# List of data elements MLDi registry

## Minimal set

Mandatory to collect

| **Minimal data element** | **Coding** |
|---|---|
| Approximate date of birth | mm/yyyy |
| Sex at birth | Male, female, unknown |
| Survival status | Alive, deceased, loss to follow-up, opted-out<br>> date of deceased/loss to follow-up/opted-out<br>> cause of death |
| Name or country of specialized center | Specify center |
| Confirmed diagnosis (checkboxes) | Yes > genetically + clinically, enzymatically + genetically, enzymatically + urinary sulfatides |
| OMIM diagnosis | 250100, 249900, 272200 |
| Date of diagnosis (age at diagnosis) | mm/yyyy<br>if unknown: antenatal, at birth, childhood, adult |
| Date at symptom manifestation (age at symptom onset) | Pre-symptomatic, age in years and months |
| Relevant other diagnosis/comorbidity | No, Yes > specify other (inherited) important conditions/prenatal history |
| Inclusion of the patient in the registry is allowed | Yes consent was given, no but exceptional circumstances apply |
| Agreement to be contacted for research purposes | Yes, no, missing, not applicable |
| Biological sample | Yes, no, unknown |
| Link or information to a biobank | If applicable, free text |

## Core set

Encouraged to collect

| **Data element** | **Coding** |
|---|---|
| Ethnic background | According to the United Nations Geoscheme<br>Northern Africa, Sub-Saharan Africa, Eastern Africa, Middle Africa, Southern Africa, Western Africa, Caribbean, Central America, South America, Northern America, Central Asia, Eastern Asia, South-eastern Asia, Southern Asia, Western Asia, Eastern Europe (including Northern Asia), Northern Europe, Southern Europe, Western Europe |
| Country of residence | Countries |
| Significant family history | No relevant family history, Parkinson's disease, other, unknown |
| Sibling with MLD | Yes, no, unknown<br>Record ID of sibling |

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| Consent to future sharing of encoded data with physicians abroad through the MLD initiative | Yes, no, unknown |
| Consent to future sharing of encoded data with researchers outside the European Union | Yes, no, unknown |
| Consent to future sharing of encoded data with companies developing new treatments for MLD and with (semi)governmental bodies involved in making healthcare policies. | Yes, no, unknown |
| Clinical trial participation | Yes (>specify), no, unknown |
| MLD type | late-infantile (<2.5 years) , early-juvenile (2.5 - 6 years), late-juvenile (6 - 16 years), adult (>16 years) |
| Both genetic mutations | • c.256C>T, p.(Arg86Trp)<br>• c.257G>A, p.(Arg86Gln)<br>• c.293C>T, p.(Ser98Phe)<br>• c.465+1G>A<br>• c.542T>G, p.(Ile181Ser)<br>• c.1210+1G>A<br>• c.1283C>T, p.(Pro428Leu)<br>• Specify other ARSA mutation<br>• Specify PSAP mutation<br>• Specify SUMF1 mutation<br>• Presence of pseudodeficiency allele (c.1055A > G, p.(Asn352Ser) + ∗96A > G) |
| ASA activity in leukocytes or fibroblasts at diagnosis | Leukocytes/Fibroblasts > in nmol/mg protein/h / nmol/17hmg protein / % from mean reference value |
| Urinary sulfatide level | In nmol/mmol creatinine |
| Symptomatic at diagnosis 1 | Which situation gave rise to the diagnosis: manifested symptoms, family screening because of affected sibling, newborn screening, other, unknown. |
| Symptomatic at diagnosis 2 & presenting symptoms | No symptoms at all, Gross motor signs (unsteady gait, clumsiness), signs of polyneuropathy, balance and coordination problems, deterioration in school performance, cognitive decline, language regression, behavioral changes, psychiatric signs, unknown, other. |
| Date of first contact with specialized center | mm/yyyy |
| Gross Motor Function Classification (GMFC-MLD) | Scale from level I - level VI<br>date of transition to other level |
| Expressive Language Function Classification (ELFC-MLD) | Scale from level I - level IV<br>date of transition to other level |
| Eating and Drinking Ability Classification System (EDACS) | Scale from level I - level V<br>date of transition to other level |
| Manual Ability Classification System (MACS) | Scale from level I - level V<br>date of transition to other level |
| Weight | Kg |
| Standing height, sitting height or length | m |
| Developmental milestones | Sitting without support, Hands-and-knees crawling, Standing with assistance, Walking with assistance, |

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| | Standing alone, Walking alone (according to WHO motor development milestones)<br><br>Exact age in months or Normal development/delayed development/unknown |
| Cognitive decline | Yes, no, unknown |
| Memory problems | Yes, no, unknown |
| Intelligence – IQ scores<br>Total IQ score (TIQ)<br>Verbal comprehension (VIQ)<br>Perceptual Reasoning Index (PIQ)<br>Processing speed<br>Working memory | 0-150 |
| Intelligence - IQ scale used for testing | Used test: Wechsler Preschool and Primary Scale of Intelligence, Wechsler Adult Intelligence Scale–Third Edition, Wechsler intelligence Scale for Children, Dutch Groninger Intelligence Test, Bayley Scales of Infant Development, Kaufman Assessment Battery for Children, Leiter International Performance Scale, Wechsler Nonverbal Scale of Ability, Mullen Scales for Early Learning, Bourdon-Wiersema test, Wechsler memory scale-revised |
| Psychiatric symptoms | Yes, no, unknown<br>>Psychotic symptoms, affective disorders, behavioral disorders (>impulsive/disinhibition, aggression, inappropriate sexual behavior, apathy, ADHD, autism spectrum disorder), anxiety disorder, obsessive-compulsive disorder, change of personality |
| Irritability | Always, mostly, rarely, never (PROM) |
| EuroQol 5D | PROM |
| Seizures | No, partial seizures only, primary or secondary generalized seizures |
| MLD Loes score | Scale from 0 - 34 |
| Permanent tube feeding | Yes, no, unknown |
| Causal treatment | |
| Causal treatment | Yes, no, decision for causal treatment not yet made, unknown<br>Hematopoietic stem cell transplantation, Autologous hematopoietic stem cell based gene therapy (Libmeldy™), Intrathecal enzyme replacement therapy (SHP611/HGT-1110/rhASA), other |
| Date of treatment | Dd/mm/yyyy<br>In case of HSCT and GT: choose date of stem cell product infusion.<br>In case of ERT: choose date of first enzyme infusion. |
| Symptoms at time of the treatment | Pre-symptomatic, early-symptomatic, symptomatic |
| Adverse events | Dd/mm/yyyy<br>Common Terminology Criteria for Adverse Events version 5.0 |

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| | In addition to CTCAE:<br>acute GvHD + grade (overall grade: 1 to 4), chronic GvHD (mild, moderate or severe: NIH criteria), graft failure (autologous reconstitution recipient >95%, aplasia), neurological deterioration (disease progression), immunoglobulins against arylsulfatase A, presence of replication competent virus, pump infection, catheter disconnection<br><br>Pregnancy after transplant (unknown, no, yes, natural, preserved) |
| ERT-related | |
| Intrathecal enzyme replacement therapy | Dose (150mg weekly, other…) |
| HSCT-related | |
| Conditioning regimen | Bu/Cy or FluBu or CloFluBu or TreoFluTT, other (free text) + dose<br>If Bu (busulfan): what was Busulfan area under the curve (AUC)? (Free text) \| |
| Serotherapy | rATG (Sanofil), rATG (neovi), hATG, Alemtuzumab, None, unknown |
| Number of infused CD34+ cells per kg | Infused number x 10^6/kg |
| Total number of infused cells per kg | Number |
| Time to engraftment neutrophils<br>Defined as: Neutrophil engraftment is defined as three consecutive days where the neutrophil count is 500 cells/mm3 or more. | Number of days |
| Time to platelet engraftment<br>Defined as: Choose the first day of the 7 consecutive days of platelets exceeding 20 x 10^9/L | Number of days |
| Full chimerism in blood (>95%) | >95%, 50-95%, 10-50%, unknown |
| Matching for HLA-A, HLA-B, and HLA-DRB1 alleles | 10/10, 9/10, 8/10, 7/10, ≤6/10<br>OR for 8 antigens: 8/8, 7/8, 6/8, 5/8, or ≤4/8<br>OR for 6 antigens: 6/6,5/6, 4/6, ≤3/6 |
| Graft-versus-Host-Disease prophylaxis | Ciclosporine, Methotrexaat, mycophenolate mofetil (MMF), Tacrolimus, Sirolimus, prednison, other (Free text) |
| Donor type | Unrelated, related carrier, related non-carrier, related carrier status unknown |
| Graft source | Bone marrow, peripheral blood, umbilical cord blood (expended cord blood) |
| ASA activity in leukocytes every 12 months | In nmol/mg protein/h / nmol/17hmg protein / % from mean reference value |
| Chimerism in blood at last follow-up | % |
| Test used to measure chimerism | FISH, PCR, VRTR, next generation sequencing, other |
| Second treatment | Yes, no, unknown |

| GT-related | |
|---|---|
| Conditioning regimen | Bu<br>What was Busulfan AUC? (Free text) \| |
| Number of infused CD34+ cells per kg | Infused number x $10^6$/kg |
| Total number of infused cells per kg | Number x $10^6$/kg |
| Time to engraftment neutrophils<br>Defined as: Neutrophil engraftment is defined as three consecutive days where the neutrophil count is 500 cells/mm3 or more. | Number of days |
| Time to platelet engraftment<br>Defined as: Choose the first day of the 7 consecutive days of platelets exceeding 20 x 10^9/L | Number of days |
| ASA activity in leukocytes every 12 months | In nmol/mg protein/h / nmol/17hmg protein / % from mean reference value |
| Second treatment | Yes, no, unknown |
| Used viral vector | Lentiviral, other |
| Vector Copy Number (VCN) per cell | Number<br>Peripheral blood/bone marrow/unknown |
| Transduced (LV+) cell engraftment | % |
| Time to transduced LV+ cell engraftment | Number of days |

## Optional set

Nice to have

| **Data element** | **Coding** |
|---|---|
| Gross Motor Function Measure-88 (GMFM-88) | % |
| Head circumference | Cm |
| Puberty development | Normal, delayed, premature, not applicable |
| Urinary continence | Diurnal continence, nocturnal continence, unknown |
| Urinary catheterization | No, intermittent, permanent |
| Cranial nerves | Eye movements (intact/not intact) > onset symptom (yes/no) > strabismus (paralytic/concomitant), nystagmus, oculomotor apraxia, hearing |
| Muscle tone | Spasticity, Rigidity, Dystonia, Paratonia, none, unknown |
| Extrapyramidal symptoms | Chorea, tremor (resting, postural, intention), tics, myoclonus, hemiballismus |
| Tendon reflexes | Normal, exaggerated upper/lower extremities, absent upper/lower extremities, unknown |
| Plantar responses left and right | Flexor, Babinski sign, indifferent |
| Gait | Normal, broad-based, spastic, foot drop, unable to walk |
| Ataxia | Yes, no, unknown |
| Trunk balance | Yes, no, unknown |
| Frequent falls | Yes, no, unknown |
| Mini-mental state examination (MMSE) | Score from 0-30 |

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| School career | None, early childhood education (preschool, kindergarten), primary education (primary/elementary school), secondary education (secondary/high school), tertiary education (higher/vocational education, academic degree) |
| Happiness | Always, mostly, rarely, never (PROM) |
| Pediatric Quality of Life Inventory (PedsQL) | Score |
| Health Utilities Index (HUI) | PROM |
| Malignancy | Gall bladder malignancy, gallbladder carcinoma, Ewing sarcoma, pilocytic astrocytoma, and malignant peripheral nerve sheath tumor, other (specify) |
| Kidney stones | Yes, no, unknown |
| MRI scale used in italian studies (gene therapy trial) - Adapted Loes score | Scale from 0 - 31.5 |
| Signs of peripheral neuropathy | Yes (>demyelinating PNP confirmed with EMG yes, no), no, unknown |
| Metabolic acidosis | Yes, no, unknown |
| Gall bladder ultrasound results | Wall thickening (>3mm), gall bladder stones, dilated bile duct (>8mm), gall bladder distension, gall bladder polyposis, collapsed gall bladder |
| Gall bladder resection | Yes, no, unknown |
| Intrathecal baclofen | Yes, no, unknown |
| Medication and year of start treatment | Spasmolytics, antiemetics, analgesics, anticonvulsants, antidepressants, antipsychotics, anxiolytics, sleep medication, hormone replacement therapy, immunomodulators other, none |
| Scale for the assessment and rating of ataxia (SARA) | Score 0 - 40 |
| Other skeletal deformities | Scoliosis, feet deformities/contracture(s), knee contracture(s), hip contracture(s), hip luxation(s), other |
| Surgical intervention for skeletal/feet deformities | Yes (>specify year, indication), no, unknown |