BHIVA
British HIV Association

The ANCHOR Study

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

Iain Reeves, Homerton Heathcare NHS Trust

Palefsky et al, N Engl J Med 2022;386:2273-82.

BHIVA
British HIV Association

Conflict of Interest

I have no conflicts of interest relevant to this presentation

Background

Population	Incidence in USA (per 100,000 person years)
General population: men	1.5
General population: women	1.9
MSM LWHIV*	89
Women LWHIV*	18.6-35.6
Other men LWHIV[+]	46

Increasing rates in UK, from mid 70s – 2009-11:

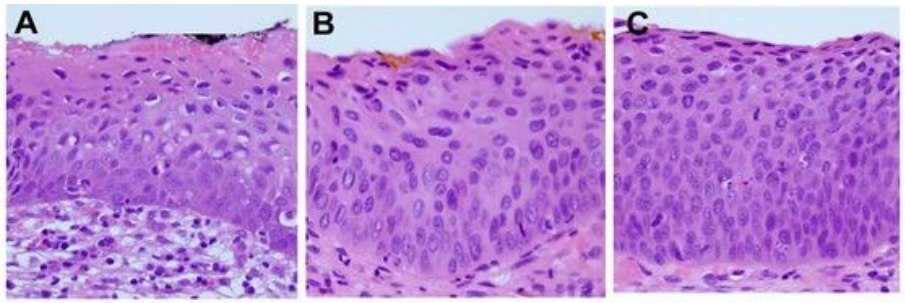
Men: 0.4 →1.2 per 100,000

Women: 0.4 →1.8 per 100,000

*Clifford et al. Int J Cancer 2021;148: 38-47. Colón-López et al. J Clin Oncol 2018;36:68-75

[+]Silverberg et al. Clin. Infect. Dis. 2012;54:1026–34

Is anal cancer preventable?



- HPV related cancer
- AIN as a precursor stage
  - HSIL (high grade squamous intra-epithelial lesion)
- Therefore analogous to cervical cancer?
  - LLETZ of transition zone > 90% success
- What are the risks vs benefits?
- Obvious anatomical differences – “anal whack-a-mole”

Study objectives

- Primary: Is treating anal HSIL effective in reducing incidence of anal cancer in men and women living with HIV?

- Secondary:
  - Safety of treatment modalities
  - Associations with HPV type, biomarkers …

Study design (outline)

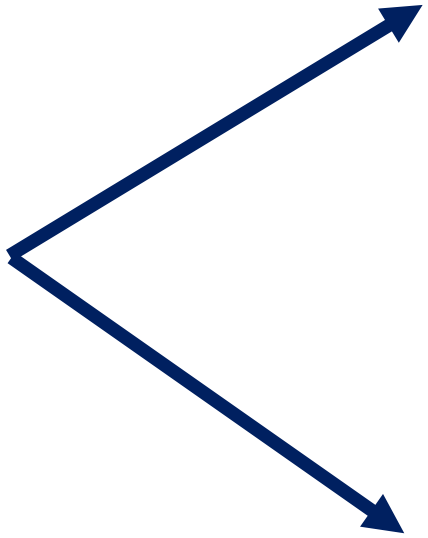
Eligible population

Inclusion:

- >35 years LWHIV
- Biopsy proven HSIL at screening
- Life expectancy > 5 years
- Contraception / conception

Exclusion

- No history of HPV related cancer / treatment of anal HSIL
- No previous HPV vaccine
- Any chronic immune-modulatory treatment
- Past Chemo/Radiotherapy



Active monitoring

- HRA every 6 months
- Biopsy minimum every year

Treatment

Treatment modalities:

- Electrocautery*
- IR coagulation
- 5-FU
- TCA
- Imiquimod

HRA every 6 months

*83.6% were treated with this modality

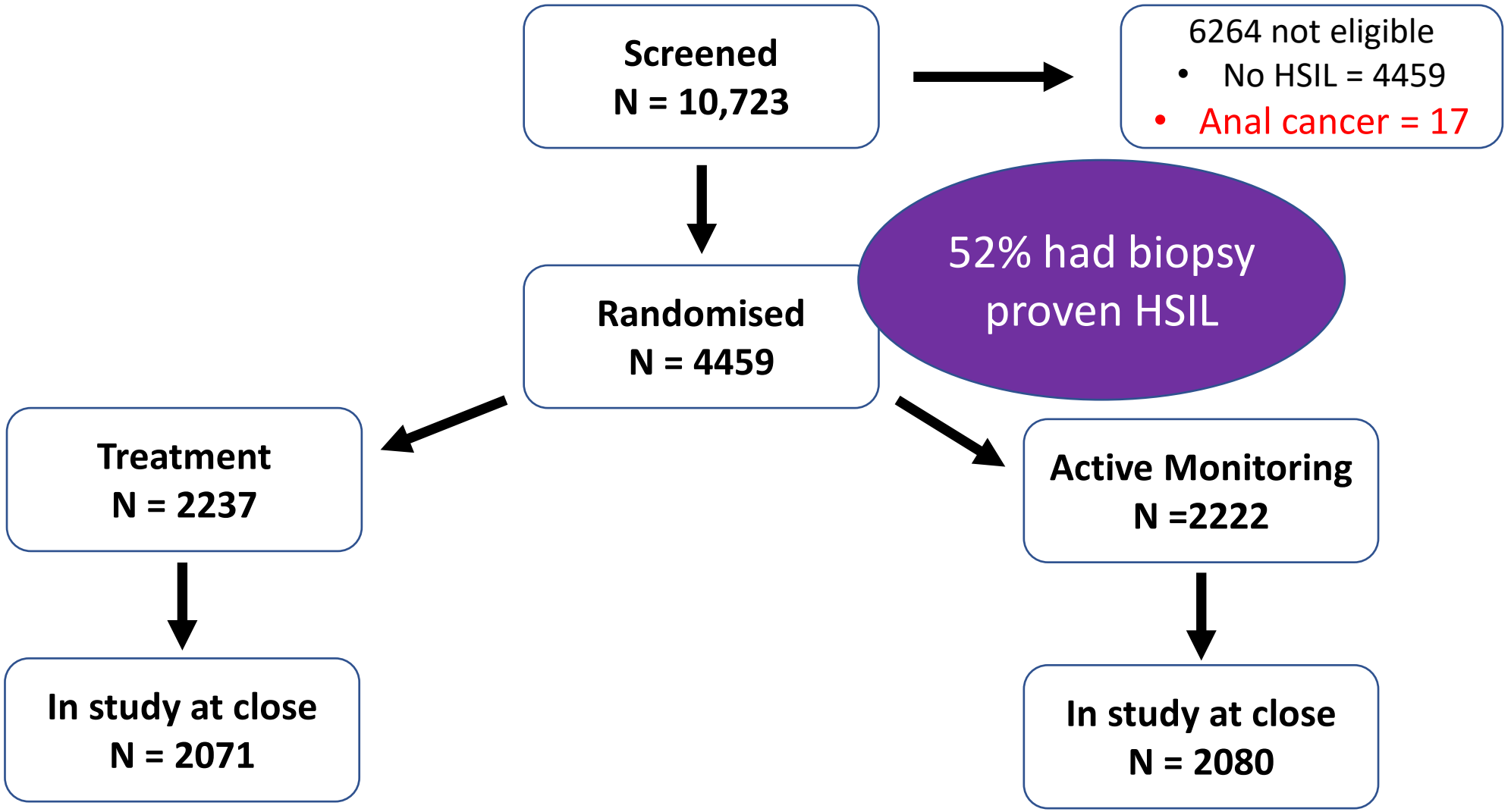
Sample size

- Conservative estimate of incidence of anal cancer in population all proven to have HSIL = 200 per 100,000 py
- Trial powered to detect difference between this incidence in monitoring arm vs 50 per 100,000 py in the treatment arm

- 5% annual drop-out rate

- Total recruitment required = 5058 participants

Consort diagram (simplified)



Baseline demographics (selected) - 1

Characteristic	Treatment arm	Active monitoring arm
Median age	51 (44-57)	51 (44-57)
Median years since HIV diagnosis	17 (10-24)	17 (10-25)
Gender (%)		
Male	1793 (80.5)	1782 (80.3)
Female	346 (15.5)	356 (16.4)
Trans	85 (3.8)	68 (3.1)
Race or ethnic group (%)		
Black	935 (42.0)	939 (42.3)
Non-Hispanic White	695 (31.2)	737 (33.2)
Non-Black Hispanic	381 (17.1)	339 (15.3)
Asian or Pacific Islander	27 (1.2)	29 (1.3)
Other/unknown	189 (8.5)	175 (7.9)
Transmission risk (%)		
MSM	1716 (77.1)	1717 (77.4)
Heterosexual	532 (23.9)	510 (23.0)
PWID	152 (6.8)	177 (8.0)
Other	89 (3.9)	78 (3.5)

Baseline demographics - 2

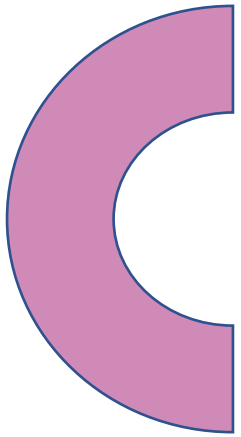
Characteristic	Treatment arm	Active monitoring arm
Viral load <50 51-199 200-1000 >1000	 83.7% 7.0% 3.8% 5.5%	 81.8% 7.3% 4.2% 6.7%
Median CD4	602 (393-827)	607 (410-837)
Nadir CD4 ≤ 200 > 200	 1130 (50.7%) 1097 (49.3%)	 1121 (50.5%) 1098 (49.5%)
HSIL size at screening: > 50% anal canal ≤ 50% anal canal	 12.8% 87.2%	 12.7% 87.3%

Results

Result	Treatment arm	Active monitoring arm
Cancer – total number	9	21
Cancer incidence, per 100,000 pyfu (95% CI)	173 (90-352)	402 (262-615)
Cumulative incidence to 48 months	0.9%	1.8%

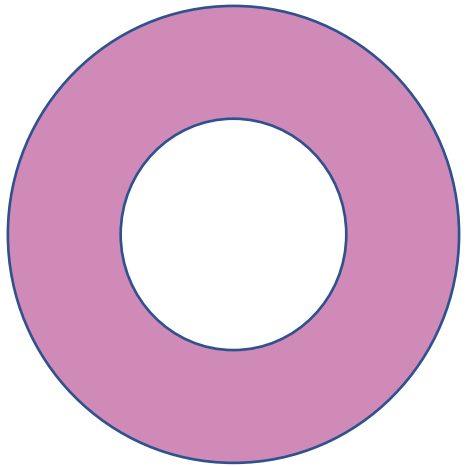
Primary outcome: 57% (95% CI 6-80, p= 0.03) reduction in progression to cancer in the Treatment arm

Effect of lesion size



≤50% anal canal

185 per 100,000 pyfu



>50% anal canal

1047 per 100,000 pyfu

Safety

Events	Treatment arm	Active monitoring arm
Adverse events	683	635
SAEs	586	568
Trial related AEs	43	4
Trial related SAEs	7	1
Deaths	55	48

Summary

- Treatment of anal HSIL reduces incidence of anal cancer
- Relatively little detail on adverse events in the paper and appendix
- NNT = 438
  - BUT everyone had to have HRA first – 41% of 10723 screened for the study did not have HSIL
- Clear relationship with lesion size
- Some cancers still occurred in treatment arm
  - Better treatment?
  - Almost all had electrocautery – what do these results mean for other treatment methods?