Short term relapse risk after switching from Fingolimod to Ocrelizumab or Cladribine – a retrospective international cohort study

Introduction

Background:
• Information on disease activity when switching MS medication from fingolimod (FTY) to ocrelizumab (OCR)/cladribine (CLAD) is scarce.
• Several studies of disease activity have been reported in smaller heterogeneous case series in around 10% of patients (irrespective of following FTY).

Design and Methods:
• Patients were recruited from several academic centers (AC) throughout Germany, Norway, and two national registries:
  - Danish MS Register (DMSR)
  - German MS Register (GMSR)

Results:

1. Background

- **Objective:** To assess the short-relapse and disability risk after switching from fingolimod (FTY) to ocrelizumab (OCR) or cladribine (CLAD) in patients with relapsing-remitting multiple sclerosis (RRMS).

- **Participants:** We included 283 adults with RMS who stopped FTY and switched to OCR or CLAD.
  - **AC:** N = 173, CLAD: N = 105, OCR: N = 68
  - **DMSR:** N = 28, CLAD: N = 15, OCR: N = 13
  - **GMSR:** N = 73, CLAD: N = 53, OCR: N = 20

- **Exclusion criteria:**
  - Treatment-free switching interval ≥6 months
  - Follow-up on OC/CLAD ≥6 months

- **Outcomes included:**
  - Number of relapses
  - Accumulated relapse rate (ARR)
  - Disease activity on MRI scans
  - Clinical measures of overall disability

- **Statistics:**
  - Descriptive figures include means and percentiles along with 95% (CI) confidence intervals
  - ARR compared by using generalized linear models

- **Figure 1:** Short-term relapse risk for patients treated with Fingolimod (FTY), fingolimod, or other disease-modifying therapies.

2. Methods

- **Academic centers (AC):**
  - Danish MS Register (DMSR)
  - German MS Register (GMSR)

- **No. of patients (%):**
  - FTY: 105 (37.3)
  - OCR: 68 (24.1)
  - CLAD: 92 (32.6)

- **Age at disease onset (yr):**
  - FTY: 27.9 ± 5.2
  - OCR: 27.1 ± 5.8
  - CLAD: 26.4 ± 6.1

- **Disease activity on OCR (n = 95% CI):**
  - OCR: 0.12 (0.05-0.25)

- **Patients with at least one relapse during switching interval (n = 95% CI):**
  - FTY: 0.12 (0.05-0.23)
  - OCR: 0.12 (0.05-0.25)

- **Patients with disease activity on brain MRI scan during switching interval (n = 95% CI):**
  - FTY: 0.12 (0.05-0.23)
  - OCR: 0.12 (0.05-0.25)

- **Patients with relapses within 3 months of switch treatment (n = 95% CI):**
  - FTY: 0.12 (0.05-0.23)
  - OCR: 0.12 (0.05-0.25)

- **Patients with relapses within 6 months of switch treatment (n = 95% CI):**
  - FTY: 0.12 (0.05-0.23)
  - OCR: 0.12 (0.05-0.25)

- **Total no. of relapses within 6 months of switch treatment:**
  - FTY: 0.12 (0.05-0.23)
  - OCR: 0.12 (0.05-0.25)

3. Conclusions

- **Around 20% of FTY switches to OCR or CLAD experienced a relapse.**
- **Most relapses occurred during the treatment free switching interval or the first 3 months on switch treatment.**
- **The relapse risk varied according to the data source and was highest in AC, reflecting potential referral bias with more severely diseased patients.**
- **Relapse rates were lower after switch to OCR compared to relapse rates under FTY, especially in academic centers, were a large number switched due to lacking efficacy.**

- **Again this reflects a cohort with very active MS disease activity on MRI scan was higher in treatment free switching interval than under switch treatment.**
- **Disease activity on MRI scan was higher under CLAD than under OCR.**

- **Our data is limited by a relatively small sample size in the CLAD cohort and the retrospective study design.**

- **Figure 2:** Patients with MS activity (measured by new Gd+ T2 lesion or T1 lesion in the considered interval (FTY treatment) (top), switching interval (middle), and OCR treatment (bottom)) with or without relapse.

- **Figure 3:** Follow-up after FTY discontinuation.

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