prevalent are c.1226A > G (N370S) and C.1448 T > C (L444P) constituting the majority of subtypes 1 and subtypes 2/3. Diagnosis can be significantly delayed due to a broad spectrum of symptoms that overlap with other conditions, compounded by a lack of disease awareness. Thus, there is a need for a simple methodology to facilitate the identification of patients for earlier diagnosis. Recently, the prototype of a GD type 1/3 point-scoring system (PSS), proposed by the panel of the Gaucher Earlier Diagnosis Consensus initiative (GED-C), was tested using electronic health record data available from 170,000 individuals previously treated at the Hospital District of Southwest Finland (HDSWF). All individuals were successfully point-scored, but not validated as GD patients. The aim of this study was to advise on further validation of the GED-C PSS and deciding which patient should be tested to confirm GD diagnosis at the HDSWF. For this, the points distributions of the GED-C PSS in true GD patients, previously diagnosed at the Oulu University Hospital, Finland, were evaluated. GD diagnosis of three patients participating in the study was confirmed. All patients were found to have deleterious *GBA* mutations, including a novel compound heterozygous mutation in one patient, and high levels of lyso-Gb1 in plasma samples and dry whole blood spots. Importantly, overall point scores of all these patients were high, although variable among individuals, when compared to the general point score distribution of the data set obtained from the HDSWF, thus further validating the GED-C PSS. This study was funded by Takeda.

doi:10.1016/j.ymgme.2019.11.379

371
Selective screening for nephropathic cystinosis among high-risk contingents of the children population in Russia

Kirill Savostyanov, Alexander Pushkov, Natalia Zhurkova, Natalia Mazanova, Lubov Muravyova, Alexander Pakhomov, Piotr Ananin, Tatyana Vashurina, Alexey Tsygin, Andrey Fisenko, *National Medical Research Center for Children's Health, Moscow, Russian Federation*

Cystinosis is a rare metabolic disease characterized by an accumulation of cystine inside the lysosomes, causing damage in different organs and tissues, particularly in the kidneys and eyes. We examined 75 blood samples from patients selected according to the following criteria: renal tubular Fanconi syndrome, glucosuria, polydipsia, polyuria, vomiting, dehydration, metabolic acidosis, failure to thrive, skeletal deformity, phosphaturia/rickets. All patients were measured concentration of cystine in leukocytes by HPLC-MS. Analysis of all coding and adjacent intron regions of the *CTNS* gene was performed by Sanger sequencing. 57 kb deletion was detected by PCR-based assay. We revealed 33 (44%) children (boys 61%, girls 39%) median aged 22 month (5 month - 145 month) with the increased concentration of cystine in leukocytes. All of them were confirmed by molecular genetics analysis. As a result, 17 different variants in the *CTNS* gene were identified. Among the mutations described earlier, a deletion of 57 kb was detected in 20 (30%) alleles. Seven mutations (41%) were not described before this study. These are one missense mutation *c.627C > A (p.S209R)*, three nonsense mutations *c.450G > A (p.Trp150*)*, *c.433C > T (p.Q145*)* and *c.785G > A (p.W262*)*, one frameshift *c.1000del (p.Thr334Profs*65)* and one splicing site mutation *c.140 + 2dup*. The cystinosis screening algorithm used, including biochemical and subsequent molecular genetic diagnostics, showed high detectability among Russian patients. The high frequency of 57 kb deletion allows to start the molecular genetic diagnosis of cystinosis with its detection.

doi:10.1016/j.ymgme.2019.11.380

372
Lyso−Gb_3 is not a predictive biomarker of treatment response in migalastat-treated patients with migalastat-amenable variants

Raphael Schiffmann[a], Daniel G. Bichet[b], Johannes M. Aerts[c], Nina Skuban[d], Atul B. Mehta[e], *[a]Baylor Scott & White Research Institute, Dallas, TX, United States, [b]Hôpital du Sacré-Coeur, University of Montreal, Montreal, QC, Canada, [c]Leiden Institute of Chemistry, Leiden, Netherlands, [d]Amicus Therapeutics, Inc., Cranbury, NJ, United States, [e]Royal Free Hospital, University College London, London, United Kingdom*

Fabry disease (FD) is a rare, progressive X-linked lysosomal disorder caused by *GLA* gene variants, resulting in functional deficiency of alpha-galactosidase A (α-Gal A) and pathological accumulation of glycosphingolipids within lysosomes. These glycosphingolipids accrue in many cell types, such as capillary endothelial, renal, cardiac, and nerve cells, and can activate Toll-like receptors, triggering inflammation and fibrosis cascades. Migalastat, an oral pharmacological chaperone available worldwide for treating patients with migalastat-*amenable GLA* variants, binds to and stabilizes endogenous α-Gal A and facilitates trafficking of the endogenous enzyme to the lysosomes. With new data that assist our understanding of FD pathophysiology, there is an increasing need for predictive biomarkers to monitor and evaluate treatment efficacy in FD. Here, we examined profiles of plasma globotriaosylsphingosine (lyso-Gb_3) in enzyme-replacement therapy (ERT)-naive and ERT-experienced patients with FD who were treated with migalastat in the phase 3 FACETS (NCT00925301) and ATTRACT (NCT01218659) studies and subsequent long-term open-label extension studies to assess the validity of lyso-Gb_3 as a predictive biomarker of treatment response. Spearman rank correlation coefficients and *P* values were calculated to assess the correlation between plasma lyso-Gb_3 and left ventricular mass index (LVMi), estimated glomerular filtration rate ($eGFR_{CKD\text{-}EPI}$), and global measure of pain per the Brief Pain Inventory Short Form. Baseline was defined as the beginning of migalastat treatment. In ERT-experienced patients, no significant correlation was identified between changes in lyso-Gb_3 and changes in LVMi, eGFR, or pain at months 18 or 30. In ERT-naive patients, there was no significant correlation between changes in lyso-Gb_3 and LVMi at months 6 or 24, or between changes in lyso-Gb_3 and eGFR at month 6. Data suggest that lyso-Gb_3 is not a predictive marker of treatment response in patients receiving treatment with migalastat for FD, consistent with published data for ERT.

doi:10.1016/j.ymgme.2019.11.381

373
Venglustat combined with imiglucerase positively affects neurological features and brain connectivity in adults with Gaucher disease type 3

Raphael Schiffmann[a], Timothy M. Cox[b], Hiroyuki Ida[c], Eugen Mengel[d], Pramod Mistry[e], Nigel Crawford[f], Sebastiaan Gaemers[g], Allena Ji[h], M. Judith Peterschmitt[i], Jyoti Sharma[f], Qi Zhang[f], Tanya Fischer[i], *[a]Baylor Research Institute, Dallas, TX, United States, [b]University of Cambridge, Cambridge, United Kingdom, [c]The Jikei University School of Medicine, Tokyo, Japan, [d]Mainz Medical University, Mainz, Germany, [e]Yale School of Medicine, New Haven, CT, United States, [f]Sanofi Genzyme, Bridgewater, NJ, United States, [g]Sanofi Genzyme, Amsterdam,*