

Multiple sclerosis: wasted opportunities

A team of authors analysed the randomised clinical trials conducted on multiple sclerosis drugs before and after their authorisation up to July 2017 (1). Eight drugs had been authorised in Europe since the market introduction of *interferon beta* and *glatiramer* (a)(1).

These eight drugs were granted marketing authorisation on the basis of 16 clinical trials, in a total of about 16 000 patients. Eleven (i.e. more than two-thirds) of these trials compared the new drug with placebo, while the other trials compared it with *interferon beta-1a* (the standard therapy, in the absence of a better alternative). The primary endpoint in 11 trials was the mean annualised relapse rate. The only trials that evaluated disability progression as the primary endpoint were the trials of *alemtuzumab*, but they did not provide any proof of efficacy (1). In other words, when first introduced on the market, most of these drugs had not been compared with the standard treatment, and their effect on disease progression in the long term had not been evaluated (1).

These authors also analysed the 52 randomised clinical trials conducted after the eight drugs had obtained marketing authorisation, 21 of which assessed *fampridine*. Only 24 of the 52 trials had been completed and their results published. Two-thirds (34) of the trials compared the drug with placebo and 17% (9 trials) with *interferon* or *glatiramer*. Only one of the trials whose final results had been published compared two drugs head-to-head: *natalizumab* versus *fingolimod*; and only one trial (on *fingolimod*) evaluated disease progression as an endpoint, without demonstrating its efficacy (1).

Given the absence of direct comparisons between new drugs, we are unable to determine the first-choice drugs for multiple sclerosis, and the opportunity provided by post-approval trials to better evaluate efficacy in slowing disease progression was wasted (1). The authors of this study called on public health authorities to fund trials to answer the questions that are most important to patients and healthcare professionals: which drugs should they choose, how effective are they, and what are their adverse effects (1)?

Multiple sclerosis is another example of a dilemma already well known in oncology: the drugs available have been so poorly evaluated, leaving so many questions unanswered, that healthcare professionals are obliged to base their treatment decisions more on personal experience, possibly influenced by key opinion leaders, than on convincing data. Inadequate drug evaluation is a waste of society's resources and a lost opportunity for patients to benefit from better treatments.

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a- These eight drugs are *alemtuzumab*, *daclizumab* (withdrawn worldwide in March 2018), *dimethyl fumarate*, *fampridine*, *fingolimod*, *peginterferon beta-1a*, *natalizumab* and *teriflunomide* (ref 1). *Ocrelizumab* was authorised after this study: see pp. 92-94 of this issue.

Sources 1- Gerardi C et al. "Preapproval and postapproval evidence on drugs for multiple sclerosis" *Neurology* 2018; 10:1212/WNL. 5561: 10 pages.

