The efficacy of topical imiquimod in high-grade cervical intraepithelial neoplasia: a systematic review and meta-analysis.

A.J.M. VAN DE SANDE, MD1, M. KENSAKUL1,2, MD, M.M. KOENEMAN, MD, PhD1, M. JOZWIAK, MD, PhD1, C.G. GERESTEIN, MD, PhD3, A.J. KRUSE, MD, PhD1,3, E.M.G. VAN ESCH, MD, PhD3, P.J. DE VOS VAN STEENWIJK, MD, PhD1,3, C.L.P. MUNTINGA, MD4, W.M. BRAMER5, H.C. VAN DOORN, MD, PhD1, F.J. VANKEMENADE, MD, PhD1, H.J. VAN BEEKHUIZEN, MD, PhD1.

1 Department of Gynecological Oncology, Erasmus MC Cancer Institute, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands, 2 Physiotherapy Chonprathan Center, Nonthaburi, Thailand, 3 Department of Obstetrics and Gynecology, Maastricht University Medical Centre, the Netherlands, 4 Department of Gynecologic Oncology, Division of Imaging and Oncology, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands, 5 Department of Obstetrics and Gynecology, Sint Maartenskliniek, Zwolle, the Netherlands.

Background:
Invasive treatment of high-grade cervical intraepithelial neoplasia (CIN) may adversely affect future fertility and pregnancy outcomes. Alternative therapies are desirable.

Objectives:
To determine the efficacy of topical imiquimod in treatment of high-grade cervical intraepithelial neoplasia (CIN), defined as regression to CIN 1 or less, and to determine the clearance rate of high-risk human papillomavirus (hr-HPV), compared to surgical treatment and placebo.

Material and Methods:
Electronic databases were searched for articles from the database inception to July 2022. Meta-analysis using random-effects models was conducted to determine the efficacy of topical imiquimod treatment.

Results:
Five studies involving 463 women with high-grade CIN were included. Imiquimod was associated with histological regression to CIN1 or less in 55% of cases versus 29% for placebo, and 93% for surgical treatment. Imiquimod-treated women had a greater odds ratio of histological regression to CIN1 or less than placebo-treated women (ORs 4.17, 95% CI 2.03-8.54). In comparison to imiquimod, surgical treatment had an odds ratio of 14.81 (95% CI 6.59-33.27) for histological regression to CIN1 or less. The hr-HPV clearance rate was 53.4% after imiquimod treatment and 66% after surgical treatment (ORs 1.53, 95% CI 0.62-23.77).

Figure 1. Forest plot displaying odds ratios of women with HSIL treated with topical imiquimod relative to LLETZ (histological regression)

Conclusion:
Histological regression is higher in imiquimod treatment than placebo. Surgical treatment, which is currently the golden standard, demonstrates the highest histological regression rate. Future studies should focus on patient selection and further development of alternative treatments.

Keywords:
Papillomavirus Infections; Papillomaviridae; Metabolic Clearance Rate; Uterine Cervical Neoplasms; Transformation zone; Treatment outcome; Squamous intraepithelial lesions.

Presenter: M. Kengsakul, MD, malika@g.swu.ac.th
Corresponding author: A.J.M. van de Sande, MD, a.vandesande@erasmusmc.nl