Introduction
Multiple Sclerosis (MS) is an autoimmune disease characterized by demyelination and axonal loss. Secondary progressive MS (SPMS), is a subtype of MS which is distinguished from its precursor, relapsing remitting MS, by steadily increasing neurological disability. There is currently no effective treatment for secondary progressive MS; however, Dirucotide (MBP8298, a synthetic peptide with a sequence corresponding to 17 amino acid residues 82-98 of human myelin basic protein) exhibits potential as a safe treatment to slow disease progression [1]. Since proton MR Spectroscopy (1H-MRS) is considered a useful technique for evaluating demyelination and axonal integrity, concentration differences seen in metabolites may be useful as markers for disease progression. Objective: to investigate the changes in absolute concentration of metabolites from baseline to week 103 between MBP8298-treated and placebo groups of subjects with SPMS.

Materials and Methods
Subjects
This was a single centre MRI substudy. SPMS subjects were randomized (double-blinded) to intravenous injection of MBP8298 every six months for a period of two years or placebo. All subjects from our centre received 1H-MRS as part of their MR scan. A total of 21 subjects treated with MBP8298, and 24 treated with placebo were included in the analysis.

MR Examinations
The MRI as well as the 1H-MRS examinations were performed on a Philips 3T Achieva MR scanner operating at 2.1 software. The single voxel 1H-MRS experiment consisted of a PRESS sequence (TR/TE=5000/35ms, voxel size = 65x45x18mm, 1024 samples) located just above the ventricles (Fig. 1). Each subject was scanned at study screening (week -4), baseline (week 0) and twice afterward, at week 52 and week 104.

Analysis
Analysis of 1H-MRS data was performed using LCModel [2]. Water-scaling was used, referencing the metabolite signal to the water signal in order to give absolute concentrations in millimolar (mM) for n-acetyl-aspartate (NAA), creatine (Cre), choline (Cho), myo-Inositol (mI) and glutamate (Glu). Metabolite concentrations were tabulated and separated based on MBP8298 and placebo treatment.

Results
The changes in NAA, Cre, Cho, ml and Glu at the pre-scan (-4 weeks), week 0, week 52 and week 104 are shown in the graphs below. The error-bars correspond to standard error.

Discussion
There is no change in absolute metabolite concentrations in either of the cohorts over the two-year period. Although Dirucotide (MBP8298) did not meet the primary endpoint of delaying disease progression, as measured by the Expanded Disability Status Scale, during the two-year MAESTRO-01 Phase III trial in patients with SPMS, MRS is a promising technique for monitoring changes in important metabolites such as NAA and may give insights into the mechanism of disease progression.

References

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