Autologous Stem Cell Transplantation versus Alemtuzumab, Ocrelizumab, Ofatumumab or Cladribine in Relapsing Remitting Multiple Sclerosis (StarMS Trial)

Brittain, G.,[1] Duffy, K. E. M.,[2] Nicholas, R.,[3] Ciccarelli, O.,[4] Scolding, N.,[5] Young, C.,[6] Venneri, A.,[7] Silber, E.,[8] Silva, T.,[9] Kazmi, M.,[8] Coles, A.,[10] Peniket, A.,[11] Giovannoni, G.,[12] Beecher, C.,[13] Cooper, C.,[2] Papaioannou, D.,[2] Walters, S.,[2] Bursnall, M.,[2] Loban, A.,[2] Petrie, J.,[2] Glover, R.,[2] Muraro, P.,[3] Sharrack, S.,[1] Snowden, J.,[1] on behalf of the StarMS trial team

1. Sheffield Teaching Hospitals NHS Foundation Trust. 2. The University of Sheffield. 3. Imperial College Healthcare NHS Trust. 4. University College London. 5. University of Bristol. 6. The Walton Centre NHS Foundation Trust. 7. Brunel University London. 8. King's College Hospital NHS Foundation Trust. 9. Imperial College of Science Technology and Medicine. 10. University of Cambridge. 11. Oxford University Hospitals NHS Foundation Trust. 12. Barts and The London Queen Mary's School of Medicine and Dentistry.13. Sheffield Hallam University.

Background

- Multiple Sclerosis (MS) is a chronic autoimmune disease affecting the central nervous system
- The immune system mistakenly attacks the protective myelin sheath of the nerves, causing damage
- MS leads to impairment in strength, sensation, balance, vision & cognition
- ~150,000 people living with MS in UK
- Symptoms include fatigue, vision, mobility & balance issues
- Autologous haematopoietic stem cell transplantation (aHSCT) is increasingly used as a treatment for patients with active MS, after failure of disease modifying therapies (DMTs)
- Unanswered questions remain about the relative efficacy and safety of aHSCT over high efficacy DMTs (standard of care) in patients with relapsing remitting MS (RRMS) or rapidly evolving severe MS (RES-MS)

Aim

Evaluate the effectiveness and safety profile of aHSCT versus high efficacy DMTs in patients with highly active relapsing remitting MS or treatment naïve rapidly evolving severe MS

Method

- **Design**: Pragmatic, parallel group, open-label superiority trial
- **Participants:** Adults aged 16-55 with diagnosis of MS
- **Sample:** n=94 across 12 UK sites from March 2021 to September 2024
- **Randomisation:** Stratified by site and baseline Expanded Disability Status Scale score (EDSS) (≤4.0 vs >4.0) to aHSCT or clinician selected DMT
- **Primary outcome:** Proportion of participants achieving "no evidence of disease activity" (NEDA) over a 2-year follow-up.
- **NEDA:** Absence of all 3 of the following; protocol defined relapse, 6 months confirmed EDSS progression of at least 1 point & any evidence of MRI disease activity
- **Secondary outcomes:** time to disease activity, immune reconstitution following aHSCT, safety, disability (EDSS), and multiple quality-of-life metrics

aHSCT

1 Mobilisation (Moving the cells)
Medication encourages stem cells into bloodstream to allow easy collection

2 Collection & freezing (Harvesting)
Blood filtered via machine that collects stem cells

3 Conditioning (The wipeout)
Chemotherapy drugs are used to eliminate the 'sick' immune system

4 The transplant (The reboot)
Stem cells from stage 2 are re-infused into blood & give rise to new generation of healthy immune cells

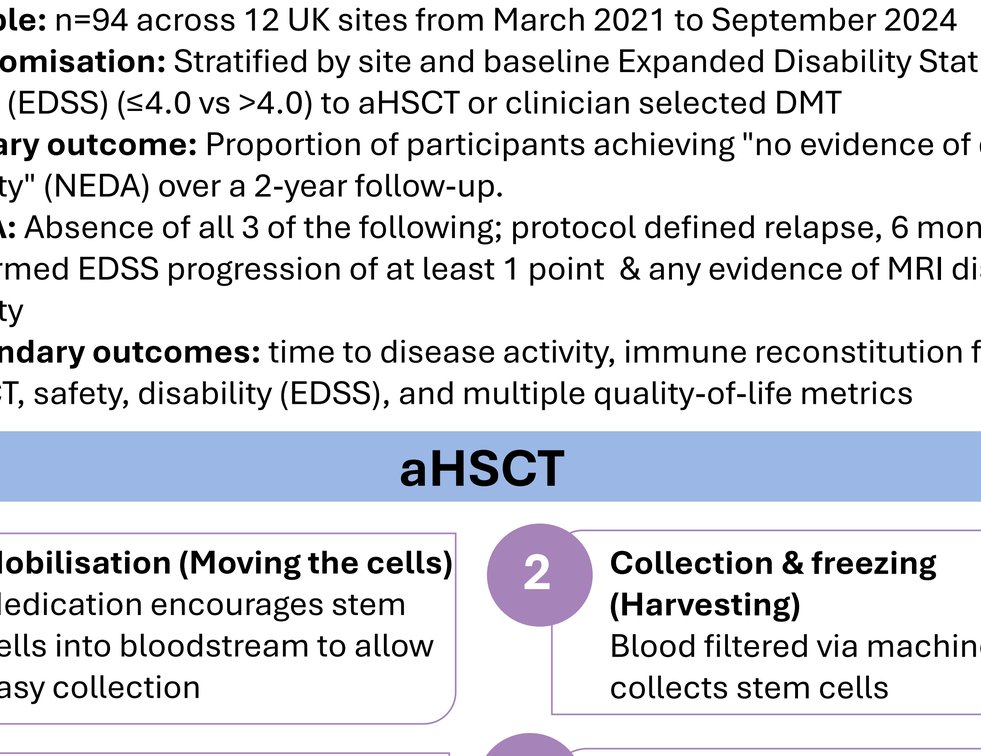
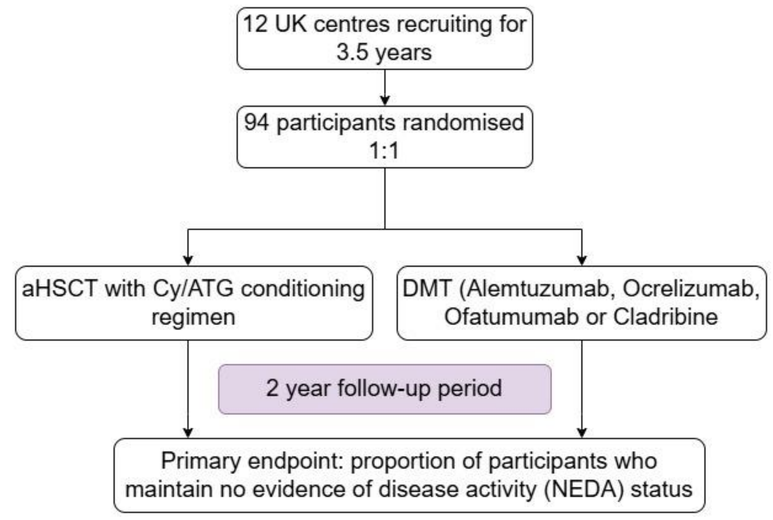


Fig 1: Patient pathway

Study flow



Sites



Fig 2: Symbol map showing recruitment in UK by trial site

Trial site	n
Sheffield	31
University College London	16
Imperial College	12
King's College	10
Nottingham	8
Southampton	6
Leeds	3
Barts	2
Edinburgh	2
St George's	2
Newcastle	1
Walton	1

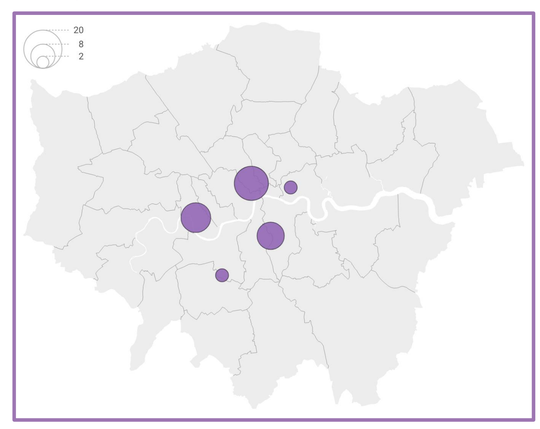


Fig 3: Recruitment by trial site in Greater London

Status

- Participants recruited between March 2021 and September 2024
- Exceeded target sample size of 90
- Last patient last visit scheduled end of September 2026
- Data to be analysed on an intention to treat and per protocol basis
- Results expected Spring 2027

Conclusions / impact

- Provides evidence on the clinical effectiveness of aHSCT compared to current high-efficacy DMTs for highly active RRMS and RES-MS
- Potential to influence MS clinical guidelines
- If aHSCT is more efficacious than the 4 DMTs, potential NHS cost savings
- Improve quality of life, patient outcomes; reduce number of relapses

References:
Brittain, G., Petrie, J., Duffy, K. E. M., Glover, R., Hullock, K., Papaioannou, D., Roldan, E., Beecher, C., Bursnall, M., Ciccarelli, O., Coles, A. J., Cooper, C., Giovannoni, G., Gabriel, I., Kazmi, M., Kyriakou, C., Nicholas, R., Paling, D., Peniket, A., Scolding, N., ... StarMS trial team (2024). Efficacy and safety of autologous haematopoietic stem cell transplantation versus alemtuzumab, ocrelizumab, ofatumumab or cladribine in relapsing remitting multiple sclerosis (StarMS): protocol for a randomised controlled trial. *BMJ open*, https://doi.org/10.1136/bmjopen-2023-083582

Contact:
star-ms@sheffield.ac.uk

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