Movement Disorders: 04

**VISUAL DYSFUNCTION PREDICTS COGNITIVE IMPAIRMENT AND WHITE MATTER DEGENERATION IN PARKINSON’S DISEASE**

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10.1136/jnnp-2022-ABN.307

**Introduction**
Visual dysfunction predicts Parkinson’s dementia but whether this translates to structural change is not known. We aimed to identify longitudinal white matter changes in Parkinson’s with low visual function and who developed mild cognitive impairment (MCI).

**Methods**
We used fixel-based analysis to examine longitudinal white matter change in Parkinson’s. Diffusion MRI and clinical assessments were performed in 77 patients (22 low/55 high visual performers; and 13 MCI/51 normal cognition) and 25 controls at baseline and after 18 months. We compared micro-structural changes in fibre density, macro-structural changes in fibre cross-section and combined fibre density and cross-section across white matter, adjusting for age, gender and intracranial volume.

**Results**
Parkinson’s with low visual performance showed worse cognition at follow-up (r=−0.386, p=0.024) and were more likely to develop MCI than those with normal vision (p=0.008). Parkinson’s with poor visual function showed diffuse micro-structural and macro-structural changes at baseline, whereas those with MCI showed fewer baseline changes. At follow-up, Parkinson’s with low visual function showed widespread macro-structural changes with up to 22% further reductions in fibre cross-section, involving the fronto-occipital fasciculi, external capsules, and middle cerebellar peduncles bilaterally. No longitudinal change was seen in baseline MCI or in MCI converters, even when combining the two groups.

**Conclusions**
Parkinson’s with poor visual function showed increased white matter damage over time, providing further evidence for visual function as a marker of imminent cognitive decline.

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**Muscle & Nerve: 02**

**SUNFISH PART 2: 24-MONTH EFFICACY AND SAFETY OF RISDIPLAM IN TYPE 2/3 SMA**

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10.1136/jnnp-2022-ABN.309

SUNFISH (NCT02908685) is a multicentre, two-part, randomised (2:1, risdiplam:placebo), placebo-controlled, double-blind study in individuals with Type 2/3 spinal muscular atrophy (SMA; inclusion criteria 2–25 years at enrolment). SUNFISH investigates efficacy and safety of risdiplam, a centrally and peripherally distributed oral survival of motor neuron 2 pre-mRNA splicing modifier. Risdiplam (EVRYSDI™) has been approved by the US Food and Drug Administration for the treatment of individuals with SMA, aged 2 months and older.

In Part 1 (N=51) the safety, tolerability and pharmacokinetics/pharmacodynamics of different risdiplam dose levels were assessed. Part 2 (N=180) assessed the efficacy and safety of the Part 1-selected dose of risdiplam versus placebo in Type 2 and non-ambulant Type 3 SMA. Individuals received risdiplam or placebo for 12 months; all individuals then received risdiplam until Month 24, when they had the opportunity to enter the open-label extension phase.

In Part 2, the primary outcome of the study was met, showing a statistically significant difference in change from baseline in 32-item Motor Function Measure total score at Month 12 between individuals treated with risdiplam (n=120)