

MS-SMART trial design and recruitment status: a multi-arm phase IIB randomised double blind placebo-controlled clinical trial comparing the efficacy of three repositioned neuroprotective drugs in secondary progressive multiple sclerosis

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Multiple Sclerosis-Secondary Progressive Multi-Arm Randomisation Trial



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Background: Drug repurposing (repositioning) provides an attractive paradigm to accelerate academic-led development of neuroprotective therapies for secondary progressive multiple sclerosis (SPMS). Having systematically reviewed all published animal and human literature to identify the leading candidates, we designed a multi-arm phase IIB trial as an efficient way to evaluate neuroprotective efficacy in SPMS.

Objective: To test if three candidate drugs – chosen from an extensive search of published animal and human literature – slow the rate of brain volume loss in SPMS measured by MRI-derived atrophy rate against placebo.

Methods: MS-SMART (ClinicalTrials.gov NCT01912059) is a multi-centre, multi-arm, double-blind, placebo-controlled phase IIB randomised controlled trial.

Study population: 440 patients with worsening SPMS have been recruited across thirteen UK sites.

Principal eligibility criteria: Patients aged 25-65 inclusive, with an EDSS score of 4.0-6.5 and not on DMT.

Interventions: Oral therapy with either placebo, amiloride 5mg bd, riluzole 50mg bd, or fluoxetine 20mg bd

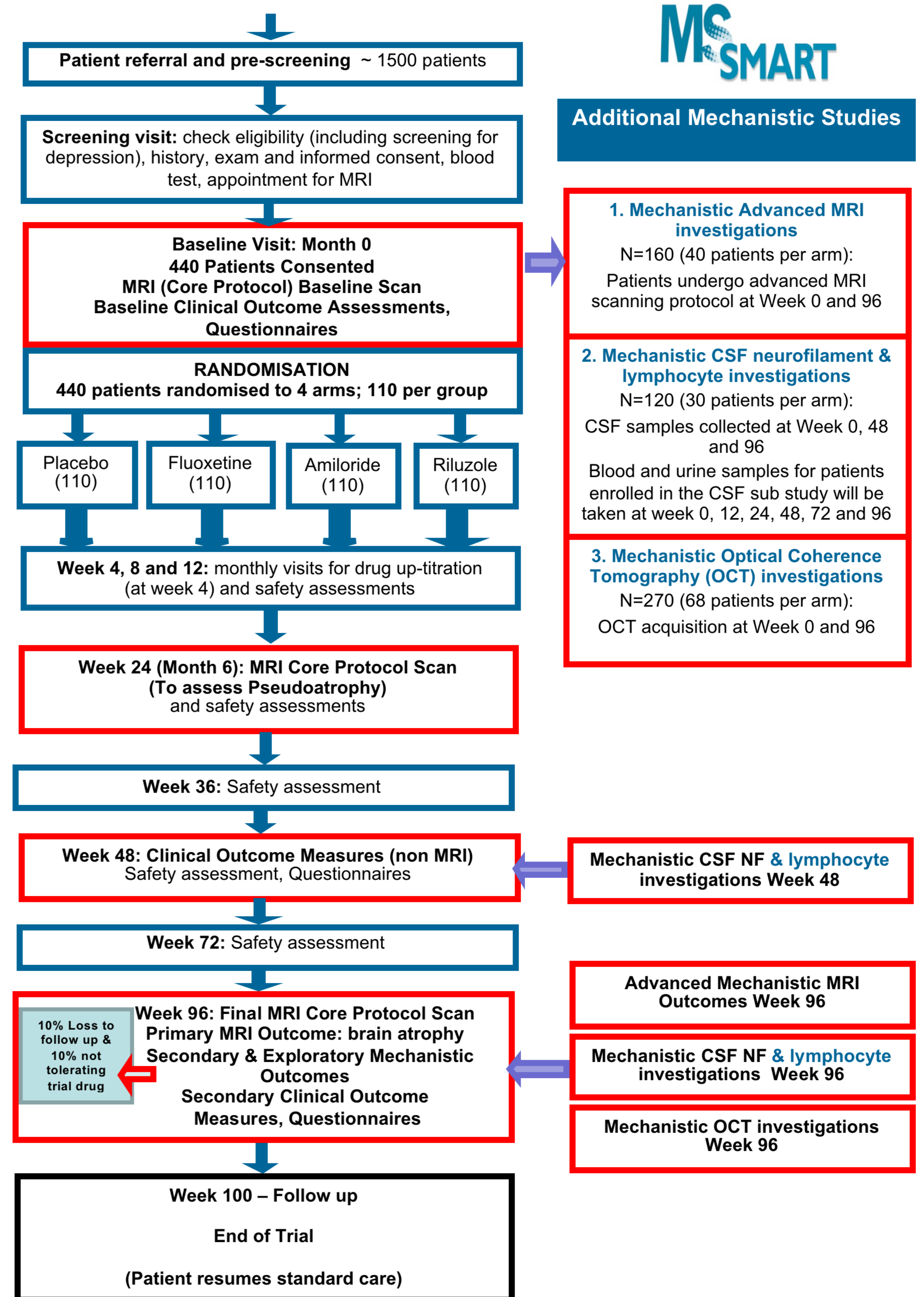
Randomisation: 1:1:1:1

Assessment schedule: Participants will be followed for 96 weeks with outcome data collected after 0, 24, 48 and 96 weeks (see figure).

Endpoints: The primary endpoint is brain atrophy (percent brain volume change) on structural MR imaging at 96 weeks. Secondary endpoints are clinician and patient reported outcome measures, including Multiple Sclerosis Impact Scale v2 and Multiple Sclerosis Walking Scale v2. Exploratory endpoints include: grey and white matter atrophy, cervical cord atrophy, Magnetic Transfer Ratio, MR spectroscopy, cerebrospinal fluid biomarkers, and Optical Coherence Tomography (OCT).

Results: Recruitment commenced in December 2014 and was completed in June 2016. The mean (sd) baseline features are: age 54yrs (7), duration of MS 22yrs (10), duration of SPMS 7yrs (5), and EDSS 5.9 (median 6). Significant co-morbidity ($\geq 10\%$) includes: hypertension, hyperlipidaemia and hypothyroidism.

Conclusion: The cohort recruited is representative of the wider UK SPMS population. The MS-SMART trial opens up a new platform for more efficient trial design and implementation in progressive MS, and will report on the efficacy of three repurposed oral neuroprotective therapies (amiloride, riluzole, and fluoxetine) in 2018.



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Efficacy and Mechanism Evaluation (EME) Programme

