Clinical Study Report Synopsis for Public Disclosure

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2. SYNOPSIS

Study identifier MRZ 92579 – 0738/ 1

Title of study
A Long-Term Open Label Extension Study to assess the Safety, Tolerability, and Efficacy of Neramexane Mesylate in Congenital Idiopathic Nystagmus and Acquired Nystagmus

Investigator(s), study site(s)

[redacted]
United Kingdom
[redacted]

Publication (reference)
None at the time of reporting.

Study period	First subject enrolled:	12-MAY-2009	**Phase 2**
	Last subject completed:	10-JUN-2010	

Objectives
The primary objective of this open-label, extension study was to evaluate the long-term safety and tolerability of daily doses of 25, 50, or 75 mg neramexane mesylate in the treatment of congenital idiopathic nystagmus (CIN) or nystagmus secondary to multiple sclerosis (MS). A further objective of the trial was to investigate the permanence of visual acuity improvement.

Study design and methodology
The clinical trial was conducted as a flexible dose, single center, non-randomized, uncontrolled, single group assignment, open-label extension study. Subjects who had successfully completed Merz Study MRZ 92579-0707/1 were offered participation in this 36-month trial; participation was to commence following a 30-day wash-out period.

Number of subjects planned
All subjects who completed the earlier double-blind cross-over trial MRZ 92579 – 0707/ 1 and fulfilled the eligibility criteria for the present extension study were to be included. However, this number was not reached, as recruitment was very poor owing to general unwillingness of the subjects to continue in the study (see also criteria for inclusion, below). The study was terminated prematurely by the sponsor according to protocol because new

scientific data became available which showed that the continuation of the study was not justified as the analysis of the main study MRZ 92579 0707/ 1 showed that the treatment with neramexane brought no detectable clinical advantage to CIN or MS patients.

Diagnosis and main criteria for inclusion
The study indications were congenital idiopathic nystagmus and nystagmus associated with multiple sclerosis. The main criteria for inclusion were completion of both study periods in the previous double-blind protocol MRZ 92579-0707/ 1 and willingness on the part of the subject, subject to the investigator's agreement, to enter the extension study. Subjects could be excluded according to defined clinical criteria (e.g. cardiac abnormalities) or if there had been serious compliance problems in the main study.

Test product
Neramexane mesylate modified release (MR) tablets (25 mg), with individual dose adjustment in 25-mg steps, with a starting dose of 25 mg and 75 mg as target dose.

Reference product
None.

Duration of study treatment
Planned: 36 months of treatment including a three-week up-titration period and a follow-up examination taking place 30–40 days after the end of treatment.

Criteria for evaluation

Efficacy
Not applicable (no efficacy analysis was performed, owing to premature termination of this study).

Pharmacodynamics
Not applicable

Pharmacokinetics
Not applicable

Safety
Adverse events, standard clinical laboratory variables, 12-lead resting electrocardiography, vital signs, body weight, intraocular pressure, peripheral visual field measurement. Body mass index was also planned as a safety measure, but was not used in the analysis.

Statistical methods
Study discontinued; descriptive safety analysis only.

Interim analysis
None.

Summary of results

Study subjects
Six subjects were enrolled by invitation after completion of the double-blind study (MRZ 92759-0707/1). Recruitment was ended early owing to the premature termination of the study as a whole.

Efficacy results
Not applicable

Pharmacodynamic results
Not applicable

Pharmacokinetic results
Not applicable

Safety results
Three adverse events occurred in more than one subject: moderate anxiety (in two CIN patients), moderate headache (in one CIN patient and the one MS patient) and hypoesthesia (oral hypoesthesia and facial hypoesthesia in one CIN patient each and hypoesthesia ("numbness of right side") in the one MS patient).
No serious or severe adverse events were recorded in this study; most were of moderate intensity. Two subjects were withdrawn because of adverse events (one because of right-side hypoesthesia and one because of tremor, dizziness, oral hypoesthesia and anxiety).

Conclusions

The study was terminated prematurely by the sponsor according to protocol because new scientific data became available which showed that the continuation of the study was not justified as the analysis of the main study MRZ 92579 0707/ 1 showed that the treatment with neramexane brought no detectable clinical advantage to CIN or MS patients. The few results available, concerning drug safety, were consistent with the known safety profile of neramexane and did not raise any new issues about its safety or tolerability.