Long-term registry-based study of patients with transfusion-dependent β-thalassemia (TDT) or sickle cell disease (SCD) treated with exagamglogene autotemcel (exa-cel)

First published: 12/03/2025

Last updated: 11/02/2026

Study Ongoing

Administrative details

EU PAS number

EUPAS1000000504

Study ID

1000000504

DARWIN EU® study

No

Study countries

France

Germany

Italy

United Kingdom

United States

Study description

Long-term, prospective observational cohort study using primary and secondary data collected by established international hematopoietic stem cell transplant (HSCT) registries: the European Society for Blood and Marrow Transplantation (EBMT) Registry and the Center for International Blood and Marrow Transplant Research (CIBMTR) Registry.

The study will follow patients who received exa-cel for treatment of TDT or SCD following approval of the therapy in Germany, France, Italy, and UK (via EBMT) and US (via CIBMTR). In addition, comparator populations of patients with TDT or SCD receiving an allo-HSCT from the same countries and same transplant centers will be invited to participate. All patients will be followed for safety and effectiveness outcomes for up to 15 years after HSCT.

Study status

Ongoing

Research institutions and networks

Institutions

Vertex Pharmaceuticals

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Center for International Blood and Marrow Transplant Research (CIBMTR)

First published: 01/02/2024

Last updated: 01/02/2024

Institution

European Society for Blood and Marrow Transplantation (EBMT)

European Union

First published: 20/02/2024

Last updated: 20/02/2024

Institution

Contact details

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Study contact

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Primary lead investigator

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Primary lead investigator

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Study timelines

Date when funding contract was signed
Planned: 09/12/2024

Actual: 09/12/2024

Study start date
Planned: 31/12/2024

Actual: 05/08/2025

Data analysis start date
Planned: 01/01/2027

Date of interim report, if expected
Planned: 31/12/2027

Date of final study report
Planned: 31/12/2043

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Vertex Pharmaceutical Incorporated

Study protocol

VX22-290-101 Protocol _Revised_v2.1_EMA_APPROVED_Redacted.pdf (586.64 KB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 1 (imposed as condition of marketing authorisation)

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Safety study (incl. comparative)

Data collection methods:

Combined primary data collection and secondary use of data

Study design:

Long-term, prospective observational cohort study using primary and secondary data collected by established international hematopoietic stem cell transplant (HSCT) registries.

Main study objective:

1. Evaluate long-term safety outcomes in patients who received exa-cel for treatment of TDT or SCD
2. Evaluate long-term safety outcomes in patients who received exa-cel for treatment of TDT or SCD in comparison to patients receiving allo-HSCT

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

CASGEVY

Study drug International non-proprietary name (INN) or common name

EXAGAMGLOGENE AUTOTEMCEL

Anatomical Therapeutic Chemical (ATC) code

(B06AX05) exagamglogene autotemcel

exagamglogene autotemcel

Medical condition to be studied

Sickle cell disease

Thalassaemia beta

Population studied

Short description of the study population

Patients with TDT or SCD treated in participating transplant centers reporting data to EBMT or CIBMTR Registry and receiving Casgevy or allogeneic-HSCT.

Age groups

- Adolescents (12 to < 18 years)
- Adults (18 to < 65 years)

Estimated number of subjects

800

Study design details

Setting

This is a study conducted in a real-world setting using primary and secondary data collected from the EBMT and CIBMTR patient registries; all transplant centers participating in this study will report data directly to their respective transplant registry. The study will include patients from Germany, France, Italy, UK, and US.

Comparators

To be eligible for inclusion, comparators must be:

• receiving an HSCT from a study-participating transplant center reporting data to the respective transplant registry; and

• receiving allo-HSCT for treatment of TDT or SCD from the date of approval of exa-cel through the end of the enrollment period

• Of an age that corresponds with the exa cel label current at the time of transplant.

All patients must additionally provide informed consent / assent for registry / study data collection.

Outcomes

Safety outcomes: Neutrophil recovery, Platelet recovery, New malignancy, New or worsening hematologic disorder, Mortality

Effectiveness Outcomes: Hemoglobin measures, Iron concentration measures, Disease-related end-organ damage / dysfunction diagnoses, Disease-related therapies

Other outcomes: Transplant-related complications, Additional laboratory measures, Pregnancy

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Data analysis plan

Descriptive statistics will be presented for all study endpoints. Cumulative incidence curves will be provided for select outcomes.

Within the TDT and SCD Exa-cel Cohorts, comparisons of the post-transplant period to pre-transplant period will be performed, as appropriate.

Between cohort results (TDT Exa-cel versus TDT Allo-HSCT; SCD Exa-cel versus SCD Allo-HSCT) will also be evaluated within each registry separately.

Subgroup analyses will be performed by age group, genotype, and/or other

patient characteristics, as appropriate. Subgroup analyses by country of transplant may be performed if sufficient patient counts are available to preserve patient anonymity. Additional ad hoc statistical analyses may be implemented, as applicable (e.g., modeling to adjust for differences in cohort characteristics in between-cohort analyses, time-to-event analyses for select outcomes). Pooled analyses of key safety outcomes are planned at pre-specified timepoints (after 5-, 10-, and 15-year duration of follow-up is accrued for all enrolled patients).

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s), other

European Society for Blood and Marrow Transplantation (EBMT) Registry
Center for International Blood and Marrow Transplant Research (CIBMTR) Registry

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

Unknown