A COLLABORATIVE STUDY ON PHTS AND VASCULAR MALFORMATIONS

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PTEN Hamartoma Tumor Syndrome (PHTS) is a rare syndrome with a broad phenotypic spectrum, including macrocephaly, autism spectrum disease, slow and high flow vascular anomalies, tissue overgrowth, hamartomas (a benign mass made up of an abnormal mixture of cells and tissues) and increased risk of breast, endometrial and thyroid cancer. Other "older" names for this syndrome, still sometimes used in the literature, are Cowden and Bannayan-Riley-Ruvalcaba syndrome (BRRS).

The hallmark of PHTS is the loss of a functional copy of the tumour suppressor gene, PTEN, most often in the germline, and on rare occasions as a somatic mutation. The PTEN gene is closely linked to the PIP3/PIK3CA/AKT pathways also responsible for the development of vascular malformations (see diagram below, PTEN gene, right upper corner).

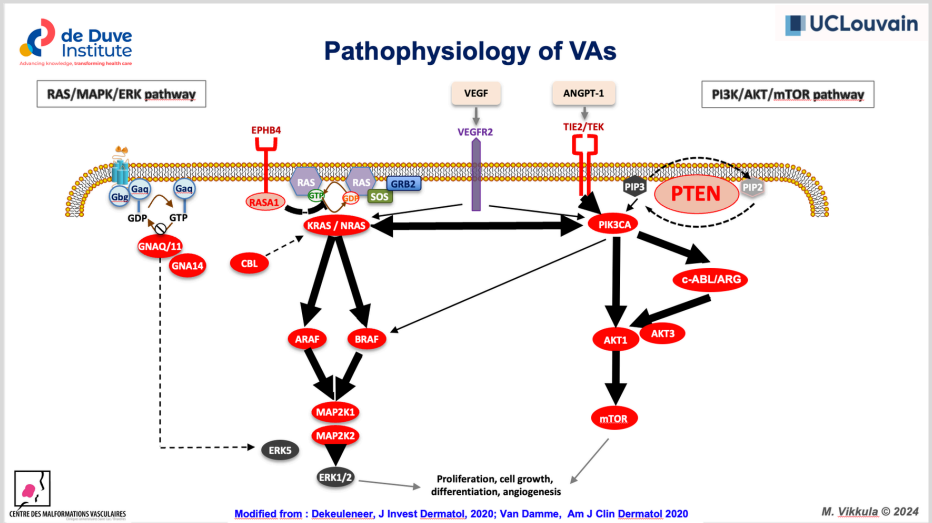
Vascular anomalies occur in 30-50% of patients with the PTEN hamartoma tumour syndrome. Most of them are small and are considered by the patient as less relevant as the focus is on the cancer risks. Research has also understandably been focused on cancer risk. However, some of the vascular malformations in these patients can behave differently from other non-PTEN related vascular malformations. The appearance, extent, progression and response to therapy (interventional radiology, surgery, medical) is different and an increased morbidity or even mortality is seen.

Despite these significant impacts of vascular anomalies in PHTS patients, there have been no studies focusing on the natural history of vascular anomalies in PHTS patients or on the efficacy of specific treatment options for these patients.

PHTS patients seem to have a more severe vascular anomaly (VA) phenotype with a more complex classification in comparison with other VA associated genetic syndromes, and therefore present significant challenges for understanding optimal treatment approaches and overall outcomes.

The consortium of the institutions below (Philadelphia, Boston, Calgary, Nijmegen, Brussels and Madrid) was formed to — as an important first step — analyse this phenotype based on a comprehensive physical exam, and radiologic and pathologic evaluations.

The analysis is needed to better define these anomalies to develop new therapeutic interventions and medical therapies. The project started in 2022, after obtaining a grant from the PTEN Research Foundation. The first results were expected by Q3 2024.



The RAS/MAPK/ERK and PI3K/AKT/mTOR pathways hyperactivated in vascular malformations

Source: Modified from Dekeuleneer, J Invest Dermatol, 2020; Van Damme, Am J Clin Dermatol 2020