(67.64%), and Mongolian spots (64.71%). There are two clinical manifestations that are markedly different between IIIA and IIIB: Hepatosplenomegaly and serrated teeth. The most common initial symptoms at diagnosis were speech delay (52.94%), hyperactivity (35.29%), and mental deterioration (29.41%). Genetic analysis of 25 patients was conducted, which identified 12 previously unreported mutations. There was no significant difference in the incidence of MPS IIIA and IIIB in this Chinese cohort. The incidence of MPS IIIC was significantly lower than that of IIIA and IIIB. No IIID patient was found. The initial clinical symptoms of MPS III were atypical. When language retardation, mental retardation, and rough facial features occur, MPS III should be considered in combination with other clinical features, such as cerebral cortex atrophy. Hepatosplenomegaly and serrated teeth can be used clinically to preliminarily distinguish IIIA from IIIB. We emphasize the importance of establishing early diagnostic procedures so that gene therapy can be carried out as soon as possible to alter the disease prognosis.

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A new look at an old disease: Is Pompe disease a neuromuscular disorder with CNS involvement?

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Pompe disease is a lysosomal disorder caused by deficiency of acid-alpha glucosidase. Lately, there have been increasing reports of white matter (WM) involvement in the brain of children with Pompe disease. Purpose of this study was to describe the extent of WM involvement and to provide new evidence of its variable rates of progression in children with Pompe disease. Methods included (1) a grading system using the Fazekas scale (quantitative assessment) on brain MRI-T2-weighted-Fluid Attenuated Inversion Recovery (T2-FLAIR) to measure WM hyperintense foci, (2) review of MRI by an experienced neuroradiologist (qualitative assessment). The Fazekas scale scoring was tailored for Pompe disease. Ten brain areas were assessed (each area scored 0–3) and each child received a total Fazekas scale score (0-absent to 30-most severe). At baseline, there were twelve children with infantile Pompe disease (IPD) and three with late-onset Pompe disease (LOPD). The total Fazekas scale score ranged from 2 (mild) to 23 (severe) for ten children with IPD. Two children with IPD and three with LOPD, each had a score of zero. For the longitudinal analyses, 13 baseline MRIs from 13 children with IPD and 15 subsequent MRIs from 6/13 children (total 28 MRIs) were examined. Superficial areas (periventricular and then subcortical) were involved prior to the deeper areas of the brain. Repeat MRIs showed variable rates of progression. There was an early involvement of the corticospinal tracts ($n = 10$), u-fibers ($n = 7$) and gray matter ($n = 2$). In conclusion, children with IPD had variable degrees of WM involvement and rates of progression. The Fazekas scale is an effective way to quantitatively assess this progression. This study underscores the need for therapies that can target the CNS. Further research is required with more longitudinal data to understand the impact of WM involvement on developmental outcomes. [Study was funded by Sanofi Genzyme].

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Mini-COMET study: Safety, immunogenicity, and preliminary efficacy for repeat avalglucosidase alfa dosing in patients with infantile-onset Pompe disease (IOPD) who were previously treated with alglucosidase alfa and demonstrated clinical decline

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Mini-COMET (NCT03019406) is an ongoing phase 2, open-label, ascending-dose, 3-cohort study, evaluating safety, pharmacokinetics, and preliminary efficacy of avalglucosidase alfa in patients aged <18 years with infantile-onset Pompe disease (IOPD). Patients had been previously treated with any stable dose of alglucosidase alfa for ≥6 months and demonstrated either clinical decline (Cohorts 1 [$n = 6$] and 2 [$n = 5$]) or sub-optimal response (Cohort 3 [$n = 11$]). Cohorts 1 and 2 received avalglucosidase alfa 20 or 40 mg/kg IV every other week (qow), respectively, for 6 months. Cohort 3 patients were randomized (1:1) to avalglucosidase alfa 40 mg/kg IV qow ($n = 5$) or alglucosidase alfa (current stable dose for previous 6 months [$n = 6$]). Thereafter, all patients may enter a study extension (≤3 years on-study) to receive avalglucosidase alfa 20 mg/kg qow (Cohort 1) or 40 mg/kg qow (Cohorts 2&3, and Cohort 1 patients with more rapid worsening of clinical decline). Interim data as of June 2019 are reported here. For Cohorts 1, 2, and 3 (only patients receiving avalglucosidase alfa), respectively: mean ages (range) at avalglucosidase alfa initiation were 7.6 (2–11), 8.1 (1–12), and 6.9 (4–10) years; mean (range) duration of avalglucosidase alfa exposure was 78.6 (63.9–88.3), 59.0 (56.1–62.1), and 21.3 (14.1–26.3) weeks; and mean (range) number of infusions was 40.2 (33–45), 30.4 (29–32), and 11.6 (8–14). Overall, treatment-emergent adverse events (AEs) were generally mild to moderate; most frequently reported treatment-related AEs (2 patients each) were fall (Cohort 1) and rash (Cohorts 2&3). Nine patients (Cohort 1: $n = 4$; Cohort 2: $n = 3$; Cohort 3: $n = 2$) presented with serious AEs unrelated to treatment. In each cohort, 2 patients had at least 1 protocol-defined infusion-associated reaction. These interim results demonstrate that avalglucosidase alfa was well-tolerated in enzyme replacement therapy-experienced IOPD patients. Updated safety data (including immunogenicity), as well as preliminary efficacy data, are planned for presentation. Funding: Sanofi Genzyme.

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