Predictors of treatment discontinuation in CIS

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Objective: Characterise treatment persistence and the main factors which influence the treatment discontinuation in Clinically Isolated Syndrome (CIS) and in early Multiple Sclerosis (MS).

Methods: The MSBase Incident Study (MSBASIS) is an observational prospective cohort study of patients with CIS occurring from 2003 onward. MSBASIS enrolls patients from 59 MS treatment centres worldwide. Data are collected by physicians using the iMed MS documentation software and aggregated in the MSBase platform. The initial data requested are the patient profile, the date and the clinical description of the CIS, the Expanded Disability Status Scale (EDSS), the cerebral Magnetic Resonance Imaging (MRI) classification and treatment. Follow-up data includes relapses, treatment starts and discontinuations and annual EDSS.

We analysed first treatment discontinuation using multivariate logistic regression and survival analysis.

Results: 2473 CIS patients were followed for a median duration of 1.73 years, of which 1364 patients relapsed clinically. 763 patients received at least one immunomodulatory treatment. There were 236 commencements of intramuscular (IM) interferon b-1a, 219 of subcutaneous (SC) INFb-1a, 172 of INFb-1b and 162 of Copaxone. The incidence rates of discontinuation for each treatment were 17.2 per 100 person-years for IM INFb-1a, 14.6 for SC INFb-1a, 15.5 for INFb-1b and 18.8 for Copaxone. For all four treatments combined, significant predictors of discontinuation identified by multivariate logistic analysis were female sex (OR= 1.63) and relapse on treatment (OR= 1.92). A reporting location of Italy was significantly associated with a reduction in discontinuation compared with Australia (OR= 0.42). MRI features, age at start of treatment, time between CIS onset and treatment onset, change in EDSS and immunomodulatory treatment choice were not significant predictors of discontinuation.

Conclusion: Treatment discontinuation is a frequent outcome. This study shows that the most important factors influencing time to discontinuation in CIS and early MS patients are female sex and relapse occurrence. Interestingly, there are also strong regional differences in treatment discontinuation rates. The choice of the immunomodulatory treatments, the EDSS evolution and the baseline MRI criteria do not have a significant influence on the treatment outcome.

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Background

Injectable disease-modifying drug therapy for early Multiple Sclerosis (MS) and Clinically Isolated Syndrome (CIS) reduces relapse rate, brain lesion accumulation and is also likely to reduce disability progression long-term. However, treatment with injectable DMD therapies causes side effects, and, as it is only partially effective, patients on DMD therapies do experience ongoing relapse activity and disability progression. Anecdotally, treatment cessation is a relatively frequent occurrence, but factors leading to treatment cessation are not well understood. Patients who cease DMD treatment are at greater risk of relapse activity and disability progression, so that an investigation of factors that influence treatment cessation could have important implications for the development of strategies to reduce this outcome.

The MSBase Incidence Study (MSBASIS) is a sub study of the MSBase Registry. It is a world-wide investigator-initiated observational cohort study which collects prospective outcomes on patients with CIS and early MS, evaluated form onset of the disease. The study is purely observational and does not prescribe or recommend any particular treatment or intervention. Routine clinical care is observed and key MS related outcomes are measured in the long term. Data are collected by physicians using the MS platform and aggregated in the MSBase platform.

Currently, 44 centres from 20 countries are contributing data (see Figure 1).

Methods

To characterise treatment persistence and the main factors which influence treatment discontinuation in Clinically Isolated Syndrome (CIS) and in early Multiple Sclerosis (MS).

- Data was extracted on 19th March 2010.
- All centres with more than 10 cases were included.
- All patients diagnosed with CIS from 2003 onwards, were seen within 12 months of onset and had cerebral Magnetic Imaging (MRI) within this time were included.

Statistical analysis

- Predictors of discontinuation were analysed with logistic regression.
- Predictors of discontinuation rate were analysed using Cox Proportional Hazards Regression.

Objective

To characterise treatment persistence and the main factors which influence treatment discontinuation in Clinically Isolated Syndrome (CIS) and in early Multiple Sclerosis (MS).

Results

2473 CIS patients were followed for a median duration of 1.73 years, of which 1364 patients relapsed clinically.

- Number of initial drug commencements:
  - 226 interferon (INF) beta-1a intramuscular (IM) injection (Avonex)
  - 219 INF beta-1a subcutaneous (SC) injection (Rebif)
  - 172 INF beta-1b SC injection (Betaferon)
  - 162 glatiramer acetate SC injection (Copaxone)

Incidence rates of discontinuation for each new treatment per 100 person years (see Figure 2).
- 17.2 INF beta-1a IM (Avonex)
- 14.6 INF beta-1a SC (Rebif)
- 15.5 INF beta-1b SC (Betaferon)
- 18.8 glatiramer acetate SC (Copaxone)

- Independent predictors of treatment discontinuation across all immunomodulatory therapies on multivariable logistic regression included:
  - female sex (OR=1.70, 95% CI: 1.16, 2.50, p=0.006);
  - a reporting location of Italy compared with Australia (OR=0.46, 95% CI: 0.26, 0.82, p=0.009) (see Figure 3); and
  - relapse on treatment (OR=1.92, 95% CI: 1.39, 2.67, p<0.001).

Significant predictors of increased rates of discontinuation on multivariable Cox regression included:
- female sex (HR=1.70, 95% CI: 1.21, 2.39, p=0.002) (see Figure 4); and
- a reporting location of Australia compared with Italy (HR=2.11, 95% CI: 1.25, 3.57, p=0.005).

- Predictors not significantly associated with discontinuation in either analysis:
  - MRI features
  - age at treatment commencement
  - time between CIS onset and treatment onset
  - EDSS change
  - immunomodulatory treatment choice

Conclusions

- Female sex and relapse-on-treatment independently predict increased likelihood of treatment discontinuation or switch
- Female sex and a reporting location of Australia both predict increased rates of discontinuation
- Choice of immunomodulatory treatment, EDSS progression and baseline MRI findings are not significantly associated with treatment discontinuation.

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