

Meeting Report: VHL International Medical Research Conference, 19-20 October 2024, Milan, Italy

Our journey to Milan for the VHL International Medical Research Conference began on a rainy Friday, 18 October. A public transport strike made for a complicated arrival, we finally got to the hotel across town. We held our Annual General Assembly for VHL in the hotel in the evening of October 18th, 2024, with members from Italy, Hungary, Denmark, France, and the Netherlands in person, and with participants joining online from Germany, France, the Netherlands.

Day 1 Highlights

RNA Interference and belzutifan in Kidney Cancer Research: Dr. Jim Brugarolas from the University of Texas Southwestern Medical Center in the USA presented a study on a new drug, ARO-HIF2, designed to block cancer-related genes associated with clear cell renal cell carcinoma (ccRCC). The study showed some promise, though neurotoxicity and limited response rates highlighted areas for improvement. Additionally, Dr. Brugarolas provided updates on the ongoing development of belzutifan, including the use of a PET scan tracer to better monitor its effects in patients.

Radiotherapy as an Option for VHL Kidney Tumours: Dr. Rachel van Leeuwen (University Medical Center Utrecht, the Netherlands) discussed the potential of radiotherapy, specifically MR-LINAC, for VHL-related kidney tumours. This non-invasive, possibly cost-effective approach offers promise for patients unable to undergo surgery, particularly those with larger tumours.

Gene Therapy and Neural Crest Cells in VHL: PhD candidate Pedram Moeini (University of Navarra, Spain) shared early findings on gene therapy using AAV vectors in kidney cancer cells, an approach with potential for long-term gene-based treatments for VHL. Meanwhile, Dr. Betty Gardie from Nantes University Hospital, France, discussed her research on neural crest cells and their link to VHL manifestations, raising the possibility that VHL may be classified as a “neurocristopathy.”

In a new feature at the conference, two young doctors pursuing their PhDs in VHL presented some challenging patient cases. Dr. Saya Ahmad from UMC Utrecht and Dr. Lucia Solerno from San Raffaele Hospital in Milan (who also spent several months working with the VHL team at UMC Utrecht) shared unique cases. They engaged a panel of experts to consider the best treatment options for these patients, creating a lively and interactive session that encouraged the audience to think along and ask questions!

Day 2 Highlights

Historical and Clinical Perspectives on VHL: Dr. Ram Srinivasan (National Cancer Institute, USA) presented a historical look at VHL treatment, from early kidney surgery practices to today’s nephron-sparing techniques. He also detailed developments since the VHL gene was identified in 1993, including the work on belzutifan, which has shown promise in stabilising tumour growth and reducing the need for surgeries, though it awaits approval from the European Medicines Agency (EMA).

Molecular and Genetic Insights into VHL-Related Tumours: Prof. Sakari Vanharanta (University of Helsinki, Finland) presented research on the role of the *PAX8* gene in kidney cancer, showing how it drives tumour growth when combined with specific mutations in ccRCC. Meanwhile, Prof. Ian Frew (University of Tübingen, Germany) explored differences in *VHL* mutations in males and females, and Prof. Ruhe Dere from Baylor College of Medicine (Houston, Texas, USA) discussed the interplay

between *SETD2* and *VHL* genes in cell division, potentially affecting tumour formation. Prof Tien Hsu (National Central University, Taiwan) team presented data that we shouldn't only focus on treating the tumour itself, but RCC can also be approached by treating the endothelial vascular cells, and it goes beyond VEGF, through another protein, Oncostatin M.

Advances in Retinal Capillary Haemangioma: Dr. Shizuo Mukai (Mass General Brigham Hospital, USA), an eye surgeon specialising in VHL, discussed advancements in treating retinal capillary haemangioma. Dr. Mukai discussed the value of early diagnosis and prompt treatment to prevent blindness. For patients with ocular symptoms alone, he advised against systemic treatments like belzutifan, recommending targeted eye care by experienced retinal specialists instead.

Advocacy and Support for VHL Patients in Europe: Dr. Rachel Giles, President of VHL Europa, highlighted the ongoing needs of European VHL patients, especially regarding access to belzutifan, which remains unavailable in many countries outside clinical trials or managed access programs. She also pointed to the unique psychosocial challenges young adults with VHL face and noted initiatives to map these needs. Janet Thompson of the VHL Alliance shared an overview of alliance activities supporting the VHL community and expanding resources for patients.

The conference hosted over 450 medical researchers and medical students. The steady progress in VHL research was wonderful to see, although addressing the challenges that remain for patients and healthcare providers alike are still substantial tasks.

After the conference, we headed to the airport, only to discover that all flights in Northern Italy had been cancelled. Arrangements had to be made for another night in Milan, and after sorting out hotels and flights home the next day, we settled in to enjoy one more evening in the city. A hassle, to be sure, but ultimately a lovely, unexpected night in Milan!





