

## **A Phase 1b, open-label study to evaluate the safety and tolerability of the putative remyelinating agent, liothyronine, in individuals with multiple sclerosis**

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### **Objective:**

To determine the safety and tolerability of ascending doses of liothyronine in individuals with multiple sclerosis (MS).

### **Background:**

While numerous immune modulating therapies exist for MS, there is an urgent need for therapies that promote remyelination and reduce neurodegeneration. Thyroid hormones play a role in early central nervous system (CNS) development including promotion of myelination, and several animal studies suggest that tri-iodothyronine (T3) can regulate oligodendrocyte differentiation and maturation. Thus liothyronine (synthetic T3) has the potential to induce remyelination and limit secondary neurodegeneration in MS.

### **Design/Methods:**

We enrolled 20 patients with relapsing (RRMS) or progressive MS in this single center trial of oral liothyronine for 24 weeks. Every participant received liothyronine according to a standardized dose-titration schedule. Eligibility criteria included euthyroid patients, 18 to 58 years old, 2010 McDonald criteria clinically definite MS and Expanded Disability Status Scale (EDSS) score of 3.0-7.5. Subjects were excluded if they had thyroid dysfunction, adrenal insufficiency, ongoing liver/renal disease, or other major medical illnesses. The primary endpoint was safety and tolerability of liothyronine. Secondary endpoints included effects on patients' clinical status (EDSS, MSFC, SDMT). Blood and spinal fluid were collected at baseline and end of study for exploratory biomarkers of treatment response.

### **Results:**

Of 20 patients enrolled, 18 completed the study; 9 women and 9 men, 11 RRMS, mean age 46.1, baseline mean EDSS 4.4. Most common adverse events included gastrointestinal distress and abnormal thyroid function tests, although no clinical thyrotoxicosis occurred. Liothyronine was overall tolerated well without treatment-related severe or serious adverse events or evidence of disease activation/clinical deterioration. Clinical and exploratory endpoints will be presented later.

### **Conclusions:**

Liothyronine appeared safe and was well-tolerated in patients with MS. A larger clinical trial will help assess whether liothyronine can promote oligodendrogenesis and enhance remyelination in vivo, limit axonal degeneration/apoptosis, and improve function.