in severity. Only 5 of 376 patients (1.3%) withdrew due to adverse events.

The efficacy of alemtuzumab in treatment of RRMS in patients who were treatment-naïve at baseline, which was noted at 2 and 3 years, was maintained at 4 years. Safety was also similar in patients who received alemtuzumab throughout the study and those who switched from interferon after the first 2 years. No new or unexpected adverse events appeared during year 4. The present data further bolster the acceptability of alemtuzumab treatment for this population of patients with MS.

RPC1063 Safe and Effective in RRMS

Written by Emma Hitt Nichols, PhD

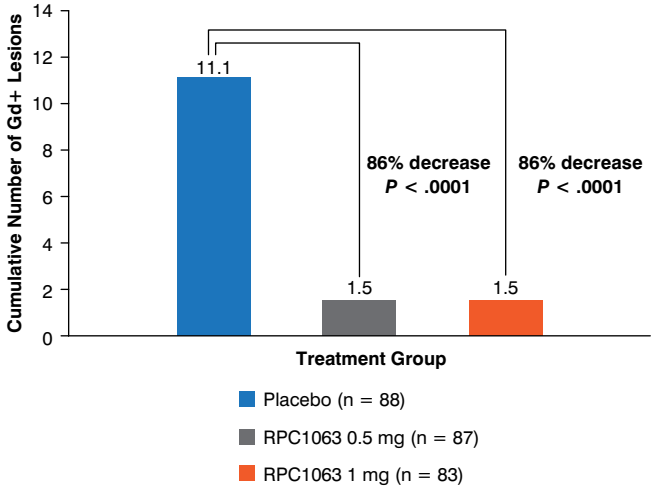
Treatment with the sphingosine 1-phosphate (S1P) receptor modulator, RPC1063, resulted in a substantial decrease in gadolinium-enhancing (Gd+) lesions and the number of new or enlarging T2 lesions in patients with relapsing-remitting multiple sclerosis (RRMS). Amit Bar-Or, MD, Montreal Neurological Institute, Montreal, Ontario, Canada, presented data from the Efficacy and Safety Study of RPC1063 in Relapsing Multiple Sclerosis Patients trial [Radiance Study; NCT01628393].

Targeting the S1P receptor family is an approach that has been explored as a treatment for patients with RRMS [Halmer R, Walter S, Fasbender K. *Cell Physiol Biochem*. 2014. RPC1063 is a novel agent that modulates S1P receptors 1 and 5, and has been previously evaluated in healthy subjects. The purpose of the Radiance Study was to further evaluate RPC1063 in patients with RRMS.

In the phase 2 Radiance Study, 258 adult patients with RRMS were randomly assigned to receive 24 weeks of 0.5 mg or 1 mg of RPC1063, or placebo. Upon completion of the treatment period, a blinded extension study was conducted in which patients who received RPC1063 continued treatment, and patients who received placebo were assigned to 0.5 mg or 1 mg of RPC1063. Patients aged 18 to 55 were eligible to enroll in the study if they had an Expanded Disability Status Scale (EDSS) score of 0 to 5.0 at baseline and met ≥1 of the RRMS criteria, which included ≥1 documented relapse within the prior 12 months, or ≥1 documented relapse plus ≥1 Gd+ lesion(s) within the previous 24 months.

The primary end point of the Radiance Study was the cumulative number of Gd+ lesions. Secondary end points included the number of Gd+ lesions at week 24, the number of cumulative or enlarging T2 lesions, and the annualized relapse rate (ARR). At baseline, the mean EDSS score ranged from 2.85 to 2.94, the mean number of relapses over 12 months from 1.3 to 1.5, and the number of Gd+ lesions from 0.9 to 1.4.

Figure 1. Effect of RPC1063 on Total Number of Gd+ Lesions Over 12 Weeks



Gd+, gadolinium-enhancing.

Reproduced with permission from JA Cohen, MD.

The cumulative number of Gd+ lesions significantly decreased by 86% ($P<.0001$) in patients who received either dose of RPC1063 as compared with patients who received the placebo from week 12 to 24 (Figure 1). In addition, at week 24, the mean number of Gd+ lesions significantly decreased by 91% and 94% ($P<.0001$ for both) in patients who received 0.5 mg and 1 mg of RPC1063, respectively, as compared with patients who received the placebo. Similarly, the cumulative number of new or enlarging T2 lesions significantly decreased by 84% and 91% ($P<.0001$ for both) in the 0.5 mg and 1 mg RPC1063 arms as compared with the placebo arm from week 12 to week 24. There was a dose-dependent trend toward a decrease in ARR, with a rate of 0.5 in the placebo arm, 0.35 in the 0.5-mg RPC1063 arm, and 0.24 in the 1-mg RPC1063 arm.

During the core, 24-week portion of the Radiance Study, the number of patients who experienced ≥1 treatment-emergent adverse event (TEAE) was 59.1% in the placebo arm, and 56% and 47% in the 0.5-mg and 1-mg RPC1063 arms, respectively. The most common TEAEs in patients who received RPC1063 included nasopharyngitis, headache, and urinary tract infection. During the study, 3 serious TEAEs were reported but deemed unrelated to the study drug. However, there were 3 cases of elevated alanine aminotransferase (≥3

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.

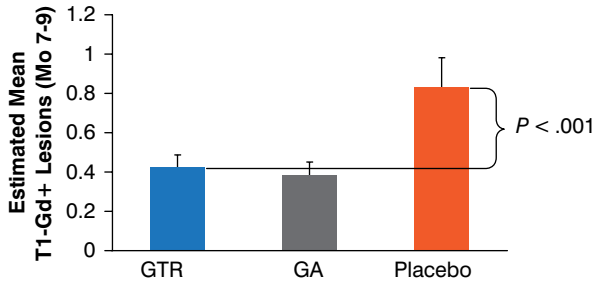
GATE is an ongoing multinational, parallel-group, equivalence study designed to demonstrate that GTR is as efficacious as GA in patients with RRMS. Men and women aged 18 to 55 years with RRMS according to the McDonald criteria (2010)—an Expanded Disability Status Scale (EDSS) score ≤ 5.5, ≥ 1 relapse 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).

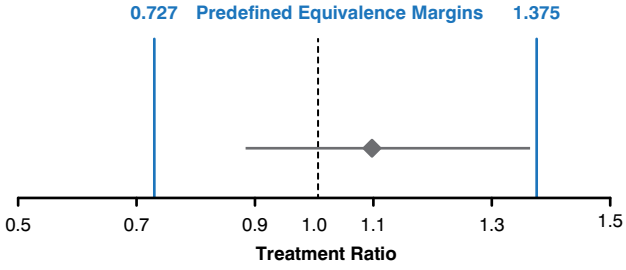
Figure 1. Study Sensitivity: T1-Gd+ Lesions



	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.
Reproduced with permission from JA Cohen, MD.