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Dermatology & Molecular Pathology

DNA METHYLATION ANALYSIS TO PREDICT REGRESSION OF HIGH-GRADE ANAL INTRAEPITHELIAL NEOPLASIA IN HIV+ MEN (MARINE): AN UPDATE OF AN ONGOING COHORT STUDY

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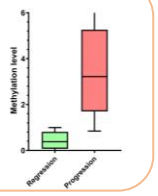
Background

Around 30% of HSIL regress within one year,[1] but current histopathological assessment is unable to distinguish between HSIL likely to regress and HSIL likely to persist or progress to cancer.

Aim

We aim to assess if host cell DNA methylation markers can predict regression of HSIL, thus determining the need for immediate treatment, or active surveillance. This could reduce overtreatment and the associated anal and psycho-sexual morbidity

In our pilot study with retrospectively collected archival HSIL samples from 18 subjects of which 9 showed regression over time and 9 showed progression to cancer, methylation levels of the "progressive" HSIL samples were extremely high compared to the "regressive" HSIL samples.



Outcomes

The primary study endpoint is spontaneous histopathological **regression** of each baseline HSIL lesion at the end of the study.

Regression is defined as: ≤LSIL in the exit biopsy at 24 months.

Regression proportions will be compared in:

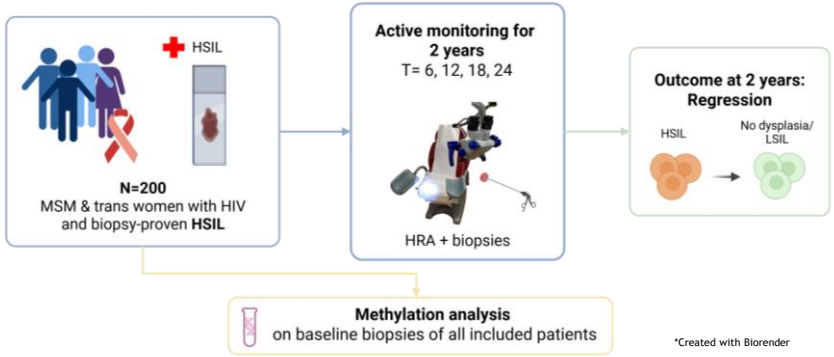
- HSIL biopsies with low vs high methylation levels
- Positivity vs negativity of immunohistochemical biomarkers

This is an ongoing clinical validation of **Methylation Markers** for **cancer risk stratification** of anal **HSIL**

Design

This is an active surveillance cohort study in the Netherlands, in 200 HIV+MSM diagnosed with HSIL in 5 centers: Amsterdam UMC, location AMC; DC Klinieken Lairesse; OLVG, locatie Oost; Maasziekenhuis Pantein; DermaHaven.

Participants are not treated but closely monitored during 24-months of follow-up with six-monthly visits including cytology, and high-resolution anoscopy (HRA) with biopsies. Methylation analysis is performed on baseline biopsies of all included patients.



*Created with Biorender

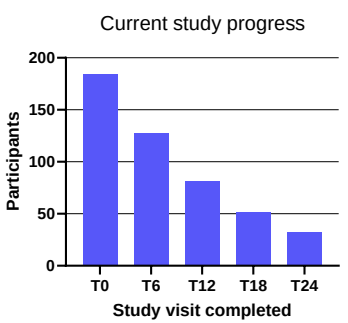
Update

184 participants were included.

32 completed the total follow-up of the study.

14 ended follow-up early. Reasons included HSIL covering >50% of anal circumference, wish for HSIL treatment, privacy concerns, and moving abroad.

Biomarker analysis is currently being performed in baseline biopsies



Ethics

Ethics approval was obtained at the local Institutional Review Board.
The main risk associated with participation in this study is progression to cancer.
However, this risk was considered to be acceptable because:

1. Short study follow-up of 2 years, thus low risk of progression to cancer in that period
2. Exclusion of patients at very high risk for cancer, i.e. patients with more than 50% of anal canal affected with HSIL, patients with abnormalities on DARE
3. Closely monitoring of participants and referral for further examination and treatment when clinical suspicion for cancer arises or biopsies confirm progression to cancer.

References

1. Goldstone et al. Clin Infect Dis 2019
Images Created with BioRender.com

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