Efficacy and safety of alemtuzumab in 159 patients with active relapsing-remitting MS: Two-year follow-up in France.


BACKGROUND
Alemtuzumab is an anti-CD52 humanized monoclonal antibody approved by the European Medicines Agency and Food and Drug administration in active relapsing remitting multiple sclerosis (RRMS). It has been shown to be effective in newly diagnosed and treatment refractory RRMS with significant reduction in clinical and MRI activity and lower rate of sustained accumulation of disability (Cohen et al., 2012; Coles et al., 2012). More recently, 5 year Follow-up data have demonstrated durable efficacy (Hardova et al., 2017; Coles et al., 2017).

OBJECTIVES
To characterize the efficacy and safety profile of alemtuzumab in patients with active RRMS treated in France.

METHODS
We retrospectively recorded clinical and radiological data of 159 patients who underwent alemtuzumab treatment since January 2015.

RESULTS:
We included 155 patients (F: 115 / M: 40) with a mean age at disease onset of 26 years (13-55).

The main clinical characteristics at baseline are shown in table 1.

Table 1: Clinical characteristics of the patients compared with phase 2 & 3 studies.

<table>
<thead>
<tr>
<th>CamMS 223</th>
<th>CARE-MS I</th>
<th>CARE-MS II</th>
<th>Present study</th>
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</thead>
<tbody>
<tr>
<td>N=112</td>
<td>N=376</td>
<td>N=426</td>
<td>N=159</td>
</tr>
<tr>
<td>Previous treatment</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Age at treatment onset</td>
<td>31.9 ± 8</td>
<td>33 ± 8</td>
<td>34.8 ± 8.4</td>
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<tr>
<td>Disease duration (y)</td>
<td>1.4 ± 0.9</td>
<td>2.1 ± 1.4</td>
<td>4.5 ± 2.7</td>
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<tr>
<td>Relapses in previous year</td>
<td>1.7 ± 0.9</td>
<td>1.8 ± 0.8</td>
<td>1.7 ± 0.9</td>
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<tr>
<td>Mean EDSS</td>
<td>1.9 ± 0.7</td>
<td>2 ± 0.8</td>
<td>2.7 ± 1.3</td>
</tr>
<tr>
<td>∆ EDSS in previous year</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Prior therapies:
- Median number of treatments: n=4 / 76% with at least 3 treatments.
- 96% had previous second line therapy or immunosuppressive drugs.

MRI characteristics at baseline (available in 140 patients):
- Gadolinium enhancing lesions: 65%.

Efficacy:
- Mean follow-up: 19 months.
- Mean relapse rate at 2 years (Figure 1): 0.26 +/- 0.6:
- 70% had no relapse during year 1 and 83% during year 2.
- EDSS change for 49 patients at 2 years (Figure 2)
  - Mean EDSS change - 0.72
  - Improvement : 38% / Stable: 42% / Worsening: 20%
- MRI at one year:
  - 40% had new T2 lesions and/or gadolinium enhancing lesions.

Safety:
- Infusion associated reactions: 58% at year 1, 36% at year 2.
- Infections: 10 patients
  - Autoimmune adverse event: 10 patients
    - Thyroid disorder: n=7
    - Immune thrombocytopenia with good recovery: n=1
    - Haemolytic anaemia: n=1
- Others: 11 patients (4 hemorrhages, 2 ischemic strokes, 1 cardiac arrest, 1 pleuropulmonary effusion, 1 epilepsy...) 11/102 patients with > 1 year follow-up did not received alemtuzumab 12 months after baseline:
  - A diverse events:
    - Progression n=1, Choice of the neurologist n=3
    - Relapse rate variation from year to year in patients with starts on the side line of treatment for patients with "Abbott",

Figure 1: Relapse rate in the year before and in the 2 years after Alemtuzumab treatment

Figure 2: Mean EDSS change 12 months before treatment, at baseline and at 1 year

Discussion and conclusion
In France, Alemtuzumab is mainly given to patients with very active disease (mean EDSS level: 5.3, mean ARR: 1.7) and refractory to several lines of treatment (median number: 4).

Our results tend to demonstrate that even in patients with advanced disease, alemtuzumab may have a significant efficacy at 2 years.

Safety findings are in line with previously published data; hemorrhagic manifestations in the absence of decreased platelet count were seen in 3% of the patients.