more common as they appear routinely in different populations. To identify them, we analysed the genotypes of MPS-I patients from thirty-five papers and calculated the frequency of every allele for each country. Additionally, Genome Aggregation Database (gnomAD) was consulted to evaluate the allele occurrence in healthy individuals. The most common mutations observed in MPS I patients were p.Trp402Ter, p.Gln70Ter and p.Pro533Arg. The first is the major allele in central Europe, in countries as Spain, Germany, Netherlands, Czech Republic and Slovakia and in the United Kingdom. From its distribution in Europe, we suggest that it has originated possibly with the Celts that once inhabited the continent, further reaching Americas and Australia with 15th century European's navigations. p.Gln70Ter's is very frequent in Finland, Norway and Russia, rareing further south. From its distribution, we suggest a possible Viking origin: they inhabited Scandinavia and migrated towards other European regions in the 8th century. United States and Australia inherited this allele with later British colonization. Finally, p.Pro533Arg is very frequent in Morocco, Algeria and Tunisia. It is also present in Spain, Italy and Turkey, meanwhile rare in Northern Europe. Considering these frequencies, we suggest that p.Pro533Arg originated in North Africa and spread towards Mediterranean countries with Moorish conquests in the Middle Age. South Europeans eventually migrated to Latin America, justifying the high frequency observed in Mexico and Brazil. Data from gnomAD mirrors what was observed in MPS-I patients. In conclusion, the distribution of the three most common IDUA mutations (p.Trp402Ter, p.Gln70Ter and p.Pro533Arg) varies around the world, with possibly different origins. This knowledge facilitates the design of new therapies based on the genotype, but also helps in fast diagnosis and, consequently, better treatment outcomes. Funding: CNPq

doi:10.1016/j.ymgme.2017.12.317

309
Open-label, single arm, pilot study of intravenous laronidase following allogeneic transplantation for Hurler syndrome

Lynda E. Polgreen[a], Troy C. Lund[b], Julie Eisengart[b], Weston Miller[b], Paul J. Orchard[b], *[a]LA BioMed at Harbor-UCLA, Torrance, CA, United States, [b]University of Minnesota, Minneapolis, MN, United States*

Mucopolysaccharidosis IH (Hurler syndrome; MPS IH) is a lysosomal disease resulting from deficiency of alpha-L-iduronidase. Infants and young children with MPS IH are treated with hematopoietic cell transplantation (HCT) due to cognitive involvement of the disease. However, enzyme replacement therapy (ERT) is also available and used to treat patients with the attenuated form of MPS I. It is unknown whether ERT can improve skeletal outcomes in patients with MPS IH previously treated with HCT. Therefore, we completed a 2-year open-label study of laronidase 0.58 mg/kg IV weekly in 10 patients with MPS IH who were <14 years at enrollment, at least 2 years since HCT, and donor engrafted. Safety, skeletal and functional outcomes were assessed every 6 months. Of the 10 patients (40% female) who completed the study (1 withdrew), median age was 9.5 years (range 5-13 years), 40% had improvements (defined for all joints as >5 degrees improvement) in shoulder range-of-motion (ROM), 30% had improvements in elbow ROM, and 50% had improvements in hip extension. Median change in handgrip strength was 1.0 kg (range -0.7 to 4.0 kg) and in 6-minute walk test was 128 feet (range -340 to +864 feet). There was no significant improvement in growth velocity compared to pre-treatment growth velocity. Median change in time to fatigue on a modified Balke Treadmill Test was 4.5 minutes (range -0.8 to 17.2 minutes). All participants had missing data for each outcome due to surgeries, pain, neurocognitive difficulties, and/or limited physical function. The fewest missing data points were for 6MWT, ROM, and height. In conclusion, laronidase initiated at least 2 years after HCT resulted in improvements in joint ROM, strength, physical function, and endurance, although results were highly variable between subjects and missing data was common.

doi:10.1016/j.ymgme.2017.12.318

310
Defining clinical measures of skeletal disease severity in mucopolysaccharidosis type I

Lynda E. Polgreen[a], Klane White[b], Kyle D. Rudser[c], Jeremiah S. Menk[d], Bradley S. Miller[d], Ellen Fung[e], Julie Eisengart[d], Troy C. Lund[d], Paul J. Orchard[f], *[a]Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA, United States, [b]University of Washington, Seattle Children's Hospital, Seattle, WA, United States, [c]University of Minnesota, Minneapolis, ME, United States, [d]University of Minnesota, Minneapolis, MN, United States, [e]UCSF Benioff Children's Hospital, Children's Hospital Oakland Research Institute, Oakland, CA, United States, [f]University of Minnesota, Mineapolis, MN, United States*

Progressive, debilitating, skeletal disease persists despite current therapies for mucopolysaccharidosis type I (MPS I). Quantifiable and easy to reproduce skeletal outcome measures are needed to advance therapies for MPS I that can treat the skeletal disease. Therefore, we conducted a cross-sectional analysis of measures of skeletal disease collected in year 6 of a 10-year longitudinal study. We identified outcomes that provided the best separation of MPS I disease severity, based on an established diagnosis of severe vs. attenuated disease, and could be easily obtained in routine clinical practice. These outcomes were then correlated with bodily pain and physical function scores from the CHQ-PF50 (for ages <18 years) and the SF-36 (for ages ≥18 years) using Pearson or Spearman correlation tests. We found that the three skeletal outcomes that provided the best separation by disease severity in these 20 patients with MPS I (14 MPS IH; 6 MPS IA) aged 8-23 years were: 1) hip dysplasia - the minimum Tonnis angle by pelvic radiograph, 2) osteoarthritis - the maximum Tonnis grade by pelvic radiograph, and 3) bone growth - height Z-score (age and sex matched). There were trends in correlations of increased hip dysplasia (higher minimum Tonnis angle) with more pain (95% CI: -0.8 to 0.1; $p = 0.08$), of increased hip osteoarthritis (higher maximum Tonnis Grade) with decreased physical function (-0.36; $p = 0.17$), and of lower height Z-score with decreased physical function (95% CI: -0.1 to 0.7; $p = 0.17$). In conclusion, we have identified easily quantifiable, clinically significant, measures of skeletal disease severity in patients with MPS I that could be used to measure effects of therapy. Additional testing of these measures in a larger population is required to validate the clinical relevance of these outcomes.

doi:10.1016/j.ymgme.2017.12.319

311
Clinical, serum lyso-Gl3 and kidney histological findings in 14 pediatric patients with classic phenotype of Fabry disease: Is it possible a correlation?

Juan Politei[a], Valeria Alberton[b], Oscar Amoreo[b], Norberto Antongiovanni[c], Maria Nieves Aran[b], Marcelo Baran[b], Gustavo Cabrera[d], Silvia Di Pietrantonio[b], Consuelo Durand[a], Alejandro Fainboim[e], Joaquin Frabasil[a], Fernando Gomez Pizarro[f], Miguel Liern[e], Fernando Perretta[g], Diego Ripeau[h], Fernanda Tognolo[i], Hernan Trimarchi[j], Dana Velasques Rivas[a], Elsa Zotta[k], Andrea Beatriz Schenone[a],

[a]Laboratorio de Neuroquímica Dr Chamoles, Buenos Aires, Argentina, [b]El Cruce Hospital, Buenos Aires, Argentina, [c]Pergamino Clinic, Buenos Aires, Argentina, [d]Del Viso Medical Center, Buenos Aires, Argentina, [e]Ricardo Gutierrez Children Hospital, Buenos Aires, Argentina, [f]San Justo Children Hospital, Buenos Aires, Argentina, [g]Dr. E. Erill Hospital, Buenos Aires, Argentina, [h]Prof. Dr. Alejandro Posadas Hospital, Buenos Aires, Argentina, [i]Pathology Diagnoses Center, Buenos Aires, Argentina, [j]Britain Hospital, Buenos Aires, Argentina, [k]IFIBIO Houssay, CONICET, Pharmacy and Biochemistry Faculty, Buenos Aires, Argentina

Introduction: The classic phenotype of Fabry disease (FD) in children presents early symptoms such as neuropathic pain, angiokeratoma, corneal opacities and gastrointestinal compromise, particularly in males. Findings in kidney biopsy in children and serum lyso-Gb3 levels were reported previously, but no correlation was presented.

Aim: to present an observational correlation between clinical parameters, serum lyso-Gb3 level and histological findings in kidney biopsy in children with classic phenotype of FD.

Patients and methods: 14 children (10 girls, media age 10.5 years old) were included before enzyme replacement therapy indication. Clinical parameters (neuropathic pain, angiokeratomas, cornea verticilatta and gastrointestinal compromise), serum lyso-Gb3 and podocituria were assessed. A kidney biopsy was performed in all patients.

Results: all patients referred at least one symptom, just the youngest male (2 years old) did not present any symptom. Serum lyso-Gb3 was measured in 11/14 patients and in all cases levels were upper the normal range. In 8/10 girls podocituria was higher than controls as well as in 2/2 boys. Even when all patients presented normal glomerular filtration rate, kidney biopsy showed: podocyte Gb3 inclusions in all samples, 12/14 showed foot-process effacement and Gb3 accumulation in distal tubules, 11/14 glomerular endothelial cells inclusions, 3/14 intersticial fibrosis and glomerular sclerosis in 2/14. We found higher level of lyso-Gb3 in girls with more symptomatic burden of the disease and the same finding was evident in cases with severe histological involvement in kidney biopsy.

Conclusion: In all children with classic FD kidney involvement was present, and signs of fibrosis and sclerosis were found in the 21% of samples. Podocituria, as an early marker of glomerular damage, was present in 80% of girls and 100% in boys. Lyso-Gb3 in serum was high in all cases and seems to correlate with symptoms and renal histological involvement in girls.

doi:10.1016/j.ymgme.2017.12.320

312
Fabry disease: Multi-disciplinary evaluation after 15 years of treatment with agalsidase beta

Juan Politei[a], Gustavo Cabrera[b], Consuelo Durand[c], Joaquin Frabasil[c], Andrea Beatriz Schenone[c], [a]Dr Chamoles, Neurochemistry Laboratory, Quilmes, Argentina, [b]Del Viso Medical Center, Buenos Aires, Argentina, [c]Dr Chamoles, Neurochemistry laboratory, Buenos Aires, Argentina

Objective: to describe the results of the multidisciplinary evaluation in 5 patients with classic phenotype of FD after 15 years of treatment with agalsidase beta.

Patients and methods: five patients from the same family were enrolled. Baseline data was measured for renal, cardiac and cerebrovascular functioning. We compared baseline quality of life scales with the current results.

Results: Male patients started ERT before 28 years old and the female at 46. Before ERT all patients showed normal eGFR. All presented microalbuminuria and just two cases showed proteinuria. After 15 years of ERT, no patient showed decrease in renal functioning. One patient decreased from proteinuria to microalbuminuria range. Before treatment left ventricular hypertrophy (LVH) was not present in any case and LV Mass Index was abnormal in the female patient. After treatment echocardiographic values did not present progression to LVH. Brain MRI showed lack of ischaemic lesions and vertebrobasilar dolichoectasia in one male, after 15 years MRI findings did not change. Quality of life showed improvement in all domains measured.

Conclusion: Our results in patients with mild organ involvement in classic phenotype of Fabry disease, showed good outcomes and support an early and continuous ERT.

doi:10.1016/j.ymgme.2017.12.321

313
Lessons learned after 5 years of treatment in adult patient with MPS VI. ERT, spinal decompression and home infusion therapy: A triangle for success?

Juan Politei, Consuelo Durand, Andrea Beatriz Schenone, *Laboratorio de Neuroquímica Dr Chamoles, Buenos Aires, Argentina*

Mucopolysaccharidosis VI (MPS VI) or Maroteaux-Lamy syndrome is an inherited metabolic disease caused by a deficiency of the lysosomal enzyme arylsulfatase B. Clinical phenotypes vary between slowly and rapidly progressive. A severe, disabling and life-threatening complication of MPS VI is narrowing of the cervical spinal canal at the craniocervical junction.

Aim: to present the outcome after 5 years of treatment in an adult patient with MPS VI. Case report: 26 years old MPS VI male patient, diagnosed at the age of 9 years, started enzyme replacement therapy (ERT) at 26 years due severe pain at the cervical level and proximal joints in 4 limbs and to prevent further complications related to MPS. One year after ERT, the 6MWT increased distance, however due progression of spinal symptomatology indication craneo-cervical decompression was performed with clear omprovement in pain and functional scales. After 4 years of ERT and spinal surgery clinical parameters, SF-36 and pain scales showed initial improvement and further stabilization. The beginning of home infusion therapy led to a new improvement of SF-36 during the last year.

Conclusion: ERT and craneal decompression have shown a positive result in previous experiences. Home infusion therapy in MPS VI was rarely reported. A better compliance with the weekly treatment regimen was improved in our patient on home therapy at the same time that quality of life scale showed a new recovery. In adult patients with mild visceral involvement, the three columns of treatment: ERT, spinal decompression and home infusion therapy may guarantee a successful outcome.

doi:10.1016/j.ymgme.2017.12.322

314
Long term renal function in patients with Fabry disease

Juan Politei[a], Ricardo Heguilen[b], Gustavo Cabrera[c], Amelia Bernasconi[b], Consuelo Durand[a], Frabasil Joaquin[a], Andrea Beatriz Schenone[a], [a]Laboratorio de Neuroquímica Dr Chamoles, Buenos Aires, Argentina, [b]Juan Fernandez Hospital, Buenos Aires, Argentina, [c]Del Viso Medical Center, Buenos Aires, Argentina

Proteinuria and progressive renal dysfunction are major findings in patients with Fabry disease. In order to prevent progressive organ