Alpelisib in Pediatric and Adult Patients With Lymphatic Malformations Associated With a PIK3CA Mutation.

Last Update: Nov 15, 2024
A Two-stage Double-blind, Randomized, Placebo-controlled Study to Assess the Efficacy, Safety and Pharmacokinetics of Alpelisib in Pediatric and Adult Patients With Lymphatic Malformations Associated With a PIK3CA Mutation.
ClinicalTrials.gov Identifier:
NCT05948943
Novartis Reference Number:CBYL719P12201
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All compounds are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation.

Study Description

The main purpose of this study in participants with PIK3CA-mutated lymphatic malformations (LyM) is to assess the change in radiological response and symptom severity upon treatment with alpelisib as compared to placebo. This is a phase II/III multi-center study with two stages:

* Stage 1 is designed to select the dose(s) for the confirmatory phase (DSCP) for alpelisib in Stage 2 and will comprise a 24-week open-label core phase in adult (≥18 years of age) and pediatric participants (6-17 years of age) with PIK3CA-mutated LyM, followed by an extension. After eligibility has been confirmed at screening, participants will be randomized to the different alpelisib doses according to their age. Depending on the results at the end of Stage 1 core phase, the Stage 2 will be opened to adult and/or pediatric participants or the study may be stopped.
* Stage 2 is designed to confirm the efficacy and assess safety of alpelisib at the DSCP in participants with PIK3CA-mutated LyM and will comprise a 24-week randomized, double blind, placebo-controlled confirmatory phase in adult (≥18 years of age) and pediatric participants 6-17 years of age followed by an open-label extension. After eligibility has been confirmed at screening participants will be randomized to alpelisib or placebo.

Additionally, in parallel, Stage 2 will include a 24-week open-label core phase in pediatric participants 2-5 years of age followed by an extension, if pediatric participants will be enrolling in Stage 2.

Based on the results of the 24-week open-label core phase of Stage 1, the dose(s) for Stage 2 will be selected by Novartis in consultation with the Steering Committee (SC). During the 24-week randomized, double blind, placebo-controlled core phase of Stage 2, an Independent Data Monitoring Committee (DMC) will conduct periodic safety reviews.

Condition
Lymphatic Malformations

Phase
Phase2, Phase3
Overall Status
Recruiting
Number of Participants
230
Start Date
Nov 24, 2023
Completion Date
May 05, 2030
Gender
All
Age(s)
2 Years - (Child, Adult, Older Adult)

Interventions

Drug

Alpelisib

In Stage 1: adult participants (≥18 years of age) will receive dose 1 or dose 2 of alpelisib; pediatric participants (6-17 years of age) will receive dose 2 or dose 3 of alpelisib. In Stage 2: Adult participants will receive alpelisib at the dose selected for confirmatory phase in adult participants; pediatric participants (6-17 years of age) will will receive alpelisib at the dose selected for confirmatory phase in pediatric participants; and pediatric participants of 2-5 years of age will receive dose 3 of alpelisib
Drug

Placebo

In Stage 2, participants will receive matching placebo for 24 weeks of the study

Eligibility Criteria

Key Inclusion Criteria:

* Participant must be willing to remain at the clinical site as required by the protocol and be willing to adhere to study restrictions and examination schedules.
* Participant has a physician confirmed and documented diagnosis of a LyM at the time of informed consent
* Participant is not considered as a candidate for or is not willing to receive local therapy options including but not limited to sclerotherapy, embolization, and surgery until the completion of Week 24 in Stage 1 and 2.
* Participant has evidence of a somatic mutation(s) in the PIK3CA gene
* Participant has at least one measurable LyM lesion confirmed by BIRC assessment prior to randomization.

Key Exclusion Criteria:

* Participant has a physician-confirmed and documented diagnosis of PROS at the time of informed consent.
* Participant has a physician-confirmed and documented diagnosis of a Central Conducting Lymphatic Anomaly, General Lymphatic Anomaly, Gorham-Stout disease, Kaposiform lymphangiomatosis at the time of

informed consent.
* Participant has a known history of Stevens-Johnson syndrome, erythema multiforme, or toxic epidermal necrolysis at the time of informed consent.
* Participant has an established diagnosis of type I diabetes mellitus or uncontrolled type II diabetes mellitus at the time of informed consent.
* Participant had previous treatment with alpelisib and/or any other PI3K inhibitors with treatment duration longer than 2 weeks at the time of informed consent.

Other inclusion/exclusion criteria may apply

Australia

Novartis Investigative Site

Recruiting

Brisbane,Queensland,4101,Australia

Belgium

Novartis Investigative Site

Recruiting

Bruxelles,1200,Belgium

France

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Bron Cedex,69677,France

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Recruiting

Caen,14033,France

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Recruiting

Lille,59000,France

Novartis Investigative Site

Recruiting

Marseille,13885,France

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Recruiting

Montpellier,34295,France

Germany

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