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IMPACT OF NONAVALENT ANTI-HPV VACCINATION ON ORAL PAPILLOMAVIRUS INFECTION

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Roberto Rossotti[1], Alice Nava[2], Chiara Baiguera[1], Maria Cristina Moioli[1], Diana Fanti[2], Federico D'Amico[1], Elvira Inglese[2,3], Daniele Calzavara[4], Chiara Vismara[2], Simona Bossolasco[4,5], Andrea Marco Tamburini[6], Massimo Cernuschi[4,5], Francesco Scaglione[2,7], Massimo Puoti[1,8].

1 Infectious Diseases Dept., ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; 2 Chemical-Clinical and Microbiological Analyses, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; 3 Brain and Behavioral Sciences Dept., Università degli Studi di Pavia, Pavia, Italy; 4 Milano Checkpoint, Milan, Italy; 5 Infectious Diseases Dept., IRCCS San Raffaele Scientific Institute, Milan, Italy; 6 Gastrointestinal Surgery Dept., IRCCS San Raffaele Scientific Institute, Milan, Italy; 7 Oncology and Hemato-Oncology Dept., Università degli Studi di Milano, Milan, Italy; 8 School of Medicine, Università degli Studi di Milano-Bicocca, Milan, Italy.

BACKGROUND

- Human papillomavirus (HPV) infection is the most common sexually transmitted infection (STI) worldwide and is one of the main risk factors for the development of oral, genital and anal carcinomas.
- Most HPV infections clear within few months while some others become persistent leading to premalignant or malignant disease. HIV infection is an additive risk factor for progression to cancer.
- HPV vaccination is a preventive strategy that could shorten persistent infection duration with a consequent decreased risk of cancer development.
- Aim of this study is to evaluate the impact of nonavalent vaccination on oral HPV infection in a cohort of MSM and TGW.

METHODS

- This multicentric, prospective study included all MSM and TGW who started nonavalent HPV vaccination from May 2019 to May 2021. Enrollment included HIV-infected subjects, PrEP users or individuals attending our Clinic for STIs screening in need of vaccination.
- Age over 45 years and previous HPV-related disease were not considered as exclusion criteria.
- Oral rinse was collected before each vaccine administration (T0, T1, T2) and six months after the third dose (T3). Cellular pellet was tested on Nimbus with Anyplex II HPV28 (Seegene).
- Demographic, clinical and behavioral data were collected at baseline. At each time point full STI screening was performed and used as a proxy to assess any possible change in sexual behavior.
- Descriptive statistics (median and interquartile range for continuous variables, absolute and relative values for categorical variables) were used. Kaplan Meier probability curves and Cox regression models for HPV acquisition and clearance were calculated.
- The study protocol was approved by the IRB of the ASST Grande Ospedale Metropolitano Niguarda, Milan. All enrolled subjects signed a written informed consent before participating to the study.

Oral HPV infection was assessed in 211 MSM and TGW before and after receiving nonavalent vaccination.
HIV-infected individuals had a higher baseline rate of oral infection (**18.8%** versus **5.4% in PrEP users** and **5.9% in others**), but no HIV-related features were associated to HPV clearance or acquisition.
The samples at baseline were positive in **14.2%** of cases, the rate of positivity **did not change** over time.

RESULTS (1)

- The analysis included 211 individuals: 202 MSM and 9 TGW with a median age of 42 (IQR 35-50) years.
- **Table 1** shows demographic and clinical status of Study population.
- The majority was HIV-infected (65%) with a good immunologic status (mean CD4 count 788 cell/mmc, IQR 600-1,047). Previous anal condylomas were registered in 25% of subjects.

Table 1. Demographic and clinical features of enrolled subjects.

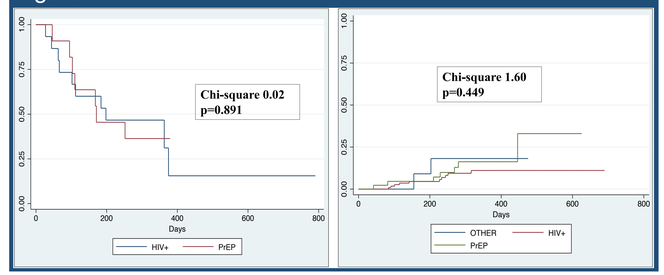
		Study population (N=211)	Negative baseline oral rinse (N=181)	Positive baseline oral rinse (N=30)	p
Age, ys, median (IQR)		42 (35-50)	42 (26-49)	41 (32-50)	0.696
	>45 ys, N (%)	77 (36.5)	64 (35.4)	13 (43.3)	0.401
Sexual behavior, N (%)	MSM	202 (95.7)	173 (95.6)	29 (96.7)	0.785
	TGW	9 (4.3)	8 (4.4)	1 (3.3)	
Italian origin, N (%)		183 (86.3)	159 (87.9)	23 (76.7)	0.100
Risk group, N (%)	HIV-positive	138 (65.4)	112 (61.9)	26 (86.7)	**0.030**
	PrEP users	56 (26.5)	53 (29.3)	3 (10.0)	
	Other STI Clinic clients	17 (8.1)	16 (8.8)	1 (3.3)	
Smoker, N (%)		85 (40.3)	72 (29.8)	13 (43.3)	0.713
Alcohol use, N (%)		128 (60.7)	110 (60.8)	18 (60.0)	0.936
Recreational drugs use, N ((%)		69 (32.7)	59 (32.6)	10 (33.3)	0.937
Previous syphilis infection, N (%)		102 (48.3)	82 (45.3)	20 (66.7)	**0.030**
Previous gonococcal urethritis, N (%)		56 (26.5)	45 (24.9)	11 (26.7)	0.175
Previous non-gonococcal urethritis, N (%)		45 (21.3)	40 (22.1)	5 (16.7)	0.501
Previous anal condylomas, N (%)		52 (24.6)	41 (22.7)	11 (36.7)	**0.099**
Calendar year of HIV diagnosis, median (IQR)		2011 (2004-2015)	2010 (2004-2015)	2013 (2005-2015)	0.839
Lymphocyte T CD4+ count, cell/mmc, median, (IQR)		788 (600-1,047)	809 (600-1,047)	767 (524-1,035)	0.431
Lymphocyte T CD4/CD8 ratio, cell/mmc, median, (IQR)		0.80 (0.58-1.10)	0.84 (0.62-1.14)	0.59 (0.48-0.82)	**0.007**
Class C, N (%)		18 (13.0)	14 (12.5)	4 (15.4)	0.841
Dual therapy, N (%)		43 (31.2)	35 (31.2)	8 (30.8)	0.895
HIV RNA target not detected , N (%)		124 (89.9)	99 (88.4)	25 (96.2)	0.372

- Oral rinse was already positive at baseline in 30 subjects (**14.2%**): 18.8% in HIV-positive subjects, 5.4% in PrEP users and 5.9% in others (**p=0.030**).
- Positivity rate **did not change over time**: 12% at T1, 13% at T2, and 9% at T3 (p=0.596), even when restricting the analysis only to high-risk genotypes (p=0.574) and to genotypes covered by vaccine (p=0.930).
- The presence of concomitant STIs remained stable (36% at T0, 29% at T2, and 34% at T3, p=0.322).

RESULTS (2)

- **Figure 1** shows Kaplan Meier curves for viral clearance and acquisition: HIV-positive individuals did not display a different trends both in terms of HPV clearance and acquisition after vaccination.

Figure 1



- Cox regression model failed to identify factors associated to viral clearance. Smoking was close to reach the statistical significance to be associated to HPV acquisition (aHR 0.40, 95% CI 0.14-1.13, p=0.083).
- **Recreational drugs use** was the only factor associated to HPV acquisition (**aHR 3.52**, 95% CI 1.22-10.10, p=0.019) although with wide confidence intervals.

CONCLUSIONS

- In our study, the rate of positivity was comparable with data from existing literature.
- Nonavalent anti-HPV vaccination had no impact on overall oral infection: the rate of positivity did not change over time and, although viral clearance was observed in the large majority of those with a positive baseline oral rinse, a significant proportion acquired a new infection.
- HIV-infected subjects had a higher rate of baseline positive oral rinse; they have also a worst inflammatory condition as suggested by a lower CD4/CD8 ratio.
- Nevertheless, no specific HIV-related factor was associated to viral clearance or acquisition.
- The only factor significantly associated to new oral infection was recreational drugs use, suggesting that risky sexual behavior plays a major role for HPV spread.
- Our data suggest that careful clinical monitoring should continue even after full nonavalent vaccination course.