MOLECULAR SUBCLASSIFICATION OF VULVAR SQUAMOUS CELL CARCINOMA: PROGNOSTIC SIGNIFICANCE AND REPRODUCIBILITY

¹EF Thompson*, ²L Hoang, ³AK Höhn, ⁴A Palicelli, ⁵KL Talia, ⁶N Tchranian, ¹J Senz, ⁷A Jamieson, ¹J Huwila, ⁷JN Mcalpine, ²CB Gilks, ⁸M Höckel, ⁹N Singh, ³LC Horn. ¹The University of British Columbia, Molecular Oncology, Vancouver, Canada; ²The University of British Columbia, Vancouver General Hospital, Pathology and Laboratory Medicine, Vancouver, Canada; ³Leipzig University, Division of Gynecologic Pathology, Leipzig, Germany; ⁴Azienda Unit Sanitaria Locale- IRCCS, Pathology Unit, Reggio Emilia, Italy; ⁵Royal Women's Hospital and VCS Foundation, Anatomical Pathology, Parkville, Australia; ⁶Barts Health NHS Trust, London, UK; ⁷The University of British Columbia, Division of Gynaecologic Oncology, Vancouver, Canada; ⁸Leipzig University, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology (Institute of Trier), Leipzig, Germany; ⁹Queen Mary University of London, Barts Health NHS Trust and Centre for Pathology at the Blizard Institute, London, UK

10.1136/ijgc-2021-ESGO.616

Introduction/Background* Vulvar squamous cell carcinoma (VSCC) is subclassified into three prognostically relevant groups: i) HPV-Associated (HPV-A), ii) HPV-Independent TP53 mutated (HPV-I p53abn), and iii) HPV-Independent TP53 wild type (HPV-I p53wt). Immunohistochemistry (IHC) for p16 and p53 are used as surrogate markers for HPV viral integration and TP53 mutational status, respectively.

We assessed the reproducibility of subclassification based on p16 and p53 IHC and evaluated the prognostic significance of VSCC molecular subgroups in a patient cohort treated by vulvar field resection (VFR) surgery.

Methodology VSCC formalin-fixed paraffin-embedded tumour tissue and patient clinicopathologic data from 68 cases treated

by vulvar field resection (VFR) were collected from the Leipzig School of Radical Pelvic Surgery. Immunohistochemistry for p16 and p53 was performed at three different institutions and evaluated independently by seven pathologists and two pathology research fellows. Tumors were classified into one of four groups: HPV-A, HPV-I p53wt, HPV-I p53abn, and Indeterminate (requiring additional investigation). Selected cases were further interrogated by HPV RNA in situ hybridisation (ISH) and TP53 sequencing.

Result(s)* Final VSCC subclassification yielded 22 tumors (32.4%) were HPV-A, 41 (60.3%) were HPV-I p53abn, and 5 (7.3%) were HPV-I p53wt; the clinicopathologic data is summarised in table 1. Interobserver agreement (overall Fleiss' kappa statistic) for the four-category classification was 0.74. No statistically significant differences in clinical outcomes between HPV-A and HPV-I VSCC were observed (figure 1).

Conclusion* Interobserver reproducibility of VSCC subclassification based on p16 and p53 IHC is very good, supporting their routine use in clinical practice. VSCCs treated by VFR surgery showed no significant difference in clinical outcomes when stratified based on HPV status. This contrasts with the significant prognostic differences between HPV-A and HPV-I VSCC demonstrated in cohorts treated by conventional conservative surgical approaches and suggests that a change in surgical approach can improve outcomes in patients with HPV-I VSCC.

Abstract 231 Table 1 Clinicopathologic features of vulvar squamous cell carcinoma stratified by HPV status

Variable	Total		HPV-associated		HPV-independent				p
					TP53 wild-type		TP53 mutated		
Total	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	
	68	100.0%	22	32.4%	5	7.4 %	41	60.3 %	
Follow-up (years, median)	2.2		3.5		3.6		1.7		
Age [years, median, (SD)]	66.1	15.2	60.5	16.0	77.0	7.9	74.0	14.1	0.01
Stage I	35	51.5%	10	45.5%	4	80.0%	21	51.2%	0.057
II	4	5.9%	4	18.2%	0		0	0.0%	
III	26	38.2%	6	27.3%	1	20.0%	19	46.3%	
IV	3	4.4%	2	9.1%	0		1	2.4%	
Grade 1	10	14.7%	3	13.6%	4	80.0%	3	7.3%	<0.001
2	31	45.6%	14	63.6%	1	20.0%	16	39.0%	
3	27	39.7%	5	22.7%	0		22	53.7%	
Tumour size [cm, median (SD)]	3.3	2.2	2.7	2.0	1.5	2.2	3.5	2.2	0.35
LVI	40	58.8%	11	50.0%	2	40.0%	27	65.9%	0.36
Positive lymph node(s) ^a	29	42.6%	8	36.4%	1	20.0%	20	48.8%	0.65
Distant Metastases	3	4.4%	2	9.1%	0		1	2.4%	0.58
Adjuvant radiotherapy	2	2.9%	1	4.5%	0		1	2.4%	1
Died of disease	11	16.2%	2	9.1%	1	20.0%	8	19.5%	0.63
Recurrent disease	9	13.2%	2	9.1%	1	20.0%	6	14.6%	1

Abstract 231 Table 2 Summary of the clinicopathologic features by ProMisE molecular subtype

Variable	Total	<i>POLE</i> mut	MMRd	NSMP	p53abn
Total	172	21 (12.2%)	47 (27.3%)	74 (43.0%)	30 (17.4%)
Age at diagnosis					
<60 years	70 (40.7%)	12 (57.1%)	18 (38.3%)	38 (51.4%)	2 (6.6%)
≥60 years	102 (59.3%)	9 (42.9%)	29 (61.7%)	36 (48.6%)	28 (93.3%)
Histotype					
Endometrioid	137 (79.7%)	18 (85.7%)	45 (95.7%)	71 (95.9%)	3 (10.0%)
Non-endometrioid	35 (20.3%)	3 (14.3%)	2 (4.3%)	3 (4.1%)	27 (90.0%)
-Serosus	15(8.7%)	0	1(2.1%)	0	14(46.7%)
-Clear cell	2(1.2%)	0	0	1(1.4%)	1(3.3%)
-Carcinosarcoma	8(4.7%)	0	0	0	8(26.7%)
-Mixed	10(5.8%)	3(14.3%)	1(2.1%)	2(2.7%)	4(13.3%)
Tumour grade					
low grade	129 (75%)	16 (76.2%)	41 (87.2%)	69 (93.2%)	2 (6.7%)
high grade	43 (25%)	5 (23.8%)	6 (12.8%)	5 (6.8%)	28 (93.3%)
Tumour size					
<2cm	31 (18.0%)	4 (19.0%)	12 (25.5%)	14 (18.9%)	1 (3.3%)
≥2cm	132 (76.8%)	17 (81.0%)	35 (74.5%)	53 (71.6%)	27 (90.0%)
unk	9 (5.2%)	0	0	7 (9.5%)	2 (6.7%)
Myoinvasion					
None	39 (22.7%)	5 (23.8%)	13 (27.7%)	16 (21.6%)	5 (16.7%)
<50%	82 (47.7%)	11 (52.4%)	19 (40.4%)	37 (50.0%)	15 (50%)
≥50%	51 (29.6%)	5 (23.8%)	15 (31.9%)	21 (28.4%)	10 (33.3%)
FIGO stage					
I-II	140 (81.4)	17 (81.0%)	43 (91.5%)	64 (86.5%)	15(50.0%)
III-IV	32 (18.6%)	4 (19.0%)	4 (8.5%)	10 (13.5%)	15 (50.0%)
LVI					
Negative	117 (68.0%)	15 (71.4%)	31(66.0%)	59 (79.7%)	12 (40.0%)
Positive	55 (32.0%)	6 (28.6%)	16 (34.0%)	15 (20.3%)	18 (60.0%)
Pelvic and Para-aortic LND					
Yes	171 (99.4%)	21 (100%)	47 (100%)	74 (100%)	29 (96.7%)
No	1 (0.6%)				1 (3.3%)
Presence of LN metastases					
	31 (18.1%)	3 (14.2%)	7 (14.9%)	8 (10.8%)	13 (44.8%)

LN, lymph node; LND, lymph node dissection; LVI, lymphovascular invasion; unk, unknown.