Can Human Papillomavirus Biomarkers Help Predict Patterns of Anal High-Grade Squamous Intraepithelial Lesion Detection in Homosexual men?

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Disclosure of interest

- Andrew Grulich: honoraria & research funding from CSL Biotherapies; honoraria & travel funding from Merck; member of Australian advisory board for Gardasil HPV vaccine
- Christopher Fairley: honoraria, travel funding & research funding from CSL & Merck; member of Australian advisory board for the Gardasil HPV vaccine; owns shares in CSL Biotherapies
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- All other authors: no conflicts of interest

Overview

- The SPANC study
  - Study design
  - Methods: biomarkers used
  - Definition of disease progression and clearance
- Baseline cohort characteristics
- Anal high-grade squamous intraepithelial lesions (HSIL) progression and clearance
  - Biomarker as predictors

Background

- Anal HPV infection and its associated cancer precursor are highly prevalent in homosexual men
- HPV detection on its own is of limited use in determining who is at risk of anal cancer due to extremely high prevalence
- The development of other biomarkers which may predict which men have high grade disease that is at risk of progressing should be a research priority

HPV biomarkers

- HPV biomarkers that are commercially available
  - Viral markers: E6/E7 mRNA
  - Cellular makers: p16/Ki67 dual staining
- Developed in cervical cancer screening to improve sensitivity
- Limited use in anal cancer research
- Potentials in predicting disease progression and persistence not adequately assessed

SPANC Study

- The Study of the Prevention of Anal Cancer (SPANC)
  - Natural history study of anal HPV infection and associated anal diseases
- Community-based
  - HIV-positive and HIV-negative homosexual men
  - 35 years and above
- 5 study visits over 3 years
  - Baseline, 6-month, and 3 annual follow-up visits
  - All participants undergo anal cytology and high resolution anoscopy at all study visits
Methods

- **HSIL composite endpoint definition**
  - Liquid based anal cytology: cytological HSIL and/or
  - High-resolution anoscopy: histological HSIL
- **Biomarker testing**
  - E6/E7 mRNA: NucliSENS EasyQ, BioMerieux
  - p16/Ki67 dual staining: CINtec PLUS, Roche

Incident disease definition

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<th>Baseline</th>
<th>1-year visit</th>
<th>Incident HSIL</th>
<th>Persistent HSIL</th>
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Cohort characteristics

- **Total participants:** 617; 220 (35.7%) HIV-positive
  - **Median age:** 49 (range: 35-79)
- **HSIL prevalence**
  - Cytological: 109 (18.5%)
  - Histological: 196 (31.8%)
  - Composite: 231 (37.5%)

<table>
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<th>Baseline status</th>
<th>n</th>
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<th>clearance (%)</th>
<th>RR</th>
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Predictors of incident HSIL

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Predictors of HSIL clearance

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Conclusions

- Anal HSIL is a very dynamic condition in homosexual men
  - High one-year cumulative incidence and clearance
- Biomarkers has the potential to predict disease progression and persistence
  - E6/E7 mRNA and p16/Ki67 can predict disease progression
  - E6/E6 mRNA can predict disease clearance
- Further biomarker studies are needed for its potential in deciding patients who warrant HSIL treatment
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HPV biomarker in the SPANC Study