Rochester Minnesota was 1 per 614. One third of these children develops DRE and half have GDD. Aetiology can be identified in 54%. Identification of aetiology is associated with DRE and GDD.

Plenary

P07 ONASEMNOGENE ABEPARVOVEC GENE-REPLACEMENT THERAPY (GRT) FOR SPINAL MUSCULAR ATROPHY (SMA): FROM BENCH TO BEDSIDE

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10.1136/archdischild-2020-rcpch.20

Aims Report onasemnogene abeparvovec (formerly AVXS-101) GRT development for SMA. Onasemnogene abeparvovec is a one-time, intravenous GRT that addresses the genetic root cause of SMA, a progressive neurological disease. Onasemnogene abeparvovec delivers the survival motor neuron gene (SMN) via a self-complementary adeno-associated serotype 9 viral vector (scAAV9) that crosses the blood-brain barrier. Onasemnogene abeparvovec is designed for immediate and sustained expression of SMN protein in non-dividing neurons, allowing for rapid onset and durable therapeutic effect.

Methods SMA mice (SMN2^{+/+}; SMNΔ7^{+/+}; *Smn*^{-/-}) received intravenous scAAV9-SMN or scAAV9-GFP at post-natal day 1; survival and motor function were assessed. Non-human primates (NHPs) received intravenous scAAV9-GFP; transduced cell types were assessed. A phase 1/2a study (START; NCT02122952) evaluated onasemnogene abeparvovec infused at low (Cohort 1, n=3) or high (Cohort 2, n=12) doses in symptomatic SMA type 1 (SMA1) infants; patients were followed for 2 years for safety/tolerability and efficacy and could enroll in a long-term follow-up (LTFU) study to assess long-term safety.

Results In SMA mice, scAAV9-SMN improved survival (>200 versus 15 days in controls), and increased motor function. In NHPs, scAAV9-GFP efficiently targeted motor neurons throughout the central nervous system. In the phase 1/2a START trial, all patients survived free of permanent ventilation at 24 months. In the high-dose cohort, 11/12 patients reached CHOP INTEND >40; 11 sat unassisted ≥5s, 10 for ≥10s, 9 for ≥30s. Two patients crawled, stood, and walked. No patient received nusinersen during the 24-month study period. In the LTFU study, 2 more patients in Cohort 2 have gained the motor milestone of standing with assistance (as of 31 Dec 2019); neither patient has ever received nusinersen. No new treatment-related serious adverse events or adverse events of special interest have occurred in LTFU (as of 31 Dec 2019). The oldest patient in Cohort 2 is aged 5.6 years, with 5.2 years of follow-up since onasemnogene abeparvovec dosing.

Conclusion Onasemnogene abeparvovec has demonstrated unprecedented outcomes in patients with SMA compared with untreated natural history. Phase 3 trials of onasemnogene abeparvovec in SMA1 are ongoing (US, EU, Asia-Pacific); additional trials are investigating presymptomatic SMA and intrathecal administration in older patients.

G32 IMPROVING SURVIVAL OF THOSE WITH CEREBRAL PALSY IN ENGLAND AND WALES OVER THE LAST 18 YEARS

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10.1136/archdischild-2020-rcpch.21

Aims To assess the rate of change in median age of death over time, where cerebral palsy (CP) is documented as a cause of death, with reference to all-cause mortality in England and Wales.

Methods Published death registration statistics for England and Wales for all-cause mortality as well as ICD 10 code 'G80 – Cerebral Palsy' were extracted from the WHO Causes of Death Query online for 2001–2016 and the Office for National Statistics for 2013–2018. This captures those who died, where cerebral palsy was documented in part 1 of the death certificate. Linear interpolation was used to calculate the median age of death for the different groups. Data was imported into SPSS and linear regression was used to assess trends.

Results Median age of death was significantly lower in the CP group compared to the general population, with the median age of death increasing from 22.5 in 2001 to 49.6 in 2018. The trends in median age of death from 2001–2018 in England and Wales are highlighted in table 1.

Abstract G32 Table 1 Change in median age of death (in life years per year) from 2001–2018 in England and Wales

	Cerebral Palsy	All Causes
Combined	+1.59 (95%CI 1.19 to 1.99)	+0.15 (95%CI 0.11 to 0.18)
Male	+1.61 (95%CI 1.23 to 1.99)	+0.14 (95%CI 0.13 to 0.15)
Female	+1.46 (95%CI 0.88 to 2.04)	+0.11 (95%CI 0.10 to 0.12)

Conclusion The increasing median age of deaths due to CP hints at improved survival due to improvements in care. The rate of this improvement is significantly greater than that of the general population.

These death registration data cannot directly report improved survival. However, this finding is supported by the absolute numbers for registration of deaths due to CP remaining constant. Prolonged survival may therefore be inferred by the increasing median age of death.

G33 EACH AND EVERY NEED – A COMPLETED AUDIT CYCLE OF ACUTE CARE RECEIVED BY CHILDREN WITH CHRONIC NEURODISABILITY

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10.1136/archdischild-2020-rcpch.22

Aims In 2018 the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) launched 'Each and Every Need: a review of the quality of care provided to patients 0–25 with chronic neurodisability' detailing the standards of care relating to both acute and community care. Our experience was that these were not being met when our complex