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## Discontinuation of first-line disease-modifying therapy in stable multiple sclerosis (DOT-MS): an early-terminated multicenter randomized controlled trial

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### Introduction:

The consequences of discontinuing first-line disease modifying therapy (DMT) in multiple sclerosis (MS) have not fully been established.

### Objectives/Aims:

To investigate whether first-line DMT can be discontinued in people with stable MS without recurrence of inflammatory disease activity.

### Methods:

The DOT-MS trial (NCT04260711) is a multicenter randomized controlled non-inferiority trial that included people with relapse onset MS aged  $\geq 18$  years without any relapses or substantial MRI activity in the previous five years. Participants were randomized into groups that discontinued or continued first-line DMT. The primary outcome measure was the number of patients with inflammatory disease activity, defined as a confirmed relapse or significant MRI activity during follow-up ( $\geq 3$  new T2-lesions or  $\geq 2$  contrast-enhancing lesions on MRI). Pre-defined interim analyses were conducted to timely detect disease activity: premature discontinuation of the trial was considered if the proportion of patients with inflammatory disease activity in the 'discontinuation' group was higher than in the 'continuation' group, and the 95%CI of this difference did not include zero.

### Results:

The trial was prematurely discontinued because of inflammatory disease activity in the discontinuation group above the predefined limit. At the moment of trial discontinuation, 89 participants had been included of whom 45 (50.6%) were randomized into the 'discontinuation' group. Most participants (67.4%) were female. Mean age at inclusion was 53.5 years (SD 7.8). Median follow-up was 12.0 months (IQR 7.0-20.0). During follow-up,

6/45 participants in the 'discontinuation' group experienced inflammatory disease activity that fulfilled the predefined criteria vs. 0/44 participants in the 'continuation' group (95% CI of difference in patient proportion: 0.04-0.27). Median time to disease activity was 9.0 months (IQR 5.3-13.5). Of the 6 participants with inflammatory disease activity, 2 experienced a relapse. Mean age of these 6 patients was 48.7 years (SD 8.6). All restarted DMT, which resulted in stabilization of disease. In addition to these 6 patients, 5 patients in the 'discontinuation' group and 1 patient in the 'continuation' group experienced radiological disease activity not fulfilling our criteria for significant disease activity.

#### **Conclusion:**

Significant inflammatory disease activity returned in 6/45 participants (13.3%) who discontinued DMT. Based on our pre-planned interim-analysis the trial was discontinued in its current design.

#### **Disclosures:**

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