ANCHOR Trial Update

Barcelona HPV Course
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Joel Palefsky, M.D.
University of California, San Francisco

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Disclosure

- Vir Biotechnology, Virion Therapeutics, Antiva Biosciences, Roche Diagnostics -consultant
- Merck- advisory board member- speaker

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Objectives

- Describe the groups in the population at highest risk of anal cancer
- Describe the main findings of the ANCHOR Study
- Describe approaches to screening people living with HIV to determine who should be referred for high resolution anoscopy

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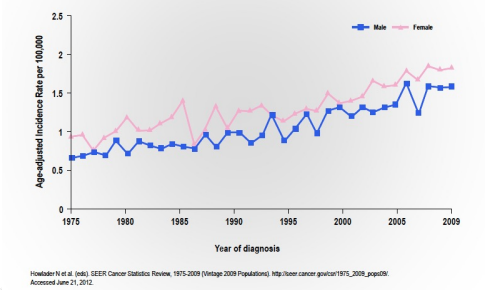
Age-Adjusted Incidence of Invasive Anal Cancer by Gender and Year of Diagnosis: United States



Howlader N et al. (eds). SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations). http://seer.cancer.gov/csr/1975_2009_pops09/. Accessed June 21, 2012.

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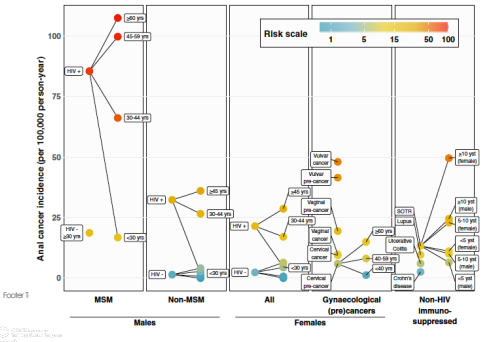
Anal cancer risk scale



Clifford et al. Int. J. Cancer. 2020;1–11. https://doi.org/10.1002/ijc.33185

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Why try to prevent anal cancer?

- Survival rate is low for more advanced disease
- Among those who do survive, there is substantial morbidity associated with standard treatment, primarily due to radiation therapy

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Why anal screening and treatment of HSIL might not work: the need for evidence fro a RCT

- In many at-risk people lesions are large and multifocal
- Clinicians may miss lesions
- Clinicians may inadequately treat lesions
- New lesions often arise- anal whack-a-mole!

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the ANCHOR study

The ANCHOR Investigators Group
Protocol A01 of the AIDS Malignancy Consortium
UM1CA121947

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the ANCHOR study

Aim 1: To determine whether treating anal high-grade squamous intraepithelial lesions (HSIL) is effective in reducing the incidence of anal cancer in PLWH

Aim 2: To determine the safety of treatment for anal HSIL

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the ANCHOR study

Aim 3: To develop and implement an instrument to measure the impact of ANCHOR procedures on QoL (ANCHOR Health-Related Symptom Index (A-HRSI)

Aim 4: Collect clinical specimens and data to create a bank of well-annotated specimens that will enable correlative science:
Identify host and viral factors in HSIL progression to cancer
Identify host and viral biomarkers of progression from HSIL to cancer

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Footer Text

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer

J.M. Palefsky, J.Y. Lee, N. Jay, S.E. Goldstone, T.M. Darragh, H.A. Dunlevy, I. Rosa-Cunha, A. Arons, J.C. Pugliese, D. Vena, J.A. Sparano, T.J. Wilkin, G. Bucher, E.A. Stier, M. Tirado Gomez, L. Flowers, L.F. Barroso, R.T. Mitsuyasu, S.Y. Lensing, J. Logan, D.M. Aboulafia, J.T. Schouten, J. de la Ossa, R. Levine, J.D. Korman, M. Hagensee, T.M. Atkinson, M.H. Einstein, B.M. Cracchiolo, D. Wiley, G.B. Ellsworth, C. Brickman, and J.M. Berry-Lawhorn, for the ANCHOR Investigators Group*

N ENGL J MED 386;24 NEJM.ORG JUNE 16, 2022

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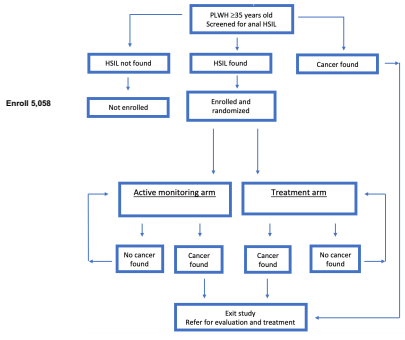
Study schema



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Methods

- Powered to detect difference between 50/100,000 PY in the treatment arm and 200/100,000 PY in the AM arm at the two-sided 0.05 significance level with power of 0.90
- Event-driven analysis, primary outcome= time-to-cancer
- N=2,529 per arm (total 5,058) to detect 31 anal cancers

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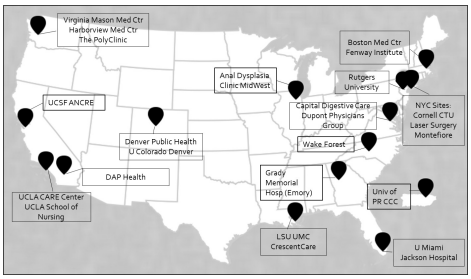
ANCHOR sites



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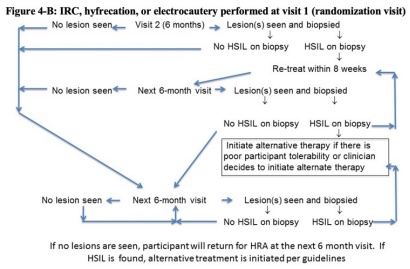
Treatment arm

- Treated immediately- hyfrecation, IRC, 5-FU, imiquimod



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Treatment arm

- Followed according to treatment algorithm
- Biopsied if suspicion for HSIL, re-treated as needed
- Examined every 6 months once treatment complete
- Seen every 3 months if concern for cancer
- Biopsied at any visit if concern for cancer

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Active monitoring arm

- Examined every 6 months
- Biopsied annually to confirm persistent HSIL
- Seen every 3 months if concern for cancer
- Biopsied at any visit if concern for cancer

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Anal HSIL and cancer at screening

- 10,723 PLWH from 9/24/2014 to 8/5/2021
- 53.3% of men
- 47.2% of women
- 67.1% of transgender individuals
- 17 individuals (0.16%, 160/100,000) were diagnosed with anal cancer

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Demographics of randomized population (1)

	Randomized population N=4,446		P value
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Median age at randomization (years, IQR)	51.0 (44.0-57.0)	51.0 (44.0-57.0)	0.79
Median years at randomization since HIV diagnosis (years, IQR)	17.0 (10.0-24.0)	17.0 (10.0-25.0)	0.96
Months of follow-up (median, IQR)	25.3 (11.7 – 42.0)	27.2 (12.0 – 42.1)	0.77
Gender identity N (%)			0.30[2]
Male	1793 (80.5)	1782 (80.3)	
Female	346 (15.5)	365 (16.5)	
Transgender	85 (3.8)	68 (3.1)	
Neither male nor female	2 (0.1)	2 (0.1)	
Decline to answer	1 (0.0)	2(0.1)	

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Demographics of randomized population (2)

	Randomized population N=4,446		P value
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Race/ethnicity N (%)			
Non-Hispanic White	695 (31.2)	737 (33.2)	0.37
African-American	935 (42.0)	939 (42.3)	
Hispanic, non-African-American	381 (17.1)	339 (15.3)	
Asian/Pacific Islander	27 (1.2)	29 (1.3)	
Other/Unknown	189 (8.5)	175 (7.9)	
CDC HIV risk group N (%)			
Homosexual	1738 (78.0)	1742 (78.5)	0.74
Heterosexual	532 (23.9)	510 (23.0)	0.48
Injection drug use	152 (6.8)	177 (8.0)	0.14
Transfusion	53 (2.4)	47 (2.1)	0.56
Hemophilia	2 (0.1)	4 (0.2)	0.41
Other high-risk group	34 (1.5)	27 (1.2)	0.37

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Demographics of randomized population (3)

	Randomized population N=4,446		P value
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Current smoker N (%)	710 (31.9)	743 (33.5)	0.26
Plasma HIV-1 RNA copies/mL at randomization N (%)			0.27
<50	1852 (83.7)	1800 (81.8)	
51-199	155 (7.0)	160 (7.3)	
200-1000	83 (3.8)	93 (4.2)	
>1000	122 (5.5)	148 (6.7)	
CD4 cells/uL at randomization (median, IQR)	602 (393-827)	607 (410-837)	0.32

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Demographics of randomized population (4)

	Randomized population N=4,446		P value[1]
	Treatment arm	Active monitoring arm	
	N=2,227	N= 2,219	
Stratification factors at randomization N (%)			
Nadir CD4 cells/uL			0.88
≤200 cells/uL	1130 (50.7)	1121 (50.5)	
>200 cells/uL	1097 (49.3)	1098 (49.5)	
HSIL size at screening			0.93[3]
>50% of anal canal/perianal region	285 (12.8)	282 (12.7)	
≤50% of anal canal/perianal region	1942 (87.2)	1937(87.3)	

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Results

For the participants in the treatment arm, initial treatment:
Office-based electrocautery ablation (86.2%)
Infrared coagulation (4.8%)
TUA (2.3%)
Topical 5-fuorouracil cream (4.5%)
Topical imiquimod (0.5%)

Over the course of the study: one treatment modality only (86%)

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Results

- Final analysis based on 30 cases
- 9 participants were diagnosed with invasive anal cancer in the treatment arm and 21 in the AM arm
- Median follow-up of 25.8 months, 57% reduction in anal cancer (95% CI 6% to 80%, chi-squared = 4.74, P=.029)
- Cancer incidence in the treatment arm was 173/100,000 PY of follow-up, compared with 402/100,000 PY in the AM arm

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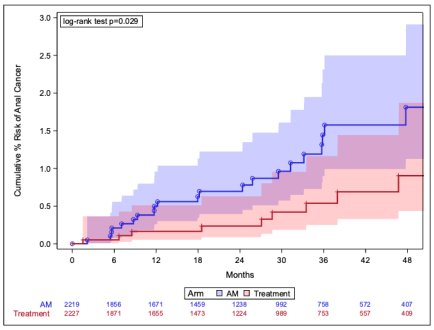
Kaplan-Meier curve of time-to-confirmed cancer cases



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Adverse events

	Treatment arm	Active monitoring arm
Adverse events (N)	683	635
Deaths	55	48
Serious adverse events (N)	586	568
Study-related adverse events (N)	43	4
Study-related serious adverse events (N)	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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Results

- DSMB recommended stopping the study for efficacy
- Recommendation made to treat all individuals in the monitoring arm
- We are following all individuals who wish to be treated and/or followed

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Progression to cancer

- Cumulative progression to cancer at 48 months was 0.9% in the treatment arm and 1.8% in the monitoring arm
- The cancer risk was 185/100,000 PY (95% CI: 115-298) and 1047/100,000 PY (95% CI: 608-1803) for those with lesions ≤50% and >50% of the anal/perianal canal, respectively (hazard ratio 5.26, 95% CI: 2.54-10.87)

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Implications of the study findings

- Rate of progression from anal HSIL to cancer is high
- Treatment of anal HSIL is effective in reducing the incidence of anal cancer
- These data should be included in an overall assessment for inclusion of screening for and treating anal HSIL as standard of care

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Implications of the study findings

- There is room for improvement in treatment of anal HSIL
- There is a need for biomarkers for HSIL progression or regression

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Implications of the study findings

- There is a need for optimization of screening algorithms for HSIL
- There is a need for a large scale-up of HRA training programs
- Extrapolation of our results to other groups at high risk of anal cancer

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There remains much to do

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What to do in the short term

- DARE on all PLWH annually
- Screen MSMLWH over 35 years and all other PLWH over 45 years IF you do HRA and treatment or you can refer to someone trained in HRA and treatment

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What does screening look like?

- Combination of anal cytology and HPV co-testing when available

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Anal cytology testing only

- If screening with anal cytology only, PWH in whom screening has been initiated should have an anal cytology testing every 12 months
- If the results of three consecutive anal cytology tests are normal, follow-up anal cytology tests should be every 3 years.
- Persons with any abnormal cytology (≥ASC-US) should be referred for HRA

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Normal anal cytology and HPV co-testing

- If co-testing with anal cytology and anal high-risk HPV testing is performed, then persons who co-test negative (i.e., a normal anal cytology and negative HPV test) can have their next anal cancer screening in 3 years
- If the initial anal HPV high-risk testing results identify HPV16 or HPV16/18, referral to HRA is recommended (regardless of cytology result)

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How to treat

- Office-based ablation (e.g., hyfrecation) for amenable lesions
- Referral to surgery for disease too bulky to treat in office
- Treat with 5-fluoro-uracil cream to de-bulk

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With deep gratitude to:

- ANCHOR Investigators Group and the study staffs at all of the ANCHOR sites
- Study participants
- ANCHOR Community Advisory Board
- AIDS Malignancy Consortium
- Emmes Corporation
- NCI/Office of HIV and AIDS Malignancies

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Muchas gracias!

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