

Supplementary data

Table S1. Clinicopathological data of the 33 patients with SNSCC

	HPV negative N=26	mRNA- positive N=8	p-value (Test)
Sex			0.194 (Fisher's exact test)
Male	20	4	
Female	6	4	
Median age (range)	58 (18-84)	51 (43-81)	0.255 (Mann-Whitney test)
Smoking history			1.00 (Fisher's exact test) [†]
Never smokers	7	4	
Current or past smokers	8	3	
Unknown	11	1	
Occupational risks			NA
Yes	1	1	
Unknown	25	7	
Tumor type			0.416 (Fisher's exact test) [‡]
K-SCC	13	6	
NK-SCC	12	2	
S-SCC	1	0	
P16 status by IHC			0.004 (Fisher's exact test)
positive	2	5	
negative	24	3	
Tumor site			NA
Nasal cavity	10	4	
Maxillary sinus	7	1	
Multiple subsites	3	0	
Other/Unknown	6	3	
Clinical stage, AJCC 7th ed.			NA
I	1	3	
II	3	0	
III	2	3	
IVa	8	0	
IVb	6	1	
IVc	2	0	
Unknown	4	1	
Grade			NA
1	4	1	
2	6	1	
3	15	6	
4	1	0	
Primary therapy			NA
Biopsy only	3	1	
Radical surgery	4	0	
Surgery+RAT	3	3	
Surgery+CHT	1	0	
Surgery+RAT+CHT	2	1	
Surgery+RAT+CHT	1	0	
CHT only	8	1	
CHT+RAT	3	2	
RAT only	1	0	
Unknown			

K-SCC: keratinizing squamous cell carcinoma (SCC), NK-SCC: nonkeratinizing SCC, S-SCC: sarcomatoid SCC, IHC: immunohistochemistry, RAT: radiotherapy, CHT: chemotherapy

[†] Test for difference between never smokers vs past/current smokers groups

[‡] Test for difference between K-SCC vs NK-SCC groups

Table S2. Logistic regression model: mRNA HPV Status ~ st

	b	SE	Wald statistics	p-value	Odds Ratios (CI95)
St I	3.87	1.55	6.26	0.0124	48.00 (2.31-9.97×10 ²)
St II	-17.21	7.63×10 ³	5.08×10 ⁻⁶	0.9982	0.00
St III	3.18	1.38	5.33	0.0210	24.00 1.62-3.57×10 ²
St IV	Baseline				
Constant	-2.77	1.03	7.24	0.0071	
Hosmer-Lemeshow test	$\chi^2=6.31\times 10^{-9}$ p=1.00				
Pseudo R² (Nagelkerke)	0.5473				
N	29				

(st = clinical stage; levels I – IV; baseline = stage IV)

Table S3. Logistic regression model with forward selection of variables

Final model: mRNA HPV Status ~ st+P16

	B	SE	Wald statistics	p-value	Odds Ratios (CI95)
St III	2.98	1.42	4.43	0.0354	19.65 (1.23-3.15×10 ²)
St IV	Baseline				
P16_1	4.08	1.53	7.16	0.0075	59.28 (2.99-1.18×10 ³)
P16_0	Baseline				
Constant	-2.96	1.03	8.34	0.0039	---
Overall model fit	$\chi^2=14.03$ p=0.0009				
Pseudo R² (Nagelkerke)	0.5736				
N	29				

(st = clinical stage; levels I – IV; baseline = stage IV; p16 = status of p16; levels 1=positive; 0=negative)

Table S4. Studies reporting transcriptionally-active HPV infections in sinonasal squamous cell carcinoma directly (through HPV mRNA) or by inference (diffuse positivity or $\geq 70\%$ neoplastic cells positive for p16/IHC and HPV DNA-positivity)

Study (Reference number)	HPV detection methods	HPV-positive cases	HPV+ / SCC subtype							Comment on prognosis
			K-SCC	NK-SCC	B-SCC	P-SCC	Ad-SCC	V-SCC	S-SCC	
El-Mofly et al. 2005 (10)	DNA PCR + p16	5/29 (17.2%)	1/21	4/8						
Alos et al. 2009 (11)	DNA PCR + p16	12/60 (20.0%)	2/42	6/11	2/5	2/2				Improved OS and PFS in HPV-positive group
Bishhop et al. 2012 (12)	DNA and mRNA ISH	2/7 (29.0%)								
Bishop et al. 2013 (13)	DNA ISH + p16	28/91 (31.1%)	0/25	15/44	4/8	4/5	5/6		0/3	A trend toward improved survival in HPV-positive group
Larque et al. 2014 (14)	DNA PCR + p16, DNA ISH, mRNA PCR	14/70 (20%)	2/49	8/14	2/51	2/2				Improved OS and PFS in HPV-positive group
Laco et al. 2015 (15)	DNA and mRNA PCR, DNA and RNA ISH	14/49 (28.6%)	1/16	11/27	2/3	0/1	0/1	0/1		A trend towards improved survival in HPV-positive group
Sahnane et al. 2019 (16)	DNA ISH + p16, DNA PCR	4/35 (11.4%)								
Current study	DNA PCR + p16, mRNA PCR and ISH	8/34 (23.5%)	6/19	2/14 (incl. 1 hybrid SCC)					0/1	A trend towards improved survival in HPV-positive group
Total		87/374 (23.3%)	12/172 (6.97%)	46/118 (38.98%)	10/21 (47.61%)	8/10 (80%)	5/7 (71.42%)		0/4 (0%)	

PCR: polymerase chain reaction, ISH: in situ hybridization, K-SCC: keratinizing squamous cell carcinoma (SCC), NK-SCC: nonkeratinizing SCC, B-SCC: basaloid SCC, P-SCC: papillary SCC, Ad-SCC: adenosquamous carcinoma, V-SCC: verrucous SCC, S-SCC: sarcomatoid SCC, OS: overall survival, PFS: progression free survival