

PW 20:
**Glycogenosis and other
metabolic myopathies**

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| PW20-242 | <p>PHENOTYPIC EXPRESSION OF LATE-ONSET POMPE DISEASE (PD) SIFI Y¹, SIFI K², BOULEFKHAD A¹, ABADI N², BENLATRECHE C², HAMRI A¹ (1) Service de neurologie, Constantine, ALGERIA. (2) Laboratoire de génétique et de biologie moléculaire, Constantine, ALGERIA.</p> |
| To contact the author:: sifimina@yahoo.fr. | <p>Introduction: Pompe disease (PD), is caused by a deficiency of the enzyme lysosomal, acid-glucosidase (GAA) resulting in the accumulation of glycogen primarily in muscle tissue. The clinical presentation of (PD) is variable with respect to the age of onset and rate of disease progression. Patients with onset of symptoms in early infancy typically exhibit rapidly progressive hypertrophic cardiomyopathy and marked muscle weakness. Most of these infants die within the first year of life from cardiac and/or respiratory failure. In the majority of cases of (PD), onset of symptoms occurs after infancy, ranging widely from the first to sixth decade of life. Progression of the disease is relentless and patients eventually progress to loss of ambulation and death due to respiratory failure The aim of this study was to characterize the clinical presentation of patients with late-onset Pompe disease.</p> <p>Patients and methods: During the period 2001- 2006 we diagnosed 04 adult cases of (PD). All patients profited from a complete clinical examination, electromyographic study, a systematic proportioning of muscular enzymes (CPK, LDH), muscular biopsy, hepatic assessment, abdominal and heart echography, pulmonary function testing (PFT) and leucocytic proportioning of acid maltase.</p> <p>Results: Four late-onset Pompe disease (PD) patients were included in this study. The average age of the first symptoms was 22 years, muscle weakness has interested upper and lower extremity proximal in all cases, Three patients (patients 2, 3, and 4) also suffered from frequent respiratory infections with a death following a respiratory insufficiency. The muscular enzymes and the hepatic assessment were disturbed at 03 patients The diagnosis was confirmed by leucocytic proportioning of acid maltase.</p> <p>Conclusion: The clinical presentation of late-onset (PD) is heterogeneous and resembles that of other myopathies, therefore definitive diagnosis needs to be confirmed by biochemical or molecular methods.</p> |

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| PW20-243 | <p>THE EVOLVING ROLE OF THE FRENCH POMPE REGISTRY DE CASTRO D¹, LALOUI K¹, DOPPLER V¹, PAYAN C¹, HOGREL J-Y¹, OLLIVIER G¹, LAFORÉT P AND THE FRENCH POMPE REGISTRY STUDY GROUP .¹ (1) Institut de Myologie, Groupe Hospitalier Pitié-Salpêtrière, Paris, FRANCE.</p> |
| To contact the author:: d.decastro@institut-myologie.org. | <p>Introduction: Recombinant human alpha al-glucosidase (rhGAA; Myozyme® Genzyme), an enzyme replacement therapy (ERT) for Pompe disease (PD; acid maltase deficiency, glycogenosis type II), was first used in France for late-onset patients in May 2005 and authorisation for European use was granted in March 2006. An 18-month international double-blind placebo-controlled efficacy study ("Late Onset Treatment Study"; AGLU02704) was completed in mid-2007. Early results show small but statistically significant improvements in the primary endpoints—vital capacity and 6-minute distance walked. Objectives: The Registry was established in 2004 as a database for PD natural history independent of industry control. Data submission to the Registry is a requirement for government funding of GAA. Certain data will be passed on to the international Genzyme PD database. Methods: Information is collected at French neuromuscular treatment centres and maintained at the Institute of Myology in Paris on a secure webserver with protected access. Adult PD patients, treated and untreated, are currently included; inclusion of infants is planned. Patients' written consent is required. Data are collected anonymously on inclusion then every 6 months for GAA-treated patients and annually for untreated patients: disease history, diagnostic results (muscle biopsies, muscle enzyme activity, genetic data), videotaped muscle strength assessments, tests of respiratory, cardiac and hearing function, and reviews of other systems. Results: Approximately two thirds (N=66) of patients currently diagnosed in France are included on the Register, of whom 47 are currently treated with GAA. 17 centres have provided data. Treatment/nontreatment comparisons at 1 yr will be presented. Conclusion: In view of the continuing increase in the number of GAA-treated patients, the principle role of the French Registry is now to monitor the long-term efficacy and safety of this very high-cost treatment. Post-treatment and natural history data are also available for use in trial design, patient selection and patient monitoring.</p> <p>Acknowledgements. This work was supported by the Association Française des Glycogénoses (AFG) and the Association Française contre les Myopathies (AFM).</p> |

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| PW20-244 | <p><u>BENEFIT OF RECOMBINANT HUMAN ACID ALPHA GLUCOSIDASE TREATMENT (MYOZYME*) IN LATE ONSET POMPE DISEASE: ABOUT FOUR CASES WITH TREATMENT FOR SIX MONTHS</u></p> <p>LEBLANC A¹, BLANCHARD C¹, ZAGNOLI F¹ (1) Service de Neurologie Hôpital d'Instruction des Armées Clermont Tonnerre, Brest, FRANCE.</p> |
| <p>To contact the author:: fabien.zagnoli@orange.fr</p> | <p>Since 2007, patients with late onset Pompe disease can be treated by recombinant human acid alpha glucosidase. Four patients were treated: 3 men and one woman. The woman was 35 old. She complained difficulties for walking and climbing stairs since 19 years old. Since 26, she could not stand up from a chair without help or carry her child. At 31 she used a wheelchair and at 33 she needed non invasive ventilation. One of the men was the first patient's brother: he was 50. The disease started when he was 40. He had walking disability but he did not need any help. He had no respiratory failure. The two others patients were 60 and 68 years old. The Pompe disease begun for 4 years. They had walking disability and both needed non invasive ventilatory. For all, the diagnosis was performed on muscle biopsy and decreased alpha glucosidase level in muscle and leucocytes. After six months of treatment (20mg/kg twice a month), the patients felt better and one reduced the duration of non invasive ventilation and could stand up longer. Measurement tests confirmed this impression: the total MFM score and the SF36 scale improved slightly for all. For one, the duration of non invasive ventilation decreased to 10hours/day, for the three others, the six minutes walking test improved until 30% . No adverse event was observed.</p> <p>After six months of treatment the quality of life of patients seems increased and clinical signs improved.</p> |

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| PW20-245 | <p>EFFECTS OF ONE YEAR ENZYME REPLACEMENT THERAPY IN SEVERE FORM OF LATE ONSET POMPE DISEASE. SEVERE LATE ONSET TREATMENT STUDY (FRENCH SLOTS).</p> <p>ORLIKOWSKI D¹, LAFORET P³, PELLEGRINI N¹, PRIGENT H², MONNET A³, CARLIER P⁴, CARLIER R⁵, EYMARD B³, LOFASO F², ANNANE D¹</p> <p>(1) Intensive care and home ventilation unit, technology investigation centre, Hopital R Poincaré, Garches, FRANCE. (2) Physiology department, technology investigation centre, Hopital R Poincaré, Garches, FRANCE. (3) Myology institute, Hopital Pitié Salpêtrière, Paris, FRANCE. (4) MRI laboratory, Myology institute, Hopital Pitié Salpêtrière, Paris, FRANCE. (5) Radiology department, Hopital R Poincaré, Garches, FRANCE.</p> |
| To contact the author:: david.orlikowski@rpc.ap hp.fr. | <p>Efficacy of Enzyme Replacement (ERT)Therapy is not fully assessed in severe late-onset forms of Pompe disease (SLO Pd). The aim of the study is to assess efficacy and tolerance of ERT in SLO Pd in a Prospective, open-label, single arm, monocenter trial.</p> <p>Five SLO Pd patients confined to wheelchair and ventilated, treated with Myozyme® 20 mg/kg I.V. every 2 weeks for 52 week. Respiratory function (slow Vital capacity sitting and supine, sVC si and su), maximal mouth pressures (Pi and Pe max), transdiaphragmatic pressure (Pdi/MIP and Pdi/MEP), quantitative (QMT) and manual muscle testing (MMT), motor functional testing (MFM), Brook and Vignos, Walton and Gardner scales, muscle morphology (MRI and ¹³C spectroscopy ¹³CNMR), quality of life (SF-36) and safety, assessed at weeks 0, 12, 26, 38 and 52.</p> <p>Age at inclusion was 48±14 years with disease history of 25.7±6.5 years. Mean sVC si and su, Pimax and Pemax were respectively 540±250 ml (15,6%), 430±170 ml (12,5%), 9.0±6 and 12.0±8.6 cm H₂O. Mean Pdi/MIP and Pdi/MEP were 3.2±3.5 and 10.40±5.22 cmH₂O. Three patients were ventilated 24h/day and 4 were tracheostomized. Total MFM, QMT arm and leg scores were respectively 38.0±8.7, 75.3±42.0 and 36.2±26.4. Muscular MRI shows a massive proximal and axial muscular atrophy in all patients. Treatment was well tolerated. One patient died because of tracheal haemorrhage at 50 weeks. At week 52, mild improvement of sVC si and su (+4/+4 and +4/0), Pimax (+7 and +5), Pemax (+6 and +2), Pdi/MEP (+4 and +4) as well as MFM score (+5 and +6) was observed in 2 patients. At week 52, 2 tracheostomized patients were able to breath free of ventilator respectively for 1 and 2 h/24h without increase of dyspnea and one wheelchair bound-patients was able to stand up. In one patient small decrease of pulmonary and muscle endpoints occurs. Quality of life improved in 4 out of 5 patients. In all patients muscle morphology remained unchanged and the glycogen/creatinine ratio decreased in 2 patients.</p> <p>.</p> |

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| PW20-246 | <p><u>A NOVEL THERAPEUTIC APPROACH FOR THE GLYCOGEN STORAGE DISEASE TYPE II</u> DOUILLARD-GUILLOUX G¹, BATISTA L¹, RABEN N², CAILLAUD C¹, RICHARD E³ (1) Institut Cochin, Paris, FRANCE. (2) NIAMSD, NIH, Bethesda, Washington, USA. (3) Inserm EO217, Université Bordeaux 2, Bordeaux, FRANCE.</p> |
| To contact the author:: douillard-guilloux@cochin.inserm.fr. | <p>Glycogen storage disease type II (GSDII) or Pompe disease is an autosomal recessive disorder caused by defects in the lysosomal acid alpha-glucosidase (GAA) gene. It is characterized by glycogen accumulation, especially in skeletal muscle and heart, leading to death in the infantile form. Enzyme replacement therapy (ERT) has recently demonstrated its efficacy on motor strength and cardiac function. However, it has been shown that type II muscle fibers are more resistant to therapy, a phenomenon probably due to large autophagic areas and altered intracellular traffic of the recombinant enzyme. Therefore, our aim is to develop a novel therapeutic approach based on the reduction of glycogen loading, especially in type II fibers.</p> <p>Small interfering RNAs targeted to the two major genes for glycogen synthesis (glycogenin and glycogen synthase) were designed and selected on C2C12 cells. Two lentiviral vectors (siRNA/GN2 and siRNA/GYS2) were tested on primary myoblasts from GSDII mice showing a significant decrease in GN/GYS expression and in glycogen synthesis (80-90% in differentiated cells). Enlarged lysosomes were not found in siRNA/GN or siRNA/GYS cells compared to non-transduced cells.</p> <p>AAV/siRNA/GYS was then constructed and administered in GSDII mice to perform a conditional disruption of the glycogen synthase. A single intramuscular injection induced a reduction in GYS mRNA expression (50%) and glycogen accumulation in the injected gastrocnemius compared to the contralateral muscle. In parallel, a double knock-out (lacking GYS and GAA) was created and used to determine the long-term effects of a permanent glycogen synthase defect. In this model, glycogen accumulation and autophagosomes were not detected in muscle. These results suggest that substrate reduction could be a potential therapeutic strategy in GSDII in association with ERT especially in type II fibers.</p> |

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| PW20-247 | <p>A NEW CASE OF MUSCLE GLYCOGEN STORAGE DISEASE 0 WITH MUTATION IN THE GYS2 MUSCLE SYNTHASE GENE</p> <p>LABARRE VILA A¹, MEZIN P¹, MONNIER N¹, VERGNAUD S¹, BAGUET JP¹, WUYAM B¹, CHABRE O¹, TOUSSAINT B¹, LUNARDI J¹</p> <p>(1) Centre de Référence Rhône-Alpes des Maladies Rares Neuromusculaires, GRENOBLE, FRANCE.</p> |
| To contact the author:: ALabarre-Vila@chu-grenoble.fr. | <p>We describe the case of a young algerian patient, now 27 years old, whose parents are cousins and one of his 5 brothers died suddenly during an effort at the age of 18 years. From age of 7 years, he complains of muscle fatigability, nausea and often feels faint favoured by stress and exercise. He presents with a moderate girdle weakness and diffuse hypotrophy. CK are normal, as glucose tolerance test. Glucagon test produced a normal increase of the glycemia, suggesting a normal hepatic glycogen storage. EMG is myopathic without myotonia. PAS reagent and electron microscopy of two muscles biopsies performed in 1997 and 2002 revealed vacuolar myopathy with absence of intrasarcoplasmic glycogen. Quantitative muscle glycogen was low. Exercise tests showed limited lactate increase, poor performance but the test was stopped as a faint occurred. Cardiac evaluation showed a mild left ventricular hypertrophy, numerous atrial extrasystoles on 24-hour recording of cardiac rhythm. The heart muscle biopsy failed as it induced a serious faint.</p> <p>This case is a new one of muscle glycogen storage disease so-called type 0, recently described in three siblings by Kollberg et al (2007). The risk of cardiomyopathy with sudden death probably responsible for his brother's death is high, and justify cardiac monitoring and prevention of stress. A defibrillator implantation is debated.</p> <p>We identified a homozygous c.678+1G>A splicing mutation in the GYS2 gene coding for the muscle isoform of the glycogen synthase. The mutation led to an in-frame exon 4 skipping and to a strong instability of the deleted transcript. Western-blot analysis confirmed the absence of the muscle glycogen synthase isoform. Both parents were carriers for the mutation.</p> |

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| PW20-248 | <p><u>AN INCREASE IN STRENGTH OF CONTRACTION ACCOMPANIES NOTEXIN INDUCED RE-EXPRESSION OF PHOSPHORYLASE BRAIN ISOFORM IN REGENERATING OVINE MCARDLE'S MUSCLE</u></p> <p>HOWELL JMC¹, CREED KE¹ (1) School of Veterinary and Biomedical Sciences, Murdoch University and Australian Neuromuscular Research Institute, Queen Elizabeth 11 Medical Centre, Needlands, Murdoch, AUSTRALIA.</p> |
| To contact the author:: J.Howell@murdoch.edu.au. | <p>There is no satisfactory treatment of McArdle's disease, a genetic deficiency of myophosphorylase. A sheep model exists and injection of a myophosphorylase expression cassette produced expression of functional myophosphorylase and re-expression of the brain and liver isoforms, as did the injection of notexin . We measured the force of contraction and the extent of fatigue in 47 strips of muscle from 17 normal sheep, 52 strips from 22 untreated McArdle's sheep, and 11 strips from 6 McArdle's sheep 21 days after the injection of 100µl of a solution containing 5 µg/ml of notexin. The contractile response to a single stimulus (twitch) was similar in the 3 groups but the tetanus twitch ratios at 20Hz and 50Hz compared with the twitch were 2.69 and 4.97 in strips from normal and 1.67 and 2.11 from McArdle's sheep. For strips from muscles injected with notexin the ratios were 2.18 and 4.45. The fatigue measurements after 2 seconds at 20 Hz and 50 Hz were 67.4% and 82.3% of the peak in normal, 66.8% and 50.2% in affected sheep and 71.9% and 91.5% after injection with notexin. The force and fatigue when measured at 50Hz in affected sheep was less than in normal sheep, and were improved in regenerating fibres after the injection of notexin towards the normal levels. Muscle biopsies from a second notexin injected site contained 2 to 600 (mean of 161.36) phosphorylase positive fibres compared to zero from affected lambs.</p> |

PW20-249

ALGLUCOSIDASE ALFA IN INFANTS AND CHILDREN WITH RAPIDLY PROGRESSIVE POMPE DISEASE

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Pompe disease is caused by a deficiency of acid alpha-glucosidase (GAA). Severe GAA deficiency manifests during infancy with rapidly progressing muscle weakness and cardiomyopathy. Most patients die by age 1 year.

Two open-label studies (S1 and S2) were conducted in patients ≤ 6 months (S1, n=18) or $>6-36$ months (S2, n=21) of age. S1 patients were randomized to alglucosidase alfa at 20 or 40 mg/kg qow; all S2 patients started at 20 mg/kg qow.

Mean age at treatment \pm SD was 5.1 \pm 2.0 months (S1) and 15.7 \pm 11.0 months (S2), respectively. Median treatment duration for both studies was 120.5 weeks (range: $<1-168$). Cox regression analyses comparing study patients to similar historical controls; (S1 n=61; S2 n=84) indicated that in patients treated at ≤ 6 months, treatment reduced the risk of death by 95% and the risk of death or invasive ventilation by 91% (both with $p < 0.0001$). In patients $>6-36$ months, treatment reduced the risk of death by 79% ($p=0.0009$) and the risk of death or invasive ventilation by 58% ($p=0.02$). Decrease in LV mass occurred in 94% (S1) and 81% (S2) of patients, respectively. In both studies, normal growth was seen in $>80\%$ of patients and clinically significant motor gains in 61%. Infusion-associated reactions occurred in 56%; IgG antibodies developed in 92%. Low IgG titres or a trend towards decreasing titres occurred in 74% of those who seroconverted. Patients with two null GAA mutations and high, sustained IgG titres were observed more frequently among those who died, needed ventilation, and/or had minimal motor response.

These findings illustrate the clinical benefit of alglucosidase alfa in infants and children with Pompe disease. A more robust response was noted in patients treated at earlier stages of disease progression, underscoring the need for early diagnosis.

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| PW20-250 | <p>SUCCESSFUL TREATMENT OF ADENOSINE MONOPHOSPHATE DEAMINASE DEFICIENCY BY D-RIBOSE IN A YOUNG GIRL LAZARO L¹, ROCHCONGAR P¹, MENARD D¹, BALL S², MARCORELLES P³ (1) Centre hospitalier universitaire, RENNES, FRANCE. (2) Birmingham Children's Hospital, BIRMINGHAM, UNITED-KINGDOM. (3) Centre hospitalier universitaire, BREST, FRANCE.</p> |
| <p>To contact the author:: leila.lazaro@chu-rennes.fr.</p> | <p>We report on a nine-year girl who was referred for early fatigue and exercise-induced pain. Those symptoms as well as cramps had developed during early childhood. CK were elevated by one and a half. On clinical examination, a mild pelvic girdle weakness was discovered and muscles strength was graduated 4. Skeletal Muscles were normal in size and the tendon reflexes were present. Screening for other inborn-errors of energy metabolism was negative. Electromyography was normal. Exercise test failed to produce ammonia.</p> <p>Muscle biopsy was performed on vastus medialis. No abnormal fiber pattern was observed. However, complete deficit of activity with AMP deaminase was detected by enzymohistochemistry on the muscle biopsy. The deficiency was confirmed by molecular analysis. A homozygous C34T mutation in the AMPD1 gene was present in the patient and both parents were heterozygous.</p> <p>As this young girl was complaining about her every day life and about school difficulties administration of D-Ribose was tested. The benefit of this treatment was obvious as exercise-induced symptoms decreased. These improvements allowed the young patient to start again a regular practice of sports. Control exercise test under D-Ribose treatment did not find any ammonia production but CK did not rise.</p> <p>As a conclusion, AMP deaminase deficiency could be suspected by a exercise test. Symptoms could be strongly improved by D-Ribose intake particularly in children. These positive results could suggest D-Ribose administration, at least as a test, every time exercise-related symptoms are present.</p> |

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| PW20-251 | <p><u>MYOPATHY WITH LACTIC ACIDOSIS IS LINKED TO CHROMOSOME 12Q23.3-24.11 AND CAUSED BY AN INTRON MUTATION IN THE ISCU GENE RESULTING IN A SPLICING DEFECT</u></p> <p>OLSSON A¹, LIND L¹, THORNELL LE², HOLMBERG M¹</p> <p>(1) Medical and Clinical Genetics Unit, Department of Medical Biosciences, Umeå University, Umeå, SWEDEN. (2) Anatomy Unit, Department of Integrative Medical Biology, Umeå University, Umeå, SWEDEN.</p> |
| <p>To contact the author:: lars-eric.thornell@anatomy.umu.se.</p> | <p>A hereditary metabolic myopathy with paroxysmal myoglobinuria was described by Larsson et al. 1964 (1). The patients showed low physical performance, resulting in physical exertion that causes early exhaustion, dyspnoea, and palpitations. Evidence for a defect in complex II of the respiratory chain (2) and reduced levels of mitochondrial aconitase and additional abnormalities, affecting proteins with iron-sulphur centres, have also been observed (3) suggested that the patients suffered from a dysfunction in iron-sulphur clusters (3). 19 individuals in nine families in northern Sweden have been identified suffering from hereditary myopathy with lactic acidosis (HML).</p> <p>We have now identified the gene for HML to chromosome 12q23.3-24.11, with a maximum lod score of 5.26. The 1.6-Mb disease-critical region contained the gene—<i>ISCU</i>—specifying a protein involved in iron-sulphur assembly. IscU is produced in two isoforms; one cytosolic and one mitochondrial, coded for by different splice variants of the <i>ISCU</i> gene. Mutational analysis revealed one intron mutation specific for the disease haplotype. We could not see any effect of the mutation on expression levels <i>in vitro</i> or <i>in vivo</i>, but a drastic difference in the splicing pattern between patients and controls. In controls the mRNA was mainly in the mitochondrial form, while in the patients a larger mRNA transcript consistent with the cytosolic form of IscU was seen. Sequencing of the product showed that the mRNA of the patient contained part of intron 5. These data reveal an intron mutation in the <i>ISCU</i> gene, resulting in an aberrant mRNA which leads to 15 incorrect amino acids and a premature stop in the translated protein.</p> <ol style="list-style-type: none"> 1. Larsson, L.E., et al (1964). <i>J Neurol Neurosurg Psych</i>, 27, 361-80. 2. Linderholm, H., Essen-Gustavsson, B. and Thornell, L.E. (1990). <i>J Intern Med</i>, 228, 43-52. 3. Hall, R.E., et al (1993). <i>J Clin Invest</i>, 92, 2660-6. |

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| PW20-252 | <p><u>THE POMPE REGISTRY: TRACKING POMPE DISEASE SYMPTOMS IN A BROAD PATIENT POPULATION</u> KISHNANI P¹, BYRNE B², CASE L³, MERLINI L⁴, VAN DER PLOEG A⁵ (1) Division of Medical Genetics, Duke University Medical Center, Durham, USA. (2) Congenital Heart Center University of Florida, College of Medicine, Gainesville, USA. (3) Division of Physical Therapy, Department of Community and Family Medicine, Duke Medical School, Durham, USA. (4) Department of Medical Genetics, University of Ferrara, Ferrara, ITALY. (5) Erasmus Medical Center, Sophia, Rotterdam, THE NETHERLANDS.</p> |
| | <p>Introduction: Pompe disease (acid maltase deficiency) is a rare, progressive, and often fatal metabolic myopathy caused by deficiency of the enzyme acid alpha-glucosidase. Clinical manifestations vary significantly with respect to age at onset, rate of disease progression, and extent of organ involvement.</p> <p>Description: To gain a better understand of the natural course of Pompe disease, a global, voluntary, observational Registry was developed to collect anonymous, longitudinal data on Pompe patients.</p> <p>Preliminary data overview: As of September 2007, 400 patients from 23 countries are enrolled in the Pompe Registry. The majority of patients (71%) are Caucasian; currently, Europe and North America enroll 85% of patients. For infants (n=78, 20%), the median age at symptom onset was 2.0 months, median age at diagnosis 4.0 months. Typically these patients experience cardiomyopathy, profound skeletal and respiratory muscle weakness, and death within the first year of life. For adults (n=238, 60%), the median age at symptom onset was 26.3 years, median age at diagnosis 34.5 years. These patients display progressive proximal skeletal and respiratory muscle weakness. Patients currently ≥ 18 years old (n=259) report the following symptoms most frequently: muscle weakness in lower extremities (81%, including inability to run [66%] and use of a walking device [45%]), upper extremities (71%), and trunk (57%); shortness of breath after exercise (61%) and at rest (33%); dependence on respiratory support (39%); sleep disturbance/apnea (37%); hypotonia (35%); orthopnea (34%); and scapular winging (31%).</p> <p>Summary: Pompe Registry data show that the time from onset of Pompe symptoms to diagnosis represents a significant lag in adults, which is often due to misdiagnosis and highlights the need for greater disease awareness. As the Pompe Registry matures, data on prevalence and age at onset of symptoms in various patient subgroups may allow physicians to identify patients at an earlier stage of disease progression.</p> |