P3.256

67th Annual Meeting of the American Academy of Neurology, April 18-25 2015, Washington DC, USA

Synthon

Similar Local Tolerability Profiles following Double-Blind Treatment with Generic or Branded Glatiramer Acetate in Multiple Sclerosis

Krzysztof Selmaj[1], Frederik Barkhof[2], Christian Wolf[3], Anna Belova[4], Janine Oberyé[5], Evelyn van den Tweel[5], Roel Mulder[5], Norbert Koper[5], Gerrit Voortman[5], Jeffrey Cohen[6] for the GATE study group

[1]Neurology Center Lodz, Lodz, Poland; [2]Image Analysis Centre, Department of Radiology and Nuclear Medicine, VU University Medical Center, Amsterdam, Netherlands; [3]Lycalis sprl, Brussels, Belgium; [4]Research Institute of Traumatology and Orthopaedy, Functional Diagnostics, Nizhniy Novgorod, Russian Federation; [5]Synthon BV, Nijmegen, Netherlands; [6]Mellen Center for Multiple Sclerosis Treatment and Research, Cleveland Clinic, Cleveland, OH, USA

INTRODUCTION

GTR (Synthon) is the first generic glatiramer acetate with a demonstrated equivalent efficacy and safety profile to branded glatiramer acetate (GA, Copaxone®, Teva)[1]. Because local injection site reactions (LISRs) are the most common adverse reactions for GA, these were further investigated to ensure the local tolerability profile supports the comparability.

METHODS

GATE: Glatiramer Acetate clinical Trial to assess Equivalence vs. Copaxone

Study population

RRMS patients aged 18-55 years with ≥1 relapse in the year prior to screening and 1-15 gadolinium-enhanced brain lesions.

Treatment

794 patients were randomized and received daily subcutaneous injections of 20 mg GTR (Synthon glatiramer acetate; N=353), 20 mg GA (Teva glatiramer acetate (Copaxone®); N=357), or placebo (N=84) in a double-blind trial for 9 months.

Local tolerability scoring

The presence and severity of LISRs 5 minutes and 24 hours after injection were recorded in diaries for two periods of 14 days starting at Day 1 and Month 3. The LISR presence score was based on the number of symptoms (pain, redness, swelling, itching, lumps) reported and ranges from 0 to 5. The severity score was reported as 0 (none), 1 (mild), 2 (moderate) or 3 (severe).

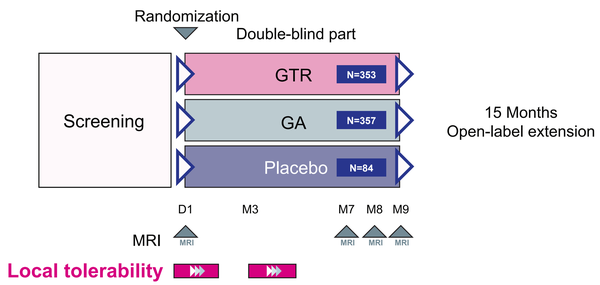
Adverse event monitoring

Local injection site reactions were reported as adverse events on those days when LISR scores were not entered in the diaries.

Statistical Analysis

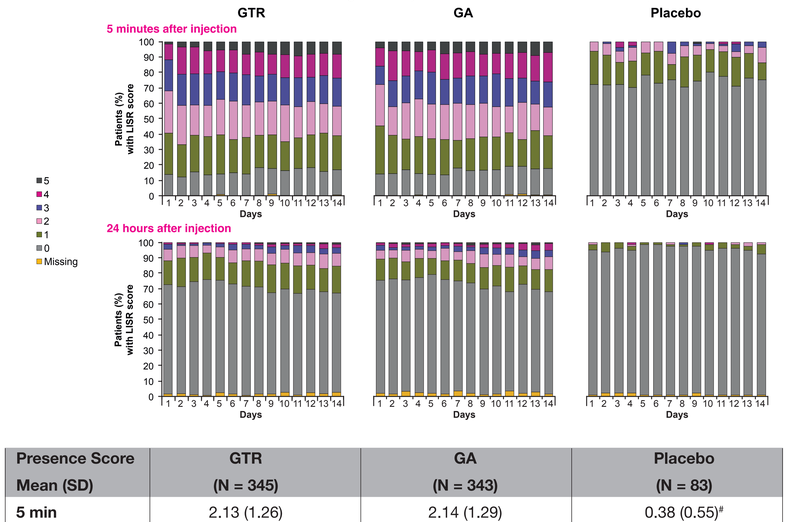
Per period and timepoint, the LISR presence score and the LISR severity score is calculated for each subject as the mean of the reported scores over the 14-day period.
Treatments were compared using a 1-way ANOVA model with the mean LISR presence and the mean LISR severity scores as response.

STUDY FLOW



RESULTS – LISR PRESENCE SCORES DURING PERIOD 1

Similar LISR presence scores for GTR and GA; significantly lower LISR presence scores for placebo.



Presence Score Mean (SD)	GTR (N = 345)	GA (N = 343)	Placebo (N = 83)
5 min	2.13 (1.26)	2.14 (1.29)	0.38 (0.55)#
24 hrs	0.49 (0.68)	0.51 (0.81)	0.05 (0.015)#

 # p< 0.001 vs. GTR and GA

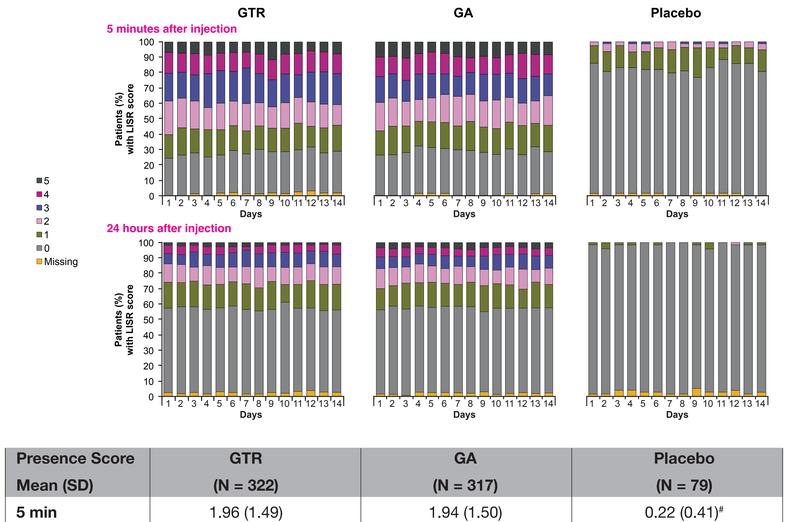
RESULTS – ADVERSE EVENTS DURING 9-MONTH DOUBLE-BLIND PART

Similar incidence of adverse events related to injection site reactions in GTR and GA group and clearly different from placebo.

Local injection site reactions	GTR (N = 353) n (%)	GA (N = 357) n (%)	Placebo (N = 84) n (%)
General disorders and administration site conditions			
Any event	**81 (22.9%)**	**82 (23.0%)**	**14 (16.7%)**
Injection site reaction	58 (16.4%)	61 (17.1%)	6 (7.1%)
Injection site swelling	14 (4.0%)	12 (3.4%)	3 (3.6%)
Injection site pain	11 (3.1%)	13 (3.6%)	1 (1.2%)
Injection site erythema	8 (2.3%)	7 (2.0%)	0 (0.0%)
Injection site pruritus	8 (2.3%)	5 (1.4%)	0 (0.0%)
Injection site induration	3 (0.8%)	3 (0.8%)	0 (0.0%)
Injection site anaesthesia	2 (0.6%)	1 (0.3%)	0 (0.0%)
Injection site oedema	2 (0.6%)	2 (0.6%)	0 (0.0%)
Injection site haematoma	1 (0.3%)	0 (0.0%)	3 (3.6%)
Injection site bruising	0 (0.0%)	0 (0.0%)	3 (3.6%)
Injection site haemorrhage	0 (0.0%)	0 (0.0%)	1 (1.2%)

RESULTS – LISR PRESENCE SCORES DURING PERIOD 2

Similar LISR presence scores for GTR and GA; significantly lower LISR presence scores for placebo.



Presence Score Mean (SD)	GTR (N = 322)	GA (N = 317)	Placebo (N = 79)
5 min	1.96 (1.49)	1.94 (1.50)	0.22 (0.41)#
24 hrs	0.93 (1.16)	0.99 (1.27)	0.01 (0.05)#

 # p< 0.001 vs. GTR and GA

RESULTS – SEVERITY SCORES

Pain and Redness were the most relevant LISR: 5 minutes post-injection 62% and 54% (GTR) and 65% and 52% (GA) of patients reported at least once moderate or severe symptoms for these domains.

Mean severity scores were similar in GTR and GA groups at both time points and significantly different from placebo.

Severity Score - Period 1* Mean (SD)		GTR (N = 345)	GA (N = 343)	Placebo (N = 83)
Pain	5 min	1.13 (0.73)	1.12 (0.69)	0.15 (0.33)#
	24 hrs	0.33 (0.49)	0.32 (0.52)	0.07 (0.22)#
Redness	5 min	0.99 (0.57)	0.93 (0.57)	0.24 (0.39)#
	24 hrs	0.27 (0.48)	0.31 (0.53)	0.06 (0.25)#

*# p<0.005 vs. GTR and GA; * Similar results for Period 2 were obtained*

CONCLUSIONS

Local tolerability of GTR is comparable to the branded GA product as reflected by similar LISR presence scores and similar LISR severity scores for all local tolerance domains, including the most frequently reported domains Pain and Redness, as well as similar incidence of reported local tolerance adverse events.

Study was supported by Synthon BV

References:1 Cohen JA, et al. Generic glatiramer acetate is equivalent to Copaxone® on efficacy and safety: results of the randomized double-blind GATE trial in multiple sclerosis. MS Journal 2014; 20: S38-S39

Disclosures: KS: grants and personal fees (Synthon BV, Roche, Biogen Idec, Novartis, Teva, Merck, Genzyme, Neuron, Receptos); FB: personal fees (Bayer Schering Pharma, Sanofi Aventis, Biogen Idec, Teva, Merck Serono, Novartis, Roche, Synthon BV, Jansen Research, Genzyme); CW: personal fees (Synthon BV, Novartis AG, Teva Ltd, BBB BV, Desitin); AB: personal fees (Synthon BV); JO, EvT, NK, RM and GV: employees of Synthon BV; JC: grants and personal fees (EMD Serono, Genentech, Genzyme, Innate Immunotherapeutics, Synthon BV, Vaccinex).

GATE
Glatiramer Acetate clinical Trial to assess Equivalence vs. Copaxone