Cladribine to halt deterioration in people with advanced MS

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Cladribine in progressive MS

Choice of compound

- Highly effective in RMS\(^1,2\)
- CNS penetrant\(^3,4\)
- Favourable safety profile\(^5-7\)
- Convenient dosing\(^1,2,5\)

\(^1\) Giovannoni, et al. NEJM 2010
\(^5\) Mao, et al. Mult Scler Rel Disord 2019
\(^6\) Pakpoor, et al. Neurol N2 2015
**Aims & objectives**

- **Aims:** To assess cladribine tablets (3.5mg/kg over 24 months) in a randomised, placebo-controlled trial (1:1) for safety, efficacy, and cost-effectiveness, and to advance mechanistic understanding in pwAMS. To provide evidence to support widespread NHS, and international, adoption of cladribine tablets in pwAMS.

- **Objective:** To investigate whether cladribine tablets 3.5mg/kg over 24 months is an effective DMT in pwAMS as measured using the 9-hole peg test (9HPT) peg speed at 24 months.
Screening Visit [V1] ~300 potential participants [M-1]

Baseline Visit & Randomisation [V2]
- n= 200 participants consented
- Baseline Clinical Outcome Assessments [M0]

Not eligible ~100

Oral cladribine 3.5mg/kg/24 months
- n= 9-10 days administration in year 1
- n= 9-10 days administration in year 2

Oral placebo over 24 months
- n= 9-10 days administration in year 1
- n= 9-10 days administration in year 2

Months 3 – 24 follow up (2 treatment cycles)
- Regular visits [V3, V4, V5, V6, V7, V8] for trial endpoints & safety assessments [M3, M6, M9, M12, M18, M24]

Lost to Follow-up Allowance ≤20%

Cladribine
- n≥ 80

Placebo
- n≥ 80

Primary endpoint analysis at 24 months

End of Study
Key inclusion criteria

EDSS 6.5-8.5
Upper limb deterioration
9HPT ≤ 180sec

Primary outcome

Screening
Randomisation

Placebo
Placebo

-1 0 1 6 12 18 24

Cladribine Tablets
Cladribine Tablets

Outcomes

9HPT

Secondary clinical
ARAT, SDMT, 25ftWT, NFI-MS, EDSS,
ABILHAND-56, SLCVA, Safety

MRI outcomes

• Whole brain volume
• C2 Cross sectional area
• T2 Lesion burden
• T1 Hypo-intense lesions
• Grey matter volumes
• Slowly expanding lesions (SELS)

Health Economics
MSIS-29, EQ-5D-5L, WPAI-GH

Exploratory
Serum neurofilament level & B-Cell subsets

PROM patient related outcome measures; 9HPT 9 hole peg test; SDMT symbol digit modality test; T25WT timed 25 foot walking test; NFI-MS Neurological fatigue index MS; EDSS Expanded disability status scale; ARAT Action research arm test; SLVCA Sloan low contrast visual acuity; MSIS-29 Multiple Sclerosis Impact Scale, WPAI-GH: Work Productivity and Activity Impairment-General Health
Cladribine to halt deterioration in people with advanced multiple sclerosis

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MS Society

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MS Charity

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North Thames

Morris-Saady Charitable Trust

Barts Health NHS Trust

Barts Health

University College Hospitals

BHR, Romford

Kings College Hospitals

Imperial College Hospitals

St. George's Hospital

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NIHR

Clinical Research Network

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SARS-CoV2 risk mitigation

• All staff involved in the conduct of ChariotMS must follow UK wide guidance, guidance provided by nationwide government and local NHS Trusts

• All staff involved in the conduct of ChariotMS will regularly be updated about the impact of new guidance regarding physical distancing and other public health and hygiene guidance issued by national health authorities

• ChariotMS trial team have updated the schedule of assessments to minimize the time participants spend at trial sites where possible

• ChariotMS trial team are exploring the possibility of remote assessments and remote visits which will be part of protocol amendment 1

• Looking into remote blood collection, couriering/delivering study treatment to participants houses & carrying out trial assessment at home under supervision

• Further changes will be made to mitigate COVID-19 risk as needed
Conclusions

• The first DMT-trial focusing on pwAMS, regardless of disease course (PPMS, SPMS) with no upper age limit.

• Developed from the outset jointly with PPI and colleagues across the UK, and beyond.

• Several important secondary and exploratory outcomes (clinical, immunology, MRI) included in patient population with very limited DMT options.

• If successful, ChariotMS will expand the DMT landscape to include pwAMS and provide a platform for add-on therapies.

• SARS-CoV2 risk mitigation under active consideration.