INTRODUCTION

In this belated newsletter, we update you on recent developments with PC Project. We update readers on progress with topical rapamycin, recent publications and the upcoming PC patient Support Meeting in London. PC patients tell us how they look after their nails. We can all learn from PC patients and it is very useful for physicians to hear the ingenious ways that patients manage problems for which we currently have no good treatment.

PC PROJECT AND PALVELLA COLLABORATING TO INITIATE PHASE 2/3 CLINICAL STUDY OF PTX-022

By: Wes Kaupinen, CEO, Palvella Therapeutics

PC Project and Palvella have been working very closely over the last several months to prepare for the imminent initiation of the Phase 2/3 study evaluating PTX-022 (novel, high strength topical rapamycin, optimized for dermal targeting) for the treatment of PC. Significant progress has been made in recent months, the most important of which is: i) The selection of a final formulation to be evaluated in the Phase 2/3 clinical study; ii) Decisions around which efficacy endpoints to prioritize for the study. Notably, the final formulation has been architected specifically for the PC patient population, and it was selected after a rigorous testing program that included more than 20 prototype formulations evaluated by Palvella and their formulation partner MedPharm, a leading global topical formulation development company based in London, UK.

With regards to efficacy endpoints, as many of you are aware, hundreds of PC patients have willingly participated in qualitative and quantitative surveys to help narrow to specific efficacy endpoints. PC is truly a condition where the patients are the experts in the disease, and hence, the ‘voice of the patient’ will play a central role in the Phase 2/3 study. In addition to the tremendous response from PC patients, a Global Pachyonychia Congenita Working Group comprised of clinicians with expertise in PC as well as rare disease regulatory experts was assembled more than 16 months ago, and that group has worked diligently to iteratively narrow to efficacy endpoints for the study.

Overall, the meaningful progress made these last few months is a testament to the tremendous collaboration that defines PC Project and the PC community worldwide. More frequent updates on the upcoming Phase 2/3 clinical study will follow in the coming weeks.

IPCC SPOTLIGHT:

EDEL O’TOOLE MD, PhD, FRCPI, FRCP

Professor of Molecular Dermatology and Centre Lead, Centre for Cell Biology and Cutaneous Research, Blizard Institute, Barts and the London School of Medicine and Dentistry. Consultant Dermatologist, Royal London Hospital, Barts Health NHS Trust, London, UK

I was born in County Mayo in the West of Ireland. I was brought up in a small village called Leenane, on the border of County Mayo and Galway beside Killary Harbour, a 16 km long fjord-like inlet. Although it was very beautiful, it rained (with varying intensity) about 300 days out of 365. I am the oldest of seven children and my father was an agricultural scientist. When I was about 9 I decided that I wanted to be a botanist. Subsequently, I fell in love with the piano and I thought I might study for a degree in Music. At age 16, I decided I could always play the piano no matter what career I pursued, and chose to become a doctor. I obtained my medical degree at University College, Galway and subsequently trained in Internal Medicine and
Dermatology in Galway and Dublin. I acquired expertise in keratinocyte biology at Northwestern University, Chicago, where I was a Dermatology Foundation Fellow followed by a Howard Hughes Medical Institute Physician Scientist Fellow with David Woodley from 1994-1998. I relocated to London in 1998 to complete my Dermatology training, obtained my PhD and became a Senior Lecturer in 2001. I was promoted to Professor of Molecular Dermatology in October 2008 at Queen Mary University of London and became Centre Lead in 2015. Our Centre has diverse interests in epithelial biology including skin cancer, keratin biology, skin genetics, epidermal barrier, hair biology and stem cells. We also have a portfolio of undergraduate and postgraduate teaching in Dermatology and Plastic Surgery.

In my early years in London, I worked with Professor Irene Leigh who stimulated my interest in palmoplantar keratodermas (PPK) including pachyonychia congenita. PPK and Ichthyosis are my main clinical specialist interests. I have two big clinics a week at the Royal London Hospital in Whitechapel in East London. Tuesday is paediatric dermatology day and Thursday is adult dermatology (with a mix of inflammatory skin disease and genetic skin disease). I supervise the inpatient acute dermatology service for 2 months of the year. I am also the rare disease lead for my hospital for 100K Genomes, a big project in the National Health Service to sequence 100,000 genomes from patients with rare disease and cancer.

I first attended an IPCC meeting in 2005 and currently am on the Medical and Scientific Advisory Board of PC Project and participate in the monthly genetics meetings. Through attending PC Project Patient Support Meetings and also participating in the genetics meetings I have learned a huge amount about PC and PPKs from sharing clinical experiences with Eli Sprecher, Alain Hovnanian, David Hansen, Phil Gard, Frances Smith and Maurice van Steensel. I am also the current Chair of the Medical Advisory Board of the UK-based Ichthyosis Support Group.

In the lab, I have a fairly broad portfolio of research. Since working with David Woodley, I have been interested in extracellular matrix and my group works on type VII collagen and laminin and normal epidermal homeostasis, in particular with regard to epidermolysis bullosa. I also have 2 active basic science projects on harlequin ichthyosis and X-linked ichthyosis. In the East End of London, I see a lot of Bangladeshi children with severe eczema and these families have enrichment in variation in filaggrin. I have just recently started a new project to recruit over 1,000 Bangladeshi children and young adults for deep phenotyping (clinical and laboratory). This is an interesting new adventure. However, this does not compare to the adventures I have had with PC Project including near collapse from dehydration on the floor of the Grand Canyon and hearing issues for several months after a trip to Salt Lake City (Sancy and Roger are you listening)! Thankfully, I am now fully recovered.

In summary, I have really enjoyed my involvement with PC Project. Progress is being made and I can definitely see a better treatment for PC patients on the horizon. However, we can still do better for all of our patients and need to work together to achieve this.

PC Project attended and participated with the Society for Pediatric Dermatology (SPD) at the annual meeting July 12-14, 2018 at Lake Tahoe. As the only patient advocacy group to be invited, this was a not-to-be-missed opportunity for PC Project to network and raise awareness among the 430 attendees. The goal of PC Project was for every single participant to learn about PC and PC Project, to join the IPCC (International PC Consortium) and to encourage every dermatologist there to invite their PC patients to join the International PC Research Registry (IPCRR).

In addition to brochures, PC Project handed out small treats with poems to educate researchers and physicians about the painful nature of PC and to entice attendees to visit the PC Project table that was located directly outside of the main presentation room. Thanks to a PC patient for his limerick-writing parenting patient advocacy.
abilities. The treats and the poems were enthusiastically received.

During the “Hurwitz Lecture—Lessons Learned from Great Thinkers,” Dr. Eulalia Baselga, the director of the Pediatric Dermatology unit at Hospital de la Santa Creu i Sant Pau in Spain, who has referred patients to PC Project and who attended the 2016 Spain and 2016 Edinburgh Patient Support Meetings, shared her positive experiences from attending PC Patient Support Meetings. Dr. Baselga told the group how she learned about current research at the patient meeting and how the meeting helped her own PC patient. Dr. Baselga encouraged doctors to attend patient support meetings with their patients. In addition, she gave an enthusiastic shout-out to PC Project!

Dr. Tracy Funk, Assistant Professor, Dermatology and Pediatrics at Oregon Health & Science University, who works with Dr. Sancy Leachman who was influential in PC Project’s creation and a founding member of the International PC Consortium (IPCC), gave an informative 30-minute presentation called, “Update on Pachyonychia Congenita.” Dr. Funk also encouraged scientists and clinicians to learn more from PC Project.

Because there are many rare diseases, to have PC and PC Project talked about twice in one conference was extraordinary. PC Project met new researchers, physicians and medical students, and reunited with IPCC members and friends such as Anna Bruckner, Amy Paller, Joyce Teng and many others. Thanks to the Society for Pediatric Dermatology for the invitation to share their annual conference with PC Project.
**RECENT PUBLICATIONS**


Krupiczocj MA and O'Toole EA. Plantar pain in pachyonychia congenita Br J Dermatol 2018;179:11-12 (Linked to Brill et al Br J Dermatol 2018;179:154-162)


Peter DCV, Thomas M, Wilson NJ, Smith FJD. Skin fragility, woolly hair syndrome with a desmoplakin mutation - a case from India. Int J Dermatol. 2018 Sep;57(9):e73-e75

**WHY ARE PATIENT SUPPORT MEETINGS IMPORTANT TO ACHIEVING THE MISSION OF PC PROJECT?**

Over 65 PC patients, plus caregivers, physicians, scientists and industry partners (approximately 140 people), will attend the 17th PC Patient Support Meeting in London, England, October 19-21, 2018.

Each year, PC Project hosts a Patient Support Meeting where PC patients and their families come together to learn from leading physicians and scientists who provide information and training on how to care for and live with this isolating, painful disease. These meetings are not only educational but emotional and even life-changing for PC patients who have never met another person with PC. In addition to adult sessions, meetings include sessions for teenagers and children who learn about the science behind PC, how to deal with pain, social issues, difficult questions, bullying, and how to stay focused on their positive strengths and characteristics.

Furthermore, PC Patient Support Meetings serve as an opportunity for clinicians, researchers and drug developers to observe and learn directly from PC patients. Various studies and focus groups conducted at Patient Support Meetings over the years have resulted in first-hand and greater knowledge about PC due to the benefit of having a gathering of rare patients to learn from.

Finally, the hope with every patient meeting is that PC patients and caregivers will leave encouraged, edified and more able to cope with this debilitating disease. Instead of feeling embarrassed and alone, patients will feel more positive about a disease they didn’t choose and feel empowered to live fulfilling lives in spite of the pain.

Quotes from Patients who have attended past Patient Support Meetings:

“At my first PSM meeting, for the first time I looked into the eyes of another person with the same disease, saw them move like me, and saw them use the same tricks that I use to get through their day. This gave me an immense feeling of no longer being alone and it’s a wonderful feeling. I would say that I’ve never been as happy and confident before the PC PSM experience.”

“Attending the PSM is the one best thing you can do to help the way you psychologically handle your PC. It has finally allowed me to be able to talk openly about my PC.”

“I have hope again.”

“Despite living with PC for my entire life (although not knowing what it was for most of that), I had never met another person with the condition. My life changed forever as I discovered the amazing community of patients, caregivers, physicians, scientists, and others who make up PC Project.”
This PC Patient Support Meeting is sponsored by Palvella Therapeutics and supported by a grant from Novartis Pharmaceuticals UK Limited. PC Project is extremely grateful to both of these organizations.

**HOW PATIENTS CARE FOR PC NAILS**

The PC community was asked how they trimmed their nails. PC nails vary between PCers in how they look, and patients trim them in different ways using many different tools. What works for one does not necessarily work for another. It is an individual choice of the tool to use, how often to trim, whether preference is wet or dry nails when trimming etc. Here is how one PCer, Roseann McGrath, has cared for her nails from childhood:

“I am a 52-year-old female, spontaneous PC-K6a mutation, where my PC presented at birth on my hands and feet. I was thankfully diagnosed shortly after my birth with having PC. As early as 6 months old, my mother & father used a General Electric (G.E.) manicure set to drill my tiny finger and toe nails weekly. As I got older I started to do it myself. In my early teens I began to use a Sears Craftsman Dremel Drill every other day on my finger nails and weekly on my toe nails.

In 2014, a fellow PCer told me about the “Upower” drill, which is just as powerful, but much easier to hold and handle than the Dremel. It is made by Urawa Corporation Upower Nail Filing System UP200C Series Controller. To this day I drill my nails down to get them as flat as I can. I paint my fingernails with a light beige nail polish to cover the green hue in our PC nails. I cannot “trim” or “drill” too low because my nerves grow through my nails, thus when they start to bleed I know I’ve gone too low. Conversely, I cannot permit my nails to remain too high, because the nails are sensitive from the thickness. Therefore, I must find the right balance of how thick or how low my nails can be. With this said, I err on the side of drilling down as far as I can to hide how thick they are and to try to make them appear somewhat normal. I unfortunately cannot hide my calluses and blisters on each finger (and foot) at each pressure point like I can my nails.”

Responses from others on tips and tools they use.

“Large pointed nail clippers (I affectionately refer to them as “hedge trimmers”) which work best on wet/soaked nails, or a Dremel tool with a dimmer switch on dry nails/skin.”

“Nails clippers for large dogs, small pointed nail clippers, Dremel and Emery board. I grind them with an electric manicure device every three weeks.”

“I use this (see left) once a week for the very thick nails of my son. Our son watches television with a favorite snack during the weekly trimmings.”

“An Emery board to maintain my nails. I’ve only been able to tolerate the Dremel on my fingers in the last couple of years. As a child, my dad soaked and trimmed my nails with arazor blade. A Dremel still hurts when used on the fingernails.”

“These are a few of my trimming tools (see right).”

“Dremel on the worst nails, nail clippers and an Emery board on the other nails.”

“I use a thing called the PediNova by Medicool. It’s essentially a Dremel tool but they provide different bits specifically for nail grooming. They include a sandpaper barrel attachment, but I find that gets incredibly hot.”

“Black & Decker drill with a fine sandpaper disk.”

“My nails are very thick, so when a podiatrist takes the clippers to them, it’s quite painful. I find that using a grinder is much more comfortable.”

“A spring-loaded toe nail clipper for the foot nails and a good nail file for the hand nails. Sometimes I use a single edge razor blade to help with the toe nails.”

**SAVE the DATE**

The annual International PC Consortium (IPCC) Symposium will be held May 7-8, 2019 in conjunction with the SID meeting in Chicago, Illinois.