3. Hua LH et al. *Mult Scler Relat Disord*. 2019;30:252-256.

Discontinuation of DMTs in Older People with MS: Randomized Clinical Trials

Discontinuation of DMTs in MS (DISCO-MS)

Study design	Randomized, single-blind, parallel assignment (discontinuation vs continuation of DMT); noninferiority over 2 years
Study population (N=259)	Age ≥55 years; RRMS, SPMS, or PPMS No relapse for ≥5 years and no new MRI lesions for ≥3 years Progression of MS • EDSS score change ≥1.0 point in last 2 years, or • Significant change in motor function in last year, unrelated to relapse Taking DMT continuously for ≥5 years and most recent DMT for ≥2 years
Preliminary results	 Noninferiority not shown Disease activity events (relapses or new lesions on MRI): 16 (12%) discontinuers; 6 (5%) continuers 15 of these events involved 1 or 2 new brain lesions, but no clinical relapse
STOP-I-SEP	
Recruiting	Randomized, open-label, parallel assignment (DMT discontinuation vs continuation) in patients older than 50 years with inactive SPMS (no evidence of focal inflammatory activity for 3 years)

EDSS=Expanded Disability Status. NCT03073603 and NCT03653273; ClinicalTrials.gov. Accessed October 8, 2022.