patients identified in the French Gaucher Disease Registry are included and exhaustive data are collected. Twenty-six women and 21 men are included, median age 46.6 years [2.4–81.1] with a median follow-up duration of 10.7 years [0.4–40.8]. Patients homozygous for N370S mutation represent 22% of the patients, and those heterozygous for L444P mutation represent 24.4%. From diagnosis to inclusion, we observe no worsening for 75% of the patients. Some clinical features improve such as fatigue or splenomegaly. However, chronic bone pain usually worsens. Biologically, hemoglobin improves, and platelets count and chitotriosidase remain stable. This study highlights the large genotypic heterogeneity of this sub-group, in which the disease is stable despite the absence of treatment. Interestingly, some of the patients experience a spontaneous improvement. Next step will be the prospective follow-up of this cohort to analyze the characteristics leading to potential complications. This study was funded by Shire, now part of Takeda.

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379
Alteration in redox homeostasis in early-onset Tay-Sachs disease mouse model

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Tay-Sachs disease is an autosomal recessively inherited lysosomal disorder. It is caused by mutations on the HEXA gene encoding α-subunit of β-Hexosaminidase A enzyme. The enzyme normally catalyzes GM2 to GM3 conversion but when it is absent or dysfunctional the GM2 degradation is interrupted. The undegraded GM2 ganglioside is progressively accumulated especially in neurons and causes neurodegenaration at the end. The *Hexa*$^{-/-}$ mice generated as Tay-Sachs model was nearly normal and a bypass mechanism mediated by a sialidase was suggested. Recently we determined that Neu3 sialidase involves in ganglioside degradation in the Tay-Sachs disease pathology and the *Hexa*$^{-/-}$*Neu3*$^{-/-}$ mice mimic the neuropathologic and clinical phenotype of the disease. It was reported that oxidative stress is triggered in neurodegenerative diseases and several lysosomal disorders. It is caused by the imbalance between antioxidant defence mechanism and production of reactive oxygen species (ROS). ROS have high chemical reactivity which react and damage DNA, protein, carbohydrates and lipids. In this study we investigated whether the oxidative stress has an effect on the pathology of *Hexa*$^{-/-}$*Neu3*$^{-/-}$ mice or not. We found that expression levels of oxidative stress markers Catalase and Ttase1 was significantly increased in *Hexa*$^{-/-}$*Neu3*$^{-/-}$ fibroblast. Furthermore, oxidized DCFDA was significantly elevated in *Hexa*$^{-/-}$*Neu3*$^{-/-}$ mice fibroblast compared to *Hexa*$^{-/-}$. There was an increase in protein level of APE1/Ref-1 which indicates cellular response to oxidative stress in cerebellum and thalamus of *Hexa*$^{-/-}$*Neu3*$^{-/-}$ mice. In addition, a significant increase in protein carbonyl level only in cerebellum region was detected by protein carbonylation assay based on detection of derivatized carbonyl groups on the side chains of the proteins. Our overall our data suggests that GM2 accumulation causes increased oxidative stress and leads to alteration in redox homeostasis which contributes pathology in early-onset Tay-Sachs disease mouse model.

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380
Analysis of rare variants in lysosomal pathway genes in patients with Gaucher disease with and without Parkinson disease

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Gaucher disease (GD) is a lysosomal disorder (LD) that results from a deficiency in the enzyme glucocerebrosidase caused by mutations in the *GBA1* gene. GD presents with a broad phenotypic spectrum, ranging from lethal to very mild symptoms, but it is clinically divided into three types: non-neuronopathic (GD1) and acute and chronic neuronopathic (GD2 and GD3, respectively). Mutations in *GBA1* are also one of the most common genetic risk factor associated with Parkinson's disease (PD), although not all mutation carriers develop PD. Recent literature (Robak et al., 2017) suggests an excessive burden of LD gene variants in PD. In order to identify possible modifier genes for PD among our cohort, we analyzed whole exome sequencing data for rare and likely damaging variations in 54 LD genes in 41 patients with both GD and PD (GD/PD) and 32 patients with GD alone. We hypothesize that multiple variants in these genes may collectively impair lysosomal function in GD/PD patients vs GD. This could contribute to the accumulation of α;-synuclein in patient's brain and lead to the development of PD later in life. Using *t*-test and Mann-Whitney *U* Test our results suggest an increased burden of rare and likely damaging variants in LD genes in the GD/PD group compared to the GD group. Variants in *ATP13A2*, *CLN6* and *CTSD* specifically were over-represented in patients with GD/PD vs GD. Since this is a pilot study, replication of the analyses in a larger patient population is needed to validate the findings and well as studies are needed to functionally characterize effects of multiple genetic hits in Parkinson disease pathogenesis in GD/PD patients.

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381
Role of 3-dimensional (3D) reconstruction of radiology images and virtual endoscopy in the assessment of airways in adult mucopolysaccharidosis patients

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Mucopolysaccharidosis (MPS) is a lysosomal disorder caused by deficiency of enzymes metabolising glycosaminoglycans (GAGs) leading to multisystem disease due to GAGs deposits. MPS patients have a complex airway and failure to recognise this prior to general anaesthesia can lead to significant morbidity and mortality. A 3D reconstruction and virtual endoscopy can be created from CT or MRI scans. We discuss our experience with these non-invasive methods in the airway assessment of MPS patients. Retrospective data was collected in MPS patients who had this performed at our centre. Patients had CT scan (2.5 mm thick slices) of the neck and thorax. 3D reconstruction of the airway and production of the virtual endoscopy were performed using the software 3D Slicer, with further video editing carried out with the software package Blender. The resulting models had axial resolution of 2.5 mm and lateral resolution of 0.7 mm, but were further processed within 3D Slicer to provide smooth surfaces. Seven adult MPS patients (MPS $I = 1$, MPS II $= 5$, MPS IV