

Supplementary Materials

Assessment of TSPAN expression profile and their role in the VSICC prognosis

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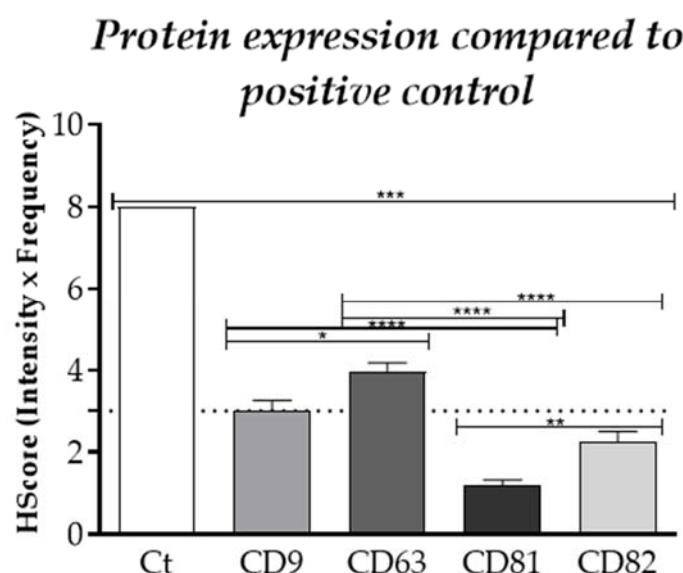


Figure S1. Tetraspanins protein expression in patient tissues compared to normal tonsil (positive control).

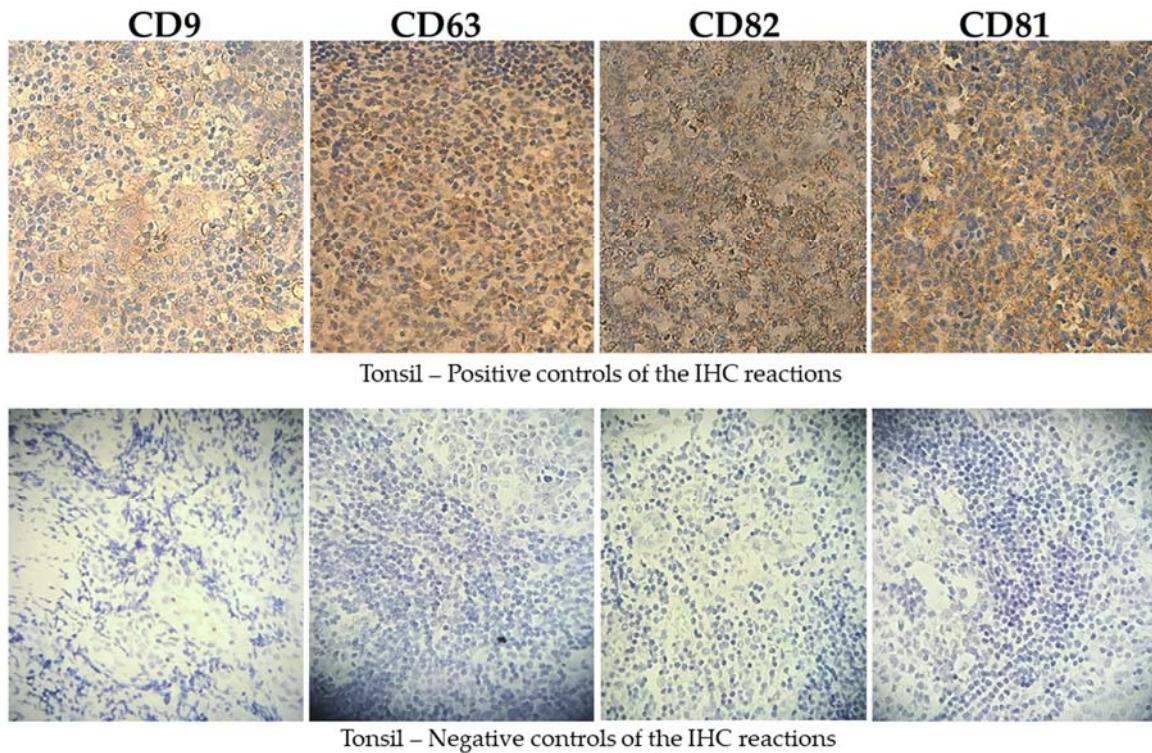


Figure S2. Positive controls for CD9, CD63, CD81 and CD82 using the tissues indicated by antibodies manufacturers' (Tonsils). Negative controls were obtained using the same tissues and omitting the primaries antibodies, as described in the method section.

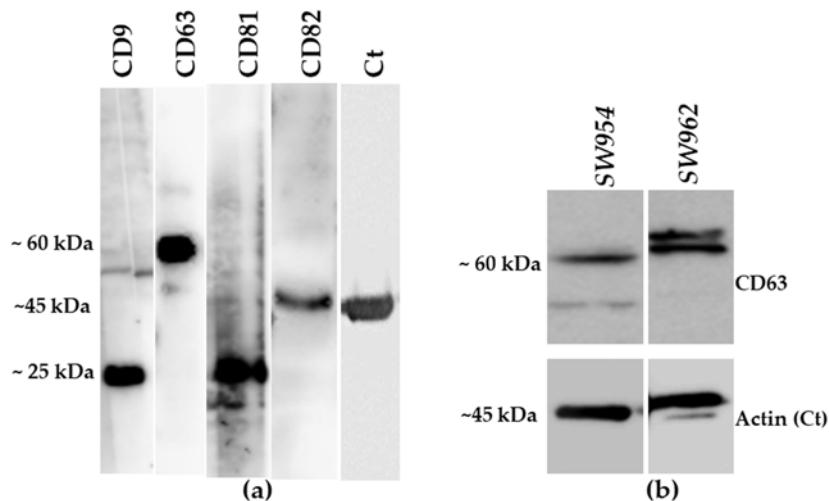


Figure S3. Specificity of anti-TSPANs by Western Blot. **(a)** Detection of CD9, CD63, CD81, CD82, and Actin-B (loading control; C) in total cell lysate from the human breast cancer cell line, MCF7. **(b)** Reactivity of anti-CD63 in total cell lysate from VSCC non-metastatic (SW954) and metastatic (SW962) cell lines. Protein sizes are indicated.

Table S1. Comparison between clinical and pathological features from patients, considering neoadjuvant chemotherapy treatment.

Variables	n	Not treated	Treated	Total	p
		n (%)	n (%)	n (%)	
Labia Majora	77				
No		35 (97)	1 (3)	36 (100)	0.060 ^b
Yes		34 (83)	7 (17)	41 (100)	
Labia Minora	77				
No		27 (96)	1 (4)	28 (100)	0.245 ^b
Yes		42 (86)	7 (14)	49 (100)	
Clitoris	76				
No		47 (94)	3 (6)	50 (100)	0.222 ^b
Yes		22 (85)	4 (15)	26 (100)	
Perineal	78				
No		58 (94)	4 (6)	62 (100)	0.015^b
Yes		11 (69)	5 (31)	16 (100)	
Tumor Size (mm ³)	77				
≤5 mm		10 (67)	5 (33)	15 (100)	0.014^a
6 to 10 mm		13 (93)	1 (7)	14 (100)	
≥10 mm		45 (94)	3 (6)	48 (100)	
Histological diagnosis	79				
VSCC 1		25 (83)	5 (17)	30 (100)	0.765 ^a
VSCC 2		33 (92)	3 (8)	36 (100)	
VSCC 3		6 (86)	1 (14)	7 (100)	
Basaloid carcinoma		5 (83)	1 (17)	6 (100)	
Adjuvant treatment	78				
No		63 (90)	7 (10)	70 (100)	0.229 ^b
Yes		6 (75)	2 (25)	8 (100)	
Lymph node metastasis	38				
No		19 (86)	3 (14)	22 (100)	1.000 ^b
Yes		14 (88)	2 (12)	16 (100)	
Depth of invasion	76				
Superficial dermis		4 (67)	2 (33)	6 (100)	0.050^a
Dermis		40 (91)	4 (9)	44 (100)	
Lower layer of the dermis		13 (87)	2 (13)	15 (100)	
Subcutaneous		9 (90)	1 (10)	10 (100)	
Rectal mucosa		0 (0)	1 (100)	1 (100)	
Inflammatory infiltrate					
1+ Low		18 (86)	3 (14)	21 (100)	0.524 ^a
2+ Moderate		43 (86)	7 (14)	50 (100)	
3+ High		8 (100)	0 (0)	8 (100)	

Vascular invasion					
No	57 (88)	8 (12)	65 (100)	1.000 ^b	
Yes	12 (86)	2 (14)	14 (100)		
Perineural invasion					
No	60 (88)	8 (12)	68 (100)	0.608 ^b	
Yes	8 (80)	2 (20)	10 (100)		
Clinical FIGO ¹ stage	78				
I (A/B) and II	35 (90)	4 (10)	39 (100)	0.974 ^a	
III A	6 (86)	1 (14)	7 (100)		
III B	4 (80)	1 (20)	5 (100)		
III C	17 (89)	2 (11)	19 (100)		
IV (A/B)	7 (88)	1 (12)	8 (100)		
Relapse	77				
No	40 (98)	1 (2)	41 (100)	0.010 ^b	
Yes	28 (78)	8 (22)	36 (100)		
Death	77				
No	30 (94)	2 (6)	32 (100)	0.457 ^b	
Yes	39 (87)	6 (13)	45 (100)		
HPV infection	41				
No	17 (100)	0 (0)	17 (100)	1.000 ^b	
Yes	23 (96)	1 (4)	24 (100)		
HPV coinfection	23				
No	16 (94)	1 (6)	17 (100)	1.000 ^b	
Yes	8 (100)	0 (0)	6 (100)		
HPV type	25				
High-risk	21 (100)	0 (0)	21 (100)	0.021 ^a	
Low-risk	2 (67)	1 (33)	3 (100)		
Both	1 (100)	0 (0)	1 (100)		

^aChi-square; ^b Fisher exact; ¹FIGO, International Federation of Gynecology and Obstetrics. Bold numbers indicate significant p values.

Table S2. Comparison of HPV types and co-infection in patients with VSCC.

HPV coinfection	High-risk n (%)	Low-risk n (%)	Both n (%)	Total	p
No	18 (90)	2 (10)	0 (0)	20 (100)	
Yes	7 (64)	1 (9)	3 (27)	11 (100)	0.048
Total	25 (80.6)	3 (9.7)	3 (9.7)	31 (100)	

Table S3. Prevalence of HPV considering patients with and without coinfection (n = 31).

HPV type	Frequency (%)	HPV Coinfection
High-risk		High-risk
16	17 (58)	16, 18, 33
33	7 (23)	16, 31
53	4 (13)	16, 33
18	2 (6)	16, 33, 82
45	3 (10)	31, 33, 82
82	2 (6)	High-risk and low-risk
31	2 (6)	16, 45, 54
67	1 (3)	16, 11
Low-risk		Low-risk
54	4 (13)	42, 54
11	2 (6)	-
42	1 (3)	-

Table S4. VSCC clinicopathological features and CD9 protein expression.

Variables	n	CD9		Total	p
		Negative n (%)	Positive n (%)		
Age	107				
≤50		7 (58)	5 (42)	12 (100)	1.000 ^b
>50		56 (59)	39 (41)	95 (100)	
Menarche	58				
11 to 14 years old		22 (55)	18 (45)	40 (100)	0.968 ^a
15 to 19 years old		10 (56)	8 (44)	18 (100)	
Menopause	62				
No		1 (33)	2 (67)	3 (100)	0.584 ^b
Yes		33 (56)	26 (44)	59 (100)	
Sexarche	31				
15 to 18 years		6 (37)	10 (63)	16 (100)	0.886 ^a
≥19 years		6 (40)	9 (60)	15 (100)	
Partners	37				
≤2		14 (40)	21 (60)	35 (100)	1.000 ^b
≥3		1 (50)	1 (50)	2 (100)	
Contraceptive	63				
No		32 (55)	26 (45)	58 (100)	0.182 ^b
Yes		1 (20)	4 (80)	5 (100)	
Alcoholism	72				
No		40 (56)	31 (44)	71 (100)	0.444 ^b
Yes		0 (0)	1 (100)	1 (100)	
Smoking	73				

No	32 (57)	24 (43)	56 (100)	0.464 ^a
Yes	8 (47)	9 (53)	17 (100)	
Labia Majora	79			
No	19 (54)	16 (46)	35 (100)	0.526 ^a
Yes	27 (61)	17 (39)	44 (100)	
Labia Minora	80			
No	15 (56)	12 (44)	27 (100)	0.801 ^a
Yes	31 (58)	22 (42)	53 (100)	
Clitoris	78			
No	26 (52)	24 (48)	50 (100)	0.173 ^a
Yes	19 (63)	9 (37)	28 (100)	
Perineal	79			
No	37 (60)	25 (40)	62 (100)	0.173 ^a
Yes	7 (41)	10 (59)	17 (100)	
Tumor Size (mm ³)	106			
≤5 mm	27 (68)	13 (32)	40 (100)	0.052 ^a
6 to 10 mm	13 (72)	5 (28)	18 (100)	
≥10 mm	22 (46)	26 (54)	48 (100)	
Histological diagnosis	111			
VSCC 1	23 (56)	18 (44)	41 (100)	0.138 ^a
VSCC 2	29 (66)	15 (34)	44 (100)	
VSCC 3	9 (75)	3 (25)	12 (100)	
Basaloid carcinoma	3 (27)	8 (73)	11 (100)	
Verrucous carcinoma	2 (67)	1 (33)	3 (100)	
Neoadjuvant chemotherapy	78			
No	37 (54)	31 (46)	68 (100)	0.732 ^b
Yes	6 (60)	4 (40)	10 (100)	
Adjuvant treatment	81			
No	38 (55)	31 (45)	69 (100)	1.000 ^b
Yes	9 (75)	3 (25)	12 (100)	
Lymph node metastasis	39			
No	13 (57)	10 (43)	23 (100)	0.986 ^b
Yes	9 (56)	7 (44)	16 (100)	
Depth of invasion	106			
Superficial dermis	4 (44)	5 (56)	9 (100)	0.161 ^a
Dermis	43 (64)	24 (36)	67 (100)	
Lower layer of the dermis	12 (63)	7 (37)	19 (100)	
Subcutaneous	3 (30)	7 (70)	10 (100)	
Rectal mucosa	0 (0)	1 (100)	1 (100)	
Inflammatory infiltrate	109			
1+ Low	21 (58)	15 (42)	36 (100)	0.974 ^a

2+ Moderate	38 (58)	27 (42)	65 (100)	
3+ High	5 (62)	3 (38)	8 (100)	
Vascular invasion	111			
No	55 (59)	38 (41)	93 (100)	0.876 ^a
Yes	11 (61)	7 (39)	18 (100)	
Perineural invasion	107			
No	55 (58)	42 (42)	97 (100)	0.514 ^b
Yes	7 (70)	3 (30)	10 (100)	
Clinical FIGO ¹ stage	80			
I (A/B) and II	27 (56)	21 (44)	48 (100)	0.996 ^a
III A	3 (60)	2 (40)	5 (100)	
III B	11 (58)	8 (42)	19 (100)	
III C	3 (50)	3 (50)	6 (100)	
IV (A/B)	1 (50)	1 (50)	2 (100)	
Relapse	78			
No	21 (53)	19 (47)	40 (100)	0.474 ^a
Yes	23 (61)	15 (39)	38 (100)	
Death	85			
No	21 (68)	10 (32)	31 (100)	0.133 ^a
Yes	27 (51)	26 (49)	53 (100)	
HPV infection	47			
No	16 (80)	4 (20)	20 (100)	0.337 ^b
Yes	18 (64)	10 (36)	28 (100)	
HPV coinfection	27			
No	14 (74)	5 (26)	19 (100)	0.114 ^b
Yes	4 (40)	6 (60)	10 (100)	
HPV type	27			
High-risk	14 (64)	8 (36)	22 (100)	0.231 ^a
Low-risk	3 (100)	0 (0)	3 (100)	
Both	1 (33)	2 (67)	3 (100)	

^a Chi-square; ^b Fisher exact; ¹FIGO, International Federation of Gynecology and Obstetrics. Bold numbers indicate significant p values.

Table S5. VSCC clinicopathological features and CD63 protein expression using two categories (Negative and Positive expression).

Variables	n	CD63		Total	p
		Negative n (%)	Positive n (%)		
Age	103				
≤50		2 (17)	10 (83)	12 (100)	1.000 ^b
>50		15 (16)	76 (84)	91 (100)	

Menarche	56				
11 to 14 years old		4 (10)	36 (90)	40 (100)	1.000 ^b
15 to 19 years old		2 (12)	14 (88)	16 (100)	
Menopause	61				
No		0 (0)	3 (100)	3 (100)	1.000 ^b
Yes		7 (12)	51 (88)	58 (100)	
Sexarche	30				
15 to 18 years		2 (13)	13 (87)	15 (100)	0.482 ^b
≥19 years		0 (0)	15 (100)	15 (100)	
Partners	35				
≤2		4 (12)	29 (88)	33 (100)	1.000 ^b
≥3		0 (0)	2 (100)	2 (100)	
Contraceptive	62				
No		7 (12)	50 (88)	57 (100)	1.000 ^b
Yes		0 (0)	5 (100)	5 (100)	
Alcoholism	69				
No		10 (15)	58 (85)	68 (100)	1.000 ^b
Yes		0 (0)	1 (100)	1 (100)	
Smoking	74				
No		8 (15)	45 (85)	53 (100)	0.182 ^a
Yes		6 (29)	15 (71)	21 (100)	
Labia Majora	75				
No		7 (21)	27 (79)	34 (100)	0.209 ^a
Yes		4 (10)	37 (90)	41 (100)	
Labia Minora	76				
No		5 (19)	21 (81)	26 (100)	0.495 ^a
Yes		6 (12)	44 (88)	50 (100)	
Clitoris	74				
No		6 (12)	43 (88)	49 (100)	0.725 ^a
Yes		4 (16)	21 (84)	25 (100)	
Perineal	76				
No		10 (17)	49 (83)	59 (100)	0.438 ^b
Yes		1 (6)	16 (94)	17 (100)	
Tumor Size (mm ³)	102				
≤5 mm		7 (18)	31 (82)	38 (100)	0.191 ^a
6 to 10 mm		5 (29)	12 (71)	17 (100)	
≥10 mm		5 (11)	42 (89)	47 (100)	
Histological diagnosis	107				
VSCC 1		7 (17)	33 (83)	40 (100)	0.316 ^a
VSCC 2		10 (24)	32 (76)	42 (100)	
VSCC 3		1 (8)	11 (92)	12 (100)	

Basaloid carcinoma	0 (0)	10 (100)	10 (100)	
Verrucous carcinoma	0 (0)	3 (100)	3 (100)	
Neoadjuvant Chemotherapy	76			
No	9 (14)	58 (86)	67 (100)	0.610 ^b
Yes	2 (22)	7 (78)	9 (100)	
Adjuvant treatment	18			
No	10 (15)	57 (85)	67 (100)	1.000 ^b
Yes	1 (9)	10 (91)	11 (100)	
Lymph node metastasis	37			
No	6 (26)	17 (74)	23 (100)	0.217 ^b
Yes	1 (7)	13 (93)	14 (100)	
Depth of invasion	102			
Superficial dermis	0	9 (100)	9 (100)	0.169 ^a
Dermis	15 (24)	49 (76)	64 (100)	
Lower layer of the dermis	2 (11)	17 (89)	19 (100)	
Subcutaneous	0 (0)	9 (100)	9 (100)	
Rectal mucosa	0 (0)	1 (100)	1 (100)	
Inflammatory infiltrate	105			
1+ Low	7 (20)	28 (80)	35 (100)	0.515 ^a
2+ Moderate	8 (13)	54 (87)	62 (100)	
3+ High	2 (25)	6 (75)	8 (100)	
Vascular invasion	107			
No	18 (20)	72 (80)	90 (100)	0.070 ^b
Yes	0 (0)	17 (100)	17 (100)	
Perineural invasion	103			
No	17 (18)	77 (82)	94 (100)	1.000 ^b
Yes	1 (11)	8 (89)	9 (100)	
Clinical FIGO ¹ stage	77			
I (B / A) and II	10 (21)	37 (79)	47 (100)	0.159 ^a
III A	1 (25)	3 (75)	4 (100)	
III B	0 (0)	18 (100)	18 (100)	
III C	0 (0)	6 (100)	6 (100)	
IV (A / B)	0 (0)	2 (100)	2 (100)	
Relapse	75			
No	8 (20)	32 (80)	40 (100)	0.202 ^b
Yes	3 (9)	32 (91)	35 (100)	
Death	80			
No	6 (19)	25 (81)	31 (100)	0.174 ^b
Yes	4 (8)	45 (92)	49 (100)	
HPV infection	47			
No	4 (21)	15 (79)	19 (100)	1.000 ^b

	Yes	6 (21)	22 (79)	28 (100)	
HPV coinfection	29				
No		4 (21)	15 (79)	19 (100)	1.000 ^b
Yes		2 (20)	8 (80)	10 (100)	
HPV type	28				
High-risk		4 (18)	18 (82)	22 (100)	0.100 ^a
Low-risk		2 (67)	1 (33)	3 (100)	
Both		0 (0)	3 (100)	3 (100)	

^aChi-square; ^b Fisher exact; ¹FIGO, International Federation of Gynecology and Obstetrics.

Table S6. Comparison between clinical and pathological features and CD63 protein expression using three categories (Negative, Moderate and Strong expression).

Variables	CD63 expression			Total n (%)	<i>p</i>
	Negative n (%)	Moderate n (%)	Strong n (%)		
Labia Majora					
No	7 (21)	27 (79)	0 (0)	34 (100)	0.2905 ^a
Yes	4 (10)	36 (88)	1 (2)	41 (100)	
Labia Minora					
No	5 (19)	20 (77)	1 (4)	26 (100)	0.2478 ^a
Yes	6 (12)	44 (88)	0 (0)	50 (100)	
Clitoris					
No	6 (12)	42 (86)	1 (2)	49 (100)	0.7087 ^a
Yes	4 (16)	21 (84)	0 (0)	25 (100)	
Perineal					
No	10 (17)	48 (81)	1 (2)	59 (100)	0.4360 ^a
Yes	1 (6)	16 (94)	0 (0)	17 (100)	
Tumor Size (mm³)					
≤5 mm	7 (18)	30 (79)	1 (3)	38 (100)	0.2816 ^a
6 to 10 mm	5 (29)	12 (71)	0 (0)	17 (100)	
≥10 mm	5 (11)	42 (89)	0 (0)	47 (100)	
Histological diagnosis					
VSCC 1	7 (17)	33 (83)	0 (0)	40 (100)	0.0022^a
VSCC 2	10 (24)	32 (76)	0 (0)	42 (100)	
VSCC 3	1 (8)	9 (75)	2 (17)	12 (100)	
Basaloid and verrucous carcinoma	0 (0)	13 (100)	0 (0)	13 (100)	
Neoadjuvant treatment					
No	9 (14)	58 (86)	0 (0)	67 (100)	0.0162^a
Yes	2 (22)	6 (67)	1 (11)	9 (100)	
Adjuvant treatment					

No	10 (15)	56 (83)	1 (2)	67 (100)	0.3074 ^a
Yes	1 (9)	9 (82)	1 (9)	11 (100)	
Lymph node metastasis					
No	6 (26)	17 (74)	0 (0)	23 (100)	0.2173 ^b
Yes	1 (7)	13 (93)	0 (0)	14 (100)	
Depth of invasion					
Superficial dermis	0 (0)	9 (100)	0 (0)	9 (100)	0.1343 ^a
Dermis	15 (24)	49 (76)	0 (0)	64 (100)	
Lower layer of the dermis	2 (10)	16 (84)	1 (6)	19 (100)	
Subcutaneous	0 (0)	8 (89)	1 (11)	9 (100)	
Rectal mucosa	0 (0)	1 (100)	0 (0)	1 (100)	
Inflammatory infiltrate					
1+ Low	7 (20)	26 (74)	2 (6)	35 (100)	0.2303 ^a
2+ Moderate	8 (13)	54 (87)	0 (0)	62 (100)	
3+ High	2 (25)	6 (75)	0 (0)	8 (100)	
Vascular invasion					
No	18 (20)	72 (80)	0 (0)	90 (100)	0.0009 ^a
Yes	0 (0)	15 (88)	2 (12)	17 (100)	
Perineural invasion					
No	17 (18)	76 (81)	1 (1)	94 (100)	0.1050 ^a
Yes	1 (11)	7 (78)	1 (11)	9 (100)	
Clinical FIGO¹ stage					
I (A/B) and II	10 (21)	37 (79)	0 (0)	47 (100)	0.2951 ^a
III A	1 (25)	3 (75)	0 (0)	4 (100)	
III B	0 (0)	17 (94)	1 (6)	18 (100)	
III C	0 (0)	6 (100)	0 (0)	6 (100)	
IV (A/B)	0 (0)	2 (100)	0 (0)	2 (100)	
Relapse					
No	8 (20)	32 (80)	0 (0)	40 (100)	0.2267 ^a
Yes	3 (8)	31 (88)	1 (4)	35 (100)	
Death					
No	6 (19)	25 (81)	0 (0)	31 (100)	0.1939 ^a
Yes	4 (8)	43 (88)	2 (4)	49 (100)	
HPV infection					
No	4 (22)	14 (78)	0 (0)	18 (100)	1.0000 ^b
Yes	6 (21)	23 (79)	0 (0)	29 (100)	
HPV coinfection					
No	4 (21)	15 (79)	0 (0)	19 (100)	1.0000 ^b
Yes	2 (20)	8 (80)	0 (0)	10 (100)	
HPV type					
High-risk	3 (14)	19 (86)	0 (0)	22 (100)	0.0552 ^a

Low-risk	2 (67)	1 (33)	0 (0)	3 (100)
Both	0 (0)	3 (100)	0 (0)	3 (100)

^a Chi-square; ^b Fisher exact; ⁱFIGO, International Federation of Gynecology and Obstetrics. Bold numbers indicate significant p values.

Table S7. VSCC clinicopathological features and CD81 protein expression.

Variables	n	CD81		Total	<i>p</i>
		Negative n (%)	Positive n (%)		
Age	101				
≤50		9 (82)	2 (18)	11 (100)	1.000 ^b
>50		71 (93)	19 (7)	90 (100)	
Menarche	55				
11 to 14 years old		28 (74)	10 (26)	38 (100)	0.304 ^b
15 to 19 years old		15 (88)	2 (12)	17 (100)	
Menopause	61				
No		2 (100)	0 (0)	2 (100)	1.000 ^b
Yes		45 (76)	13 (24)	59 (100)	
Sexarche	30				
15 to 18 years old		12 (75)	4 (25)	16 (100)	1.000 ^b
≥19 years old		11 (79)	3 (21)	14 (100)	
Partners	36				
≤2		25 (74)	9 (26)	34 (100)	1.000 ^b
≥3		2 (100)	0 (0)	2 (100)	
Contraceptive	61				
No		45 (80)	11 (20)	56 (100)	0.574 ^b
Yes		5 (100)	0 (0)	5 (100)	
Alcoholism	69				
No		57 (84)	11 (16)	68 (100)	1.000 ^b
Yes		1 (100)	0 (0)	1 (100)	
Smoking	72				
No		45 (80)	11 (20)	56 (100)	1.000 ^b
Yes		13 (81)	3 (19)	16 (100)	
Labia Majora	75				
No		32 (94)	2 (6)	34 (100)	0.029 ^b
Yes		30 (73)	11 (27)	41 (100)	
Labia Minora	76				
No		21 (81)	5 (19)	26 (100)	0.754 ^b
Yes		42 (84)	8 (16)	50 (100)	
Clitoris	74				
No		40 (87)	6 (13)	46 (100)	0.189 ^a

		Yes	21 (75)	7 (25)	28 (100)	
Perineal	76					
No		49 (82)		11 (18)	60 (100)	1.000 ^b
Yes		13 (81)		3 (19)	16 (100)	
Tumor Size (mm ³)	100					
≤5 mm		30 (81)		7 (19)	37 (100)	0.479 ^a
6 to 10 mm		16 (89)		2 (11)	18 (100)	
≥10 mm		34 (76)		11 (24)	45 (100)	
Histological diagnosis	105					
VSCC 1		32 (84)		6 (16)	38 (100)	0.900 ^a
VSCC 2		32 (78)		9 (22)	41 (100)	
VSCC 3		9 (75)		3 (25)	12 (100)	
Basaloid carcinoma		9 (82)		2 (18)	11 (100)	
Verrucous carcinoma		2 (67)		1 (33)	3 (100)	
Neoadjuvant Chemotherapy	75					
No		55 (85)		10 (15)	65 (100)	0.023 ^b
Yes		5 (50)		5 (50)	10 (100)	
Adjuvant treatment	77					
No		54 (82)		12 (18)	66 (100)	0.439 ^b
Yes		8 (73)		3 (27)	11 (100)	
Lymph node metastasis	37					
No		16 (73)		6 (27)	22 (100)	1.000 ^b
Yes		11 (73)		4 (27)	15 (100)	
Depth of invasion	100					
Superficial dermis		7 (88)		1 (12)	8 (100)	0.289 ^a
Dermis		50 (79)		13 (21)	63 (100)	
Lower layer of the dermis		14 (78)		4 (22)	18 (100)	
Subcutaneous		9 (90)		1 (10)	10 (100)	
Rectal mucosa		0 (0)		1 (100)	1 (100)	
Inflammatory infiltrate	103					
1+ Low		26 (84)		5 (16)	31 (100)	0.671 ^a
2+ Moderate		50 (77)		15 (23)	65 (100)	
3+ High		6 (86)		1 (14)	7 (100)	
Vascular invasion	105					
No		70 (80)		18 (20)	88 (100)	1.000 ^b
Yes		14 (82)		3 (18)	17 (100)	
Perineural invasion	101					
No		72 (79)		19 (21)	91 (100)	0.681 ^b
Yes		9 (90)		1 (10)	10 (100)	
Clinical FIGO ¹ stage	70					
I (B / A) and II		39 (87)		6 (13)	39 (100)	0.474 ^a

III A	3 (60)	2 (40)	5 (100)	
III B	15 (79)	4 (21)	19 (100)	
III C	4 (67)	2 (33)	6 (100)	
IV (A / B)	1 (100)	0 (0)	1 (100)	
Relapse	74			
No	33 (90)	6 (10)	39 (100)	0.554 ^b
Yes	27 (77)	8 (23)	35 (100)	
Death	80			
No	28 (93)	2 (7)	30 (100)	0.039 ^b
Yes	37 (74)	13 (26)	50 (100)	
HPV infection	48			
No	17 (85)	3 (15)	20 (100)	1.000 ^b
Yes	24 (86)	4 (14)	28 (100)	
HPV coinfection	29			
No	18 (90)	2 (10)	20 (100)	0.568 ^b
Yes	7 (78)	2 (22)	9 (100)	
HPV type	28			
High-risk	20 (87)	3 (13)	23 (100)	0.534 ^a
Low-risk	2 (67)	1 (33)	3 (100)	
Both	2 (100)	0 (0)	2 (100)	

^aChi-square; ^b Fisher exact; ¹FIGO, International Federation of Gynecology and Obstetrics. Bold numbers indicate significant p values.

Table S8. VSCC clinicopathological features and CD82 protein expression.

Variables	n	CD82		Total	p
		Negative n (%)	Positive n (%)		
Age	102				
≤50	7 (58)	5 (42)	12 (100)	1.000 ^b	
>50	48 (53)	42 (47)	90 (100)		
Menarche	56				
11 to 14 years old	23 (67)	16 (33)	39 (100)	0.674 ^a	
15 to 19 years old	9 (65)	8 (35)	17 (100)		
Menopause	59				
No	1 (33)	2 (67)	3 (100)	0.568 ^b	
Yes	33 (59)	23 (41)	56 (100)		
Sexarche	29				
15 to 18 years old	8 (53)	7 (47)	15 (100)	0.263 ^b	
≥19 years old	4 (29)	10 (71)	14 (100)		
Partners	36				
≤2	15 (44)	19 (56)	34 (100)	0.500 ^b	

≥ 3	0 (0)	2 (100)	2 (100)	
Contraceptive	63			
No	32 (55)	26 (45)	58 (100)	0.654 ^b
Yes	2 (40)	3 (60)	5 (100)	
Alcoholism	70			
No	39 (56)	30 (44)	69 (100)	1.000 ^b
Yes	1 (100)	0 (0)	1 (100)	
Smoking	71			
No	30 (56)	24 (44)	54 (100)	0.505 ^a
Yes	11 (65)	6 (35)	17 (100)	
Labia Majora	75			
No	20 (57)	15 (43)	35 (100)	0.975 ^a
Yes	23 (57)	17 (43)	40 (100)	
Labia Minora	77			
No	18 (67)	9 (33)	27 (100)	0.159 ^a
Yes	25 (50)	25 (50)	50 (100)	
Clitoris	74			
No	28 (58)	20 (42)	48 (100)	0.709 ^a
Yes	14 (54)	12 (46)	26 (100)	
Perineal	77			
No	34 (57)	26 (43)	60 (100)	0.874 ^a
Yes	10 (59)	7 (41)	17 (100)	
Tumor Size (mm^3)	102			
$\leq 5 \text{ mm}$	15 (39)	23 (61)	38 (100)	0.027 ^a
6 to 10 mm	14 (78)	4 (22)	18 (100)	
$\geq 10 \text{ mm}$	24 (52)	22 (48)	46 (100)	
Histological diagnosis	107			
VS CC 1	18 (46)	21 (54)	39 (100)	0.536 ^a
VS CC 2	26 (60)	17 (40)	43 (100)	
VS CC 3	6 (55)	5 (45)	11 (100)	
Basaloid carcinoma	4 (36)	7 (64)	11 (100)	
Verrucous carcinoma	2 (67)	1 (33)	3 (100)	
Neoadjuvant Chemotherapy	76			
No	38 (57)	29 (43)	67 (100)	1.000 ^b
Yes	5 (56)	4 (44)	9 (100)	
Adjuvant treatment	77			
No	41 (61)	26 (39)	67 (100)	0.004 ^b
Yes	1 (10)	9 (90)	10 (100)	
Lymph node metastasis	37			
No	11 (50)	11 (50)	22 (100)	0.5490 ^a
Yes	9 (60)	6 (40)	15 (100)	

Depth of invasion	102				
Superficial dermis		1 (12)	7 (88)	8 (100)	0.181 ^a
Dermis		35 (54)	30 (46)	65 (100)	
Lower layer of the dermis		9 (50)	9 (50)	18 (100)	
Subcutaneous		6 (60)	4 (40)	10 (100)	
Rectal mucosa		1 (100)	0 (0)	1 (100)	
Inflammatory infiltrate	105				
1+ Low		14 (44)	18 (56)	32 (100)	0.268 ^a
2+ Moderate		38 (58)	27 (42)	65 (100)	
3+ High		3 (47)	5 (63)	8 (100)	
Vascular invasion	107				
No		45 (50)	45 (50)	90 (100)	0.265 ^a
Yes		11 (65)	6 (35)	17 (100)	
Perineural invasion	103				
No		49 (53)	44 (47)	93 (100)	0.747 ^b
Yes		6 (60)	4 (40)	10 (100)	
Clinical FIGO ¹ stage	78				
I (B / A) and II		26 (58)	19 (42)	45 (100)	0.743 ^a
III A		2 (50)	2 (50)	4 (100)	
III B		9 (47)	10 (53)	19 (100)	
III C		5 (71)	2 (29)	7 (100)	
IV (A / B)		1 (33)	2 (67)	3 (100)	
Relapse	75				
No		20 (51)	19 (49)	39 (100)	0.391 ^a
Yes		22 (61)	14 (39)	36 (100)	
Death	79				
No		17 (55)	14 (45)	31 (100)	0.901 ^a
Yes		27 (56)	21 (44)	48 (100)	
HPV infection	48				
No		13 (65)	7 (35)	20 (100)	0.959 ^a
Yes		18 (64)	10 (36)	28 (100)	
HPV coinfection	29				
No		15 (79)	4 (21)	19 (100)	0.051 ^b
Yes		4 (40)	6 (60)	10 (100)	
HPV type	29				
High-risk		16 (70)	7 (30)	23 (100)	0.462 ^a
Low-risk		2 (67)	1 (33)	3 (100)	
Both		1 (33)	2 (67)	3 (100)	

^aChi-square; ^b Fisher exact; ¹FIGO, International Federation of Gynecology and Obstetrics. Bold numbers indicate significant p values.