Background

- Many disease-modifying therapies (DMTs) are currently available for adults with relapsing-remitting multiple sclerosis (RR-MS) but no medication has completed testing for pediatric MS (ped-MS) in randomized placebo-controlled trials. In recent years several pediatric MS trials have been launched.
- The high frequency of relapses in ped-MS, especially in the first years, with a relapse rate higher than that of adults, and the pattern of MRI lesions, with more pronounced inflammatory aspects, support the use of DMT in the pediatric population as they mainly target the inflammatory component.
- Use of DMT in ped-MS remains off-label in many countries, especially for nevertheless they are widely used in the treatment of children and adolescents with RR-MS.
- Several observational studies have provided data on safety and efficacy of interferon-beta (IFNb) and glatiramer acetate (GA) in the ped-MS population, but data are not available after a long-term follow-up.

Objectives

In 2009 we reported the results of immunomodulatory treatment in a cohort of 130 ped-MS patients after 4–6 years of follow-up. We describe here the results update to 2016.

Methods

- Type of study: multicenter, observational retrospective.
- Population included: all ped-MS patients initiating GA or IFNb included in previous work of our group and regularly followed for at least 5 years.
- Data collected: demographic characteristics, clinical outcomes (including the first events as a relapse) and treatments received.
- Statistical analysis performed:
  - Comparison of annual relapse rate (ARR) and EDSS score before Vs after therapy initiation (Friedman and Wilcoxon tests) in the whole cohort and in two groups divided by type of therapy received during the whole follow-up (first-line and second-line/other therapies).
  - Multivariate analysis to predict the clinical course of MS (measured by 3 endpoints: last EDSS score, ARR during follow-up and EDSS score worsening of 1 point at last observation) using seven baseline variables (see results for details).
  - Comparison of baseline demographics and clinical outcomes in patients starting treatment before Vs after 12 years of age using independent sample tests (Chi-square, Spearman rank).

Results

Clinical outcomes of the whole cohort

Baseline clinical and demographic characteristics of the whole cohort

97 patients

<table>
<thead>
<tr>
<th>Gender (Female/Male)</th>
<th>Age of MS onset (years)</th>
<th>Type of Rx</th>
<th>Rx at last observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>67/30</td>
<td>12.3±2.5 (6-16)</td>
<td>IFNβ2a</td>
<td>1.8±0.7 (0.3-6.0)</td>
</tr>
</tbody>
</table>

Of the 130 ped-MS patients of the previous cohort we lost to follow-up 33 of them, mainly because they moved to other MS centers. Baseline characteristics are shown as number of cases (es. Female/Male) or as mean±SD (v. standard deviation). The figure shows baseline and subsequent therapies after a mean follow-up of 12.5 years, according to the three classification:

- Number of switches performed
- Type of therapy (Rx) received defined as first-line (IFN, GA, TFU, DMF) and second-line/other therapies (NAT, FTY, ALZ, SCT, CTX, MTX, AZA, AIV)
- Last ongoing therapy at the end of follow-up

Legend: Rx, therapy; IFN, interferon; GA, glatiramer acetate; FTY, fingolimod; ALZ, azathioprine; SCT, sarcoplasmic reticulum Ca2+ ATPase inhibitor; CTX, cyclophosphamide; MTX, methotrexate; AIZ, azathioprine; AIV, intravenous immunoglobulin; No Rx, no therapy for at least 6 months.

Clinical outcomes of the whole cohort

- After the first therapy ARR drastically reduced with respect to the pre-therapy period, and it remained significantly low also at last observation. Mean EDSS score showed a slight increase after first therapy (not significant) and at last observation (significant). During the follow-up period one patient reached EDSS score of 10 and died because of MS, as shown in the bar graph on the right.

Conclusions

- Over 12 years of follow-up 43% of ped-MS patients remained on first-line therapies, while 57% patients switched to second-line or other treatments. At last observation about 10% of ped-MS patients was still on the first therapy;
- ARR was drastically reduced by the first treatment and remained low during the whole follow-up. This finding suggest that it is appropriate to shift soon non-responders to other treatment;
- At last observation the large majority of patients had an EDSS 3.5, about 10% had EDSS4e, and one patient (1%) died because of MS;
- Starting therapy after 12 years of age was the main predictor of a worse MS course. This finding could be related to the higher inflammatory pattern of ped-MS, compare to the adult form, and to its better capability to compensate brain damage. This pattern could be even more relevant in the pre-pubertal stage.

References