**Appendix Table E3. Neurocognitive and neurodevelopmental outcomes for treatment (HSCT) and comparators (ERT, substrate reduction therapy) of inherited metabolic diseases with both rapid and slow progression**

| **Disease** | **Neurocognitive** **Pre-Intervention** | **Neurocognitive** **Post-Intervention** | **Neurodevelopmental****Pre-Intervention** | **Neurodevelopmental** **Post-Intervention** | **Study****(record #), treatment, study design (N)** |
| --- | --- | --- | --- | --- | --- |
| Farber disease | **Type 2/3, with no CNS involvement**nr | **Type 2/3, with no CNS involvement**nr | **Type 2/3, with no CNS involvement**# subcutaneous nodules:pt 1: 58pt 2: 39pt 3: 18# joints with limited motion:pt 1: 26pt 2: 24pt 3: 10 | **Type 2/3, with no CNS involvement**# subcutaneous nodules:pt 1: 8 at 1.2 yrs postpt 2: 14 at 0.5 yrs postpt 3: 0 at 0.7 yrs post# joints with limited motion:pt 1: 2 at 1.2 yrs postpt 2: 4 at 0.5 yrs postpt 3: 4 at 0.7 yrs post | Ehlert K, Germany, 2006 (4690), HSCT, case series (N=3) |
| **Type 2/3, with no CNS involvement**nr | **Type 2/3, with no CNS involvement**nr | **Type 2/3, with no CNS involvement**# subcutaneous nodules:pt 1: 58pt 2: 39# joints with limited motion:pt 1: 26pt 2: 24 | **Type 2/3, with no CNS involvement**# subcutaneous nodules:pt 1: 8pt 2: 12# joints with limited motion:pt 1: 2pt 2: 2 | Vormoor J, Germany, 2004 (9420), HSCT, case series (N=2) |
| **Type 1, with CNS involvement**normal myelination at 0.75 yrsBayley Scales of Infant Development: developmental age and real age equivalent at time of transplant (0.75 yrs) | **Type 1, with CNS involvement**normal myelination at 0.3 yrs post, decrease in grey and white matter differentiation at 0.7 yrs post, poor grey and white matter contrast at 1.3 yrs postdevelopment age plateaued at 0.6 yrs at real age of 1.3 yrs and 2.1 yrs | **Type 1, with CNS involvement**wt, ht, and head circumference: 10th-25th percentile | **Type 1, with CNS involvement**wt, ht, and head circumference:5th percentile at 0.8 yrs post<5th percentile at 1.5 yrs post | Yeager AM, US, 2000 (14880), HSCT, case report |
| **Type 1, with CNS involvement**mental regression | **Type 1, with CNS involvement**mental regression worsened, cerebral atrophy seen in brain imaging | **Type 1, with CNS involvement**unable to standdecreased tendon reflexes | **Type 1, with CNS involvement**regression of motor abilitiesincreasing tremor | Hoogerbrugge, PM, Netherlands, 1995 (21780D), HSCT, case series (n=1) |
| GM1 ganglio-sidosis | **juvenile form:**nr | **juvenile form:**normal language development at 0.6 yrs postlanguage declining at 1.7-2.1 yrs postdemyelination and diffuse cerebral function at 2.4 yrs postno language at 4.0 yrs post | **juvenile form:**nr | **juvenile form:**walking at 0.6 yrs postbecame clumsy at 1.7-2.1 yrs postlimited motor skills at 4.0 yrs postwheelchair at 6.0 yrs post | Shield JPH, England, 2005 (6720), HSCT, case report |
| Tay-Sachs disease | **form not specified:**nr | **form not specified:**nr | **form not specified:**nr | **form not specified:**nr | Page KM, US, 2008 (1280A), HSCT, case series (n=1) |
| **form not specified:**mental regressionbrain imaging showed widened subarachnoidal spaces | **form not specified:**vegetative stateno brain imaging follow-up | **form not specified:**psychomotor retardationmyoclonic jerks | **form not specified:**vegetative state | Hoogerbrugge PM, Netherlands, 1995 (21780C), HSCT, case series (n=1) |
| **juvenile form:**nr | **juvenile form:**MRI shows cerebral atrophy at 0.5 yrs postworsening neuropsychological test scores at 0.5 yrs postspeech deteriorating at 0.5 yrs post | **juvenile form:**nr | **juvenile form:**motor skills deteriorating at 0.5 yrs postDeterioration of this pt similar to deterioration of untreated older sister | Jacobs JFM, Netherlands, 2005 (6740), HSCT with substrate reduction therapy added at 2 yrs post, case report |
| **juvenile form:**pt 1: mild cognitive impairment, attends regular school with assistancept 2: severe cognitive impairment, generalized seizures | **juvenile form:**pt 1: at 15 mos acute psychotic eventpt 2: at 15 mos marked increase in seizures, alertness deteriorated, at 24 mos spasticity increased | **juvenile form:**pt 1: mild muscle weakness, moderate muscle impairment, independent feeding and ambulationpt 2: needs support for ambulation | **juvenile form:**pt 1: at 6 mos handwriting deteriorated, at 12 mos fine tremor in hands, from 12-24 mos, progressive muscle atrophypt 2: at 15 mos muscle bulk decreased markedly, at 24 mos wheelchair dependent | Maegawa GHB, Canada, 2009 (56590B), substrate reduction therapy, single arm (n=2) |
| ceroid lipo-fuscinosis |  cerebral cortical atrophy:moderate in one pt, not detectable in 2 ptsperiventricular white matter hyperintensity:mild in 1 pt, not detectable in 2 pts | cerebral cortical atrophy:moderate became severe in one pt, not detectable became moderate in two ptsperiventricular white matter hyperintensity:mild became severe in one pt, not detectable became moderate in two pts | one pt mildly symptomatic and two pts asymptomatic | all three pts by end of follow-up at 2-4 yrs of age were hypotonic and spastic, with some head control remaining | Lonnquist T, Finland, 2001 (12960), HSCT, case series (N=3) |
| Sandhoff’s disease | nr | nr | nr | nr | Ringden O, Sweden, 2006 (5940B), HSCT, case series (n=1) |
| pt 1: severe cognitive dysfunction, hallucinations, agitation, scores 1.5 yrs below agept 2: episodic psychosis, cognitive function well-preserved, works part timept 3: 2 episodes of psychosis, IQ=75 | pt 1: neuropsych scores unchangedpt 2: 18 mos post, neuropsych scores stable, speech less intelligible, hallucinations reduced, anxiety ongoingpt 3: at 16 mos post, spasticity developed, anxiety aggravated, neuropsych scores stable | pt 1: muscle wasting, fully dependent for feeding and ambulationpt 2: moderate skeletal muscle weakness, independent ambulation, feeding, bathingpt 3: independent ambulation, feeding, and bathing | pt 1: 3 mos incoordination progressed, 15 mos wheelchair, 21 mos can't standpt 2: at 18 mos gait disturbance progressed & muscle strength reducedpt 3: 6 mos gait disturbance, 16 mos notable wt losspt 2 and pt 3 stopped tx at 21 mos due to excessive weight loss | Maegawa GHB, Canada, 2009 (56590A), substrate reduction therapy, single arm (n=3) |