



# Risk of progression of high grade anal dysplasia to invasive squamous cell carcinoma of the anus in the HIV infected population

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## INTRODUCTION

- The incidence of invasive squamous cell carcinoma of the anus (SCCA) is 30- to 80-fold higher in the HIV infected population relative to the general population (1, 2)
- Anal dysplasia is mediated by persistent HPV infection (3)
- Anal intraepithelial neoplasia, grade 3 (AIN 3) is thought to be the precursor lesion to SCCA (3)
- The rate and predictors of progression of AIN 3 to SCCA are not well defined (4-9)

## OBJECTIVE

- To use population-based data to describe the incidence of SCCA among cases of AIN3 in the HIV infected population

## METHODS

- We identified 592 HIV infected cases of incident, pathologically-confirmed AIN 3 from the Surveillance, Epidemiology, and End Results (SEER) database linked to Medicare claims from 2000-2011 (10, 11)
- We identified cases who had undergone anal cytology prior to AIN 3 diagnosis (screening) and following AIN 3 diagnosis (surveillance)
- Treatment of AIN 3 was defined as both surgical (local excision) and non-surgical (thermal ablation, laser tumor destruction, electrocautery, and fulguration) within 30 days of diagnosis of AIN 3
- We used SEER data and Medicare claims to ascertain the incidence of SCCA at 12, 24, 36, and 60 months
- We fitted Cox regression models to adjust for potential confounders

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**Table 1.** Patient characteristics (N=592)

<b>Male sex, N (%)</b>	565 (95)
<b>Age, years, median (IQR)</b>	45.7 (41.4-52.1)
<b>Race, N (%)</b>	
Non-Hispanic White	372 (63)
Non-Hispanic Black	84 (14)
Hispanic	55 (9)
Other	81 (14)
<b>Year of AIN 3<sup>a</sup> Diagnosis, N (%)</b>	
2000-2002	67 (11)
2003-2005	138 (23)
2006-2008	196 (33)
2009-2011	191 (32)
<b>Site, N (%)</b>	
Anus, not otherwise specified <sup>b</sup>	209 (35)
Anal canal	378 (64)
Overlapping lesion of rectum, anus, and anal canal	<11 <sup>c</sup>
<b>Charlson comorbidity index, mean (SD)</b>	0.37 (0.93)
<b>Smoking (current or past), N (%)</b>	108 (18)
<b>History of anogenital condylomata, N (%)</b>	262 (44)
<b>Anal cytology, screening,<sup>d</sup> N (%)</b>	386 (65)
<b>Anal cytology, surveillance,<sup>e</sup> N (%)</b>	428 (72)
<b>Treated for AIN 3,<sup>f</sup> N (%)</b>	349 (62)
<b>Follow up time, months, median (IQR)</b>	69 (46-97)

<sup>a</sup> AIN 3 = anal intraepithelial neoplasia, grade 3  
<sup>b</sup> Excludes skin of anus and perianal skin  
<sup>c</sup> Value suppressed for confidentiality  
<sup>d</sup> Anal cytology, screening = cytology within two years prior to AIN 3 diagnosis  
<sup>e</sup> Anal cytology, surveillance = cytology thirty days or more following AIN 3 diagnosis  
<sup>f</sup> Treatment = cryosurgery, electrocautery, laser ablation, or local excision within 30 days of AIN 3 diagnosis

**Table 3.** Unadjusted and adjusted analyses of predictors of progression to SCCA<sup>a</sup>

	Unadjusted		Adjusted	
	HR <sup>b</sup> (95%CI)	P	HR <sup>b</sup> (95%CI)	P
<b>Male sex</b>	1.4 (0.3-5.8)	0.7	1.9 (0.4-8.5)	0.4
<b>Age</b>	1.0 (1.0-1.0)	0.8	1.0 (1.0-1.0)	0.8
<b>Race</b>				
Non-Hispanic White	REF	--	REF	--
Non-Hispanic Black	2.8 (1.3-6.0)	0.01	2.1 (0.8-4.6)	0.1
Hispanic	1.1 (0.3-3.7)	0.9	1.2 (0.3-4.1)	0.8
Other	0.2 (0.0-1.9)	0.2	0.3 (0.0-1.8)	0.2
<b>Year of AIN 3<sup>c</sup> diagnosis</b>				
2000-2002	REF	--	REF	--
2003-2005	N/A	--	N/A	N/A
2006-2008	N/A	--	2.2 (0.7-6.7)	0.2
2009-2011	N/A	--	1.7 (0.6-5.0)	0.3
<b>History of anogenital condylomata</b>	2.4 (1.2-5.0)	0.02	2.1 (0.9-4.6)	0.07
<b>Smoking (current or past)</b>	1.8 (0.9-4.0)	0.1	1.3 (0.6-3.1)	0.5
<b>Anal cytology, screening</b>	0.5 (0.3-1.0)	0.05	0.6 (0.3-1.2)	0.2
<b>Treatment of AIN 3<sup>c</sup></b>	1.9 (0.8-4.3)	0.2	1.0 (0.4-2.5)	0.9

<sup>a</sup> SCCA = squamous cell carcinoma of the anus  
<sup>b</sup> HR = hazard ratio  
<sup>c</sup> AIN 3 = anal intraepithelial neoplasia, grade 3

**Table 2.** Cumulative incidence rates of SCCA<sup>a</sup> among those with baseline AIN 3<sup>b</sup> diagnosis, unadjusted

	%	95% CI
12 months	1.2	0.6-2.5
24 months	2.6	1.6-4.3
36 months	3.7	2.4-5.6
60 months	5.7	4.0-8.1

<sup>a</sup> SCCA = squamous cell carcinoma of the anus  
<sup>b</sup> AIN 3 = anal intraepithelial neoplasia, grade 3

## RESULTS

- The study sample was composed mostly of young, non-Hispanic White males
- Median follow up time was 69 months (IQR 46-97 months)
- There were 33 cases of SCCA over the study period
- The cumulative incidence of SCCA among HIV infected patients with baseline AIN 3 was 1.2% (95% CI 0.6%-2.5%) at 1 year and 5.7% at 5 years (95% CI 4.0%-8.1%)
- Unadjusted analysis showed increased hazard of progression to SCCA among patients with Black race (p = 0.01), history of anogenital condylomata (p = 0.02), and who had undergone anal cytology prior to AIN 3 diagnosis (p = 0.05)
- No predictors were statistically significantly associated with progression to SCCA on adjusted analyses

## DISCUSSION

- This is the first population-based study examining the rate of AIN 3 progression to SCCA
- We found a risk of progression of AIN 3 to SCCA of 1.2% at 1 year and 5.7% at 5 years in the ART era
- These rates fall within the wide range seen in similar studies (4,5, 7-9, 12)
- Large percentage of cases with anal cytology prior to AIN 3 diagnosis suggest that our study sample is composed largely of HIV infected patient undergoing anal cancer screening
- Our study lacks detailed data regarding treatment patients received for AIN 3 lesions and information regarding the severity of HIV-related disease

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