

Since this is a very extensive table, the format and content has not been edited by ActaDV.

Table SII Summary of tumor level characteristics of cutaneous squamous cell carcinoma (cSCC)

Tumor characteristics	Total	Non- metastatic	Metastatic	P value	
Tumors included, n	303	218	85		
Gender, ref n	303	218	85		
Male, n (%)	198 (65.3)	141 (64.7)	57 (67.1)	.70	
Female, n (%)	105 (34.7)	77 (35.3)	28 (32.9)	.70	
Age at exact tumor diagnosis, ref n	303	218	85		
Median (IQR), y	78.0 (68-85)	78.0 (66-85)	77.0 (70.5-83)	.82	
Mean, y	75.6	75.6	75.5		
Range, y	27-102	42-102	27-95		
Age bands					
<50, n (%)	11 (3.6)	8 (3.7)	3 (3.5)		
50-59, n (%)	14 (4.6)	12 (5.5)	2 (2.4)		
60-69, n (%)	61 (20.1)	49 (22.5)	12 (14.1)		
70-79, n (%)	88 (29.0)	50 (22.9)	38 (44.7)	.006	
80-89, n (%)	101 (33.3)	75 (34.4)	26 (30.6)		
≥90, n (%)	28 (9.2)	24 (11.0)	4 (4.7)		
Primary tumor location ^a , ref n	303	218	85		Metastatic tumor percentage
Head and neck, n (%)	226 (74.6)	156 (71.6)	70 (82.4)		31.0
Male, n (% of head and neck)	142 (62.8)	94 (60.3)	48 (68.6)		33.8
Female, n (% of head and neck)	84 (37.2)	62 (39.7)	22 (31.4)		26.2
M:F ratio ^b	0.9	0.8	1.1		
Scalp, n (% of head and neck)	14 (6.2)	11 (7.1)	3 (4.3)		21.4
Male, n (% of scalp)	10 (71.4)	7 (63.6)	3 (100.0)		30.0
Female, n (% of scalp)	4 (28.6)	4 (36.4)	0 (0.0)		0.0
M:F ratio ^b	1.3	0.9	NA		
Forehead, n (% of head and neck)	10 (4.4)	6 (3.8)	4 (5.7)		40.0
Male, n (% of forehead)	4 (40.0)	2 (33.3)	2 (50.0)		50.0

Female, n (% of forehead)	6 (60.0)	4 (66.7)	2 (50.0)		33.3
M:F ratio ^b	0.4	0.3	0.5		
Temple, n (% of head and neck)	39 (17.3)	29 (18.6)	10 (14.3)		25.6
Male, n (% of temple)	30 (76.9)	23 (79.3)	7 (70.0)		23.3
Female, n (% of temple)	9 (23.1)	6 (20.7)	3 (30.0)		33.3
M:F ratio ^b	1.8	2.1	1.1		
Orbita, n (% of head and neck)	4 (1.8)	0 (0.0)	4 (5.7)	<.001	100.0
Male, n (% of orbita)	2 (50.0)	0 (0.0)	2 (50.0)		100.0
Female, n (% of orbita)	2 (50.0)	0 (0.0)	2 (50.0)		100.0
M:F ratio ^b	0.5	NA	0.5		
Nose, n (% of head and neck)	16 (7.1)	13 (8.3)	3 (4.3)		18.8
Male, n (% of nose)	7 (43.8)	5 (38.5)	2 (66.7)		28.6
Female, n (% of nose)	9 (56.3)	8 (61.5)	1 (33.3)		11.1
M:F ratio ^b	0.4	0.3	1.0		
Upper lip, n (% of head and neck)	4 (1.8)	2 (1.3)	2 (2.9)		50.0
Male, n (% of upper lip)	2 (50.0)	0 (0.0)	2 (100.0)		100.0
Female, n (% of upper lip)	2 (50.0)	2 (100.0)	0 (0.0)		0.0
M:F ratio ^b	0.5	NA	NA		
Lower lip, n (% of head and neck)	13 (5.8)	3 (1.9)	10 (14.3)	<.001	76.9
Male, n (% of lower lip)	5 (38.5)	0 (0.0)	5 (50.0)		100.0
Female, n (% of lower lip)	8 (61.5)	3 (100.0)	5 (50.0)		62.5
M:F ratio ^b	0.3	NA	0.5		
Cheek ^c , n (% of head and neck)	45 (19.9)	41 (26.3)	4 (5.7)	<.001	8.9
Male, n (% of cheek)	18 (40.0)	16 (39.0)	2 (50.0)		11.1
Female, n (% of cheek)	27 (60.0)	25 (61.0)	2 (50.0)		7.4
M:F ratio ^b	0.4	0.3	0.5		
Preauricular, n (% of head and neck)	32 (14.2)	20 (12.8)	12 (17.1)		37.5
Male, n (% of preauricular)	20 (62.5)	14 (70.0)	6 (50.0)		30.0
Female, n (% of preauricular)	12 (37.5)	6 (30.0)	6 (50.0)		50.0
M:F ratio ^b	0.9	1.3	0.5		
Auricle, n (% of head and neck)	35 (15.5)	23 (14.7)	12 (17.1)		34.3
Male, n (% of auricle)	33 (94.3)	21 (91.3)	12 (100.0)		36.4
Female, n (% of auricle)	2 (5.7)	2 (8.7)	0 (0.0)		0.0

M:F ratio ^b	8.7	5.7	NA		
Tumor characteristics	Total	Non-metastatic	Metastatic	P value	Metastatic tumor percentage
Retroauricular, n (% of head and neck)	6 (2.7)	3 (1.9)	3 (4.3)		50.0
Male, n (% of retroauricular)	6 (100.0)	3 (100.0)	3 (100.0)		50.0
Female, n (% of retroauricular)	0 (0.0)	0 (0.0)	0 (0.0)		NA
M:F ratio ^b	NA	NA	NA		
Neck, n (% of head and neck)	8 (3.5)	5 (3.2)	3 (4.3)		37.5
Male, n (% of neck)	5 (62.5)	3 (60.0)	2 (66.7)		40.0
Female, n (% of neck)	3 (37.5)	2 (40.0)	1 (33.3)		33.3
M:F ratio ^b	0.9	0.8	1.0		
Trunk, n (%)	12 (4.0)	10 (4.6)	2 (2.4)		16.7
Male, n (% of torso)	11 (91.7)	10 (100.0)	1 (50.0)		9.1
Female, n (% of torso)	1 (8.3)	0 (0.0)	1 (50.0)		100.0
M:F ratio ^b	5.8	NA	0.5		
Shoulder, n (% of torso)	2 (16.7)	1 (10.0)	1 (50.0)		50.0
Male, n (% of shoulder)	1 (50.0)	1 (100.0)	0 (0.0)		0.0
Female, n (% of shoulder)	1 (50.0)	0 (0.0)	1 (100.0)		100.0
M:F ratio ^b	0.5	NA	NA		
Thorax, n (% of torso)	5 (41.7)	5 (50.0)	0 (0.0)		0.0
Male, n (% of thorax)	5 (100.0)	5 (100.0)	0 (0.0)		0.0
Female, n (% of thorax)	0 (0.0)	0 (0.0)	0 (0.0)		NA
M:F ratio ^b	NA	NA	NA		
Abdominal, n (% of torso)	1 (8.3)	1 (10.0)	0 (0.0)		0.0
Male, n (% of abdominal)	2 (100.0)	1 (100.0)	0 (0.0)		0.0
Female, n (% of abdominal)	0 (0.0)	0 (0.0)	0 (0.0)		NA
M:F ratio ^b	NA	NA	NA		
Back, n (% of torso)	2 (16.7)	2 (20.0)	0 (0.0)		0.0
Male, n (% of back)	2 (100.0)	2 (100.0)	0 (0.0)		0.0
Female, n (% of back)	0 (0.0)	0 (0.0)	0 (0.0)		NA
M:F ratio ^b	NA	NA	NA		
Pelvic, n (% of torso)	2 (16.7)	1 (10.0)	1 (50.0)		50.0
Male, n (% of pelvic)	2 (100.0)	1 (100.0)	1 (100.0)		50.0
Female, n (% of pelvic)	0 (0.0)	0 (0.0)	0 (0.0)		NA

M:F ratio ^b	NA	NA	NA		
Upper limb, n (%)	35 (11.6)	29 (13.3)	6 (7.1)		17.1
Male, n (% of upper limb)	26 (74.3)	22 (75.9)	4 (66.7)		15.4
Female, n (% of upper limb)	9 (25.7)	7 (24.1)	2 (33.3)		22.2
M:F ratio ^b	1.5	1.7	1.0		
Brachium, n (% of upper limb)	3 (8.6)	3 (10.3)	0 (0.0)		0.0
Male, n (% of brachium)	1 (33.3)	1 (33.3)	0 (0.0)		0.0
Female, n (% of brachium)	2 (66.7)	2 (66.7)	0 (0.0)		0.0
M:F ratio ^b	0.3	0.3	NA		
Antebrachium, n (% of upper limb)	11 (31.4)	10 (34.5)	1 (16.7)		9.1
Male, n (% of antebrachium)	8 (72.7)	7 (70.0)	1 (100.0)		12.5
Female, n (% of antebrachium)	3 (27.3)	3 (30.0)	0 (0.0)		0.0
M:F ratio ^b	1.4	1.3	NA		
Wrist, n (% of upper limb)	1 (2.9)	0 (0.0)	1 (16.7)		100.0
Male, n (% of wrist)	0 (0.0)	0 (0.0)	0 (0.0)		NA
Female, n (% of wrist)	1 (100.0)	0 (0.0)	1 (100.0)		100.0
M:F ratio ^b	NA	NA	NA		
Hand, n (% of upper limb)	20 (57.1)	16 (55.2)	4 (66.7)		20.0
Male, n (% of hand)	17 (85.0)	14 (87.5)	3 (75.0)		17.6
Female, n (% of hand)	3 (15.0)	2 (12.5)	1 (25.0)		33.3
M:F ratio ^b	3.0	3.8	1.5		
Lower limb, n (%)	29 (9.6)	22 (10.1)	7 (8.2)		24.1
Male, n (% of lower limb)	19 (65.5)	15 (68.2)	4 (57.1)		21.1
Female, n (% of lower limb)	10 (34.5)	7 (31.8)	3 (42.9)		30.0
M:F ratio ^b	1.0	1.2	0.7		
Thigh, n (% of lower limb)	6 (20.7)	5 (22.7)	1 (14.3)		16.7
Male, n (% of thigh)	4 (66.7)	4 (80.0)	0 (0.0)		0.0
Female, n (% of thigh)	2 (33.3)	1 (20.0)	1 (100.0)		50.0
M:F ratio ^b	1.1	2.2	NA		
Knee, n (% of lower limb)	1 (3.4)	0 (0.0)	1 (14.3)		100.0
Male, n (% of knee)	1 (100.0)	0 (0.0)	1 (100.0)		100.0
Female, n (% of knee)	0 (0.0)	0 (0.0)	0 (0.0)		NA
M:F ratio ^b	NA	NA	NA		
Shin, n (% of lower limb)	21 (72.4)	16 (72.7)	5 (71.4)		23.8

Male, n (% of shin)	13 (61.9)	10 (62.5)	3 (60.0)		23.1
Female, n (% of shin)	8 (38.1)	6 (37.5)	2 (40.0)		25.0
M:F ratio ^b	0.7	0.9	0.7		
Foot, n (% of lower limb)	1 (3.4)	1 (4.5)	0 (0.0)		0.0
Male, n (% of foot)	1 (100.0)	1 (100.0)	0 (0.0)		0.0
Female, n (% of foot)	0 (0.0)	0 (0.0)	0 (0.0)		NA
M:F ratio ^b	NA	NA	NA		
Tumor characteristics	Total	Non-metastatic	Metastatic	P value	Metastatic tumor percentage
Unknown, n (%)	1 (0.3)	1 (0.5)	0 (0.0)		0.0
Male, n (% of unknown)	0 (0.0)	0 (0.0)	0 (0.0)		NA
Female, n (% of unknown)	1 (100.0)	1 (100.0)	0 (0.0)		0.0
Side, ref n	303	218	85	.24	
Middle line, n (%)	25 (8.3)	21 (9.6)	4 (4.7)		
Right, n (%)	123 (40.6)	83 (38.1)	40 (47.1)		
Left, n (%)	146 (48.2)	105 (48.2)	41 (48.2)		
Unknown, n (%)	9 (3.0)	9 (4.1)	0 (0.0)		
Tumor diameter prior to 1 st diagnosis of metastasis, ref n	303	218	85		Metastatic tumor percentage
<10mm, n (%)	97 (32.0)	89 (40.8)	8 (9.4)	<.001	8.2
10-19,9mm, n (%)	112 (37.0)	85 (39.0)	27 (31.8)		24.1
20-29,9mm, n (%)	38 (12.5)	19 (8.7)	19 (22.4)	<.001	50.0
30-39,9mm, n (%)	20 (6.6)	7 (3.2)	13 (15.3)	<.001	65.0
≥40mm, n (%)	35 (11.6)	18 (8.3)	17 (20.0)	<.001	48.6
Unknown, n (%)	1 (0.3)	0 (0.0)	1 (1.2)		
Histological differentiation, ref n	303	218	85		
Good, n (%)	140 (46.2)	123 (56.4)	17 (20.0)	<.001	12.1
Moderate, n (%)	110 (36.3)	70 (32.1)	40 (47.1)	<.001	36.4
Poor, n (%)	46 (15.2)	22 (10.1)	24 (28.2)	<.001	52.2
Unknown, n (%)	7 (2.3)	3 (1.4)	4 (4.7)		
AK or cSCCIS among or confirmedly preceding primary tumor, ref n	303	218	85		

Yes, n (%)	78 (25.7)	66 (30.3)	12 (14.1)	.006	15.4
No, n (%)	222 (73.3)	152 (69.7)	70 (82.4)	.006	31.5
Unknown, n (%)	3 (1.0)	0 (0.0)	3 (3.5)		
Necrosis detected among primary tumor	303	218	85		
Yes, n (%)	22 (7.3)	10 (4.6)	12 (14.1)	.002	54.5
No, n (%)	274 (90.4)	208 (95.4)	66 (77.6)	.002	24.1
Unknown, n (%)	7 (2.3)	0 (0.0)	7 (8.2)		
Developed into chronic ulcer and/or Dermatitis, ref n	303	218	85		
Yes, n (%)	17 (5.6)	9 (4.1)	8 (9.4)	.09	47.1
No, n (%)	286 (94.4)	209 (95.9)	77 (90.6)	.09	26.9
Invasiveness, ref n	303	218	85		
Clark's level					
Clark 2-4, n (%)	177 (58.4)	169 (77.5)	8 (9.4)	<.001	4.5
Clark 5, n (%)	114 (37.6)	47 (21.6)	67 (78.8)	<.001	58.8
Unknown, n (%)	12 (4.0)	2 (0.9)	10 (11.8)		
Diffuse growth pattern					
Yes, n (%)	19 (6.3)	6 (2.2)	13 (15.3)	<.001	68.4
No, n (%)	278 (91.4)	212 (97.2)	65 (76.5)	<.001	23.4
Unknown, n (%)	7 (2.3)	0 (0.0)	7 (8.2)		
Invasion beyond fat					
Yes, n (%)	67 (22.1)	20 (9.2)	47 (55.3)	<.001	70.1
No, n (%)	230 (75.9)	198 (90.8)	32 (37.6)	<.001	13.9
Unknown, n (%)	6 (2.0)	0 (0.0)	6 (7.1)		
Invasion into muscle					
Yes, n (%)	32 (10.6)	5 (2.3)	27 (31.8)	<.001	84.4
No, n (%)	264 (87.1)	213 (97.7)	51 (60.0)	<.001	19.3
Unknown, n (%)	7 (2.3)	0 (0.0)	7 (8.2)		
Invasion into cartilage					
Yes, n (%)	13 (4.3)	6 (2.8)	7 (8.2)	.05	53.8
No, n (%)	283 (93.4)	212 (97.2)	71 (83.5)	.05	25.1
Unknown, n (%)	7 (2.3)	0 (0.0)	7 (8.2)		
Within auricle location					
Yes, n (%)	10 (28.6)	5 (21.7)	5 (41.7)	.26	50.0
No, n (%)	25 (71.4)	18 (78.3)	7 (58.3)	.26	28.0
Invasion into bone					

Yes, n (%)	10 (3.3)	3 (1.4)	7 (8.2)	.004	70.0
No, n (%)	286 (94.4)	215 (98.6)	71 (83.5)	.004	24.8
Unknown, n (%)	7 (2.3)	0 (0.0)	7 (8.2)		
Invasion into parotid gland					
Yes, n (%)	5 (1.7)	0 (0.0)	5 (5.9)	.001	100.0
No, n (%)	291 (96.0)	218 (100.0)	73 (85.9)	.001	25.1
Unknown, n (%)	7 (2.3)	0 (0.0)	7 (8.2)		
Invasion into CNS					
Yes, n (%)	2 (0.7)	2 (0.9)	0 (0.0)	>.99	0.0
No, n (%)	294 (97.0)	216 (99.1)	78 (91.8)	>.99	26.5
Unknown, n (%)	7 (2.3)	0 (0.0)	7 (8.2)		
PNI, n (%)	2 (0.7)	1 (0.5)	1 (1.3)	.46	50.0
Vascular invasion, n (%)	1 (0.3)	0 (0.0)	1 (1.3)	.26	100.0
Lymphatic invasion, n (%)	4 (1.4)	2 (0.9)	2 (2.6)	.28	50.0
Tumor characteristics	Total	Non-metastatic	Metastatic	P value	Metastatic tumor percentage
BWH, ref n	303	218	85		
TX, n (%)	11 (3.6)	3 (1.4)	8 (9.4)		72.7
T1, n (%)	170 (56.1)	157 (72.0)	13 (15.3)	<.001	7.6
T2a, n (%)	57 (18.8)	37 (17.0)	20 (23.5)		35.1
T2b, n (%)	56 (18.5)	18 (8.3)	38 (44.7)	<.001	67.9
T3, n (%)	9 (3.0)	3 (1.4)	6 (7.1)	<.001	66.7
AJCC-8, ref n	226	156	70		
TX, n (%)	5 (2.2)	0 (0.0)	5 (7.1)		100.0
T1, n (%)	136 (60.2)	120 (76.9)	16 (22.9)	<.001	11.8
T2, n (%)	14 (6.2)	11 (7.1)	3 (4.3)		21.4
T3, n (%)	64 (28.3)	22 (14.1)	42 (60.0)	<.001	65.6
T4a – T4b, n (%)	7 (3.1)	3 (1.9)	4 (5.7)		57.1
Local recurrence(s) prior to metastasis detection, ref n	303	218	85		
Yes, n (%)	52 (17.2)	24 (11.0)	28 (32.9)	<.001	53.8
No, n (%)	251 (82.8)	194 (89.0)	57 (67.1)	<.001	22.7
Number of local recurrences					
0, n (%)	251 (82.8)	194 (89.0)	57 (67.1)	<.001	22.7
1, n (%)	42 (13.9)	21 (9.6)	21 (24.7)	<.001	50.0

2, n (%)	4 (1.3)	1 (0.5)	3 (3.5)	<.001	75.0
3, n (%)	3 (1.0)	0 (0.0)	3 (3.5)	<.001	100.0
4, n (%)	1 (0.3)	1 (0.5)	0 (0.0)		0.0
5 or more, n (%)	2 (0.7)	1 (0.5)	1 (1.2)		50.0
Local recurrence(s) overall, ref n	303	218	85		
Yes, n (%)	59 (19.5)	24 (11.0)	35 (41.2)	<.001	
No, n (%)	244 (80.5)	194 (89.0)	50 (58.8)	<.001	
Time from the last resection of primary tumor to the histopathologic diagnosis of 1 st clinical recurrence (n=54)					Missing info n
Median (IQR), d	161 (63-366)	224 (68-669)	127 (62-204)	.06	5
Mean, d	279	376	212		5
≤6 months, n (%)	32 (59.3)	9 (40.9)	23 (71.9)		5
≤1 year, n (%)	41 (75.9)	15 (68.2)	26 (81.2)		5
≤2 years, n (%)	49 (88.9)	17 (77.3)	31 (96.9)		5
Margins (information about primary tumor resection prior to local recurrence)	Overall (303)	No local recurrence (244)	Locally recurrent (59)		Locally recurrent tumor percentage
Invasive tumor-free resection was performed, n (%)	66 (21.8)	60 (24.6)	6 (10.2)		9.1
Pathologist established that tumor has been resected with clear margins without presenting exact margins, n (%)	65 (21.5)	54 (22.1)	11 (18.6)		16.9
Cases without information of margins, n (%)	18 (5.9)	11 (4.5)	7 (11.9)		38.9
Exact margin expressed, n (%)	154 (50.7)	119 (48.6)	35 (59.3)		
Median (IQR), mm	2.0 (3.0)	2.5 (1.0-4.0)	0.4 (0.0-2.0)	<.001	
Mean, mm	2.8	3.3	1.3		
Smallest margin:					
0mm (unradical), n (% exact margins)	21 (13.6)	6 (5.0)	15 (42.9)	<.001	71.4
> 0mm ≤ 1mm, n (% exact margins)	33 (21.4)	24 (20.2)	9 (25.7)		27.2
> 1mm ≤ 2mm, n (% exact margins)	31 (20.1)	27 (22.7)	4 (11.4)		12.9
> 2mm ≤ 3mm, n (% exact margins)	27 (17.5)	24 (20.2)	3 (8.6)		11.1

> 3mm ≤ 4mm, n (% exact margins)	16 (10.4)	15 (12.6)	1 (2.9)		6.3
> 4mm ≤ 5mm, n (% exact margins)	11 (7.1)	9 (7.6)	2 (5.7)		18.2
> 5mm, n (% exact margins)	15 (9.7)	14 (11.8)	1 (2.9)		6.7
0mm – 1mm, n (%)	54 (35.1)	30 (25.2)	24 (68.6)	<.001	44.4
> 1mm, n (%)	100 (64.9)	89 (74.8)	11 (31.4)	<.001	11.0
0mm – 2mm, n (%)	85 (55.2)	57 (47.9)	28 (80.0)	.001	32.9
> 2mm, n (%)	69 (44.8)	62 (52.1)	7 (20.0)	.001	10.1
0mm – 3mm, n (%)	112 (72.7)	81 (68.1)	31 (88.6)	.02	27.7
> 3mm, n (%)	42 (27.3)	38 (31.9)	4 (11.4)	.02	9.5

^aOnly statistically significant P values via Bonferroni method from analysis including every detailed location are visualized regarding location. ^bM:F ratio indicates male:female ratio for primary tumor location adjusted for total number of cSCCs on males and females. ^cExcluding preauricular region.

AJCC-8: 8th edition of American Joint Committee on Cancer tumor staging, applied solely for head and neck tumors; AK: actinic keratosis; BWH: Brigham and Women's hospital tumor staging, applied regarding every location; CNS: central nervous system; cSCCIS: cSCC *in situ*; IQR: interquartile range; NA: not applicable; PNI: perineural invasion.