Sponsor: Sanofi **Drug substance(s):** GZ402673 – alemtuzumab, Trade name: Lemtrada®	**Study Identifiers:** IND: 10717 EudraCT number: 2016-003100-30 NCT: 03368664 WHO: U1111-1180-6352 Other: EMEA/H/C/003718 **Study code:** EFC13429

Title of the study:

A multi-center, open-label, single-arm, before and after switch study to evaluate the efficacy, safety and tolerability of alemtuzumab in paediatric patients with relapsing remitting multiple sclerosis (RRMS) with disease activity on prior disease modifying therapy (DMT) (LemKids)

Study center(s):

This study was conducted at 9 centers that enrolled participants in Italy, Russian Federation, United Kingdom, France, Poland, and Türkiye.

Study period:

Date first study participant enrolled: 23/10/2017

Date last study participant completed: 08/09/2025

Study Status: Study EFC13429 was terminated by Sponsor due to low recruitment and an EMA Article-20 Pharmacovigilance review of Alemtuzumab in adult RRMS.

Phase of development: Phase 3

Objectives:

Primary objectives:

- To evaluate the efficacy, safety and tolerability of alemtuzumab (IV) in paediatric patients from 10 to <18 years of age with RRMS who have disease activity on prior DMT.

Secondary objectives:

- To assess the pharmacokinetics (PK), pharmacodynamics (PD), antidrug antibody (ADA) formation, and potential effects of alemtuzumab on other MS disease characteristics such as cognition and quality of life.

Methodology:

The Study EFC13429 was an open-label, rater-blinded, single-arm, before and after switch study of efficacy, safety, and tolerability of alemtuzumab in pediatric participants with RRMS.

The study consisted of a screening period (up to 28 days) followed by a prior DMT phase (approximately 4 months) during which participants received their prior DMT, the alemtuzumab treatment phase (approximately 2 years), and finally the safety monitoring phase (approximately 3 years).

Number of study participants:

The study enrolled 16 participants. Of them 12 completed the prior DMT phase, 11 were exposed to first course of alemtuzumab and 7 participants completed both courses of alemtuzumab.

Diagnosis and criteria for inclusion:

The study enrolled pediatric participants from 10 to <18 years of age with RRMS with disease activity on prior DMT.

Study products

Investigational medicinal product(s):

Alemtuzumab

Formulation/ Form & composition: infusion

Route(s) of administration: intravenous (IV)

Dose regimen: 12 mg/day for participants ≥50 kg and 0.24 mg/kg/day for participants <50 kg

Duration of treatment/participation:

2 courses of alemtuzumab were administered (5 consecutive infusions at baseline followed by 3 consecutive infusions one year later). Total duration of alemtuzumab treatment phase was approximately 2 years.

Criteria for evaluation

Endpoints

Primary endpoints:

The number of new or enlarging T2 lesions on brain MRI, during continuation of prior DMT (Period 1) compared to an equal period after the first course of alemtuzumab treatment (Period 2).

Secondary endpoints:

Efficacy endpoints

- The number of patients with new or enlarging T2 lesions during continuation of prior DMT (Period 1) compared to an equal period after the first course of alemtuzumab treatment (Period 2).
- Expanded Disability Status Scale (EDSS) (descriptive statistics, eg, percentages of stable/improved/worsened since the end of Period 1).
- Annualized relapse rate (ARR) at Year 2.
- Cognition test scores: Brief Visuospatial Memory Test - Revised (BVMT-R) and Symbol Digit Modality Test (SDMT); administered at least every 6 months over 2 years.

Quality of life (QoL)

- Established generic paediatric QoL measures (PedsQL questionnaire, Paediatric NeuroQoL questionnaire) administered every 6 months over 2 years.

Pharmacokinetics (PK)/Pharmacodynamics (PD)

- PK serum concentration and PK parameters (C_{max}, T_{max}, AUC, AUC_{last}, $T_{1/2z}$) calculated where possible.
- PD assessment including lymphocyte subsets.

Safety endpoints

- Adverse event (AE), including adverse events of special interest (AESI) and infusion-associated reactions (IARs) at each visit.
- Physical examination and vital signs.
- Monthly monitoring of clinical chemistry laboratories, hematology, serum creatinine urinalysis with microscopy; thyroid function testing (TSH and if abnormal, T3 and T4) every 3 months; hepatitis B and C testing, HPV serology testing, tuberculosis test screening, pregnancy testing.
- Tanner staging.
- Antidrug antibody formation (ADA) throughout the study.

Statistical methods: Not applicable.

Summary Results

Population characteristics:

Demographic and other baseline characteristics:

Forty-six patients with RRMS were screened and 16 participants were enrolled in the study. Most participants were males (12/16, 75%). One participant had a history of hypothyroidism. Mean (standard deviation [SD]) age at baseline was 14.5 (2.2) years. Mean (SD) time from MS diagnosis was 2.79 (2.07) years; mean (SD) number of relapses within a year prior to enrollment was 2.1 (1.3). Of 11 participants exposed to alemtuzumab, 6 had progressed with prior interferons and 5 with prior glatiramer acetate during the prior DMT before the switch.

At baseline, mean (SD) Expanded Disability Status Scale (EDSS) score was 1.78 (1.13), mean (SD) volumes of T2- and T1-hyperintense lesions were 12.27 (6.33) and 2.19 (2.09), respectively.

Exposure:

Eleven participants received first course of alemtuzumab, 10 of them completed all 5 infusions while 1 participant received only 3 infusions. All 7 participants who started the second course of alemtuzumab received 3 infusions as planned per the protocol.

Efficacy results:

Despite the small sample size limiting the ability to interpret the data, alemtuzumab was associated with a reduction in the number of new or enlarging T2 lesions compared with prior DMT phase (7 lesions during alemtuzumab treatment phase versus 178 during DMT phase). The relative risk (RR) for the adjusted number of these lesions per month was 0.04 (95% confidence interval [CI]: 0.01 to 0.14).

Of 11 participants, 10 (90.9%) participants during the prior DMT phase and 3 (27.3%) participants during the alemtuzumab treatment phase had at least 1 new or enlarging T2 lesion. Treatment with alemtuzumab was associated with lower odds of developing these lesions with an odds ratio (OR) of 0.02 (95% CI: 0.00 to 0.15).

Four participants exposed to alemtuzumab experienced 1 relapse each with an adjusted ARR at 2 years of 0.53 (95% CI: 0.12 to 2.37).

EDSS, Brief Visuospatial Memory Test – Revised (BVMT-R), and Symbol Digit Modality Test (SDMT) scores were difficult to interpret due to small sample size but appeared rather stable in participants exposed to alemtuzumab.

Safety results:

Ten (62.5%) of 16 participants had at least 1 pre-treatment adverse event (AE) and 3 (18.8%) participants had at least 1 pre-treatment serious adverse event (SAEs) (either RRMS relapse or pseudo relapse).

The most frequent pre-treatment AEs at the system organ class (SOC) level were Infections and infestations (7 [43.8%] participants), Nervous system disorders (5 [31.3%] participants), General disorders and administration site conditions (3 [18.8%]) participants), Psychiatric disorders (2 [12.5%] participants), and Gastrointestinal disorders (2 [12.5%] participants).

At the preferred term (PT) level, the most frequent pre-treatment AEs were Nasopharyngitis, Rhinitis, and Multiple sclerosis relapse (3 [18.8%] participants each) and Ear infection (2 [12.5%] participants), respectively. None of the participants experienced an adverse event of special interest (AESI) or discontinued the study due to AE during the pre-treatment period.

All 11 participants exposed to alemtuzumab had at least 1 treatment-emergent adverse event (TEAE), all participants except 1 had a TEAE related to study treatment.

Infusion-associated reactions (IARs), defined as any AEs occurring during alemtuzumab infusion or within 24 hours post-infusion, were the most common TEAEs, reported in 10 (90.9%) participants, all were mild or moderate in intensity. The most frequent IARs (reported in ≥2 participants) by PT were Urticaria (6 [54.5%] participants), Headache (5 [45.5%] participants), Bradycardia, Nausea, and Non-cardiac chest pain (each reported in 2 [18.2%] participants).

Most frequent TEAEs by SOC level were Skin and subcutaneous tissue disorders (10 [90.9%] participants), Infections and infestations (9 [81.8%] participants), Nervous system disorders, Gastrointestinal disorders, Investigations, and General disorders and administration site conditions (7 [63.6%]) participants each), Respiratory, thoracic and mediastinal disorders (6 [54.5%] participants), Psychiatric disorders, Cardiac disorders, Ear and labyrinth disorders, and Injury, poisoning and procedural complications (4 [36.4%] participants each), Muskuloskeletal and connective tissue disorders (3 [27.3%] participants), Endocrine disorders, Blood and lymphatic system disorders, Eye disorders, Pregnancy, puerperium and perinatal conditions, and Renal and urinary disorders (2 [18.2%] participants each). At the PT level, the most frequent TEAEs were Nasopharyngitis, Urticaria, and Headache (6 [54.5%] participants each), Fatigue (5 [45.5%] participants), Diarrhoea, Nausea, Vomiting, and Pyrexia (4 [36.4%] participants), Rhinitis, Upper respiratory tract infection, Epistaxis, Abdominal pain, and Influenza like illness (3 [27.3%] participants each), Pharyngitis, Urinary tract infection, Insomnia, Vertigo, Bradycardia, Cough, Constipation, Toothache, Dermatitis allergic, Pruritus, Rash, Myalgia, Pregnancy, Non-cardiac chest pain, Oedema peripheral, Weight increased, Ligament sprain, and Hyperthyroidism (2 [18.2%] participants each). TEAEs assessed by the Investigator as related to study treatment included the PTs of Urticaria in 6 (54.5%) participants, Fatigue in 4 (36.4%) participants, Nausea, Vomiting, Abdominal pain, and Pyrexia (each reported in 3 [27.3%] participants), Nasopharyngitis, Rhinitis, Bradycardia, Diarrhoea, Non-cardiac chest pain (each reported in 2 [18.2%] participants), Urinary tract infection, Herpes zoster, Respiratory tract infection, Hyperthyroidism, Insomnia, Dizziness, Dysgeusia, Paraesthesia, Presyncope, Ear pain, Palpitations, Abdominal discomfort, Abdominal pain upper, Dermatitis allergic, Pruritus, Rash, Acne, Myalgia, Arthralgia, Pain in extremity, Dysuria, Oedema peripheral, Asthenia, Chest discomfort, Cough, Discomfort, Blood pressure increased, Eosinophil count increased, Heart rate increased, and Tri-iodthyronine increased (each

reported in 1 [9.1%] participants). Treatment-emergent SAEs were reported in in 3 (27.3%) participants, including PTs or Urticaria (2 [18.2%] participants) and Multiple sclerosis relapse (1 [9.1%] participant).

Seven (63.6%) participants experienced a treatment-emergent AESI including PTs of Urticaria in 6 (54.5%) participants, Hyperthyroidism in 2 (18.2%) participants, and Dermatitis allergic, and Alanine aminotransferase (single [9.1%] participant each). Two female participants became pregnant during the study.

There were no discontinuations due to a TEAE.

Potentially clinically significant abnormalities (PCSA) for laboratory evaluation parameters, vital signs, and physical examination were infrequent and few of them were considered clinically meaningful.

Pharmacokinetic results:

Not applicable.

Pharmacodynamic results:

Not applicable.

Other results:

In the evaluable anti-drug antibody (ADA) population (n=11), a single participant had pre-existing ADA and other 10 participants had a treatment-emergent ADA at Month 1.

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