

[*A Whirlwind*] Research Update

**Sussex MND Care & Research Network Study Day
Tuesday 12th November 2024**

Dr Andrew Barritt

Consultant Neurologist and Honorary Senior Lecturer

MND Research in Sussex



Population Studies

MND Register

Cog. & Behav. Studies

Carers' Support

Biomarker Studies

Brain
(MIROCALS ancil.)



MIROCALS
Modifying Immune Response & Outcomes
in Amyotrophic Lateral Sclerosis

Spinal Cord
(CordiALS)

Non-coding / micro RNAs
Preclinical models of MND

Clinical Trials with IMPs

MND-SMART
new IMP being added

MND-SMART
Clinical trials for MND

New IMP Studies
aiming for 2025!

MRI
New TBC

CTIMPs: **MND-SMART**

= MND Systematic Multi-Arm Adaptive Randomised Trial

= Double-blind, placebo-controlled, Phase 2-3 trial

Aim:

To assess clinical effects of *potential* neuroprotective drugs

Intervention:

Medicines already approved in humans for another disease thus licensed with established safety / regulatory record.

Medicines which can be taken safely via NGT / gastrostomy

CTIMPs: **MND-SMART**

IMPs can be dropped after pre-defined interim analyses
...and new IMP treatment arms initiated

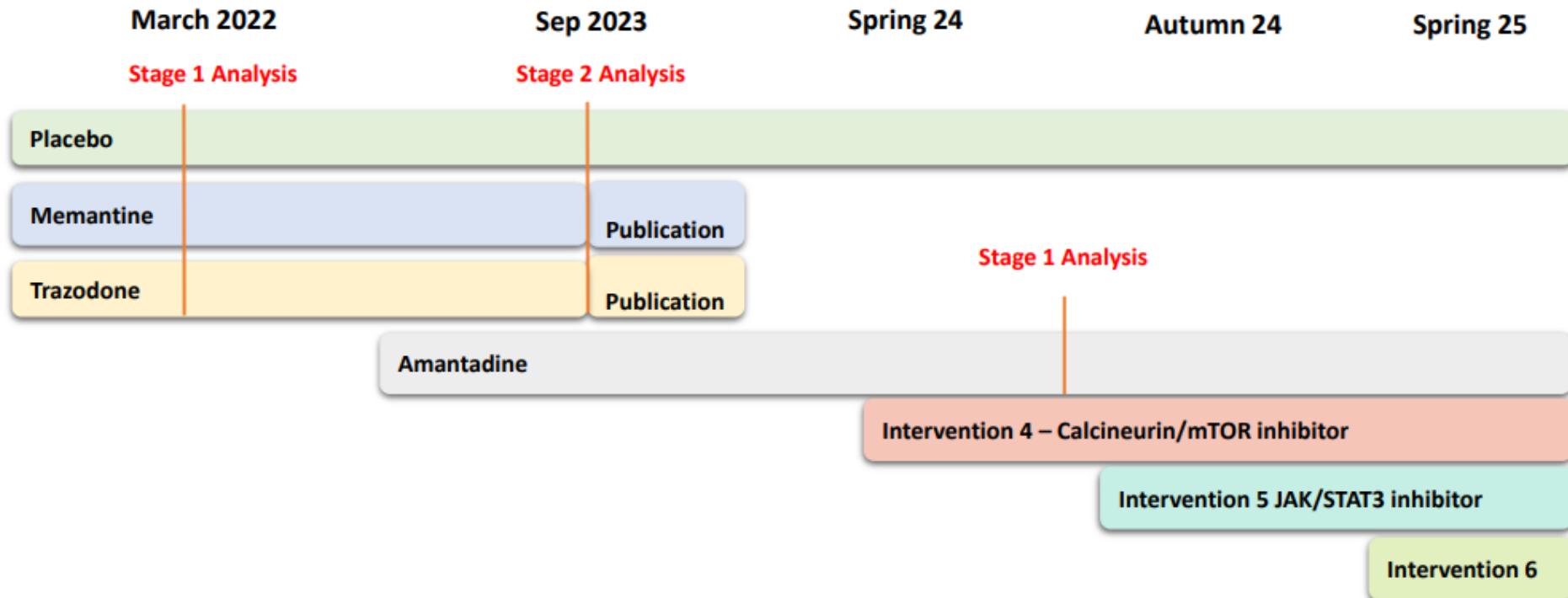
Study Population: ALS (El-Escorial poss-def), PMA and PLS
+/- gastrostomy +/- NIV

Primary Endpoints: = rate of change in ALSFRS-R over 18mo;
= survival

Secondary Endpoints: = time to King's stage 4a or 4b
= change in ECAS, FVC, HADS, EQ-5D-5L

CTIMPs: MND-SMART

MND-SMART
Clinical trials for MND



MND SMART PPI Event March 2024

Future randomisation:

1 : 1 : 1 either to placebo or Amantadine or Tacrolimus
...and patients from dropped arms can re-enrol

CTIMPs: **MND-SMART**

Amantadine

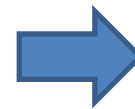
= anti-viral, anti-parkinsonian and anti-hyperalgesic activities.

= UK license for Parkinson's Disease, post-herpetic neuralgia
and Influenza A

= also used in MS for fatigue (unlicensed)

= ?reduces nerve cell toxic damage

= ?clears TDP-43 aggregates



*So hence its
selection for
MND-SMART*

<https://mnd-smart.org/>

<https://www.mndcsg.org.uk/clinical-research/studies/mnd-smart>

CTIMPs: TBC

Brighton is in discussions to open a Phase 2 study Spring 2025
and has expressed interest in another in development

Interventional Studies: [PIC site]

Virtual peer-to-peer support programme for carers of MND

Intervention: Weekly sessions over 3 months

Study Population: Informal carers of people living with MND who are also being considered for NIV, cough assist or gastrostomy

Outcome: Caregivers' mood and coping strategies

CTIMPs: [via other sites]

Lighthouse II

...as of Sept 2024

Current IMP: Trimueq (anti-retroviral therapy)

Study Population: ALS (Gold Coast Criteria)
not if patient is HLA-B*5701 positive

Interventional Studies: [via other sites]

OptiCALS

Increasing energy available for nerve cells may make them more resistant to the neurodegenerative process but the ideal way to achieve that is not known

- Intervention:** Access to online portal “OptiCALS package”
= Videos, Dietary Info & Interactive tools
with daily calorie targets & feedback
- Study Population:** ALS (Gold Coast Criteria) within 2.5 yr
- Outcomes:** Disease progression; QoL

Observational Studies: [via other sites]

ALS Biomarkers Study: (King's)

Data Collected: Clinical & repeated samples of:
Blood +/- CSF, Skin biopsy,
Urine and Stool

Study Population: ALS (El-Escorial prob-def), PMA and PLS
and healthy controls



Gene-specific Studies [via other sites]

MAGNET Platform (King's): Multi-arm, Adaptive, Group sequential trial NETwork to evaluate drug efficacy in pwALS

Current IMP: Lithium (Prelude Study)

Study Population: ALS (El-Escorial poss-def)
patients with homozyg.UNC13A variation

ACORN / C9orf72 Cohort Study (Oxford):

Data Collected: Clinical, Imaging & Blood et al. samples

Study Population: pwALS + C9orf72 mutation,
family members and healthy controls

Gene-specific Studies [via other sites]

Ionis FUS-ALS Trial: Phases 1-3 (King's)

IMP: ION363 to reduce FUS production

Population: ALS with confirmed FUS mutation

ATLAS Trial: Phase 3 (Sheffield)

IMP: BIIB067 aka Tofersen

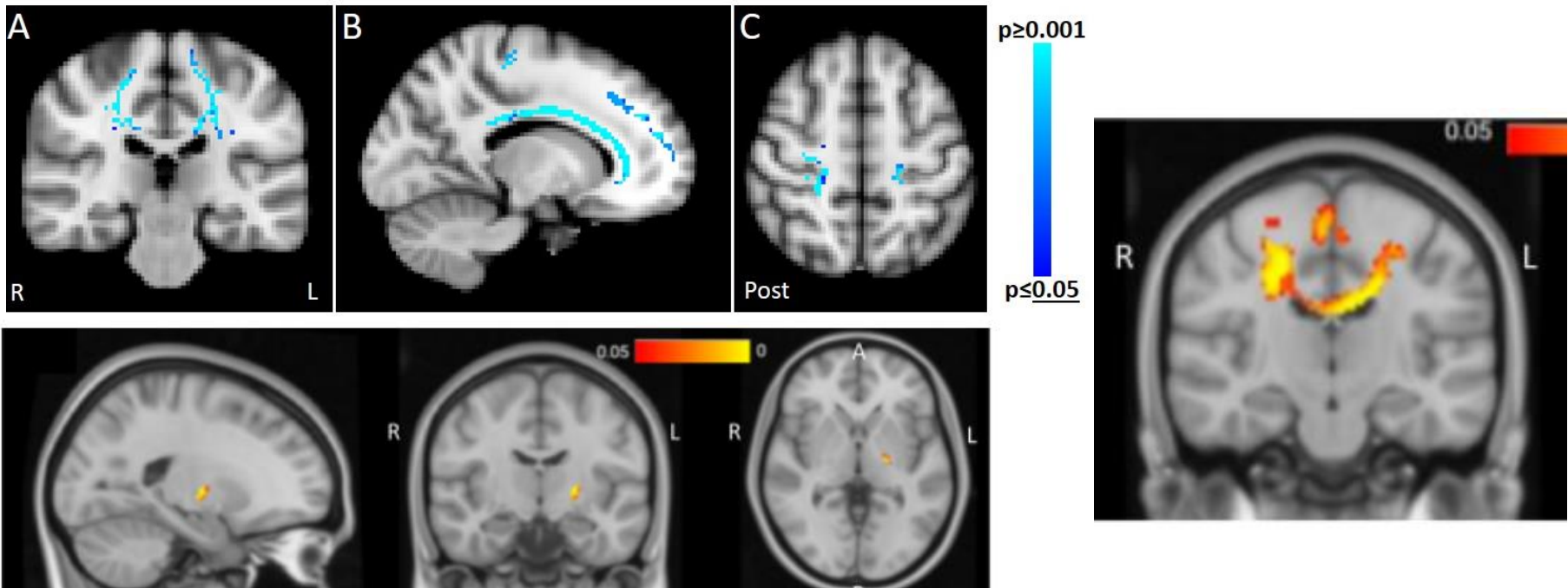
Population: Pre-symptomatic carriers of SOD1 mutations
(albeit very specific mutations...)



Local Biomarker Studies: **MIROCALS MRI**

Brain MRI scans: NODDI (and other types)

Aim: to understand mechanisms of neurodegeneration in ALS using advanced forms of brain MRI (called NODDI) and associations with clinical measures as well as blood & spinal fluid markers



Local Biomarker Studies: **CordiALS**

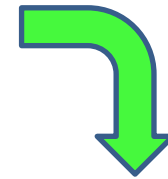
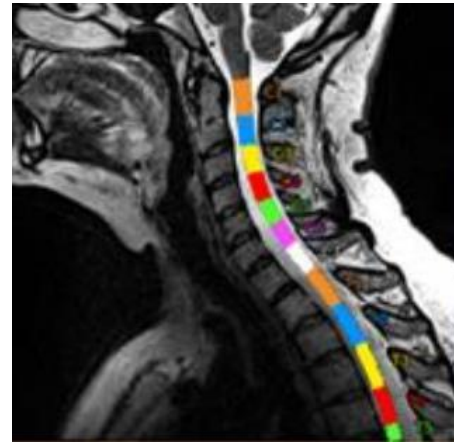
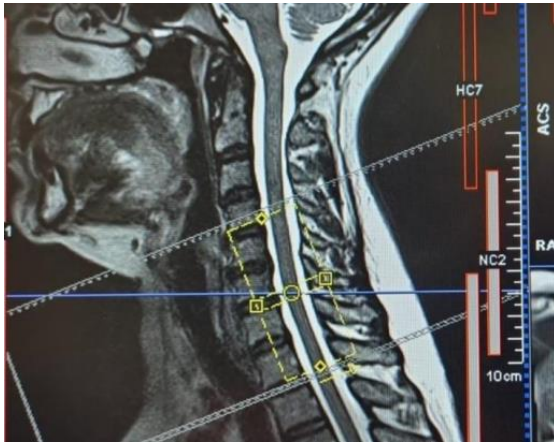
Cervical Spinal Cord MRI scans: NODDI (and other types)

Pilot study with Dr Samira Bouyagoub at UoS

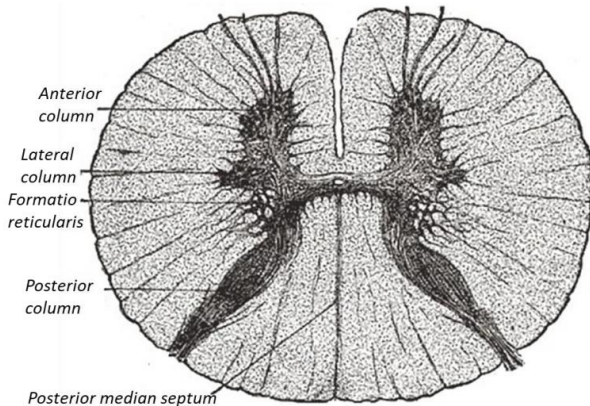
Participants: 15 pwALS + upper limb symptoms
+ 15 Controls
recruitment closing

Investigating differences between pwALS and controls to power a combined brain + cord study (*grant in preparation*)

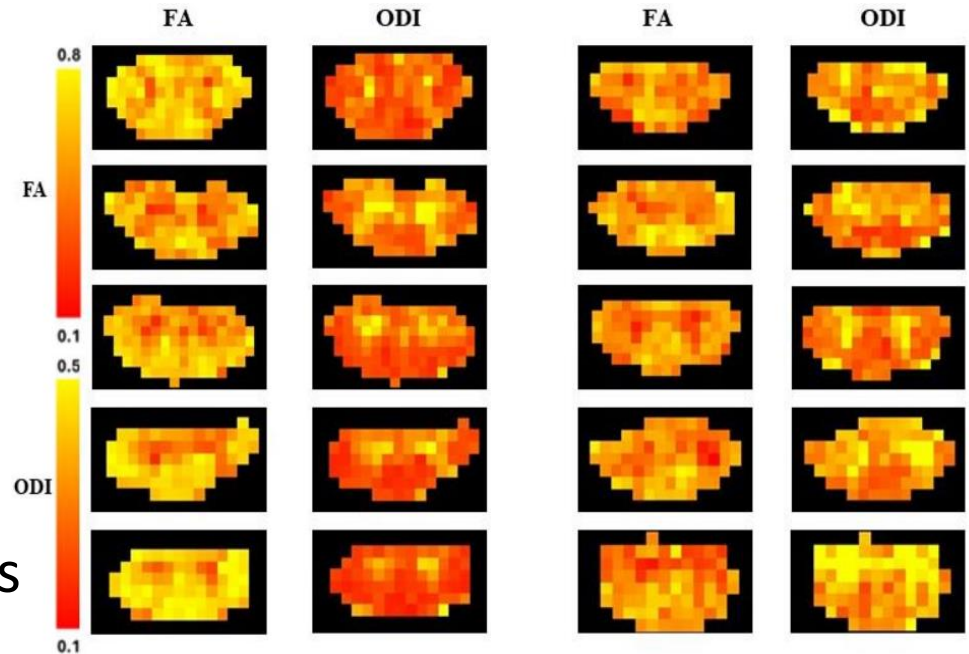
Biomarker Studies: CordiALS Imaging



ALS



Controls



With Alexandra Ford
& Dr Samira Bouyagoub

Biomarker Study: **CLIMB-ALS**

A combined brain + cord MRI study using NODDI

...coupled with blood biomarkers (neurofilament levels)

Grant proposal submitted – watch this space!

Other Clinical Research Trials

Trials potentially available at other sites:

MND Association

<https://www.mndassociation.org/research/clinical-trials/treatment-trials>

UK MND CSG

Collaboration Research Teams to improve access to studies

<https://www.mndcsg.org.uk/>

Acknowledgements



CISC

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