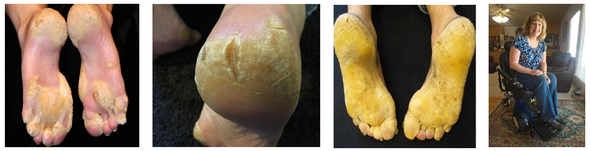
Loss of Mobility and Exquisite Plantar Pain due to Pachyonychia Congenita, a Rare Disease of Mutated Keratin Genes

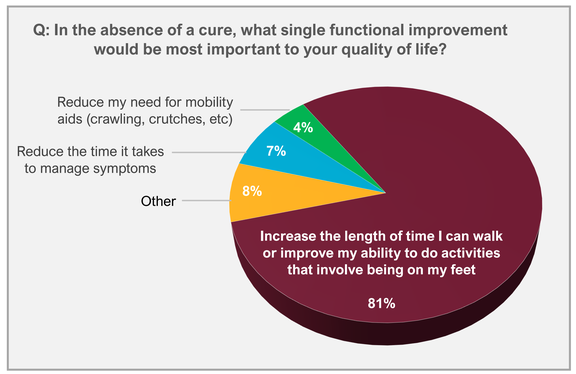
BACKGROUND: Pachyonychia congenita (PC) is a rare, chronically debilitating and lifelong monogenic disease caused by mutations in genes responsible for keratin production. These mutations lead to faulty keratin filament synthesis, increased skin fragility and impaired skin barrier function on the palms of the hands and plantar surface of the feet.



Figures Provided by Pachyonychia Congenita Project

PC patients often experience a partial or total loss of ambulation as a result of plantar pain from blistering, callus formation (keratoderma), neurovascular structures, and inflammation of the feet.

In a poll of PC patients attending the 2018 Externally Led Patient-Focused Drug Development Meeting (EL-PFDD) at FDA, lack of mobility was the primary functional improvement that would impact QoL. Of those polled, 91% reported some level of pain with every step walked.



PC POPULATION: A retrospective observational study of 400 U.S. dermatologists was published in 2019 that estimates the current population of PC patients in the U.S. to be between 8,900 and 9,800. (Gallagher et al *J Dermatol Dis* 2019)

DERMATOLOGIST AWARENESS: Gallagher et al found dermatologists were ~58X more likely to report managing a patient for prominent symptoms of PC (palmar keratodermas, follicular hyperkeratosis or leukokeratosis) than for PC, suggesting a substantial population of undiagnosed patients with PC.

Gene Mutations Often Leave Individuals with Pachyonychia Congenita **Unable to Walk** Due to **Severe Plantar Pain**

"The first steps a toddler with PC takes will begin to cause tissue trauma on their feet due to faulty keratin filament production and increased keratinocyte fragility. From this young age through adulthood, these individuals battle the pain and lack of mobility associated with PC. Increased awareness among pediatricians and dermatologists can help patients and their families adjust, but what is really needed is an effective treatment that targets the faulty keratin genes."

C. David Hansen, M.D.
University of Utah School of Medicine

For more information on PC Project

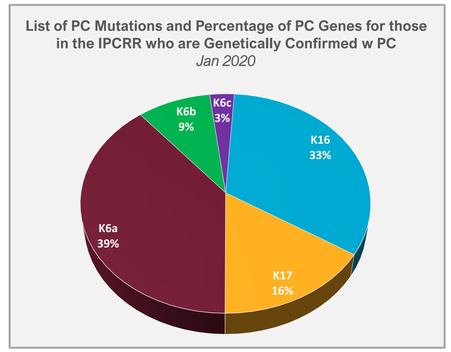
For more information on Palvella

SYMPTOM MANAGEMENT: There are currently no FDA- or EMA-approved treatments for PC. Patients self-manage their symptoms by shaving their keratoderma, lancing blisters and cysts, using OTC pain medication, soaking their feet and using creams or ointments to prevent cracking and additional pain.

EXPERIMENTAL TREATMENT: PC Project partnered with Palvella Therapeutics on their randomized, placebo-controlled, Phase 2/3 VALO Study of PTX-022 (QTORIN™ rapamycin), an experimental targeted treatment for PC.

Patient recruitment has concluded in VALO and results are expected this year.

INTERNATIONAL PC RESEARCH REGISTRY: More than 100 mutations within five keratin genes have been discovered through PC Project's International PC Research Registry (IPCRR). Revisions to the PC classification system have been introduced based on its data. Patients for the VALO study were identified and enrolled via the PC Registry.



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Pachyonychia Congenita Project
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