What is PROS, and what causes it?

- PROS is a term for a medical condition made up of rare and diverse signs and symptoms. It stands for “PIK3CA-related overgrowth spectrum,” and it is caused by mutations in a gene called PIK3CA.
- Different kinds of mutations in this gene can cause different types of tissues in the body to grow abnormally.
- Some people with PROS may have changes to their blood vessels or lymphatic system; these changes are known as vascular anomalies. Some people may have abnormal growth in multiple areas (segmental overgrowth), while others may have abnormal growth in one area of the body (focal overgrowth). Two people with PROS are exactly alike.
- The different clinical picture that one person with PROS will have, relative to other people with PROS, depends on the type of mutation in the PIK3CA gene, as well as when and where the change first occurred during fetal development.
- In PROS, PIK3CA mutations are random, spontaneous changes, and are not inherited from parent to child. If a person with PROS has children, they will not necessarily pass the PIK3CA mutation to their children. These mutations are known as somatic mutations and are only present in some cells in the body.
- After the first mutation within an embryo, both abnormal cells and normal cells continue to multiply, resulting in a “mosaic” pattern hard to find in people with PROS. If someone with PROS symptoms receives a negative test result, it doesn’t always mean a mutation is not present.

How is PROS treated?

- People with PROS are often treated for their symptoms and complications, such as bleeding, clotting, pain, conditions that affect the bones, and the inability to carry out certain physical functions.
- Many, but not all, people with PROS are treated with surgery to remove abnormal growth (lesions), but it must often be repeated because these lesions come back. Unfortunately, there is not an effective therapy available to treat the underlying genetic changes that cause PROS.
- There are no medicines that have been approved specifically for PROS, but some patients have received a medicine called sirolimus. Sirolimus has been shown to help some people by acting on some of the changes indirectly caused by the mutations in the PIK3CA gene.

What is alpelisib?

- Alpelisib is an oral medicine that works by blocking the growth of tissue caused by mutations in the PIK3CA gene; it is approved in the United States to treat a certain kind of breast cancer.
- In a recently published article, the authors reported that children and adults with PROS given alpelisib had improvements in their lesions, symptoms, and complications in 6 months.

Glossary

- Alpelisib: A medicine being tested in the EPIK-P2 study that may reduce overgrowth or vascular anomalies in PROS.
- Double-blind: A kind of clinical trial in which neither the doctor nor the person being treated knows if the medicine being given is the active drug or a placebo.
- Lesion: An area of abnormal tissue.
- Mutation: Any change in the DNA sequence of a gene.
- MRI: A type of scan that makes detailed images of organs and tissues inside the body.
- Overgrowth: An abnormal increase in the size of the body or a body part.
- PIK3CA: A gene that, when mutated, causes the abnormal tissue growth in PROS.
- Placebo-controlled: A kind of clinical trial in which a medicine’s effects are tested by comparing it to a sugar pill with no active medication.
- PROS: PIK3CA-related overgrowth spectrum.
- Prospective: A kind of clinical trial in which participants are followed after being identified.
- Somatic mutations: New mutations that are not inherited and are typically only present in some cells or some areas of the body.
- Vascular anomalies: Abnormal growths or differences in blood (veins, arteries, capillaries) or lymphatic vessels.

References


Acknowledgments

This study was sponsored by Novartis Pharmaceuticals Corporation. Medical writing assistance was provided by Rob M. Camp, PhD, of Healthcare Consultancy Group, LLC, which was funded by Novartis Pharmaceuticals Corporation.