Pharmacokinetics, Safety and Efficacy of the Selumetinib Granule Formulation in Children Aged ≥1 to <7 Years With NF1-related Symptomatic, Inoperable PN

Status: Recruiting

Eligibility Criteria

Age: 1 year to 6 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

1. Male and female participants aged ≥ 1 to < 7 years of age at the time their legally authorised representative (parent or guardian) signs the informed consent. 2. All study participants must be diagnosed with NF1 with symptomatic inoperable PN as defined in protocol. 3. Participants must have at least one measurable PN, defined as a PN of at least 3 cm measured in one dimension, which can be seen on at least 3 imaging slices and have a reasonably well-defined contour. Participants who have undergone surgery for resection of a PN are eligible provided the PN was incompletely resected and is measurable. The target PN will be defined as the clinically most relevant PN, which is symptomatic, inoperable and measurable by volumetric MRI analysis. 4. Performance status: Participants must have a Lansky performance of ≥ 70 except in participants who are wheelchair bound or have limited mobility secondary to a need for mechanical breathing support (such as an airway PN requiring tracheostomy or continuous positive airway pressure) who must have a Lansky performance of ≥ 40. 5. Participants must have a BSA ≥ 0.4 and ≤ 1.09 m2 at study entry (date of ICF signature). 6. Mandatory provision of consent for the study signed and dated by a participant's legally authorised representative (parent or guardian) along with the paediatric assent form, if applicable.

Exclusion Criteria:

1. Participants with confirmed or suspected malignant glioma or MPNST. Participants with low grade glioma (including optic glioma) not requiring systemic therapy are permitted. 2. History of malignancy except for malignancy treatment with curative intent with no known active disease ≥ 2 years before the first dose of study intervention and of low potential risk of recurrence. 3. Refractory nausea and vomiting, chronic gastrointestinal disease, inability to swallow the formulated product, or previous significant bowel resection that would preclude adequate absorption, distribution, metabolism, or excretion of selumetinib. 4. A life-threatening illness, medical condition, organ system dysfunction or laboratory finding which, in the Investigator's opinion, could compromise the participant's safety, interfere with the absorption or metabolism of selumetinib, or put the study outcomes at undue risk. 5. Participants with clinically significant cardiovascular disease as defined in the protocol. 6. Liver function tests: Bilirubin > 1.5 × the ULN for age with the exception of those with Gilbert syndrome (≥ 3 × ULN) or AST/ALT > 2 × ULN. 7. Renal Function: Creatinine clearance or radioisotope glomerular filtration rate < 60 mL/min/1.73 m2 or Serum creatinine > 0.8 mg/dL (for participants aged ≥ 1 to < 4 years) or > 1.0 mg/dL (for participants aged ≥ 4 years). 8. Participants with ophthalmological findings/condition as listed in the protocol. 9. Have any unresolved chronic toxicity with CTCAE Grade ≥ 2 which are associated with previous therapy for NF1-PN (except hair changes such as alopecia or hair lightening) 10. Participants who have previously been treated with a MEKi (including selumetinib) and have had disease progression, or due to toxicity have either discontinued treatment and/or required a dose reduction. 11. Have inadequate haematological function defined as: An absolute neutrophil count < 1500/µL or Haemoglobin < 9g/dL or Platelets <100,000/µL or Have had a transfusion (of red cells or other blood derived products) within the 28 days prior to study entry (date of ICF signature). 12. Have received or are receiving an IMP or other systemic NF1-PN target treatment (including MEKi) within 4 weeks prior to the first dose of study intervention, or within a period during which the IMP or systemic PN target treatment has not been cleared from the body (eg, a period of 5 'half-lives'), whichever is longer. 13. Has received radiotherapy in the 6 weeks prior to start of study intervention or any prior radiotherapy directed at the target or non-target PN. 14. Receiving herbal supplements or medications known to be strong or moderate inhibitors of the CYP3A4 and CYP2C19 enzymes or inducers of the CYP3A4 enzyme unless such products can be safely discontinued at least 14 days or 5 half-lives (whichever is longer) before the first dose of study medication. 15. Inability to undergo MRI and/or contraindication for MRI examinations. Prosthesis or orthopaedic or dental braces that would interfere with volumetric analysis of target PN on MRI.

Conditions & Interventions

Interventions:

Drug: Selumetinib granule formulation, Drug: Selumetinib capsule formulation

Conditions:

Neurofibromatosis Type 1

More Information

Contact(s): AstraZeneca Clinical Study Information Center - information.center@astrazeneca.com

Principal Investigator:

Phase: Phase 1/Phase 2

IRB

Number:

System ID: NCT05309668
