While I would heartily applaud Aaron Miller’s choice of the two papers presenting the BG-12 phase 3 trial data and agree with their importance, (not because I was a minor co-author in the CONFIRM study), I would respectfully choose another paper.

I chose the paper by Doug Goodin on the 21-year follow-up of the participants in the original beta interferon-1b (IFNB-1b)(Betaseron) study.1,2 For years, sceptical neurologists, particularly in the UK, have questioned the use of modestly effective disease modifying therapies in relapsing remitting multiple sclerosis (RRMS). Their argument was that the effect of beta-interferons or glatiramer acetate on disability progression was minimal (or not there at all), was not cost-effective, and that short-term trials demonstrating relapse suppression would not translate into longer-term benefits in relation to secondary progression and death. Such was their doubt, and their influence upon the National Institute for Clinical Excellence (NICE), that a long time elapsed before these therapies became available to people with RRMS in the UK. A medico-political contrivance (a “risk-sharing scheme”), was devised by the Blair government in 2002 in order to make these medicines, used widely in USA and Europe, available to patients with RRMS in the UK.3,4 However, back to the paper under consideration. Goodin and his colleagues have managed the remarkable feat of following up 98.4% (366 of 372) of the patients enrolled in the original study published in 19932 with a median follow-up of 21 years; anyone involved in long-term studies will recognize what an achievement that was.1 The criticism directed at such studies, that the patients lost to follow-up are the ones who did badly (severely disabled/died) and thus the good results, does not apply here. In the original study, 372 patients were randomized to one of three arms, low dose IFNB-1b, standard dose IFNB-1b, or placebo, for a mean of 3.3 years.2 When the trial ended patients were offered treatment with the active agent at a standard dose. The main difference between the three groups was that the placebo group received no active therapy in the trial for a mean of 3.3 years. The authors acknowledge that the patients randomized to placebo had more than three years without an active therapy, and it is difficult to be certain whether the survival advantage in the two actively treated study arms compared to placebo was due to early treatment, or to the longer duration of active therapy. The mechanisms underlying the survival advantage for the active groups are unknown; this may not be just an anti-inflammatory effect. Nevertheless, to my mind these data, taken with the natural history studies of the association between the frequency of early relapses and reduced life expectancy, indicate that we can extrapolate from relapse suppression early in the course of the illness to long-term survival.

By taking the message from this unique long-term study on board, neurologists can be more confident in our daily practice. Effective control of demyelinating disease activity, with a now increasing range of potent therapies, will have a longer-term effect on patient health in reducing disability progression and preventing death due to multiple sclerosis.

Disclosures

Michael Hutchinson served on a medical advisory board for the CONFIRM study [BG00012] for Biogen-Idec, serves on the editorial board of the Multiple Sclerosis Journal, has received speaker’s honoraria from Novartis, Biogen-Idec and Bayer-Schering and receives research support from Dystonia Ireland and the Health Research Board of Ireland.

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The best clinical paper on multiple sclerosis in 2012: Commentary

Michael Hutchinson

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