Manuscript title: MD1003 (high dose Pharmaceutical grade Biotin) for the treatment of chronic visual loss related to optic neuritis in multiple sclerosis: A randomized, double-blind, placebo-controlled study

Journal: CNS Drugs

Authors: Ayman Tourbah, Olivier Gout, Alain Vighetto, Véronique Deburghgraeve, Jean Pelletier, Caroline Papeix, Christine Lebrun-Frenay, Pierre Labauge, David Brassat, Ahmed Toosy, David-Axel Laplaud, Olivier Outteryck, Thibault Moreau, Marc Debouverie, Pierre Clavelou, Olivier Heinzlef, Jérôme De Sèze, Gilles Defer, Frédéric Sedel, Carl Arndt

Corresponding author: Professor Ayman Tourbah, Department of Neurology and Faculty of Medicine, CHU de Reims, and UCRA, Reims, France, LPN EA 2027 Université Paris 8, Saint-Denis. Email: atourbah@chu-reims.fr

Online Resources 2. Inclusion and exclusion criteria

Inclusion criteria

- Signed and dated written informed consent form in accordance with local regulations: having freely given their written informed consent to participate in the study
- Diagnosis criteria of multiple sclerosis (MS) fulfilling the actualized McDonald criteria (Polman et al., 2011)
- Uni-or bilateral optic neuropathy with worst eye visual acuity (VA)≤ 5/10 confirmed at 6 months
- Worsening of VA during the last 3 years (at least 1/10 point)
- Patient aged 18–75 years
- Likely to be able to participate in all scheduled evaluations and complete all required study procedures
- In the opinion of the Investigator, the patient was likely to be compliant and had a high probability of completing the study.

Exclusion criteria

- Optic neuritis (ON) relapse within the 3 months before inclusion
- Presence of other ocular pathology (glaucoma, cataract, retinopathy, anterior uveitis, myopia >7 dioptrics, intraocular pressure >20 mmHg, amblyopia, retinal or optic head abnormalities (drusen, dysversion)
- Bilateral VA < 1/20

- Visual impairment caused by ocular flutter or nystagmus
- Patients with uncontrolled hepatic disorder, renal or cardiovascular disease, or cancer
- Patients with hypersensitivity to excipients in biotin or MD1003
- Patients treated with any new medication for MS (immunomodulators, immunosuppressive) but fampridine, initiated less than 3 months prior to inclusion
- Treatment with fampridine initiated less than 1 month prior to inclusion
- Laboratory tests out of normal range according to the reference laboratory values. Deviations could be accepted if considered clinically insignificant for the conduct of study by the Investigator
- Patients with history or presence of alcohol abuse or drug addiction
- Pregnant or breastfeeding women
- Patients likely to be non-compliant to the study procedures or for whom a long-term follow-up seemed difficult to achieve
- Normal Retinal Nerve Fiber Layer (RNFL) at optical coherence tomography (OCT)
- Women of childbearing age without effective contraception (oral pill or intrauterine contraceptive device).

References

Polman CH, Reingold SC, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Ann Neurol. 2011;69:292-302.