## Title

15 Long term outcome of treatment of high grade squamous intraepithelial lesions (HSIL) in patients with five years follow up



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*Background:* Transplant recipients have significantly elevated risk of anal cancer, compared to the general population. We sought to determine the presence of high risk human papilloma virus (hrHPV) and anal cytological abnormalities in kidney transplant recipients, and assess the feasibility of an anal cancer screening intervention.
*Methods:* Kidney transplant recipients, over 18 years old, attending a Transplant Clinic, had anal swab specimens collected. These were then eluted into liquid-based cytology collection vials for cytological examination and HPV genotyping by Linear Array.
*Results:* Of 102 participants approached, 73 (72%) consented to join the study and completed testing. The mean age was 47 (range 20–76 years). 64 (88%) had technically satisfactory cellularity. Of these, 8 (12.5%) were abnormal; 6 (9.4%) LSIL; 2 (3.1%) HSIL and 56 negative. 70 (96%) specimens were assessable for genotyping and 15 (21%) had HPV detected. 63 had both HPV and cytology assessable. Of the 15 with HPV, 4 (27%) had abnormal cytology, compared to 4 (7%) of 48 with no HPV. However, there was no evidence of an association between any HPV detection (low or high risk) and abnormal anal cytology (OR 2.75, 95% CI 0.82–11.84); $p=0.12$). Both participants with cytological HSIL had histological HSIL on HRA, both with multiple hrHPV.
*Conclusions:* Transplant recipients were generally willing to consent to the study procedures, including anal swabbing. The prevalence of abnormal cytology was 12.5% and high risk HPV genotypes 12.3%. Anal swabbing was able to identify individuals at increased risk of anal cancer for future close monitoring.

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## Adjudicated response of anal high-grade squamous intraepithelial (HSIL) to topical therapy assessed by high-resolution anoscopy (HRA)

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*Background:* Response to treatment is determined by HRA guided-biopsies. Complete response (CR) indicates resolution of HSIL; partial response (PR) indicates clinically-significant improvement in HSIL (Table 1). HRA may be inexact with missed or obscured lesions. We evaluated potential confounding factors affecting assessment of response in a double-blind study comparing topical Chinese medicine vs. placebo (28 per arm).
*Methods:* HRA adjudication of 36 responses including all CR and PR was performed by two clinicians blinded to study arm and each other's classifications (Table 2). HRA descriptions and photodocumentation were reviewed, comparing exams during and at 12-weeks post-treatment. Clinicians determined if resolved or improved lesions were missed, recurred, had late clinical response (LCR) post-treatment, or biopsy-induced regression. Disagreements were downgraded to the lesser response.
*Results:* 17/36 responses were reclassified: 11 PR to NR, 3 PR to LCR, 2 NR to CR with recurrence, and 1 NR to PR. 2/10 CR were considered possibly biopsy-induced or too small for evaluation, but were not reclassified. Reasons for reclassification included: missed lesions, $<50\%$ improvement, biopsy-induced, uninterpretable due to obscuring or diffuse warts.
*Conclusions:* Determination of treatment efficacy is related to HRA quality. CR was confirmed in all 10 cases, but additional 4 LCR were considered post-treatment effect, which has been noted for other topical therapies. The majority of PR was reclassified. PR may indicate clinically-important response but was difficult to validate. Exclusion of patients with obscured exams or small lesions and better documentation may assure more accurate determination of response. Blind HRA adjudication may help verify findings.

Table 1 Definition of response.

| | |
|---|---|
| Complete Response (CR) | Absence of HSIL cytology and histology at week 48 |
| Late Complete Response (LCR) | Absence of HSIL cytology and histology at week 60 |
| Partial Response (PR) | Regression of HSIL histology with HSIL cytology or $\geq$50% reduction in size or number of HSIL. |
| No response (NR) | Presence of HSIL histology with no change in lesions number, size or characteristics. |
| Progression (Ca) | Increase in lesion number, size, or characteristics development of anal cancer |

Table 2 Responses pre and post-adjudication.

| Response | Pre Adjudication | | Post Adjudication | |
|---|---|---|---|---|
| | Treatment Arm | Placebo | Treatment Arm | Placebo |
| Complete Response | 7 | 3 | 7 | 3 |
| Late Complete Response | 0 | 0 | 3 | 1 |
| Partial Response | 11 | 10 | 5 | 5 |
| No response | 10 | 15 | 13 | 19 |
| Progression | 0 | 1 | 0 | 0* |
| Total | 28 | 29 | 28 | 28 |

*Adjudication determined SISCCA was present at study entry and was excluded from analysis.

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## Long term outcome of treatment of high grade squamous intraepithelial lesions (HSIL) in patients with five years follow up

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*Background:* Office-based or surgical ablation of HSIL may prevent anal cancer; however, limited data exist on long-term outcome regarding HSIL or cancer. It is not established that treating HSIL reduces the incidence of cancer, but long-term remission of HSIL may be a good clinical indicator necessary for cancer prevention.

*Methods:* Between 2006 and 2008, 369 new patients were diagnosed with HSIL. Follow-up data were extracted in 285/369 patients with HSIL (follow-up not determined in 84). 133 (46.7%) were followed for more than 5 years. As a preliminary analysis, every third patient was analyzed for outcome defined as no HSIL for at least 2 years (HSIL-free) (n=50).
*Results:* Forty-six patients were men (39 HIV-positive) and 4 were women (1 HIV-positive) ranging in age from 26 to 67 years (mean 45.7 years) and followed from 5.1 to 11.4 years (mean 8.8 years). Patients had between 1–10 (mean 2.58, median 2) ablations to become HSIL-free. Three patients never became HSIL-free; 1 with inadequate follow up and treatment developed cancer at 5.1 years. There was no recurrence of HSIL in 31 patients (62%) followed for 3.2 to 10.1 years (mean 7.0 years). HSIL recurred in 16 patients (32%) at 2.1 to 6.2 years (mean 3.8 years) and only four had another recurrence after becoming HSIL-free.
*Conclusions:* In patients with more than five years follow-up, 94% became HSIL-free with treatment. Although HSIL recurred in 16 patients, most became HSIL-free. Only 1 patient developed cancer as a result of inadequate treatment. Becoming HSIL-free after ablation may effectively prevent anal cancer.

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## Preventing anal cancer: Qualitative study among foreign-born Hispanic HIV-Infected Gay and Bisexual Men

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*Background:* This study explores foreign-born Hispanic HIV-infected gay and bisexual men's (GBM) anal cancer primary and secondary prevention understanding. These populations may be at greater risk for developing anal cancer given their reduced likelihood to engage and be sustained in HIV primary care.
*Methods:* Between August 2015 and December 2016 researchers conducted 33 semi-structured in-depth interviews with foreign-born Hispanic HIV-infected Hispanic GBM. Interview questions sought to determine participants' perceived barriers and facilitators to anal cancer primary and secondary prevention. Researchers analyzed interview transcripts using a qualitative content analysis approach.
*Results:* For primary prevention, men reported lack of knowledge about the human papillomavirus (HPV) vaccine. However, for secondary prevention roughly 60% of participants had previously screened for anal dysplasia via anal Pap smear. Provider recommendation was the most common screening facilitator. Men reported stigma related to their HIV status, sexual orientation, and anal Pap smear procedures as barrier to HIV primary care retention and, in turn, anal cancer screening adherence. Participants reported willingness to use a self-screening anal Pap smear test if it were commercially available.
*Conclusions:* Health providers continue to be the leading source of health information. Therefore, provider recommendation for HPV vaccination and anal cancer screening among age-eligible Hispanic HIV-infected GBM is critical. More work is needed to destigmatize HIV and sexual orientation to influence positive health behaviors among this population. Future intervention research could test the effects of provider-led interventions and also media campaigns aimed at influencing HPV vaccine uptake and anal cancer screening among this population.

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## Screening for anal dysplasia in women with a history of human papillomavirus related lower genital tract pathology

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*Background:* Women with a human papillomavirus related history of cervical, vaginal or vulvar high-grade dysplasia or cancer are at increased risk to develop anal dysplasia or anal cancer. Screening for anal cancer precursors (squamous intraepithelial lesions (SIL)) with high resolution anoscopy (HRA) in high-risk populations is subject of debate. In this study we evaluated standardized intra-anal SIL screening using HRA in high-risk female patients.
*Methods:* A retrospective observational study was performed to evaluate the prevalence of intra-anal SIL in women with a history of vulvar high-grade SIL (HSIL) and perianal HSIL diagnosed at the Netherlands Cancer Institute, who were referred for intra-anal SIL screening using HRA in the MC Slotervaart between 2015 and 2017.
*Results:* 22 female patients were screened for anal SIL using HRA. 19 females had a history of biopsy proven vulvar HSIL and 19 females had a history of biopsy proven perianal HSIL. Eleven (50%) patients had a history of multizonal HSIL at three or more perianogenital locations. No anal cancer was found at screening, 7 (32%) patients were diagnosed with anal HSIL and 7 (32%) patients with low-grade anal SIL.
*Conclusions:* We found a high prevalence of anal HSIL in women with HPV related lower genital tract dysplasia. Intra-anal SIL screening using HRA in this high risk population seems to be justified. However, HRA is an invasive screening method. Studying other, less invasive screening methods remains important.

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## Identification of productive and transforming anal intraepithelial neoplasia using immunohistochemical markers p16INK4a and HPV E4

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