gene (SMN1). Copies of a similar gene (SMN2) modify disease severity. In a phase 1 study, SMN GRT onasemnogene abeparvovec (AVXS-101) improved outcomes of symptomatic SMA patients with two SMN2 copies (2xSMN2) dosed ≤6 months. Because motor neuron loss can be insidious and disease progression is rapid, early intervention is critical. This study evaluates AVXS-101 in presymptomatic SMA newborns.

Methods SPR1NT is a multicenter, open-label, phase 3 study (NCT03350309) enrolling ≥27 SMA patients with 2–3xSMN2. Asymptomatic infants ≤6 weeks receive a one-time intravenous AVXS-101 infusion (1.1×10¹⁴ vg/kg). Safety and efficacy are assessed through study end (18 [2xSMN2] or 24 months [3xSMN2]). Primary outcomes: independent sitting for ≥30 seconds (18 months [2xSMN2]) or assisted standing (24 months [3xSMN2]).

Results From April–September 2018, 7 infants received AVXS-101 (4 female; 6 with 2xSMN2) at ages 8–37 days. Mean baseline Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) score was 41.7 (n=6), which increased by 6.8, 11.0, 18.0, and 22.5 points at day 14 (n=4), month 1 (n=3), 2 (n=3), and 3 (n=2). As of January 31, 2019, 15 asymptomatic infants have been enrolled in SPR1NT and dosed with AVXS-101. Updated data available at the time of the congress will be presented.

Conclusions Preliminary data from SPR1NT show rapid motor function improvements in presymptomatic SMA patients.

016 ONE DISEASE OR THREE: IS FRONTOTEMPORAL DEMENTIA – MOTOR NEURON DISEASE A DISTINCT ENTITY?

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Introduction Frontotemporal dementia-motor neuron disease (FTD-MND) is diagnosed when patients meet criteria for the diagnosis of both FTD and MND, but the mode presentation of this disorder is currently unknown. This study aimed to compare the mode of presentation, and profiles of behavioural and language disturbances, of FTD-MND with that of other FTD phenotypes using a data-driven approach.

Methods 31 FTD-MND, 119 bvFTD, 47 PNFA, 42 SD patients and 127 controls underwent comprehensive clinical, neuropsychological and neuroimaging assessments. Z-transformed scores were used to compare the severity of behavioural and language domains in each disease group. Two-step cluster analysis profiled patient subgroups. Voxel-based morphometry investigated differential patterns of cortical atrophy between groups.

Results Overall, FTD-MND patients presented with behavioural or language disturbances less frequently than FTD phenotypes, but mixed behavioural-language presentations were more common. FTD-MND patients demonstrated less severe disinhibition, apathy and semantic deficits relative to bvFTD and SD respectively. Behavioural and language deficits were of comparable severity in FTD-MND, unlike other FTD phenotypes where behaviour was worse than language (bvFTD) or language worse than behaviour (PNFA, SD). In cluster analysis, FTD-MND patients were evenly distributed across three subgroups designated as ‘mild mixed’, ‘language dominant’ and ‘behavioural dominant’. Relative to the ‘mild mixed’ group, ‘language dominant’ patients demonstrated more atrophy of the anterior temporal lobe and peri-insular regions, while ‘behavioural dominant’ patients displayed more prefrontal atrophy.

Conclusions FTD-MND does not present as a uniform syndrome. Rather, there may be at least three subgroups that demonstrate distinctive cognitive, behavioural, and neuroanatomical characteristics.