times the upper level of normal), but without associated clinical signs. There were no cases of discontinuation due to an AE.

In conclusion, Dr Cohen indicated that treatment of patients with RRMS with RPC1063 resulted in substantial reductions in magnetic resonance imaging measures and disease activity, with an overall good safety profile found with this phase 2 Radiance Study. A phase 3 portion of the Radiance Study [NCT02047734] is ongoing and a phase 3 SUNBEAM trial, evaluating RPC1063 vs interferon beta-1a, is in the planning phase.

GATE: Generic GA as Effective and Safe as Copaxone for Patients With RRMS

Written by Maria Vinall

Results from the Efficacy and Safety of GTR in Comparison to Copaxone trial [GATE; NCT01489254] reported by Jeffrey A. Cohen, MD, Cleveland Clinic, Cleveland, Ohio, USA, show that GTR, a generic form of glatiramer acetate (GA), is as effective and safe as the brand-name drug for the treatment of patients with relapsing-remitting multiple sclerosis (RRMS).

Medications contribute significantly to the cost of care for patients with multiple sclerosis (MS). Generic versions of GA that may help reduce treatment costs are being evaluated, but neither the US Food and Drug Administration nor the European Medicines Agency has issued a final guidance for establishing bioequivalence for GA.

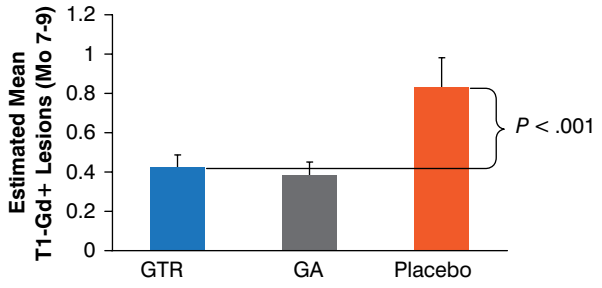
GATE is an ongoing multinational, parallel-group, equivalence study designed to demonstrate that GTR is as efficacious as GA in patients with RRMS. Men and women aged 18 to 55 years with RRMS according to the McDonald criteria (2010)—an Expanded Disability Status Scale (EDSS) score ≤ 5.5, ≥ 1 relapse in the year before screening, and 1 to 15 T1-gadolinium enhanced (Gd+) lesions on magnetic resonance imaging (MRI) at screening—were eligible to enroll. Participants were randomized to GTR (n = 353) or GA (n = 357) 20 mg, or placebo (n = 84), daily for 9 months, followed by 15 months of open-label treatment with GTR. Centrally analyzed MRI was performed at baseline and at months 7, 8, 9, 12, 18, and 24. Patients completed the EDSS at baseline and at months 6, 9, 12, 18 and 24. The primary study end point of the double-blind portion was the number of T1-Gd+ lesions at months 7 to 9 of treatment. Safety was assessed by adverse event (AE) reporting and tolerability, which was assessed at the initiation of therapy, and at months 3, 9, and 12. Dr Cohen reported the 9-month results.

At baseline, patients (mean age, approximately 33 years; approximately 67% women) had a mean disease duration of 5.5 to 6.4 years, a median of 2 Gd+ lesions (mean, 2.5-2.8), and a mean 1.9 relapses within the 2 years prior to study enrollment. More than 90% of participants completed the double-blind phase of the trial.

Both GTR and GA significantly reduced the number of T1-Gd+ lesions as compared with the placebo ($P < .001$; Figure 1).

GTR was equivalent to GA in reducing the number of T1-Gd+ lesions based on the predefined equivalence margins (Figure 2).

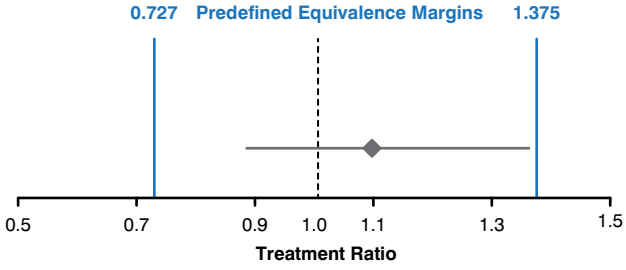
Figure 1. Study Sensitivity: T1-Gd+ Lesions



	Geometric Mean Ratio	95% CI
Full Analysis Set (N=794)	0.488	(0.365 to 0.651)
Per Protocol Set (N=733)	0.481	(0.357 to 0.647)

GA, glatiramer acetate; GTR, a generic form of GA; T1-Gd+, T1-gadolinium enhanced.
Reproduced with permission from JA Cohen, MD.

Figure 2. Equivalence: T1-Gd+ Lesions



	Geometric Mean Ratio	95% CI
Full Analysis Set (N=794)	1.097	(0.884 to 1.362)
Per Protocol Set (N=733)	1.099	(0.881 to 1.370)

T1-Gd+, T1-gadolinium enhanced.
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Table 1. Clinical End Points at Month 9

	GTR (n = 353)	GA (n = 357)	Placebo (n = 84)
Annualized relapse rate [95%CI]	0.31 (0.20 to 0.48)	0.41 (0.27 to 0.63)	0.39 (0.22 to 0.67)
Subjects without relapse (%)	281 (79.6%)	263 (73.7%)	62 (73.8%)
Change in EDSS (Median (min–max))	0.0 (–2.5 to 2.0)	0.0 (–3.0 to 4.5)	0.0 (–2.0 to 1.5)
Free from disease activity (%)	33 (9.3%)	32 (9.0%)	6 (7.1%)

EDSS, Extended Disability Status Scale; GA, glatiramer acetate; GTR, a generic form of GA.

There were no differences between the 2 active treatments in other MRI end points at 9 months: change in T2 lesion number or volume (mm^3), change in T1-hypo lesion volume (mm^3), or change in brain volume (cm^3). Clinical end points were similar between GTR and GA (Table 1).

Overall safety and tolerability were excellent and similar for GTR and GA. The most common drug-related AEs were injection site reaction (16.4% of GTR-treated patients vs 17.1% of GA-treated patients) and immediate postinjection reaction (6.8% and 5.0%, GTR vs GA, respectively). The rate of serious or severe AEs was low. Drug-related serious AEs were reported by 3 (0.8%) GTR-treated patients and 4 (1.1%) GA-treated patients. No patients died. Local tolerability (pain, itchiness, redness, swelling, lumps) was similar between the GTR and GA groups.

Data from the open-label study is expected in 2015 and will include 2-year safety and efficacy data, data on switching (from GA to GTR), and immunogenicity data for both the core and open-label portions of the study.

Postrelapse MS Treatment With Alemtuzumab Better Than SC IFN-β-1a

Written by Brian Hoyle

Subgroup analyses, entitled An Extension Protocol for Multiple Sclerosis Patients Who Participated in Genzyme-Sponsored Studies of Alemtuzumab [NCT00930553; Barkhof F et al. ACTRIMS/ECTRIMS 2014 (poster P075)], of an ongoing, open-label extension of the Comparison of Alemtuzumab and Rebif Efficacy in Multiple Sclerosis, Study Two [CARE-MS II; Coles AJ et al. *Lancet.* 2012], have confirmed the superiority of treatment of MS using the anti-CD52 humanized monoclonal antibody, alemtuzumab, over subcutaneous interferon beta-1a (SC IFN-β-1a) in magnetic resonance imaging (MRI) outcomes. The subgroup analyses were based on baseline demographics and disease characteristics, as well as prior use of SC IFN-β-1a. Alemtuzumab's superiority was, in most cases, a holdover from treatment received 2 years previously.

The latest findings from the subgroup analyses based on the phase 3, randomized, rater-blinded, active-controlled, head-to-head CARE-MS II study were presented by Frederik Barkhof, MD, VU University Medical Center, Amsterdam, the Netherlands.

CARE-MS II has established the significant superiority of alemtuzumab throughout 2 years compared with SC IFN-β-1a at reducing the risk of the development or enlargement of gadolinium-enhancing (Gd+) lesions and reducing brain volume loss [Coles AJ et al. *Lancet.* 2012], and in lessening the number of hypointense lesions [Arnold DL et al. ECTRIMS 2012). Eligible patients (n = 667) aged 18 to 55 years with active relapsing-remitting MS and a baseline Expanded Disability Status Scale (EDSS) score ≤ 5 (n = 667) were randomized 2:1 to receive alemtuzumab 12 mg/d intravenously for 5 consecutive days at baseline and 3 consecutive days 12 months later (n = 426), or to receive SC IFN-β-1a 44 µg 3 times a week on an ongoing basis (n = 202) [Coles AJ et al. *Lancet.* 2012]. The groups were similar at baseline concerning demographic and relevant clinical parameters.

The core phase ran for 2 years. In the subsequent extension phase, patients initially randomized to alemtuzumab could continue their treatment if they relapsed or presented with MRI signs of progression. This retreatment was unnecessary in 80% of cases.