Post-Authorisation Safety Study of Paediatric Patients Initiating Selumetinib: A Multiple-Country Prospective Cohort Study

First published: 03/03/2022

Last updated: 20/05/2026

Study Ongoing

Administrative details

EU PAS number

EUPAS45972

Study ID

48033

DARWIN EU® study

No

Study countries

- Austria
- France
- Germany
- Israel

Italy
Netherlands
Portugal
Spain
Switzerland
United Kingdom

Study description

This is a cohort study of paediatric patients (aged 3 to <18 years of age) with NF1 with symptomatic, inoperable PNs who begin selumetinib treatment at study sites across several European countries where selumetinib has been marketed for use. Selumetinib treatment will remain a decision of the treating clinicians and is not mandated by this study protocol. All patients prescribed selumetinib at the study sites in the usual manner and according to the terms of the marketing authorisation will be invited to participate in the study. Patients who meet the eligibility criteria, including parental/legal guardian consent to participation, will be enrolled. One hundred and twenty-five patients (approximately 100 patients of which will be in the Nested Prospective Cohort) will be enrolled over a period of up to 3 years and assigned an index date (Day 1) defined as the date of first prescription of selumetinib. Baseline data will be collected at enrolment through retrospective chart abstraction from Day -365 to Day -1 (baseline period).The Nested Prospective Cohort of patients (aged 8 to < 18 years who have not reached Tanner Stage V on the index date) will be followed prospectively to further characterise the safety of selumetinib. Data from this cohort will be collected on the occurrence of the safety outcomes of interest identified in Section 4.6 (Table 1). Enrolment will occur at approximately 52 sites in up to 12 European countries and Israel, after selumetinib is commercially available in the country and patients are able to receive.

Study status

Ongoing

Research institutions and networks

Institutions

Sana Klinikum Duisburg

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Institution

Kinder & Jugendmedizin

IRCCS Foundation “Carlo Besta” Neurological Institute

Italy

First published: 26/11/2025

Last updated: 26/11/2025

Institution

Hospital/Clinic/Other health care facility

Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Italy

First published: 26/11/2025

Last updated: 26/11/2025

Institution | Hospital/Clinic/Other health care facility

Institut Curie (IC)

France

First published: 27/11/2025

Last updated: 27/11/2025

Institution | Hospital/Clinic/Other health care facility

- Inselspital - Universitaetsklinik Bern für Pneumologie
- Complexo Hospitalario Universitario de Santiago (CHUS) - Hospital Clínico Universitario
- Sana Kliniken Duisburg
- Hôpital Necker - Enfants Malades
- Azienda Ospedaliera Universitaria Citta della Salute e della Scienza di Torino - Ospedale Molinette

- Azienda Ospedaliera di Padova
- Hôpitaux Universitaires de Strasbourg - Hôpital de Hautepierre
- Medizinische Universitaet Wien - Universitaetsklinik fuer Kinder und Jugendheilkunde
- Universitätsklinikum Hamburg-Eppendorf (UKE)
- Instituto Português Oncologia de Lisboa Francisco Gentil, EPE
- CHU Hopitaux de Bordeaux - Groupe Hospitalier Pellegrin
- Centre Hospitalier Universitaire Vaudois Lausanne (CHUV)
- Universitätsklinikum Tübingen Klinik für Kinder- und Jugendmedizin Kinderheilkunde I
- IRCCS Ospedale Pediatrico Bambino Gesù
- Hospital Sant Joan de Déu Barcelona
- Schneider Children's Medical Center of Israel
- University Children's Hospital Basel

- Hôpital des Enfants - Toulouse
- Istituto Giannina Gaslini
- CHU Amiens Sud
- Centre Oscar Lambret
- Centre Léon Bérard
- Hospital Universitario Vall d'Hebron
- Hospital Universitario 12 de Octubre
- Fondazione IRCCS Policlinico San Matteo
- Great Ormond Street Hospital for Children NHS Foundation Trust - Great Ormond Street Hospital
- Manchester University NHS Foundation Trust - Royal Manchester Children's Hospital
- Hospital Universitario Virgen del Rocío
- Universitätsklinikum Carl Gustav Carus Dresden
- Centre Hospitalier Universitaire (CHU) de Rennes - Hopital Anne de Bretagne (Hopital Sud)
- Dr. von Haunersches Kinderspital
- Fondazione I.R.C.C.S. Istituto Neurologico Carlo Besta

- CHU Nancy - Hôpital Brabois
- Tel Aviv Sourasky Medical Center
- Azienda Ospedaliero Universitaria Meyer
- Ostschweizer Kinderspital - Sankt Gallen
- Hospital Infantil Universitario Nino Jesus
- Centre Hospitalier Regional et Universitaire de Tours - Hopital Clocheville
- Chaim Sheba Medical Center
- CHU Hôpital de la Timone
- Centre Hospitalier Universitaire d'Angers
- Istituto di Ricovero e Cura a Carattere Scientifico Materno-Infantile - Burlo Garofolo
- The Newcastle upon Tyne Hospitals NHS Foundation Trust - The Great North Children's Hospital

Networks

FINPEDMED

Contact details

Study institution contact

Clinical Trial Transparency

ClinicalTrialTransparency@astrazeneca.com

Study contact

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Primary lead investigator

THORSTEN ROSENBAUM

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 22/02/2022

Actual: 22/02/2022

Study start date

Planned: 23/05/2022

Actual: 23/05/2022

Data analysis start date

Planned: 12/07/2028

Date of final study report

Planned: 31/03/2029

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

AstraZeneca AB

Study protocol

D1346R00004_Protocol V 2.0_05Nov2021_Redacted.pdf (359.51 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 2 (specific obligation of marketing authorisation)

Other study registration identification numbers and links

D1346R00004

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

To characterise the safety of selumetinib, including up to 5 years of long-term safety, in paediatric patients with NF1-related symptomatic, inoperable PN, 8 to < 18 years old who have not reached Tanner Stage V at the start of selumetinib treatment (Nested Prospective Cohort).

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Prospective cohort

Study drug and medical condition

Medicinal product name

KOSELUGO

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

SELUMETINIB

Anatomical Therapeutic Chemical (ATC) code

(L01EE04) selumetinib

selumetinib

Medical condition to be studied

Neurofibromatosis

Population studied

Short description of the study population

The target population for this study are patients with NF1 in the EU with symptomatic,
inoperable PN who have been prescribed at least 1 dose of selumetinib and who are aged
3 to < 18 years at the start of selumetinib treatment, except for those patients receiving
treatment with a mitogen-activated protein kinase inhibitor before the index date.

The study will enrol 2 cohorts:
1 The Base Cohort includes all enrolled patients aged 3 to <18 years.
2 The Nested Prospective Cohort will include the subset of Base Cohort patients aged 8

to <18 years who have not reached Tanner Stage V on the index date.

Age groups

- Children (2 to < 12 years)
- Adolescents (12 to < 18 years)

Estimated number of subjects

125

Study design details

Setting

This study will be conducted in up to 52 specialist clinics for the treatment of paediatric patients with NF1 across up to 12 European countries and Israel. The study observation period was anticipated to begin in Q2 of 2022, with some variation by country (actual start date was 23 May 2022). Patients will be enrolled after selumetinib access
is commercially available and patients are able to receive the medicine as part of local clinical practice. To meet study timelines and minimise any delay in delivering the study results, countries where selumetinib is first available will be selected for the study.

Outcomes

1. LVEF reduction 2. Physeal dysplasia 3. Rise of serum creatine phosphokinase levels AND concurrent musculoskeletal symptoms 4. Rise in transaminase (ALT and AST) and concurrent rise in bilirubin 5. Abnormalities of ophthalmological examination (eg, vision changes, IOP, etc) 6. Abnormal pubertal development, 1. Demographics: Age, sex, height, weight, Tanner staging level, and ethnicity (where allowed by GDRP/privacy laws) 2. Clinical characteristics: PN(s) (number,

location, classification and morbidities), prior medication and relevant procedures, concomitant medications, comorbidities, date of initial NF1 and PN diagnosis, NF1 origin (familial or spontaneous), and any genetic testing results.

Data analysis plan

Tabular summaries will be provided for the baseline characteristics of the Base Cohort. Demographic and clinical characteristics data obtained at baseline will be summarised using descriptive statistics: mean, standard deviation, median, minimum and maximum for continuous variables and number and percentages for categorical variables. Safety outcomes of interest will be summarised at each follow-up visit. For each outcome cumulative incidence and incidence rate with 2-sided 95% exact confidence interval will be provided. Descriptive summary statistics will be obtained for duration of exposure to selumetinib, cumulative exposure to selumetinib, and number of dose reductions, discontinuations, or interruptions. The frequency of missing values for each variable will be examined and evaluated to determine whether data are missing at random in the data source.

Documents

Abstract of study report

D1346R00004-PASS Annual Progress Report 1_Redacted.pdf (3.04 MB)

D1346R00004-PASS Annual Progress Report 2_Redacted.pdf (4.52 MB)

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 sources (types)

Electronic healthcare records (EHR)

Other

Data sources (types), other

Prospective patient-based data collection, Patient medical records

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

No