**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: 58  pt 2: 39  pt 3: 18  # joints with limited motion:  pt 1: 26  pt 2: 24  pt 3: 10 | **Type 2/3, with no CNS involvement**  # subcutaneous nodules:  pt 1: 8 at 1.2 yrs post  pt 2: 14 at 0.5 yrs post  pt 3: 0 at 0.7 yrs post  # joints with limited motion:  pt 1: 2 at 1.2 yrs post  pt 2: 4 at 0.5 yrs post  pt 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: 58  pt 2: 39  # joints with limited motion:  pt 1: 26  pt 2: 24 | **Type 2/3, with no CNS involvement**  # subcutaneous nodules:  pt 1: 8  pt 2: 12  # joints with limited motion:  pt 1: 2  pt 2: 2 | Vormoor J, Germany, 2004 (9420), HSCT, case series (N=2) |
| **Type 1, with CNS involvement**  normal myelination at 0.75 yrs  Bayley 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 post  development 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 stand  decreased tendon reflexes | **Type 1, with CNS involvement**  regression of motor abilities  increasing 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 post  language declining at 1.7-2.1 yrs post  demyelination and diffuse cerebral function at 2.4 yrs post  no language at 4.0 yrs post | **juvenile form:**  nr | **juvenile form:**  walking at 0.6 yrs post  became clumsy at 1.7-2.1 yrs post  limited motor skills at 4.0 yrs post  wheelchair 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 regression  brain imaging showed widened subarachnoidal spaces | **form not specified:**  vegetative state  no brain imaging follow-up | **form not specified:**  psychomotor retardation  myoclonic 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 post  worsening neuropsychological test scores at 0.5 yrs post  speech deteriorating at 0.5 yrs post | **juvenile form:**  nr | **juvenile form:**  motor skills deteriorating at 0.5 yrs post  Deterioration 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 assistance  pt 2: severe cognitive impairment, generalized seizures | **juvenile form:**  pt 1: at 15 mos acute psychotic event  pt 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 ambulation  pt 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 atrophy  pt 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 pts  periventricular 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 pts  periventricular 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 age  pt 2: episodic psychosis, cognitive function well-preserved, works part time  pt 3: 2 episodes of psychosis, IQ=75 | pt 1: neuropsych scores unchanged  pt 2: 18 mos post, neuropsych scores stable, speech less intelligible, hallucinations reduced, anxiety ongoing  pt 3: at 16 mos post, spasticity developed, anxiety aggravated, neuropsych scores stable | pt 1: muscle wasting, fully dependent for feeding and ambulation  pt 2: moderate skeletal muscle weakness, independent ambulation, feeding, bathing  pt 3: independent ambulation, feeding, and bathing | pt 1: 3 mos incoordination progressed, 15 mos wheelchair, 21 mos can't stand  pt 2: at 18 mos gait disturbance progressed & muscle strength reduced  pt 3: 6 mos gait disturbance, 16 mos notable wt loss  pt 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) |