Appendix B. Appendix Data Abstraction Tables

**Clinical Trials of Enzyme Replacement Therapy for Lysosomal Storage Diseases**

| **Disease/ERT** | **Author, Year, Country** | **Study Design** | **Comparator** | **No.** **of Patients** | **Disease Stage/Type** | **Mean Age at 1st Infusion (range) yrs** | **Length of Follow-up (wks)** | **Outcomes Measured** | **Adverse** **Events** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| MPS I/ Aldurazyme® (α-L-ironidase) (laronidase) | Clarke,1 2009, international | open label extension to Wraith et al, 20042 | none | 40 | attenuated | 16 (6-43) | 182 | - urinary substrate levels- liver volume- 6-min walk test- pulmonary function- range of motion- mental development- visual acuity- sleep apnea- IgG | - infusion-associated reactions- IgG antibody development |
| Giugliani,3 2009, international | dose optimization trial | 0.58 mg/kgwkly vs 1.2 mg/kg EOW, 1.2 mg/kg wkly, and 1.8 mg/kg EOW | 33 | severe (n=10) and attenuated (n=23) | 8.9 (1.4-20.7) | 26 | - urinary substrate levels- liver volume- 6-min walk test | - infusion-associated reactions- IgG antibody development- 1 death in pt w/ severe form, considered unlikely related to treatment |
| Wraith,4 2007, international | open label trial for children <5 yrs of age | none | 20 | severe (n=16) and attenuated (n=4) | 2.9 (0.5-5.1) | 52 | - urinary substrate levels- liver size- cardiac involvement- sleep apnea- growth- mental development | - infusion-associated reactions- IgG antibody development |
| Wraith,2 2004, international | randomized, double-blind, placebo-controlled trial | placebo | laronidase: 22placebo: 23 | severe (n=1) and attenuated (n=44) | laronidase:15.6 (7-43)placebo:15.4 (6-39) | 26 | - pulmonary function- 6-min walk test- urinary substrate levels- liver size- sleep apnea- range of motion | - infusion-associated reactions- IgG antibody development |
| MPS II/ Elaprase® (idursulfase) | Okuyama,5 2010, Japan | open label trial for adults | none | 10 | attenuated | 30.1 (21.1-53.9) | 52 | - urinary substrate levels- liver size- 6-min walk test- pulmonary function- range of motion- cardiac involvement- sleep apnea- spleen volume | - infusion-associated reactions- IgG antibody development |
| Muenzer,6 2011N = 94 | extension study of phase II/III randomized double-blind, placebo-controlled trial (Muenzer, 2006 7) | 0.5 mg/kg weekly | treatment groups had same distribution baseline disease scores from 2-6 | 5-31 |  |  | - 6-min walk test- pulmonary function- substrate level- liver volume- spleen volume- range of motion |  |
| Muenzer,8 2007, US | phase I/II, randomized, double-blind, placebo-controlled trial  | 3 treatment groups:0.15, 0.5, and 1.5mg/kg EOW, and placebo | idursulfase: 9placebo: 3 | attenuated | overall: 14 (6-20)0.15 mg/kg: 11 (9-14)0.5 mg/kg: 20 (20)1.5 mg/kg: 8 (6-10)placebo: 17 (13-20) | double-blind trial: 24open label extension:26 | - urinary substrate levels- liver and spleen volume- 6-min walk test- range of motion- pulmonary function- cardiac involvement- sleep apnea | - infusion-associated reactions- IgG antibody development |
| Muenzer,7 2006, international | phase II/III, randomized double-blind, placebo-controlled trial | 3 treatment groups:1) 0.5 mg/kg wkly, 2) 0.5 mg/kg EOW, and 3) placebo | 1) 322) 323) 32 | each treatment grp had the same distribution of baseline disease scores ranging from 2-6 | 1) 15.1 (6.3-26.0)2) 14.4 (5.4-30.9)3) 13.1 (5.0-29.0) | 53 | - 6-min walk test- pulmonary function- substrate level- liver volume- spleen volume- range of motion | - infusion-associated reactions- IgG antibody development |
| MPS VI/ Naglazyme® (galsulfase ) | Harmatz,9 2010, international  | extension to phase I/II, II, III trials reporting results up to 48 wks, Harmatz 200410 | 1) 0.2 mg/kg or 1.0 mg/kg2) 0.2 mg/kg3) 0.2 mg/kg | 1) 72) 103) 39 | symptomatic | phase I/II: 12 (7-16)phase II: 12.1 (6-21)phase III: 13.7 (5-29) | up to 240 weeks | -pulmonary function-height | not reported |
| Harmatz,43 2006, international | Phase III, randomized double-blind placebo-controlled trial | 1. 1.0 mg/kg wkly
2. placebo
 | 1. 19
2. 20
 | symptomatic | 13.7 (5-29) | 48 weeks | 6 and 12 minute walks - 3 minute stair climb- urinary substrate levels | not reported |
| Harmatz,11 2005, international | open label | none  | 10 | rapidly advancing disease | 12.7 (6-22) | 48 | -mobility and physical function-6 and 12 minute walks-3 minute stair climb-oxygenation during sleep-ophthalmology evaluation-liver volume-spleen volume-height | -asthma attack- infusion-associated reactions- IgG antibody development |
| Harmatz,442004international | phase I/II randomized, two-dose, double-blind | 1)0.2 mg/kg weekly2)1.0 mg/kg weekly | 1) 42) 3 | entire severity spectrum  | 11 (7-16) | 48 | -mobility and physical function-6 minute walk-pain-urinary substrate levels | not reported |
| Fabry/ Fabrazyme® (agalsidase beta) | Wraith,12 2008, international | open label trial for children | none | 16 | no information provided | 12.1 (8.5-11.7) | 48 | - skin and plasma substrate levels- renal function- cardiac function- growth- quality of life- school attendance- low, moderate, high energy level- general health | - infusion-associated reactions- IgG antibody development |
| Banikazemi,13 2007, international | randomized double blind, placebo controlled trial | placebo | agalsidase β: 51placebo: 31 | no information provided | agalsidase β: 46.9 (SD: 9.8)placebo: 44.3 (SD: 9.2) | mean: 74up to 152  | - renal function- cardiac function- cerebro-vascular events | - infusion-associated reactions |
| Germain,14 2007, international | open label extension trial | none | 58 | no information provided | 31.1 (17-62) | up to 234 | - plasma substrate level- renal function- cardiac function- pain scores | - infusion-associated reactions- IgG antibody development- 5 patients experienced stroke or TIA |
| Eto, 2005,15 Japan | open label phase 2 bridging study | none | 13 | no information provided | 26.6 (16-34) | 20 | - renal function- kidney, urine, and plasma substrate levels | - infusion-associated reactions- 1 pt hospitalized with malaise and limb pain |
| Fabry/ Fabrazyme® (agalsidase beta) | Vedder,16 2008, Netherlands | dose optimization trial | 2 treatment groups:1) 0.2 mg/kg beta2) 1.0 mg/kg beta | 1) 132) 21 | no information provided | 1) 47 (19-62)2) 49 (25-73)3) 48 (27-70) | 52 | - urinary substrate levels- renal function- cardiac function | - IgG antibody development |
| Vedder,17 2007, Netherlands | open label randomized, controlled trial | 0.2 mg/kg EOW beta | 1) 182) 16 | stratified within each grp by disease severity | 1) 42 (19-60)2) 48 (24-76 | 52-104 | - cardiac function- renal function- pain scores- urine and plasma substrate levels | in 1 beta pt:- sensomotor polyneuropathy- oesophagitis |
| Gaucher/ Cerezyme® (imiglucerase) | Kishnani,18 2009, international | open label, randomized, phase IV, dose frequency trial | 2 treatment groups:1) monthly dose biwkly, 2) monthly dose every 4 wks | 1) 332) 62 | at least 2 yrs on imiglucerase | Age at 1st imiglucerase infusion:1) 35.9 (10-74)2) 41.9 (11-75) | 104 | - anemia- hepato-megaly- spleno-megaly- skeletal pathology- physical score- mental score | - infusion-associated reactions |
| Sims,19 2008, United States | open label, single cohort prospective  | none  | 33 | symptomatic | median 43.0 (12.0-70.0) | 208 | -splenomegaly-hepatomegaly-thrombocyto-penia-anemia-bone pain-bone crisis-bone mineraldensity-medullary infarction-osteoarticularInfarction-lytic lesions-fractures | -infusion-associated reactions |
| de Fost,20 2007, Netherlands | randomized, controlled trial | 2 treatment groups:1) original dose (weekly or EOW)2) dose every 4 weeks | 1) 52) 6 | symptomatic | overall 51 (34-75) | 52 | -splenomegaly-hepatomegaly-thrombocyto-penia-anemia-Chitotriosid-ase-Hexosamini-dase | not reported |
| Gaucher/ Cerezyme® (imiglucerase) | Grabowski,21 1995, United States | randomized,double-blind, parallel trial | 2 treatment groups:1) 60 U/kg EOW Ceredase2) 60 U/kg EOW Cerezyme | 1) 152) 15 | symptomatic | 1)28 (12-52)2)39 (13-69) | 39 | -hepatic volume-splenic volume-thrombocyto-penia-anemia | - infusion-associated reactions- IgG antibody development |
| Gaucher/ Velaglucerase® (velaglucerase alfa) | Elstein,22 2011, Israel (same study population as Zimran 2010) | open label, phase I/II study with extension  | none | phase I/II: 11extension (those who have data up to 208 wks): 8 | symptomatic | extension: 39 (18-62) | phase I/II: 39extension:up to 208 | - anemia- thrombo-cytopenia- hepato-megaly- spleno-megaly- skeletal pathology | not reported |
| Zimran,23 2010, Israel(same study population as Elstein 2010) | open label, phase I/II study with extension | none | phase I/II: 11extension: 8 | symptomatic | phase I/II: 41 (18-69) | phase I/II: 39extension:up to 208 | - anemia- hepato-megaly- spleno-megaly | - infusion-associated reactions- IgG antibody development- gastro-intestinal disorders- musculo-skeletal/connective tissue disorders |
| Pompe/ Myozyme® (alglucosidase alfa) | van der Ploeg,242010, international | randomized, double-blind, placebo controlled trial | placebo | Treatment: 60Placebo: 30 | juvenile/adult form | treatment: 45.3 (15.9-70)placebo: 42.6 (11.6) | 78 | -6-minute walk test-predicted FVC-quantitative muscle testing, leg and arm-maximum inspiratory and expiratory pressure-SF-36 score | - infusion-associated reactions- IgG antibody development- nervous system disorders- skin and subcutaneous tissue disorders- gastro-intestinal disorders-musculoskeletal and connective tissue disorders-eye disorders-ear and labyrinth disorders-vascular disorders |
| Strothotte,25 2010, Germany | open label | none | 44 | juvenile/adult form | 48.9 (21-69) | 52 | -arm function test-Walton Gardner Medwin Scale-timed function tests-6 minute walk test-MRC sum score-PFT measured by FVC-SF-36-liver enzyme and CK | -moderate allergic reactions-hand edema-acute hearing loss-herpes simplex infection-pollakisuria-prickling in the muscles |
| Kishnani,26 2009, United States | open label randomized extension to Kishnani, 200627  | 1) 20 mg/kg EOW2) 40 mg/kg EOW | 16 | infantile form | mean age at end of study: 2.8 (1.7-3.5) | 60-150 | -survival-ventilator use-cardiac parameters-motor development | - infusion-associated reactions- IgG antibody development |
| Nicolino,28 2009,United States | open label | historical control group  | 21 | infantile and juvenile form | mean age (in months):15.7 (3.7-43.1) | up to 168 | -survival-ventilator use-cardiac function-muscle GAA activity-motor development-functional independence-physical growth-cognitive function | - infusion-associated reactions-6 patients died, none attributed to treatment |
| Levine,29 2008, international | open label, phase II trial for children, extension study to Kishnani 200627 | none | 8 | infantile form | mean age (in months):6.1 (2.7-14.6) | 52 | - cardiac function- pulmonary function | not reported |
| McDowell,30 2008, international | retrospective study on patients who were in open label trial for children | 1) patients with arrhythmias2) patients without arrhythmias  | 1) 72) 31 | infantile form | 1) median (in months): 7 (6-13)2) median (in months): 8 (1-43) | 78 | -cardiac function (QTc, LVMi, EF) | -arrhythmias  |
| Kishnani,27 2006, international | phase II, open label trial for children, same population as Kishnani 200926 | none  | 8 | infantile form | median age (in months) at first treatment: 4.7 (2.7-14.6) | up to 153 | -survival-ventilator-free survival-cardiac response-motor response-mental and behavioral development-growth-hearing results-analysis of skeletal muscle | - infusion-associated reactions- IgG antibody development |
| Orlikowski,31 2011, France | open label trial in adults | none  | 5 | juvenile/adult form | 48 (28-62) | 52 | -respiratory function-muscle strength-SF-36 -glucose tetrasaccharides | - infusion-associated reactions- IgG antibody development-1 patient died, not attributed to treatment |