Interferon β-1a decreased the risk for conversion to clinically definite multiple sclerosis

Comi G, Filippi M, Barkhof F, et al., and the Early Treatment of Multiple Sclerosis Study Group. **Effect of early interferon treatment on conversion to definite multiple sclerosis: a randomised study.** Lancet. 2001 May 19;357:1576-82.

QUESTION

In patients with a first episode of neurologic dysfunction suggesting multiple sclerosis (MS), does early treatment with low-dose interferon β-1a decrease the risk for conversion to clinically definite MS?

DESIGN

Randomized (allocation concealment*), blinded (clinicians and patients),* placebo-controlled trial with 2-year follow-up.

SETTING

57 centers in 14 European countries.

PATIENTS

308 patients (mean age 28 y, 64% women) who had presented with a first neurologic episode (unifocal or multifocal involvement of the central nervous system) suggesting MS in the previous 3 months, with ≥ 1 abnormality evident during the neurologic examination and a positive magnetic resonance imaging (MRI) scan result. Exclusion criteria included immunosuppressive or immunomodulatory treatment, participation in any experimental procedure during the year before the study, and serious comorbid systemic illnesses or psychiatric disorders.

INTERVENTION

154 patients were allocated to interferon β-1a (22 μg), and 154 patients were allocated to placebo. The treatments were administered by subcutaneous injection once a week for 2 years.

MAIN OUTCOME MEASURES

Conversion to clinically definite MS. The major secondary clinical outcome was time to occurrence of the second relapse in 30% of the patients.

MAIN RESULTS

Fewer patients who received interferon β-1a converted to clinically definite MS than did patients who received placebo (P = 0.047) (Table). Time to occurrence of the second relapse in 30% of patients was shorter in the placebo than in the interferon group (252 vs 569 d, P = 0.034).

CONCLUSION

In patients with a first episode of neurologic dysfunction suggesting multiple sclerosis, early treatment with low-dose interferon β-1a decreased the risk for conversion to clinically definite multiple sclerosis.

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*See Glossary.

Interferon β-1a vs placebo for multiple sclerosis†

Outcome at 2 y	Interferon β-1a	Placebo	RRR (95% CI)	NNT (CI)
CDMS	34%	45%	25% (0.3 to 43)	9 (5 to 886)

†CDMS = clinically definite multiple sclerosis. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

This well-designed short-term multicenter study by Comi and colleagues showed that interferon β-1a begun soon after the first sign of neurologic symptoms suggestive of MS (supported by MRI changes) could delay or prevent a second attack within the 2-year study period. Does this result suggest that we should treat patients at the first event suggestive of MS if the MRI yields a positive result? Most of the MS trials in the past decade were short-term studies of a lifelong disease; they measured and found the effects of treatment on acute attacks. However, it is unclear whether these effects (reducing acute attacks) translate into long-term benefits. The inference, without evidence, is that if a therapy can reduce attacks and activity confirmed by MRI, it should result in decreased long-term progression. To interpret this study, or the similar study by Jacobs and colleagues (1), as indicating that we should treat patients at the first evidence of MS would be premature until convincing and reproducible studies have shown that early therapy reduces long-term progression of the disease.

Despite the excitement about new therapies, the results to date have been modest. The glass is not even half full. A modest but definite reduction has occurred in the number and severity of acute attacks, but most patients still have attack rates and severity as if they had not been treated. For instance, in this 2-year study, 45% of patients in the placebo group had a second attack within 2 years, but so did 34% of the treated group—a significant but modest difference, especially considering the expense and inconvenience of the therapy.

Treating every patient who has an event suggesting MS would include non-MS patients and the 10% of "benign" patients who do well without therapy over subsequent decades. Such a recommendation would add substantial financial burden to the health care system and to patients and their families. Plans exist to continue evaluating the patients who completed this trial and those in the trial by Jacobs and colleagues. However, these plans are fraught with difficulty because most of the patients have been switched to long-term therapy and are not interested in continuing the studies.

We have had many short-term studies that are more important to marketers than to clinicians, but the relevant questions about whether these expensive therapies have any long-term effect on the outcome of patients with MS remain.

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Reference

1. **Jacobs LD, Beck RW, Simon JH, et al.** Intramuscular interferon beta-1a therapy initiated during a first demyelinating event in multiple sclerosis. N Engl J Med. 2000;343:898-904.