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

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BACKGROUND

Alemtuzumab is an anti-CD52 humanized monoclonal antibody approved by 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). Considering its safety profile, the French National Authority for Health (HAS) has restricted its use to radiologically and clinically active RRMS and currently, its use relies on a special authorization.

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.

Indication of Alemtuzumab:

- Treatment failure: 69%.
  - Relapses 61% / relapses & MRI activity 25% / MRI activity only 7% / other (no gad injection, etc…) 7%.
- PML risk under Natalizumab: 25%.
  - Direct switch from Natalizumab ➔ 10 patients
  - Rebound after Natalizumab withdrawal ➔ 29 patients
- Other: 6% (NA 3% / other 2% / first therapy 2 patient).

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 <u>for 49 patients at 2 years</u> (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 pleuropericardial effusion, 1 epilepsy…)
- 11/102 patients with > 1 year follow-up did not received alemtuzumab12 months after baseline:
  - Adverse event n=7, Progression n=1, Choice of the neurologist n=3

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

	CAMMS 223 N=112	CARE-MS 1 N=376	CARE-MS 2 N=426	Present study N=159
Previous treatment	No	No	Yes	Yes (99%)
Age at treatment onset	31.9 ± 8	33 ± 8	34.8 ± 8.4	37 ± 9
Disease duration (y)	1.4 ± 0.9	2.1 ± 1.4	4.5 ± 2.7	**11 ± 6**
Relapses in previous year	1.7 ± 0.9	1.8 ± 0.8	1.7 ± 0.9	1.7 ± 1.1
Mean EDSS	1.9 ± 0.7	2 ± 0.8	2.7 ± 1.3	**5.3 ± 2.2**
Δ EDSS in previous year	NA	NA	NA	0.78 ± 1.3

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

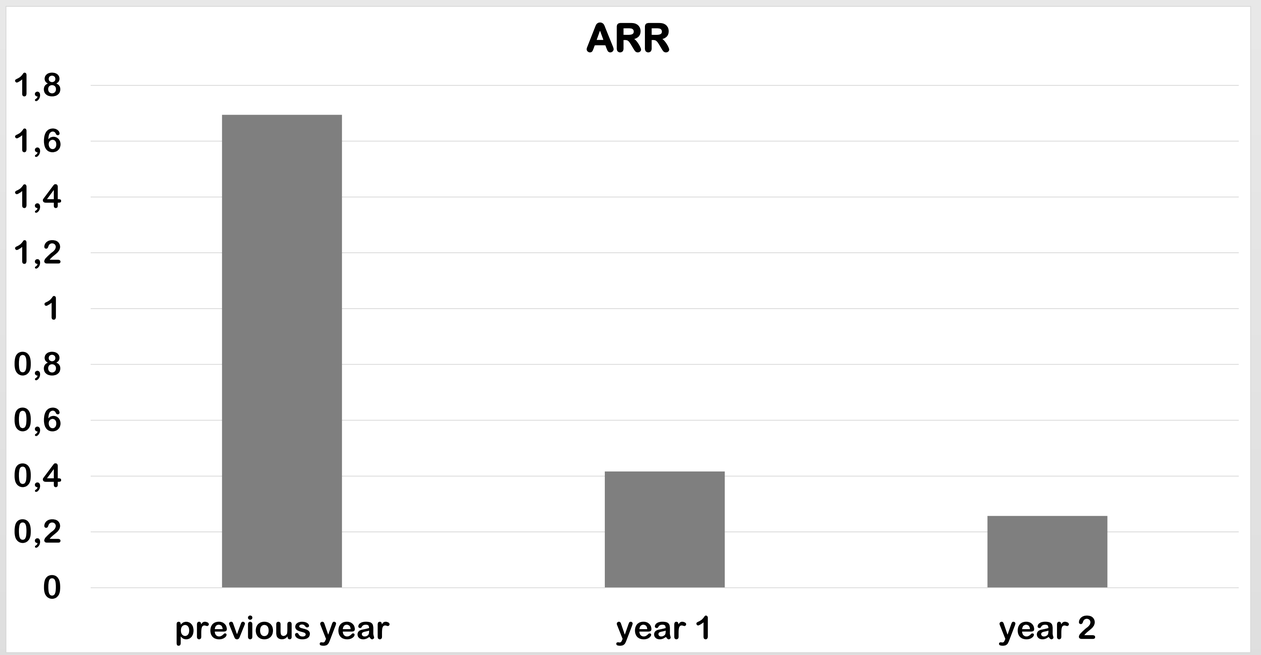
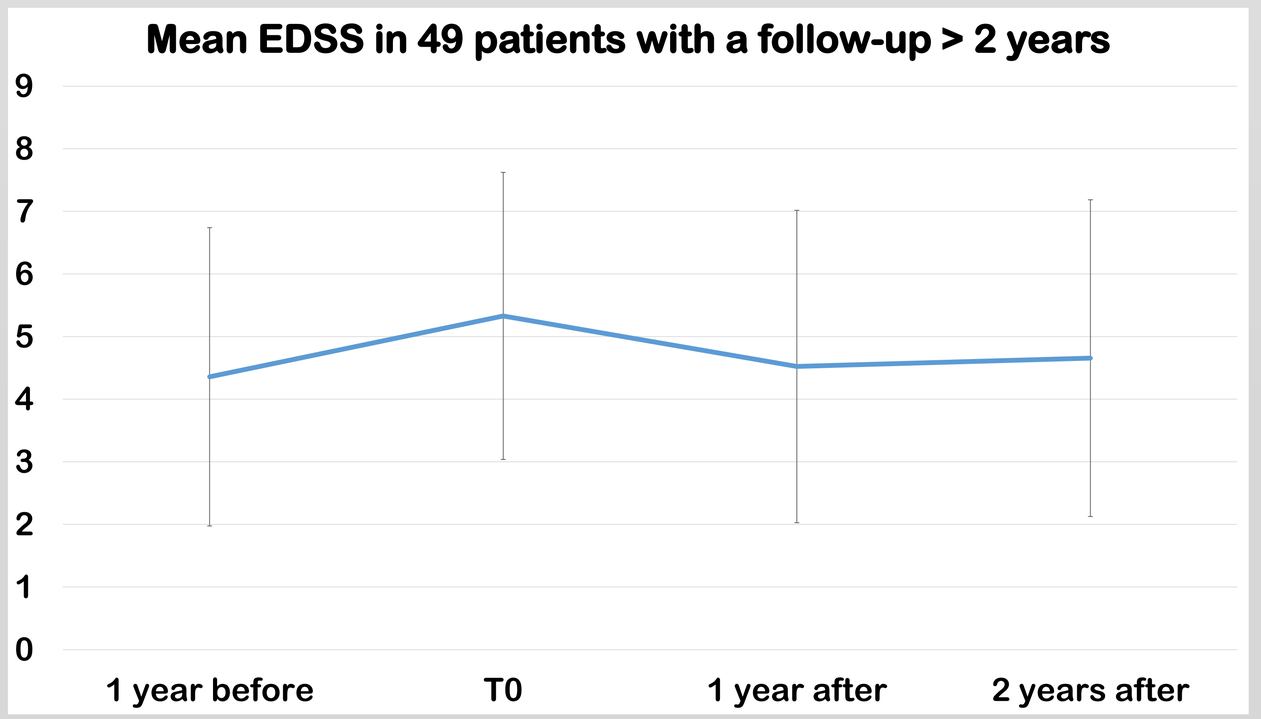


Figure 2: Mean EDSS change 12 months before treatment, at baseline and at 1 year



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 treatments (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.