Anal Cancer and ANCHOR Study

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- Review the incidence of anal cancer
- Understand the role of HPV in the development of dysplasia cancer
- Identify risk factors for dysplasia and cancer
- Discuss ANCHOR study



Anal Cancer

- Rare malignancy involving the anal canal or perianal skin
- Squamous cell carcinoma comprises 90% of anal cancers
- American Cancer Society estimates 9,760 new cases in 2023
- National Cancer Institute data shows the average age of diagnosis is 60
- Anal squamous cell cancer is a common non-AIDS defining malignancy



Incidence of Anal Cancer



Source: Deshmukh AA, et al. JNCI, 2019:djz219 Cancer.gov



Human Papillomavirus

Male: Tools frammer (2003) Alone and/or Alon

- Double-stranded DNA virus
- Spread through skin-to-skin contact
- Prevalence of HPV infection in anal cancer is 90%
- >120 types
- Classified by low and high-risk types
- Causes warts, low-grade dysplasia, and high-grade dysplasia (pre-cancer)
- High–grade squamous intraepithelial lesion (HSIL) is a precursor to cancer



Risk Factors for Anal Cancer

- Persistent HPV infection
- History of vulva, vaginal and cervical cancer
- Anogenital warts
- Multiple lifetime sexual partners: 10 or more
- Receptive anal intercourse
- Immunosuppression
- HIV infection: low CD4 nadir; high HIV viral load
- Tobacco use



Diagnosis of Anal Dysplasia



- Regular screening increases the likelihood that cancer is detected early
- Screening modalities:
 - Digital Anal Rectal Examination (DARE)
 - Anal cytology (PAP test)
 - High resolution anoscopy (HRA)
 - HPV testing



Treatment for Anal Dysplasia

- Topical treatment options: Imiquimod or 5-Fluorouracil
- Ablative therapy options: Electrocautery or Infrared Coagulation
- Excisional treatment under anesthesia for widespread HSIL





Does Treating HSIL Reduce Cancer Risk?

- Anal Cancer HSIL Outcomes Research (ANCHOR STUDY)
- Published in NEJM June 16, 2022
- Multisite, randomized, U.S. trial
- Recruited 4446 men and women with HIV >35 yo
- Biopsy-proven HSIL
- Randomized to two arms: treatment or active monitoring q 6 mo using HRA
- Examined the efficacy and safety of HSIL treatment for the prevention of anal cancer



ANCHOR Study: Goal

Study goals:

- 1. Determine if treatment of HSIL decreases anal cancer incidence
- 2. Evaluate quality of life with screening and treatment of HSIL
- 3. Biospecimen collection: molecular pathogenesis of anal cancer in HIV patients



ANCHOR Study: Inclusion Criteria

Eligibility Criteria:

- Age > 35 years
- HIV+
- Screening visit: biopsy-proven anal HSIL
- No prior history of anal cancer
- History of HSIL treatment is allowed if it was performed > 6 months prior
- HPV vaccination allowed



ANCHOR Study: Protocol



Outcome: Development of Cancer? If yes, exit study for cancer treatment **Goal**: Follow for 5 years



Treatment Arm: Medications

- Options for topical treatment:
- Imiquimod intra-anally, peri-anally or both thrice weekly for up to 16 weeks
- Fluorouracil twice daily for 5 days every 2 weeks for up to 16 weeks

Treatment Arm: Ablation

- Ablative treatment:
- Infrared photocoagulation therapy
- Hyfrecation/electrocautery (thermal ablation therapy)

Control Arm

- Active monitoring with examinations for clinical observation every 6 months
- Every 12 months, patients undergo biopsies of visible lesions
- Cytology sampling performed at every visit

ANCHOR Study: Results

- Enrollment: 4,446 participants
- Start date: September 24, 2014
- Halted September 2021 due to early success
- Mean age: 52.7 yo



ANCHOR Study: Results

- 57% risk reduction of cancer in treatment group
- Low incidence of serious adverse events



Invasive Anal Cancer (Median Follow-up, 25.8 Mo)



ANCHOR Study: Conclusion

 ANCHOR trial shows that treatment of high-grade squamous intraepithelial lesions (HSIL) significantly reduced the risk of progression to anal cancer



Multidisciplinary Clinic

- Providers: Dr Buchwald, Dr Gabre-Kidan, NP Morris and myself
- Perform HRA, pap smear, and HPV test
- Medical, ablative, and surgical treatment



Conclusion

- Anal squamous cell cancer is a common non-AIDS defining malignancy
- Incidence rates higher in PLVH, MSM, anogenital warts, cervical dysplasia, and immunosuppressed populations
- Anal Squamous Cell Cancer is caused by persisting HPV infection and preceded by HSIL
- ANCHOR trial shows that treatment of high-grade squamous intraepithelial lesions (HSIL) significantly reduced the risk of progression to anal cancer
- Healthcare providers should know when to refer to an experienced specialist in anal cancer and dysplasia

Thank you



Comments: Adverse Events

7 Serious adverse events related to trial in treatment group (ulceration, abscess, pain with treatment or biopsy)586 Adverse events in treatment group

- 44 grade 5 AEs (deaths)—all unrelated to protocol
- 73 grade 4 AEs (life-threatening)—all unrelated to protocol



Comments: Disadvantages

- 80% male, 15-16% female, 3% transgender, 0.1 % nonbinary
- 42% black, 31 % white, 1% Asian, 17% Hispanic
- Mean CD4 count 600, 80% HIV RNA<50, 50% Nadir CD4 count <200
- 30% current smoker, 56-61% past smoker
- 10% has previous HSIL treatment



References

- IANS webinar Anchor Update 1/19/21 Dr Joel Palefsky
- Anchor press release
- NIH Clinical Trials Site
- AMC Site
- N Engl J Med 386;24 June 16, 2022 Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer J.M. Palefsky