negative in serum and cerebrospinal fluid. There was imaging improvement with limited functional recovery following initial treatment with intravenous methyl prednisone, plasma exchange, intravenous immunoglobulin, and rituximab. This case also highlights the need to identify candidate biomarkers associated with seronegative neuromyelitis optica spectrum disorder to improve early diagnosis and early management.

2595 EFFICACY AND SAFETY OF AVALGLUCOSIDASE ALFA IN PARTICIPANTS WITH LATE-ONSET POMPE DISEASE AFTER 145 WEEKS' TREATMENT: PHASE 3 COMET TRIAL

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Objectives Report efficacy/safety of avalglucosidase alfa (AVAL) in participants with late-onset Pompe disease in the extended-treatment period (ETP) of COMET (NCT02782741) at 145 weeks from treatment initiation.

Methods Following a 49-week primary-analysis period (PAP), participants could enter the ETP. 100 participants (age 16–78 years) enrolled in the PAP.

Results All 51 who received AVAL 20mg/kg every 2 weeks (qow) in the PAP (AVAL-arm) continued this in the ETP. Of 49 who received alglucosidase alfa (ALGLU) 20mg/kg qow in the PAP, 44 entered the ETP switching to AVAL 20mg/kg qow (Switch-arm). Improvement or stabilization trends from Baseline to Week 145 were observed for primary and secondary outcomes of respiratory and motor function. Changes (LS mean[SE]) in upright forced vital capacity%predicted: AVAL-arm, +1.40(1.21); Switch-arm, +1.18(1.32) and 6-minute walk test distance: AVAL-arm, +20.65(9.60)m; Switch-arm, +0.29(10.42)m. Similar trends occurred in other Week-145 outcomes. Treatment-emergent adverse events (AEs) in the ETP occurred in 49(96.1%) AVAL-arm and 43(97.7%) Switch-arm participants. Five discontinued during the ETP for 6 treatment-emergent AEs; 4 treatment-related (ocular hyperemia, erythema [in same participant], urticaria, respiratory distress) and 2 non-treatment-related (acute myocardial infarction, pancreatic adenocarcinoma). In the ETP, 13(25.5%) AVAL-arm and 12(27.3%) Switch-arm participants had treatment-emergent serious AEs (SAEs); 3 and 2 of them, respectively, had treatment-related SAEs. Switch-arm participants showed no safety/immunogenicity-related concerns.

Conclusions Week 145 results show sustained treatment effect and continued benefit with AVAL beyond the PAP, and stabilization of treatment effect after switching from ALGLU to AVAL, supporting long-term maintenance of clinically meaningful outcomes with AVAL.

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2597 RARE VARIANTS OF SUPEROXIDE DISMUTASE 1 – THERAPEUTIC RELEVANCE

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Background A genetic cause for amyotrophic lateral sclerosis (ALS) is evident in 10–15% of patients. Mutations in superoxide dismutase 1 (SOD1) are the second most commonly implicated linkage, comprising 14% of genetic cases. More than 185 variants of SOD1 mutations have been identified, with few variants linked to a defined clinical phenotype. Of relevance, the antisense oligonucleotide (ASO) therapy tofersen is being trialled for SOD1 ALS patients, prompting discussion about which variants should be considered pathogenic.

Case Three patients living with rare SOD1 mutations, all with slow disease progression, are presented. Case 1 (49F): SOD1 mutation A-G, H43R has a 15 year history of disease with only bulbar symptoms and mild weakness of distal upper limbs. Case 2 (39M): SOD1 mutation Asn66Ser has an 11 year history of distal lower limb weakness, still able to mobilise with aids (AFO, SPS), with disease progression to distal upper limbs and no bulbar symptoms. Case 3 (61M): SOD1 mutation His49Arg has a 22 year history of disease, initially right lower limb onset ALS which has progressed to weakness of all limbs. He uses a mobility scooter though remains independent for transfers, with no bulbar symptoms.

Discussion The present case series highlights the complexities of 3 patients with rare SOD1 variants, unified by remarkably slow disease progression. In the context of focussed genetic therapies for ALS such as ASO, patients and clinicians need precise information about rare variants to project individual disease trajectory and thereby establish the optimal time to commence therapy.

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