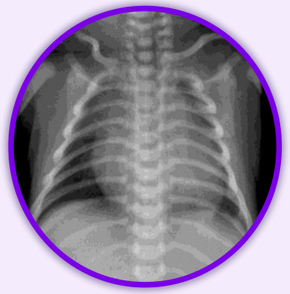
Clinical Studies in Patients with Infantile-Onset Pompe disease (IOPD)

Sanofi has pioneered the development and delivery of therapies for patients affected by rare and debilitating diseases for over 30 years. With a focus on rare disease, multiple sclerosis, immunology, oncology and rare blood disorders, we are dedicated to making a positive impact on the lives of patients and families we serve. This goal guides and inspires us every day.

Infantile Onset Pompe Disease (IOPD)

also known as acid maltase deficiency and glycogen storage disease type 2, usually presents prior to one year of age and is characterized by profound muscle weakness and cardiomyopathy. IOPD is rapidly progressive typically leading to death by cardiorespiratory failure by two years of age if left unmanaged. IOPD is caused by the deficiency of acid apha glucosidase (GAA) that results in the accumulation of lysosomal glycogen.[1]

Hypotonia and head lag[2]

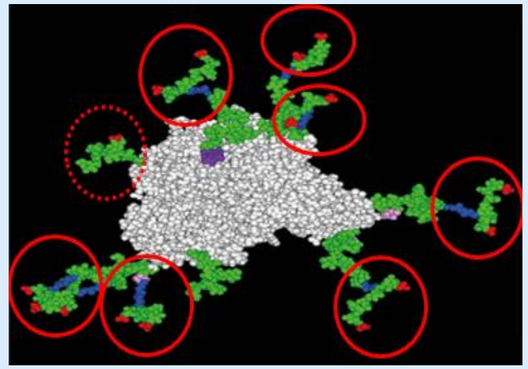


Chest X-ray of a 1-day-old female newborn[3]

1. American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM). Muscle Nerve. 2009;40:149-160
2. Image reproduced with permission from John R Bach, MD, published by Medscape CME & Education, *New* Clinical Findings in Pompe Disease, Also Known as Acid Maltase Deficiency: Evidence-Based Cases in Infantile- and Late-Onset Patients, 2007,
3. Pompe Disease: Early Diagnosis and Early Treatment Make a Difference. Yin-Hsiu Chienb, Wuh-Liang Hwu,, Ni-Chung Lee

Avalglucosidase Alfa is a GAA enzyme replacement therapy designed with increased mannose-6-phosphate (M6P) and bis-M6P content.

Avalglucosidase alfa
~15 mol M6P/mol rhGAA



Legend:

- **N-linked glycosylation sites (complex-type-N-glycans and bis mannose-6-p hosphate neoglycans)**
- **Aminooxy linker AAA**
- **Terminal glycan phosphate**
- **Fucose**

Reprinted (adapted) with permission from Zhou Q, et al. *Bioconjugate Chem* 2011;22:741–751. Copyright 2011 American Chemical Society. Zhou Q, et al. *Bioconjugate Chem*. 2013;24:2025–2035. [2]Zhu Y, et al. *Mol Ther*. 2009 Jun;17(6):954-63. *GAA*, acid α-glucosidase

The use of avalglucosidase alfa in the BabyCOMET study is investigational and the safety and efficacy of this use have not been evaluated by any regulatory authority.

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IOPD Observational Study

NCT:04848779

This is a multinational, multicenter, observational, noninterventional, prospective, follow-up study to assess the efficacy and safety of alglucosidase alfa in patients with IOPD which will serve as an external comparator for Baby-COMET.

The primary outcome is efficacy on survival and ventilator-free survival after 52 weeks of treatment.

Secondary outcomes include the effect on survival and invasive ventilator-free survival at 12 & 18 months of age; change in LVM Z-score; AIMS score; body length & weight, head circumference Z scores; urinary Hex4; Pompe-PEDI, Motor Milestones checklist, Bayley Scale of Infant and Toddler development.

Key Inclusion Criteria:

- Infants ≤ 6 months
- Confirmed diagnosis of IOPD with established CRIM status available
- ERT therapy planned or initiated with alglucosidase alfa
- Presence of cardiomyopathy at time of diagnosis

Key Exclusion Criteria:

- Ventilator use, major congenital abnormalities
- Previous use of any other Pompe disease specific therapy

baby COMET

NCT:04910776

This is a single group, phase 3, multinational, multicenter, open label study of avalglucosidase alfa 40 mg/kg QOW in treatment naive IOPD patients.

The primary outcome is efficacy on survival and ventilator-free survival after 52 weeks of treatment.

Secondary outcomes include the effect on survival and invasive ventilator-free survival at 12 and 18 months of age; change in LVM Z-score; AIMS score; body length and weight, head circumference Z scores; urinary Hex4; Pompe-PEDI, Motor Milestones checklist, Bayley Scale of Infant and Toddler development.

Key Inclusion Criteria:

- Infants ≤ 12 months
- Confirmed diagnosis of IOPD with established CRIM status available
- Treatment naïve
- Presence of cardiomyopathy at time of diagnosis

Key Exclusion Criteria:

- Ventilator use, major congenital abnormalities
- Previous use of ERT or any other Pompe disease specific therapy

For more information, please contact your local Sanofi representative or visit:

https://clinicaltrials.gov

https://sanofistudies.com

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