Novartis announces findings from a real-world study of alpelisib demonstrating clinical benefit in people with PIK3CA-Related Overgrowth Spectrum (PROS)

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- PROS is a spectrum of rare disorders caused by PIK3CA mutations and is characterized by atypical, visible overgrowths and anomalies in blood vessels, the lymphatic system and other tissues
- At 24 weeks, 38% of patients achieved ≥20% reduction in the volume of the PROS lesions assessed in the primary endpoint analysis; no patients experienced disease progression or death
- Alpelisib is the first potential treatment to specifically address the root cause of PROS conditions
- EPIK-P1 study findings presented at ESMO Virtual Congress 2021 support FDA submission

EAST HANOVER, N.J., Sept. 17, 2021 - Novartis today announced important findings from a real-world study evaluating the safety and efficacy of alpelisib for people living with PIK3CA-Related Overgrowth Spectrum (PROS) who received treatment daily for at least 24 weeks. Results from EPIK-P1 showed alpelisib effectively reduced volume of clinically significant PROS-related lesions and improved signs and symptoms in pediatric and adult patients. Results were presented at the European Society of Medical Oncology (ESMO) Virtual Congress 2021 [LBA23].

"There are few options available to manage PROS conditions, and they are mainly focused on addressing worsening symptoms. It is devastating for patients to be without treatments that address the underlying cause of PROS," said Guillaume Canaud, MD, PhD, Necker-Enfants Malades Hospital – AP-HP, the Paris Descartes University, Inserm (INEM Institute Necker Enfants Malades – Centre for Molecular Medicine). "The EPIK-P1 findings show robust clinical benefit for adult and pediatric patients and a potential new path forward for those impacted by PROS conditions."

In EPIK-P1, alpelisib reduced target lesion volume and improved PROS-related symptoms and manifestations. The primary endpoint analysis conducted at week 24 in patients with complete cases (n=32) showed 38% of patients achieving a response to treatment which was defined as 20% or greater reduction in the sum of PROS target lesion volume. Nearly three in four patients (74%) showed some reduction in target lesion volume, with a mean reduction of 13.7%, and no patients experienced disease progression at time of primary analysis.

Additionally, at week 24, investigators reported patient improvements from baseline in pain (90%), fatigue (76%), vascular malformation (79%), limb asymmetry (69%), and disseminated intravascular coagulation (55%) across the full study population (n=57).

"Thanks to the data from patients and physicians included in the analysis of EPIK-P1, we have findings to help validate the potential of alpelisib in PROS and have taken an important step toward reimagining medicine for the PROS community," said Jeff Legos, Executive Vice President, Global Head of Oncology & Hematology Development. "We will continue to discuss this real-world evidence with the FDA in an effort to bring this treatment to people in need as quickly as possible."

Adverse events (AEs) and treatment-related AEs (TRAEs) were experienced by 83% and 39% of patients, respectively. Most AEs were mild to moderate in severity, and there were no AEs leading to treatment discontinuation. The most common AEs of any grade were diarrhea (16%), hyperglycemia (12%), aphthous ulcers (11%), and stomatitis (5%). The most common grade 3/4 AE was cellulitis (4%); one adult case was considered treatment-related.

PROS is a wide-ranging spectrum of disorders caused by a mutation in the PIK3CA gene. PROS conditions are rare and visually diverse, and are typically characterized by atypical growths and anomalies in blood vessels, the lymphatic system and other tissues. PROS conditions can look different from each other in size, shape, and type of growth or malformation based on where in the body the mutation is found.[1,2] PROS can disrupt mobility and cognitive function in some patients and may lead to life-threatening complications.[3-5]

There are no approved medical therapies for PROS conditions. PROS management varies by patient, and surgery and radiologic embolization are common with patients often undergoing multiple procedures due to frequent regrowth following surgery.[1,3,4,6-9] There is a significant need for treatment options for PROS that reduce overgrowth, address symptoms, and improve quality of life.[3,9-10]

The U.S. Food and Drug Administration (FDA) granted alpelisib Breakthrough Therapy Designation on November 13, 2019, and discussions with FDA about alpelisib for PROS are ongoing.

About PIK3CA-Related Overgrowth Spectrum (PROS)

The PROS classification was proposed at the National Institutes of Health in a workshop in 2013 to unite a group of rare overgrowth conditions caused by PIK3CA mutations.[1,2] Specific conditions associated with PROS include KTS, CLOVES syndrome, ILM, MCAP/M–CM, HME, HHML, FIL, FAVA, macrodactyly, muscular HH, FAO, CLAPO syndrome and epidermal nevus, benign lichenoid keratosis, or seborrheic keratosis.[1,2] The estimated prevalence of PROS conditions is approximately 14 people per million.[6] To learn more, visit understandingpros.com.

About EPIK-P1

EPIK-P1 is a global, site-based retrospective non-interventional medical chart review of pediatric and adult male and female patients aged 2 years or older with PIK3CA-Related Overgrowth Spectrum (PROS) who received alpelisib via a compassionate use program. Primary endpoint is proportion of patients with response at 24 weeks, defined as achieving at least 20% reduction from index date in the sum of measurable target lesion volume via central imaging. Data were obtained from medical charts of 57 patients (39 pediatric, 18 adult) at seven sites in five countries. There were 32 complete cases, meaning there were complete scans for comparison at baseline and date of analysis, and one patient discontinued prior to week 24 due to lack of clinical efficacy.

Alpelisib is not approved by any regulatory authority for the treatment of PROS conditions.

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