Efficacy and tolerability of topical imiquimod cream against high-risk anal human papillomavirus infection in men who have sex with men living with HIV: A single-arm, open-label pilot clinical trial

Authors:
Durukan D [1,2], Philips T[1,2], Ong JJ[1,2], Murray G[3,4] Grulich AE[5], Poynten IM[5], Jin F[5], Bradshaw CS[1,2], Chen MY[1,2],Aguirre I[2], Silvers J[2], Kent H[2], Atchison S[3,4], Balgovind P[4], Cornall A[3,4], Fairley CK[1,2]*,Chow EPF[1,2,6*]

*co-last authorships
[1] Central Clinical School, Monash University, Melbourne, Victoria, Australia
[2] Melbourne Sexual Health Centre, Alfred Health, Carlton, Victoria, Australia
[3] Murdoch Children's Research Institute, Parkville, Victoria, Australia
[4] Centre for Women's Infectious Diseases, The Royal Women's Hospital, Parkville, Victoria, Australia
[5] The Kirby Institute, UNSW Sydney, Sydney, NSW, Australia
[6] Melbourne School of Population and Global Health, The University of Melbourne, Melbourne, Australia

Background:
Men who have sex with men (MSM) living with HIV have a high prevalence of anal high-risk human papillomavirus (hrHPV), and consequent high incidence of anal cancer. All hrHPV types, particularly HPV16 and 18 can cause anal cancer and no proven treatments exist for anal hrHPV or related anal cancer precursor lesions. Imiquimod is effective against anogenital warts caused by low-risk HPV types. We conducted an open-label pilot clinical trial to assess the efficacy and tolerability of intra-anal imiquimod cream against hrHPV among MSM living with HIV [ACTRN12617001355369].

Methods:
The trial was conducted at Melbourne Sexual Health Centre between April 2018 and June 2020. MSM aged ≥18 years, living with HIV, positive for any anal hrHPV at baseline were eligible. Participants were instructed to apply half a sachet of 5% imiquimod cream (6.25 mg) intra-anally, 3 days/week for 16 weeks (Phase 1), followed by a maintenance dose of 1 day/week for 48-weeks (Phase 2). Anal swabs were collected and genotyped using the Seegene Anyplex™ II HPV28 Detection assay (Seegene, Seoul, Korea) on week 16 (Phase 1), and weeks 24 and 48 (Phase 2). SMS and questionnaires were used for adverse event (AE) follow-up.

Results:
Thirty MSM were enrolled, 27 completed phase 1 and 13 completed phase 2. Baseline prevalence of HPV16 or 18 was 51.9% (95%CI 40.0-69.3). By study completion, 9 men cleared HPV16 or 18 (64%, 95%CI 38.7-83.6): six in phase 1, and three in phase 2. In phase 1, 66.6% (18/27, 95%CI 47.8-81.4) experienced mild to moderate local AEs that lead to dose reduction or temporary interruption of treatment. The most common AEs were irritation, tenderness, and itching. AEs were persistent during ongoing treatment and resolved spontaneously following dose reduction.

Conclusion:
Intra-anal use of 5% imiquimod cream at 3 days/week caused persistent AEs and was not well-tolerated.

Disclosure of Interest Statement:
This trial was funded by an Australian National Health and Medical Research Council (NHMRC) Program Grant (GNT568971). E.P.F.C. is supported by an NHMRC Emerging Leadership Investigator Grant (GNT1172873). C.K.F. and C.S.B. are supported by an NHMRC Leadership Investigator Grant (GNT1172900 and GNT1173361, respectively). All other authors have no conflicts of interest to declare.