Screening for Anal Cancer: When to Screen and What to Do With the Results

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Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years:

Dr Ellsworth has no relevant financial affiliations to disclose. (Updated 04/01/22)

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Learning Objectives

After attending this presentation, learners will be able to:

- Describe the incidence rates of anal cancer in persons with HIV
- Determine which persons to screen for anal cancer precursors or high grade squamous intraepithelial lesion (HSIL) and learn how to screen for anal HSIL
- Quantify the expected reduction in anal cancer incidence in persons with HIV that undergo treatment of anal HSIL

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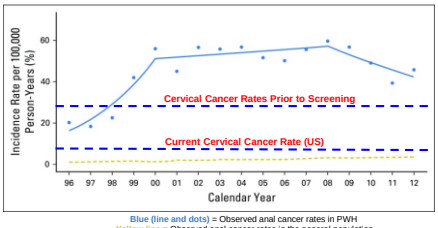
Anal Cancer Rates in HIV

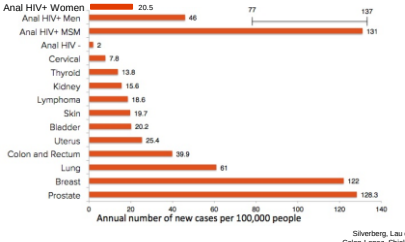


Blue (line and dots) = Observed anal cancer rates in PWH
Yellow line = Observed anal cancer rates in the general population

Slide 4

Colon-Lopez, Shiels et al. J Clin Oncol. 2017;

Anal Cancer Rates: Perspective



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Silverberg, Lau et al. Clin Infect Dis. 2012.
Colon-Lopez, Shiels et al. J Clin Oncol. 2017.
www.anchorstudy.org

Anal Cancer Rates

Population	SIR	Incidence Rate (per 100,000 PY)
PLWH[1]	19.1	50.7
MSM	38.7	89.0
Men (non-MSM)	9.4	32.5
Women	9	20.5
HIV-[2]	~1	0-2
HIV- MSM[3]		19

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1. Colon-Lopez, Shiels et al. J Clin Oncol. 2017
2. Silverberg, Lau et al. Clin Infect Dis. 2012
3. Clifford, Georges et al Cancer Epi. 2020

Anal Cancer Rates

Recent data (Danish HIV Cohort):

5-year anal cancer risk in PWH with AIN 3 is 14.1%!

Faber MT, et al. Cancer Epidemiol Biomarkers Prev. (2020) 29 (1): 185–192.

HIV+ MSM 19

1. Colon-Lopez, Shiels et al. J Clin Oncol. 2017
2. Silverberg, Lau et al. Clin Infect Dis. 2012
3. Clifford, Georges et al Cancer Epi. 2020

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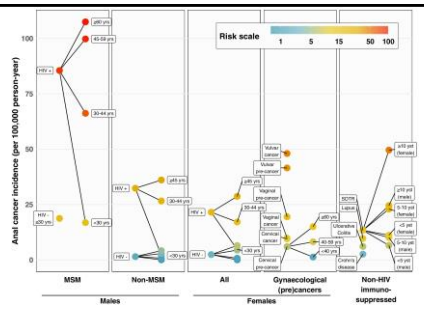

Clifford GM, et al. Int. J. Cancer. 2021; 148: 38-47.

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Who and When to Screen

- Persons with HIV
- Women with HIV
  - Prevalent histologic HSIL in 26-46% of screened women[1,2,3]
  - High rates of HSIL irrespective of sexual "risk factors"
- ≥ 35 years-old[4]
- **Symptomatic** individuals
- Consider
  - HIV-negative MSM
  - Chronically Immunosuppressed
  - HIV-negative women with cervical HPV 16 infection ≥ 45 years-old[5]

[1]Gaisa M, Ita-Nagy F, et. al. Clin Infect Dis. 2017. 64(3): 289-294.
[2]Stier EA, Lensing SY, et. al. Clin Infect Dis. 2020. 70(8): 1701-1707.
[3]Palefsky J. CROI. 2022.
[4]Deshmukh AA, Chiao EY. Cancer. 2017. 123(23):4709-4719.
[5]Chunqing L, et. al. Lancet Infect Dis. 2019;19(8):880-891

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Anal Cytology as a Screen for Anal Cancer

- Performance (≥ ASCUS)
  - Sensitivity 69 to 93% and Specificity 23 to 59%
- Recommendations:
  - No preps, no anal sex 48 hours prior
  - Prior to DARE or HRA (no lubricant)
  - Moistened polyester swab
  - Separate anal verge
  - Insert to rectal wall
  - Spiral motion with pressure and withdraw slowly (10 s)
  - Adequate agitation in cytology medium

Chiao EY, Lensing SY. AIDS. 2020 Dec 1;34(15):2249-2258
Chiao EY, Giordona TP. Clin Infect Dis 2006;43(2):223-33

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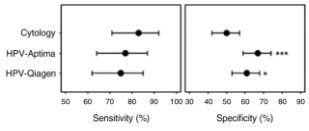
HPV Based Screening

- High prevalence anal HPV infection in MSM
- High-risk HPV screening in women living with HIV (WLWH): 41 and 45% prevalence:



Burgos J, Hernández-Losa. AIDS 2017;31(16):2227-2233
Chiao EY, Lensing SY. AIDS. 2020 Dec 1;34(15):2249-2258

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Optimized HPV Screening of Women with HIV

	Sensitivity, % (95% CI)	Specificity, % (95 % CI)
Anal Cytology	87 (74, 94)	49 (40, 57)
Unmodified Xpert	89 (78, 96)	49 (40, 57)
Xpert Optimized (ROC)	75 (61, 85)	84 (76, 89)
Xpert Optimized (Recursive Partitioning)	75 (61, 85)	86 (80, 92)

Ellsworth G, et. al. J Acquir Immune Defic Syndr. 2021;87(3):978-984.

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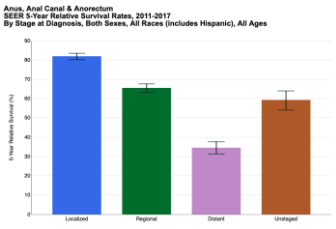
Digital Anorectal Exam (DARE)

- Anal cancer survival related to stage
  - Superficially invasive cancer is treated only surgically
- Examine:
  - **Circumference** and length of anal canal and distal rectum
  - Anal margin: 5 cm distal to anal verge
  - Prostate
  - Pouch of Douglas



Hillman RJ, Berry-Lawhorn JM, J Low Genit Tract Dis. 2019 Apr;23(2):138-146

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Cervical Cancer Prevention

- Treatment of cervical HSIL reduces the incidence of cervical cancer
- Why would a similar strategy not work in the anus?
  - Lesions are large, multifocal
  - Lesion recur, new lesions appear
  - HSIL eradication is difficult
    - 30% (probably more) of patients undergoing treatment will still have HSIL at one year[1]
  - Issues with tolerance/safety of high resolution anoscopy and HSIL ablation/treatment

[1] Goldstone SE, Lensing SY, et. al. Clin Infect Dis. 2019. 68(7) 1204-1212.

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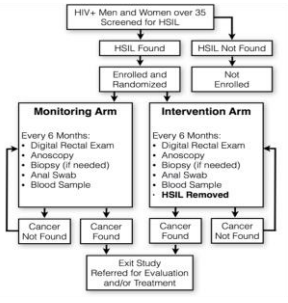
the ANCHOR study

Primary Endpoint: Time to anal cancer

Secondary Endpoint: Adverse events related to treatment of HSIL



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ANCHOR sites

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Methodology

- Visits every 6 months
  - Every 3 months if concern for cancer
- Collect
  - Anal cytology
  - Swabs
  - Blood (serum)
- Digital anorectal exam
- HRA

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Methodology

Treatment Arm

- HSIL treated:
  - at Visit 1
  - at interim visits if found on biopsy at 6 month visits
- Modalities (14% treated with > 1 modality):
  - Electrocautery (93%)
  - Infrared coagulation (6%)
  - Treatment with anesthesia (5%)
  - Topical 5-fluorouracil (7%)
  - Topical imiquimod (1%)

Active Monitoring Arm

- HSIL biopsied annually
  - Or more frequently if concern for progression to cancer

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Screened Population

- Screened 10,723 (9/24/2014 to 8/5/2021)
- 52% found to have HSIL
  - 53% of men
  - 46% of women
  - 63% of transgender persons
- 17 individuals (0.16%, 160/100,000 PY) diagnosed with cancer at screening

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Randomized Population

	Randomized N=4,446	
	Treatment N=2,227	Active Monitoring N=2,219
Age (median years, IQR)	51 (44-57)	51 (44-57)
Years since HIV diagnosis (median, IQR)	17 (10-24)	17 (10-25)
Gender Identify N (%)		
Male	1793 (81)	1782 (80)
Female	346 (16)	365 (17)
Transgender	85 (4)	68 (3)

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Randomized Population

	Randomized N=4,446	
	Treatment N=2,227	Active Monitoring N=2,219
Race N (%)		
Non-hispanic White	695 (31)	737 (33)
African-American	935 (42)	939 (42)
Hispanic, non-African-American	381 (17)	339 (15)
Asian/Pacific Islander	27 (1)	29 (1)
Other	189 (9)	175 (8)

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Randomized Population

	Randomized N=4,446	
N (%)	Treatment N=2,227	Active Monitoring N=2,219
HIV Risk Group		
Homosexual	1738 (78)	1742 (79)
Heterosexual	532 (24)	510 (23)
IVDU	152 (7)	177 (8)
Smoker	710 (32)	743 (34)
Baseline HIV RNA < 50 copies/mL	1852 (84)	1800 (82)
Baseline CD4 (median cells/µL, IQR)	602 (393-827)	607 (410-837)

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Stratification Factors

	Randomized N=4,446	
N (%)	Treatment N=2,227	Active Monitoring N=2,219
Nadir CD4 ≤ 200 cells/µL	1130 (51)	1121 (51)
HSIL size > 50% of anal canal/perianus	285 (13)	282 (13)

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Results

	Treatment	Active Monitoring	Overall
Invasive Cancer Cases	9	21	30
Cancer Incidence (per 100,000 PY)	173	402	-
Months of follow-up (median, IQR)	25 (12-42)	27 (12-42)	25.8

Treatment resulted in a 57% reduction in anal cancer (95% CI, 6% to 80%, P=.029)

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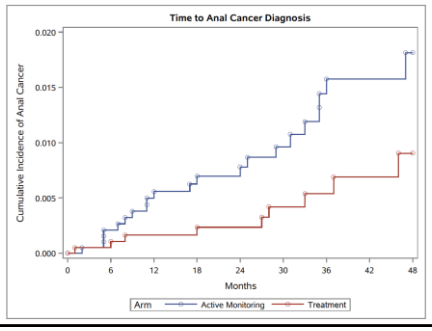

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Adverse Events

	Treatment arm	Active monitoring
Adverse events	683	635
Serious adverse events	586	568
Study-related adverse events	43	4
Study-related serious adverse events	7	1
Skin ulceration due to 5-fluorouracil	1	0
Anal abscess due to electrocautery	1	0
Pain due to electrocautery	1	0
Pain due to treatment under anesthesia	1	0
Pain due to infrared coagulation	1	0
Infection or abscess due to anal biopsy	2	1

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Current Status of ANCHOR Study

- DSMB recommended:
  - Stopping study for efficacy
  - Treat all participants in the monitoring arm
- Study is currently offering treatment and follow up to all interested participants.

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Conclusions

- Treatment of anal HSIL is an effective strategy to reduce the incidence of anal cancer in persons with HIV
- Recommendations to screen for and treat anal HSIL should be included in guidelines as standards of care

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Persisting Controversies

- There is a need to improve HSIL treatment efficacy
  - Improve clinical skills
  - Novel or adjunctive therapies
- There is not widespread access to quality HRA
  - Need for large scale training programs
  - Improved screening tools (biomarkers) and algorithms
  - No proven biomarkers for HSIL regression/progression
- Can ANCHOR results be extrapolated to other at-risk groups?
- Need for updated cost-effective analyses

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What can be done?

- Access to HRA?
  - Screen patients and refer for HRA
- No access to HRA?
  - Symptom-based screening and DARE!
  - Develop HRA programs

2012-2022
Celebrating a decade of service and education
International Anal Neoplasia Society

https://iansoc.org/HRA-Course-Overview

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Acknowledgements

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Question-and-Answer Session