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/kg  wkly 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: 22  placebo: 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 2011  N = 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: 9  placebo: 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: 24  open 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) 32  2) 32  3) 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/kg  2) 0.2 mg/kg  3) 0.2 mg/kg | 1) 7  2) 10  3) 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,44  2004  international | phase I/II randomized, two-dose, double-blind | 1)0.2 mg/kg weekly  2)1.0 mg/kg weekly | 1) 4  2) 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: 51  placebo: 31 | no information provided | agalsidase β: 46.9 (SD: 9.8)  placebo: 44.3 (SD: 9.2) | mean: 74  up 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 beta  2) 1.0 mg/kg beta | 1) 13  2) 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) 18  2) 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) 33  2) 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 mineral  density  -medullary infarction  -osteoarticular  Infarction  -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) 5  2) 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 Ceredase  2) 60 U/kg EOW Cerezyme | 1) 15  2) 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: 11  extension (those who have data up to 208 wks): 8 | symptomatic | extension: 39 (18-62) | phase I/II: 39  extension:  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: 11  extension: 8 | symptomatic | phase I/II: 41 (18-69) | phase I/II: 39  extension:  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,24  2010, international | randomized, double-blind, placebo controlled trial | placebo | Treatment: 60  Placebo: 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 EOW  2) 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 arrhythmias  2) patients without arrhythmias | 1) 7  2) 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 |