Kirby Institute

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

Fengyi Jin, I Mary Poynten, Alyssa Cornall, Samuel Phillips, Jennifer Roberts, Annabelle Farnsworth, Richard J Hillman, David J Templeton, Suzanne M Garland, Christopher K Fairley, Andrew E Grulich, Sepehr N Tabrizi on behalf of the SPANC Study Team

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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

		1-year visit	
		-	+
Baseline	-		Incident HSIL
	+	HSIL clearance	Persistent HSIL

Cohort characteristics

- Total participants: 617; 220 (35.7%) HIV-positive
  - Median age: 49 (range: 35-79)
- HSIL prevalence

	Cytological	Histological	Composite
HSIL	109	196	231
(%)	18.5	31.8	37.5

- Incident composite HSIL (342 men)

		1-year visit	
		-	+
Baseline	-	183	32 (14.9%)
	+	51 (40.2%)	76

Predictors of incident HSIL

	Baseline status	n	N	Incidence (%)	RR	95% CI	P value
HPV16 mRNA	-	19	177	10.7	1	---	<0.001
	+	13	29	44.8	4.18	2.32-7.50	
HPV18 mRNA	-	28	198	14.1	1	---	<0.001
	+	4	7	57.1	4.04	1.95-8.36	
HPV16/18 mRNA	-	18	173	10.4	1	---	<0.001
	+	14	33	42.4	4.07	2.26-7.36	
P16/Ki67 dual stain	-	5	53	9.4	1	---	0.014
	+	10	31	32.3	3.42	1.29-9.09	

Predictors of HSIL clearance

	Baseline status	n	N	clearance (%)	RR	95% CI	P value
HPV16 mRNA	-	31	58	53.5	1	---	0.004
	+	18	67	26.9	0.50	0.32-0.80	
HPV18 mRNA	-	41	104	39.4	1	---	0.910
	+	8	21	38.1	0.97	0.53-1.75	
HPV16/18 mRNA	-	26	48	54.2	1	---	0.007
	+	23	77	29.9	0.55	0.36-0.85	
P16/Ki67 dual stain	-	5	10	50.0	1	---	0.385
	+	25	68	36.7	0.74	0.37-1.47	

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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