Mitoxantrone slowed progression of disability and reduced relapses in multiple sclerosis


QUESTION: In patients with worsening relapsing remitting or secondary progressive multiple sclerosis (MS), is mitoxantrone effective for slowing progression of disability and reducing relapses?

Design
Randomised (allocation concealed*), blinded (patients and outcome assessors),* placebo controlled trial with 24 months of follow up.

Setting
17 centres in Belgium, Germany, Hungary, and Poland.

Patients
194 patients 18–55 years of age who had worsening relapsing-remitting or secondary progressive MS. Additional inclusion criteria included Kurtzke Expanded Disability Status Scale (EDSS) score 3.0–6.0 and worsening by ≥ 1 EDSS point during the 18 months before enrolment. 188 patients (97%) (mean age 40 y, 52% women) completed follow up.

Intervention
Patients were allocated to mitoxantrone, 12 mg/m² (n=63), 5 mg/m² (n=66), or placebo (n=65) administered intravenously every 3 months for 24 months. By design, only patients in the mitoxantrone 12 mg and placebo groups were included in the primary analysis.

Main outcome measures
The primary outcome was a composite of 5 clinical measures, including change from baseline EDSS at 24 months, change from baseline ambulation index at 24 months, number of relapses treated with corticosteroids, time to first treated relapse, and change from baseline ambulation index at 24 months, tested in 1 combined hypothesis of stochastic ordered alternatives.

Main results
Analysis was by intention to treat. Progression of disability was slower, and number of relapses fewer in the mitoxantrone 12 mg group than in the placebo group (assessed on the composite outcome as well as on the individual components) (table).

Conclusion
In patients with worsening relapsing-remitting or secondary progressive multiple sclerosis, mitoxantrone was effective for slowing progression of disability and reducing relapses.

*See glossary.