SAFETY AND EFFICACY OF TERIFLUNOMIDE IN PATIENTS WITH RELAPSING MULTIPLE SCLEROSIS TREATED WITH INTERFERON-BETA

M.S. Freedman[1], J.S. Wolinsky[2], G. Comi[3], L. Kappos[4], A.E. Miller[5], T.P. Olsson[6], J. Liang[7], D. Dukovic[7],
M. Benamor[8], P. Truffinet[9], P.W. O'Connor[10] for the TERACLES study group
[1]University of Ottawa and the Ottawa Hospital Research Institute, Ottawa, ON, Canada; [2]University of Texas Health Science Center at Houston, Houston, TX, USA; [3]University Vita-Salute San Raffaele, Milan, Italy; [4]University Hospital Basel, Basel, Switzerland; [5]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [6]Karolinska Institute, Stockholm, Sweden; [7]Genzyme, a Sanofi company, Bridgewater, NJ, USA; [8]Sanofi R&D, Chilly-Mazarin, France; [9]Genzyme, a Sanofi company, Chilly-Mazarin, France; [10]University of Toronto, Toronto, ON, Canada
mfreedman@toh.on.ca

BACKGROUND: Teriflunomide is a once-daily oral immunomodulator approved for relapsing–remitting multiple sclerosis (MS). TERACLES (NCT01252355) is a study assessing the effect of teriflunomide in combination with interferon-beta (IFNβ) on relapses and MRI activity in patients with relapsing MS.
OBJECTIVES: To report key outcomes from TERACLES.
METHODS: Eligible patients were aged 18–55 years, receiving IFNβ for ≥6 months, with ≥1 relapse or ≥1 gadolinium (Gd)-enhancing T1-lesion on MRI, and baseline EDSS score ≤5.5. Primary and key secondary endpoints were annualised relapse rate (ARR) and total number of Gd-enhancing T1-lesions per MRI scan. The company sponsor decided to terminate the study early.
RESULTS: 534 patients (planned N=1455) were randomised 1:1:1 to teriflunomide 14mg+IFNβ, 7mg+IFNβ or placebo+IFNβ. Average treatment duration was <300 days/treatment group. The combination of teriflunomide 14mg+IFNβ led to greater reductions in ARR and number of Gd-enhancing T1 lesions/scan as compared with IFNβ alone (20.3%; NS and 70.8%; p=0.0061, respectively); non-significant reductions were observed with 7mg+IFNβ. No new safety signals were identified versus teriflunomide monotherapy studies.
CONCLUSIONS: An incremental beneficial effect on MRI activity and relapses was observed with the addition of teriflunomide 14mg to IFNβ when IFNβ alone was unable to contain disease activity. Although the early termination of the study limited its power and interpretability, these results suggest a potential benefit in combining teriflunomide+IFNβ, two therapies with different mechanisms of action. The combination was generally well tolerated, suggesting no concern about immediate switching between IFNβ and teriflunomide therapies.
Study supported by Genzyme, a Sanofi company.