Need for optimization of screening methods for anal intraepithelial neoplasia in people living with HIV

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Stefan Esser[1], Alexander Kreuter[2], Anja Potthoff[3], Norbert H. Brockmeyer[3], Mark Oette[4], Aylin Yavuz[1], Karl-Heinz Jöckel[5,6], Laven Mavarani[5], Hildegard Lax[5,6], Konstantinos Bilbilis[5,6], Ulrike Wieland[7]

[1]Clinic of Dermatology, Department of Venereology, University Hospital Essen, Essen, Germany
[2]Department of Dermatology, Venereology and Allergology, Helios St. Elisabeth Hospital Oberhausen, University Witten-Herdecke, Oberhausen, Germany
[3]Department of Dermatology, Venereology and Allergology, Interdisciplinary Immunological Outpatient Clinic, Center for Sexual Health and Medicine, Ruhr University Bochum, Bochum, Germany
[4]Department of General Medicine, Gastroenterology and Infectious Diseases, Augustinerinnen Hospital, Cologne, Germany
[5]Institute for Medical Informatics, Biometry and Epidemiology (IMIBE), University Hospital Essen, Essen, Germany
[6]Centre for Clinical Studies Essen (ZKSE), c/o IMIBE, University Hospital Essen, Essen, Germany
[7]Institute of Virology, National Reference Center for Papilloma and Polyomavirus, University of Cologne, Faculty of Medicine and University Hospital of Cologne, Cologne, Germany

BACKGROUND

The detection rate of histologically confirmed high grade anal intraepithelial neoplasia (HGAIN) and anal carcinoma by screening with anal cytological smears and/or human papilloma virus (HPV) typing in HIV-positive individuals (HIV+) has been examined in the TECAIN Study.

METHODS

The TECAIN study is a prospective, randomized, controlled, clinical trial, conducted in multiple sites in Germany with the aim to compare efficacy and safety of local treatment with 85% trichloroacetic acid to electrocaustic ablation of histologically confirmed anal intraepithelial neoplasia (AIN) in HIV+ since 2015. Biopsies of AIN lesions, anal cytological swabs and HPV typing were performed at baseline and follow-up visits. The cytological findings were divided according to the Bethesda classification. Depending on their oncogenic potential HIV types were distinguished into high risk (HR) and low risk (LR) HPV. The consistencies between HPV types, the cytological results and histologic findings were analyzed.

RESULTS

292 examinations in 184 male HIV+ included during the TECAIN Study were analyzed until September 12, 2019. In the study population at baseline 175 (95%) were of Caucasian ethnicity, the median age was 48 (±10.9) years, 180 (98%) of HIV+ took antiretroviral therapy and 151 (82%) were MSM.

Evaluation of TECAIN RCT data showed that simultaneous screening with anal *cytological* AND *virological* smears detect high grade anal intraepithelial neoplasia (HGAIN) much more reliable than cytology alone.

Histology

108 examinations (37%) showed AIN I as the highest grade HPV-associated lesion, 84 (29%) AIN II and 100 (34%) AIN III. Thus in 184 examinations (63%) HGAIN were detected.

Cytology

At the same time, LSIL was diagnosed in 84 (29%), ASC-US in 76 (26%), HSIL in 99 (34%) and negative results in 33 (11%) cases. The cytological screening found no HSIL in 66.3% of all histologically confirmed HGAIN cases.

Virology

In 251 cases (86%) at least one HR-HPV could be diagnosed and 28 (10%) LR-HPV. No HPV was detected in 13 (4%) examinations. No HR-HPV was detected in 12% of all HGAIN cases.

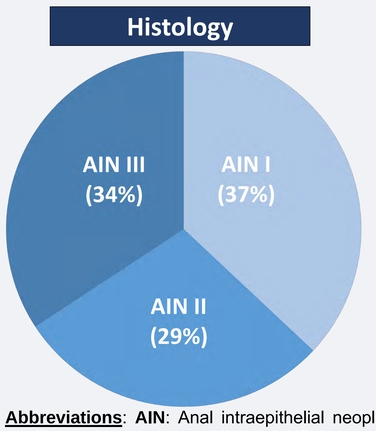
Cytology vs. Virology

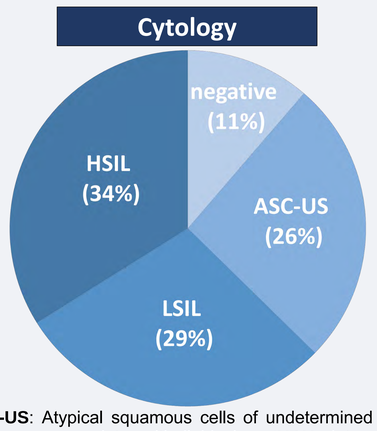
If both cytology and virology results were considered together, only 10.3% of all HGAIN cases showed no higher grade abnormalities.

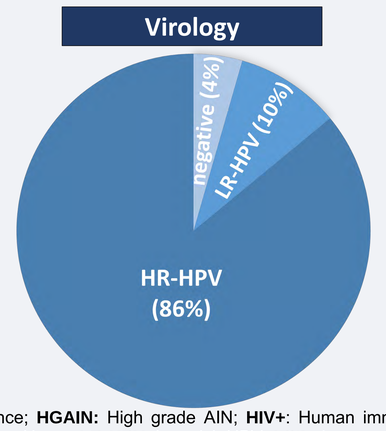
Limitations

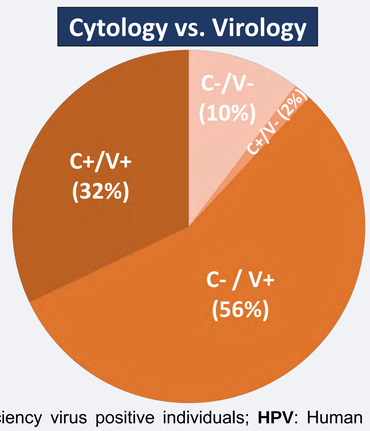
The study population consisted of a small cohort of male HIV+ patients with histopathologically confirmed AIN. Therefore a calculation of positive/negative predictive values was not possible.

Specifications in 184 male HIV+ at baseline	*n (%) or mean ± SD*	*missings n (%)*
HIV transmission risk		- (-)
MSM	151 (82.07)	
Hetero	7 (3.80)	
IVDU	3 (1.63)	
Unknown	22 (11.96)	
Other	1 (0.54)	
HIV CDC stage [1993]		1 (0.54)
HIV A	73 (39.89)	
HIV B	62 (33.88)	
HIV C (AIDS)	48 (26.23)	
CD4 count [cells/µl]	636.27 ± 311.80	14 (7.61)
CD4/CD8 [ratio]	0.83 ± 0.49	15 (8.15)
Antiretroviral Therapy [ART]		- (-)
None	4 (2.17)	
≥ 1	180 (97.83)	
Viral load	121.17 ±1067.62	18 (9.78)
> 50 HIV-RNA copies/ml	8 (4.35)	
≤ 50 HIV-RNA copies/ml	158 (85.67)	
Smoking Status		- (-)
Never-Smoker	72 (39.13)	
Ex-Smoker	43 (23.37)	
Active Smoker	69 (37.50)	
Body Mass Index [BMI]	25.09 ± 3.40	- (-)









Abbreviations: **AIN**: Anal intraepithelial neoplasia; **ASC-US**: Atypical squamous cells of undetermined significance; **HGAIN:** High grade AIN; **HIV+**: Human immunodeficiency virus positive individuals; **HPV**: Human papilloma virus; **HR-HPV**: High risk HPV; **HSIL**: high grade squamous intraepithelial lesion; **IVDU**: Intravenous Drug Users; **LR-HPV**: Low risk HPV; **LSIL**: low grade squamous intraepithelial lesion; **MSM**: Men who have sex with men; **TECAIN**: Efficacy and safety of topical **t**richloroacetic acid vs. **e**lectro**c**autery for the treatment of **a**nal **i**ntraepithelial **n**eoplasia in HIV-positive patients (TECAIN) – a randomized controlled trial

CONCLUSIONS

Collection of cytological anal smears for Bethesda classification is still standard of care in anal cancer screening. The results of the TECAIN study show that cytology alone fails to detect the majority of high-grade lesions. Whereas simultaneous screening with anal cytological and virological smears detects HGAIN much more reliable. Comparable results in gynecology have led to an extension of routine diagnostics by the addition of HPV typing to cervical cancer screening guidelines in Germany. The high resolution anoscopy combined with targeted mucocutaneous biopsies after tissue staining (acetic acid, Lugol's solution) is still essential for anal cancer screening.

ACKNOWLEDGMENTS

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Registration:

The TECAIN study was registered in:

- ClinicalTrials.gov ➔ NCT02615860
- German Clinical Trials Register ➔ DRKS00009692