

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

**First published:** 03/03/2022

**Last updated:** 05/06/2025

Study

Ongoing

## Administrative details

### EU PAS number

EUPAS45972

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### Study ID

48033

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### DARWIN EU® study

No

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### Study countries

- ☐ Austria
- ☐ France
- ☐ Germany
- ☐ Israel

- ☐ Italy
  - ☐ Netherlands
  - ☐ Portugal
  - ☐ Spain
  - ☐ Switzerland
  - ☐ United Kingdom
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## **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.

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## Study status

Ongoing

## Research institutions and networks

### Institutions

Sana Klinikum Duisburg

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Institution

Kinder & Jugendmedizin

- Inselspital - Universitätsklinik Bern für Pneumologie
- Complejo Hospitalario Universitario de Santiago (CHUS) - Hospital Clínico Universitario
- Sana Kliniken Duisburg
- Hôpital Necker - Enfants Malades
- Azienda Ospedaliera Universitaria Città 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)
- Institut Curie
- Instituto Português Oncologia de Lisboa  
Francisco Gentil, EPE
- Fondazione Policlinico Universitario Agostino  
Gemelli
- 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

[ClinicalTrialTransparency@astrazeneca.com](mailto:ClinicalTrialTransparency@astrazeneca.com)

### Primary lead investigator

THORSTEN ROSENBAUM

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Planned: 22/02/2022

Actual: 22/02/2022

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### Study start date

Planned: 23/05/2022

Actual: 23/05/2022

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**Data analysis start date**

Planned: 12/07/2028

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**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)

[CSP redacted.pdf](#)(4.88 MB)

[d1346r00004-pass-clinical-study-report\\_Redacted.pdf](#)(2.24 MB)

## Regulatory

**Was the study required by a regulatory body?**

Yes

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**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 type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**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**

Other

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## Non-interventional study design, other

Prospective cohort

## Study drug and medical condition

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

SELUMETINIB

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### Medical condition to be studied

Neurofibromatosis

## Population studied

### Age groups

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

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### Estimated number of subjects

125

## Study design details

### 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 GDPR/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.

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### **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.

## 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)

Other

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### 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

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### Check completeness

Unknown

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### Check stability

Unknown

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### Check logical consistency

Unknown

## Data characterisation

### Data characterisation conducted

No