Long-term outcomes of IFNβ-1a in RRMS

In an extension of the PRISMS study, Kappos et al. report data on 2/3 of the original cohort of 560 patients; 72% were still on treatment up to 8 years later. Patients originally randomized to IFN, particularly those on the higher dose, retained clinical and MRI benefits. No new safety concerns were identified.

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The editorial by John Noseworthy notes that although pivotal trials have demonstrated partial, short-term benefit from treatment with immunomodulatory agents in patients with either clinically isolated syndromes (patients at high risk of developing multiple sclerosis [MS]) or relapsing-remitting MS (RRMS), these benefits largely reflect the outcomes of relapse behavior and sensitive MRI measures of disease activity in randomized placebo-controlled studies. There is no definitive evidence that treatment protects against progression in disability. The Kappos et al. article exemplifies the challenges facing investigators of contemporary MS practice. Nearly 32% of those randomized in PRISMS elected not to participate in the extension study, thus the protection against bias afforded by randomization was largely lost in the extension trial. Patients and physicians originally blinded became aware of the treatment received, physicians evaluating outcomes had access to previous evaluations, and whereas patients were seen at 3-month intervals in the first 3 years, and twice yearly for the next 2 years, the final 1 to 2 years of follow-up represented the findings recorded at a single exit visit. I am not certain that "patients with RRMS can experience sustained benefit over many years from early use of IFNβ-1a."

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Publication bias in acute stroke studies

Liebeskind et al. ascertained the presence of publication bias in the stroke literature. Their analysis of all acute ischemic stroke clinical trials reported over 5 decades confirms the impact of bias and underscores the need for critical appraisal of published reports and prospective trial registration.

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Longitudinal costs in AD

Zhu et al. followed up on their earlier work in clinical features associated with baseline costs in Alzheimer disease and estimated long-term trajectories of direct costs. Between baseline and year 4, direct costs more than doubled from $9,239 to $19,925. Comorbidities and functional capacity were associated with higher costs over time.

There is a Patient Page on this topic: www.neurology.org.

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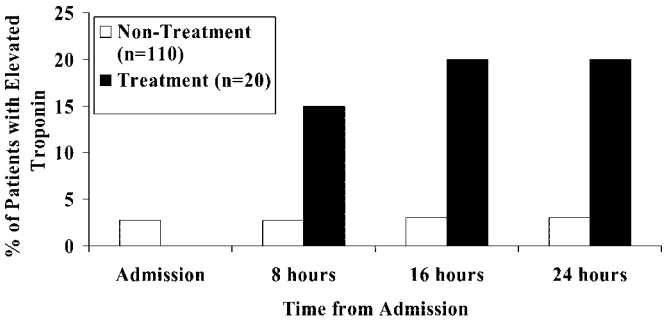
Myocardial injury with recombinant factor VIIa treatment



Sugg et al. report a significant increase in the occurrence of elevated cardiac enzymes and myocardial infarction in patients with intracerebral hemorrhage treated with recombinant factor VIIa.

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Does hydrocephalus occur with recombinant factor VIIa treatment?

Subramaniam et al. report that acute treatment of ICH with activated factor VIIa may increase the chance of developing acute obstructive hydrocephalus.

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The editorial by Steven M. Greenberg about these two articles notes that the rationale for use of rFVIIa in acute ICH is its ability to act in complex with tissue factor, calcium, and phospholipids to activate factor X and initiate coagulation via the extrinsic pathway. The requirement for exposed tissue factor is postulated to help localize rFVIIa-induced coagulation to the vicinity of recent vessel injury, but could also lead to coagulation in diseased coronary arteries and consequent MI. The mechanism by which rVIIa might cause hydrocephalus is less clear, but the authors' suggestion that a pro-coagulant could impair clearance of intraventribular blood is plausible. (Indeed, the reverse approach of intraventricular thrombolysis following intraventricular hemorrhage has been proposed to treat hydrocephalus.) As the initial study of rFVIIa was designed and powered to measure the effects of rVIIa on ICH expansion rather than outcome, the encouraging results require confirmation in a currently ongoing phase III study. Approval of rFVIIa by the US Food and Drug Administration in 1999 for treatment of certain hemophilias makes it possible for US physicians to prescribe rFVIIa off-label for ICH. These make it clear that whether benefit offsets the risks of rFVIIa has yet to be demonstrated.

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Cabergoline ameliorates sleep in restless legs syndrome

Oertel et al. investigated the long-acting dopamine agonist cabergoline in restless legs syndrome (RLS) in a placebo-controlled polysomnography study. Two milligram single evening cabergoline was efficacious and well-tolerated treatment for sensorimotor symptoms of RLS and associated sleep disturbances.

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Pramipexole for restless legs syndrome

In this 12-week randomized trial, Winkelman et al. allocated 86 patients to placebo and 258 to pramipexole at 0.25 to 0.75 mg/day. As rated by clinicians and by patients, the active agent was significantly superior, beginning at 1 week, and had a favorable safety profile.

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Sex effects in spontaneous cervical artery dissection

Arnold et al. analyzed sex differences in 696 patients with spontaneous cervical artery dissection. Younger women more often had multiple dissections, migraine, and tinnitus, and less frequently had hypertension.

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The editorial by Tobias Brandt and Steven R. Levine notes that the question of whether female sex is a risk factor for recurrent or multiple dissection is not settled by this study. More long-term follow-up and data estimating risk of recurrent CAD are needed. Although a previous study of 200 patients found that 11 of 13 (85%) multiple CAD were in women, another study observed a clear male preponderance with 6/7 (86%) in 90 followed. Since the question of how dangerous CAD is on long-term follow-up is frequently asked by patients, a large, prospective international study is needed.

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