2322 RESULTS OF THE AUSTRALIAN RESCUE-ALS TRIAL: A PHASE 2, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF CNM-AU8 TO SLOW DISEASE PROGRESSION IN ALS

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Objective The objective of RESCUE-ALS was to evaluate the efficacy and safety of CNM-Au8, a suspension of catalytic gold nanocrystals that enhance cellular energy metabolism, as a disease-modifying treatment for amyotrophic lateral sclerosis (ALS).
Methods Participants were randomized 1:1 (active:placebo). The primary endpoint was the percent change in the summated motor unit index (MUNIX) scores for four selected limb muscles after 36 weeks of treatment. Secondary/exploratory endpoints included respiratory function, ALS disease progression, and quality of life.
Results In total, 49 participants were screened and 45 enrolled (73% limb onset, 27% bulbar). In the CNM-Au8 30mg cohort, there was significant reduction of ALS disease progression (occurrence of death, tracheostomy, or need for non-invasive ventilatory support or gastrostomy tube placement; 37% absolute risk reduction, p=0.02), improved proportion free from > 6-point ALSFRS-R decline (49% vs. 8%; p=0.04, chi-square test), improved quality of life (LS mean difference: 0.9; 95% CI: 0.2 to 1.6; p=0.02). Additionally, there was a trend for improvement in the summated MUNIX score to week 36 (primary endpoint) that was more prominent in limb-onset ALS (LS mean difference: 20.9%, 95% CI: -2.2% to 44.0%, p=0.074), and a trend for improvement of respiratory dysfunction. CNM-Au8 was well-tolerated, and no safety signals were observed.
Conclusions CNM-Au8, in combination with riluzole, was safe and well-tolerated in ALS. CNM-Au8 may provide functional benefit by slowing ALS disease progression.

2344 THE 1H-MRS METABOLITE SIGNATURE OF CORTICAL HYPEREXCITABILITY IN ALS

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Cortical hyperexcitability is an established clinical feature present in the earliest stages of disease onset in ALS and can be used to detect subclinical upper motor neuron dysfunction. The abnormality is believed to reflect an underlying glutamate-induced excitotoxicity implicated in disease pathogenesis and linked to functional motor impairment. While a large body of TMS and MRS research have independently documented the disease signature of ALS, their association remains to be investigated.
Objectives Characterize the relationship between cortical motor hyperexcitability and metabolite abnormalities.

Examine asymmetry differences in hemispheric cortical motor integrity.
Methods 32 non-familial ALS patients and 17 age-education matched healthy controls were recruited. All participants received an MRI scan (3T GE MR750; 32-channel head coil) and single-voxel 1H-MRS (PRESS) data was sequentially acquired from the hand region of the left and right motor cortices. All patients underwent TMS to determine presence of cortical hyperexcitability based on SICI threshold (≤ 5.5).
Results As a whole, ALS patients demonstrated a consistent reduction in NAA/Cr in the left (p=0.02) and right (p=0.01) hand region, without evidence of hemispheric imbalance relative to controls. Patients with cortical hyperexcitability, however, demonstrated significantly higher levels of Glu/Cr and NAA/Cr across both hemispheres (p values < 0.05), relative to patients with a normal SICI. Interestingly, patients with a normal SICI demonstrated a significantly higher degree of hemispheric NAA/Cr imbalance (p=0.04).
Conclusions Cortical excitability is associated with a consistent pattern of metabolite abnormality across cortical hemispheres underlying hand motor function in ALS.

2424 HALLUCINATIONS IN NON-PARKINSON'S NEURODEGENERATIVE DISORDERS: COGNITIVE AND NEUROIMAGING EVIDENCE FOR A TRANS-DIAGNOSTIC ATTENTIONAL THEORY OF HALLUCINATION GENERATION

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Objective To determine the rate of hallucinations across non-Parkinson's neurodegenerative disorders including Frontotemporal Dementia and explore the underlying cognitive and neural basis for the development of these symptoms
Methods Patients were recruited (n=429) and assessed over a 10-year period at the FRONTIER FTD multidisciplinary research clinic. Patients were assessed at their first visit by means of a clinical interview, a battery of neuropsychological tests and MRI. Data was analysed according to 3 tiers; 1) rate of hallucinations across neurodegenerative disorders; 2) the relationship between neural structures, cognition, behaviour and hallucinations and 3) the impact of the *C9orf72* expansion on expression of hallucinations.
Results Tier 1: The majority of cases of hallucinations occurred in patients with bvFTD (22%), Alzheimer's disease (13%), LPA and Corticobasal syndrome (11%). Rate of hallucinations were low for posterior cortical atrophy (9%), Primary progressive aphasia (PPA) including left and right Semantic Dementia (SD; 6%), PPA-non-fluent variant and Progressive supranuclear palsy (0%; p<0.006). Tier 2: Attentional measures differed between groups (all p<0.02) with hallucinators making more frequent attentional and processing speed errors while structural changes affected regions of attentional networks centred on the prefrontal cortex (p<0.001). Tier 3: Attentional processes were also implicated in *C9orf72* carriers with hallucinations as well as visual

functions including memory and spatial abilities ($p<0.05$) while structural changes were focused on the thalamus ($p<0.001$).

Conclusion Hallucinations are present across neurodegenerative syndromes and highest in FTD. Attentional subsystems and networks are implicated in the generation of these features that dissociate across *C9orf72* and sporadic bvFTD.

2431 PREDICTIVE ACUTE NYSTAGMUS CHARACTERISTICS IN POSTERIOR CIRCULATION STROKE DIAGNOSIS

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Objectives The acute nystagmus characteristics of posterior circulation stroke (PCS) were assessed and compared to acute vestibular neuritis (AVN) in the emergency department (ED)

Methods Video-nystagmography (VNG) was prospectively conducted in ED at one Australian metropolitan tertiary referral hospital over a three-year period, recording ictal nystagmus in 101 patients with radiologically confirmed PCS and 104 patients with AVN.

Results PCS locations were in the brainstem alone (34.7%), cerebellum alone (29.7%), both cerebellum and brainstem (19.8%) or other/multiple locations (15.8%) were recruited. Common PCS territories included: posterior-inferior-cerebellar-artery (38.6%), multiple-territories (20.8%), pontine-perforators (18.8%), anterior-inferior-cerebellar-artery (6.9%) and posterior-cerebral-artery (5.9%).

In PCS, 50.5% of patients had no spontaneous nystagmus. Remaining PCS patients had primary position horizontal (37.2%), vertical (8.9%) and torsional (3.9%) nystagmus. Horizontal nystagmus was 51.7% ipsiversive and 48.3% contraversive in 29 lateralised PCS. 28.4% of PCS patients had pathologic gaze-evoked nystagmus. Most PCS patients with horizontal nystagmus (60.5%) had unidirectional 'peripheral-appearing' nystagmus

In contrast, AVN patients almost universally (98.1%) had primary position horizontal nystagmus. No AVN patient had gaze-evoked nystagmus. Horizontal nystagmus with SPV$\geq$5.4 / s distinguished AVN from PCS with sensitivity and specificity of 90.3% and 89.1%.

Absent nystagmus, gaze-evoked direction-changing nystagmus, and vertical/torsional nystagmus were all highly specific for PCS (100%, 100% and 98.1%).

Conclusion Most patients with PCS had concerningly benign features such as absent nystagmus or unidirectional 'peripheral-appearing' horizontal nystagmus acutely. Comparatively, all AVN patients had nystagmus acutely. This study reinforces a new paradigm in vestibular neurology that absence of findings does not equate to absence of pathology.

2212 PRETREATMENT PERIPHERAL IMMUNE CELL RATIOS AS PROGNOSTIC BIOMARKERS IN GLIOMA PATIENTS

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Background In the glioma microenvironment, elevated immune cell ratios are posited to reflect systemic response to malignancy. Given the dearth in clinically significant molecular markers to predict prognosis, there is potential for immune cell ratios to serve as low-cost and readily available prognostic markers.

Objectives This study evaluated the ability for pretreatment peripheral immune cell ratios (Neutrophil-to-Lymphocyte Ratio, NLR, and Monocyte-to-Lymphocyte Ratio, MLR) to predict overall survival (OS) and modified Rankin Scale (mRS) at admission, 6 months and 12 months post-diagnosis. It also explored relationships between immune cell ratios and clinicopathological parameters (tumour location, tumour size, tumour grade, IDH-1 mutation, MGMT promoter methylation status).

Methods Pretreatment NLR and MLR were analysed retrospectively in 64 glioma patients from Royal Melbourne Hospital. OS was evaluated with the Kaplan-Meier method. Prognostic factors for OS and mRS were evaluated with univariate and multivariable regression analyses.

Results Higher pretreatment NLR (>4.7), compared to lower pretreatment NLR (≤4.7), predicted higher mean admission mRS ($p<0.001$) and 6-month mRS ($p=0.02$). Higher NLR was associated with poor functional outcome (mRS 3–6) at admission ($p<0.001$) and 6 months ($p=0.001$). Higher pretreatment MLR (>0.35) predicted poorer OS ($p=0.02$). Higher NLR was associated with larger tumour diameter ($\geq$5cm) ($p=0.02$).

Conclusion To our knowledge, this was the first study to evaluate the association between immune cell ratios and mRS. This study demonstrated that NLR and MLR can serve as prognostic markers to predict functional outcomes and OS in glioma patients, which allows us to identify high-risk patients in need of further treatment.

2275 IVIG-EXPOSURE AND THROMBOEMBOLIC EVENT RISK: COHORT STUDY USING THE UK BIOBANK

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