Sponsor: Sanofi **Drug substance(s):** Fabrazyme® (agalsidase beta)	**Study Identifiers:** NCT00230607; EudraCT Number: 2006-001910-33 **Study code:** AGAL02603/MSC12868

Title of the study:

A Multicenter, Multinational Study of the Effects of Fabrazyme® (agalsidase beta) Treatment on Lactation and Infants

Study center(s):

This study was conducted at 3 centers that enrolled participants in the United States (US) and United Kingdom (UK). Initially the study protocol was submitted to US, UK, Northern Ireland, and Austria. The only site in Austria was closed with no enrolled patient and there was no activity in Northern Ireland.

Study period:

Study initiation date: 28 May 2006

Study completion date: 09 Feb 2024

Study Status: Terminated (Per FDA decision, the 2003 Post Marketing commitment has been fulfilled.)

Phase of development: Phase 4

Objectives:

Primary

- To determine whether αGAL (alpha-galactosidase A) activity is present in the breast milk of mothers with Fabry disease who are being treated with Fabrazyme® during lactation.
- To measure breast milk production and composition (volume, protein and fat content) in women with Fabry disease who received Fabrazyme® during lactation.
- To determine whether Fabrazyme® affects the growth, development, and immunologic response of infants born to mothers with Fabry disease who received Fabrazyme® during lactation.

Methodology:

AGAL02603 is a Phase 4, multicenter, multinational study to evaluate the effects of Fabrazyme® on lactation and on the growth, development, and immunologic response of infants born to mothers with Fabry disease who are treated with Fabrazyme® during lactation. The study protocol included 3 participation scenarios: mother/infant full participation, mother full participation/infant development only, and mother full participation/infant no participation.

The lactation status of the mother was assessed at each visit. At Months 1, 3, and 6, breast milk samples were collected immediately prior to Fabrazyme® infusion, just after the end of the infusion, and 2 hours after the end of the infusion. Breast milk samples were analyzed for volume, presence of αGAL activity, total fat content, and total protein concentration. Blood samples from the mother were drawn for pharmacokinetic (PK) analysis prior to each breast milk sample collection. If infant genotyping was performed on the umbilical blood cord sample collected at the Baseline visit, a buccal cell sample was obtained from the mother to rule out contamination of the cord blood sample with maternal DNA.

If the parent(s)/legal guardian(s) consented to infant participation, the infant's growth and development were assessed. The infant was also tested for the formation or continued presence of serum IgG and IgM antibodies to r-hαGAL and for genotype.

For the purposes of this study, the mother and the infant were each considered as study participant respectively. The mother must have been enrolled in the Fabry Registry and was followed using the Fabry Registry schedule of assessments and CRFs, as well as this study's CRF. During this study, infants were evaluated, i.e., the infant was tested for IgG and IgM antibodies to r-hαGAL at birth and Months 2, 6, and 12 and was tested developmentally at each visit for 24 months, or until the parent(s)/legal guardian(s) withdrew consent and discontinued the infant's study participation, the infant was discontinued from the study by the Investigator, or the study is terminated.

If the mother was no longer lactating, the mother discontinued the study. The infant was followed for development only for the remainder of this 24-month study.

Number of study participants:

Approximately 10 mothers and up to 10 infants were planned to be enrolled in this study.

Five mothers and 2 infants were enrolled in the study.

Five mothers and 2 infants were evaluated for safety.

Four mothers were evaluated for pharmacokinetic.

Two infants were evaluated for immunogenicity.

Diagnosis and criteria for inclusion:

Mothers who are receiving Fabrazyme® while lactating and agree to adhere to the Fabry Registry recommended schedule of assessments for medical history, pregnancy outcome, genotyping, and antibody testing.

Study products:

Study intervention: Fabrazyme®

Route of administration: Intravenous

Duration of study intervention:

This study was planned to last for up to 2 years (24 months). When the mother was no longer lactating or if they were no longer receiving Fabrazyme®, the mother was to be discontinued from the study. The infant was to be followed for development until the end of the 24-month study period.

Criteria for evaluation:

Primary

- To list as appropriate for the mothers: the level of αGAL in breast milk samples.
- To list as appropriate for the mothers: the volume, and fat and protein content in breast milk samples.
- To list as appropriate for the infants:

- Medical history
- Physical examination
- Gender
- Genotype
- APGAR score at 1 minute and 5 minutes after birth
- Denver II Developmental Screening Test
- IgM antibodies to r-hαGAL – presence, time to development, level of titers present
- IgG antibodies to r-hαGAL – presence, time to development, level of titers present
- Frequency of adverse events (AEs)
- Frequency of concomitant medications.

Statistical methods:

Per the statistical analysis plan, since fewer than 5 mothers and/or 5 infants have been enrolled, the collected data are presented in subject listings. The listings include disposition, demographics and baseline characteristics, pharmacokinetics (αGAL activity in plasma and breast milk), anti-drug antibody (ADA), physical examinations, and lactation status.

Summary Results:

Demographic and other baseline characteristics:

A total of 7 participants were enrolled.

Safety results:

Based on the low enrolment number, no data is reported here in order to protect and maintain participant privacy/confidentiality.

Pharmacokinetic results:

Evaluable data was collected for 3 participants only; and thus, was not presented to protect participant confidentiality.

Other results:

Immunogenicity

Based on the low enrolment number (7 participants), no data is reported here in order to protect and maintain participant privacy/confidentiality.

Breast milk composition (fat and protein)

Evaluable data was collected for 3 participants only; and thus, was not presented to protect participant confidentiality.

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