

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

Table SI. Summary of patient-level characteristics of cutaneous squamous cell carcinoma (cSCC)

Patient characteristics	Total			Non-metastatic			Metastatic			
Patients in total, n (%)	207 (100)			125 (100)			82 (100)			
Age at 1st cSCC diagnosis	M+F	Male	Female	M+F	Male	Female	M+F	Male	Female	
Median (IQR), y	78.0 (71-85)	77.0 (69-82)	81.0 (73-87)	80.0 (71-85)	77.0 (69-84)	81.5 (73-88)	77.0 (71-83)	75.0 (68-80)	78.0 (73-86)	
Mean, y	76.7	74.9	79.5	77.8	76.1	80.0	75.0	73.3	78.6	
Range	27-102	27-95	55-102	47-102	47-92	55-102	27-95	27-95	60-93	
Age bands										
<50, n (%)	3 (1.4)	3 (2.4)	0 (0.0)	1 (0.8)	1 (1.4)	0 (0.0)	2 (2.4)	2 (3.6)	0 (0.0)	
50-59, n (%)	10 (4.8)	9 (7.1)	1 (1.2)	6 (4.8)	5 (7.0)	1 (1.9)	4 (4.9)	4 (7.3)	0 (0.0)	
60-69, n (%)	33 (15.9)	22 (17.5)	11 (13.6)	20 (16.0)	13 (18.3)	7 (13.0)	13 (15.9)	9 (16.4)	4 (14.8)	
70-79, n (%)	68 (32.9)	45 (35.7)	23 (28.4)	33 (26.4)	20 (28.2)	13 (24.1)	35 (42.7)	25 (45.5)	10 (37.0)	
80-89, n (%)	77 (37.2)	41 (32.5)	36 (44.4)	52 (41.6)	27 (38.0)	25 (46.3)	25 (30.5)	14 (25.5)	11 (40.7)	
≥90, n (%)	16 (7.7)	6 (4.8)	10 (12.3)	13 (10.4)	5 (7.0)	8 (14.8)	3 (3.7)	1 (1.8)	2 (7.4)	
Patient characteristics	Total			Non-metastatic			Metastatic			P value
Patients in total, n (%)	207 (100)			125 (100)			82 (100)			
Gender, ref n	207			125			82			
Male, n (%)	126 (60.9)			71 (56.8)			55 (67.1)			.14
Female, n (%)	81 (39.1)			54 (43.2)			27 (32.9)			.14
Occupation, ref n	207			125			82			
High UV-exposure, n (%)	27 (13.0)			14 (11.2)			13 (15.9)			.32
Low UV-exposure, n (%)	119 (57.5)			74 (59.2)			45 (54.9)			.32
Occupation unknown, n (%)	61 (29.5)			37 (29.6)			24 (29.3)			
Farmer (High), n (%)	15 (7.2)			7 (5.6)			8 (9.8)			
Smoking, ref n	207			125			82			
Yes, n (%)	23 (11.1)			12 (9.6)			11 (13.4)			.55
No, n (%)	82 (39.6)			37 (29.6)			45 (54.9)			.55
Data not available, n (%)	102 (49.3)			76 (60.8)			26 (31.7)			
Immunosuppression (patient with at least one of following), n (%)	42 (20.3)			26 (20.8)			16 (19.5)			.82
SOTR, n (%)	8 (3.9)			6 (4.8)			2 (2.4)			.48
Kidney, n (%)	7 (3.4)			5 (4.0)			2 (2.4)			
Heart, n (%)	1 (0.5)			1 (0.8)			0 (0.0)			
HIV, n (%)	1 (0.5)			0 (0.0)			1 (1.2)			.40
Immunosuppressive medication ^a , n (%)	32 (15.5)			21 (16.8)			11 (13.4)			.51
No of cSCCs										.84
1 cSCC, n (% of above)	23 (71.9)			16 (76.2)			7 (63.6)			
2-9 cSCCs, n (% of above)	7 (21.9)			4 (19.0)			3 (27.3)			
Hematologic malignancy										
CLL, n (%)	9 (4.3)			5 (4.0)			4 (4.9)			.74
Non-Hodgkin lymphoma, n (%)	10 (4.8)			7 (5.6)			3 (3.7)			.74

Patient characteristics	Total	Non-metastatic	Metastatic	P value
Number of primary cSCCs per patient, ref n	207	125	82	
Median (IQR), n	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	.63
Mean, n	1.6	1.5	1.9	
Range, n	1-26	1-11	1-26	
Bands				.75
1 cSCC, n (%)	151 (72.9)	92 (73.6)	59 (72.0)	
2-9 cSCCs, n (%)	53 (25.6)	32 (25.6)	21 (25.6)	
≥10 cSCCs, n (%)	3 (1.4)	1 (0.8)	2 (2.4)	
Comorbidities, ref n	207	125	82	
Hypertension, n (%)	116 (56.0)	69 (55.2)	47 (57.3)	.76
MCC, n (%)	66 (31.9)	42 (33.6)	24 (29.3)	.51
T2DM, n (%)	41 (19.8)	24 (19.2)	17 (20.7)	.75
AF/AFL, n (%)	44 (21.3)	22 (17.6)	22 (26.8)	.11
COPD, n (%)	8 (3.9)	3 (2.4)	5 (6.1)	.27
Asthma, n (%)	11 (5.3)	9 (7.2)	2 (2.4)	.21
Rheumatoid arthritis, n (%)	9 (4.3)	6 (4.8)	3 (3.7)	>.99
Gout, n (%)	15 (7.2)	9 (7.2)	6 (7.3)	.98
Hypothyroidism, n (%)	15 (7.2)	12 (9.6)	3 (3.7)	.11
Hyperthyroidism, n (%)	3 (1.4)	2 (1.6)	1 (1.2)	>.99
Pernicious anemia, n (%)	5 (2.4)	5 (4.0)	0 (0.0)	.16
Earlier stroke, n (%)	19 (9.2)	12 (9.6)	7 (8.5)	.80
Pacemaker, n (%)	4 (1.9)	1 (0.8)	3 (3.7)	.30
Epilepsy, n (%)	4 (1.9)	2 (1.6)	2 (2.4)	.65
Meniere's disease, n (%)	3 (1.4)	1 (0.8)	2 (2.4)	.56
Earlier tuberculosis, n (%)	4 (1.9)	3 (2.4)	1 (1.2)	>.99
Comorbidities (dermatologic), ref n	207	125	82	
Psoriasis, n (%)	4 (1.9)	3 (2.4)	1 (1.2)	>.99
Seborrhoeic dermatitis, n (%)	6 (2.9)	4 (3.2)	2 (2.4)	>.99
Lichen simplex chronicus, n (%)	6 (2.9)	4 (3.2)	2 (2.4)	>.99
Acne rosacea, n (%)	7 (3.4)	7 (5.6)	0 (0.0)	.04
Stasis dermatitis, n (%)	5 (2.4)	3 (2.4)	2 (2.4)	>.99
Herpes zoster, n (%)	4 (3.2)	4 (3.2)	0 (0.0)	.15
Co-malignancy (excluding keratinocyte-derived), ref n	207	125	82	
Yes, n (%)	82 (39.6)	54 (43.2)	28 (34.1)	.19
No, n (%)	125 (60.4)	71 (56.8)	54 (65.9)	.19
Number of co-malignancies				.14
Zero, n (%)	125 (60.4)	71 (56.8)	54 (65.9)	
One, n (%)	68 (32.9)	42 (33.6)	26 (31.7)	
Two, n (%)	11 (5.3)	10 (8.0)	1 (1.2)	
Three, n (%)	2 (1.0)	1 (0.8)	1 (1.2)	
Four, n (%)	1 (0.5)	1 (0.8)	0 (0.0)	
Co-malignancy in relation to 1 st cSCC				.23
Prior to, n (% of co-malignancies)	49 (49.0)	30 (43.5)	19 (61.3)	
After, n (% of co-malignancies)	40 (40.0)	30 (43.5)	10 (32.3)	
Concurrently, n (% of co-malignancies)	11 (11.0)	9 (13.0)	2 (6.5)	
Prostate cancer, n (%)	19 (9.2)	12 (9.6)	7 (8.5)	.80
In males, n (%)	19 (15.1)	12 (16.9)	7 (12.7)	.52

Breast cancer, n (%)	7 (3.4)	5 (4.0)	2 (2.4)	.71
In females, n (%)	7 (8.6)	5 (9.3)	2 (7.4)	>.99
Uterine cancer (corpus +cervical), n (%)	2 (1.0)	0 (0.0)	2 (2.4)	.16
HNSCC, n (%)	4 (1.9)	3 (2.4)	1 (1.2)	>.99
Neuroendocrine (parvocellular) ca, n (%)	1 (0.5)	1 (0.8)	0 (0.0)	>.99
Non-Hodgkin lymphoma, n (%)	10 (4.8)	7 (5.6)	3 (3.7)	.74
Hodgkin's lymphoma, n (%)	3 (1.4)	2 (1.6)	1 (1.2)	>.99
CLL, n (%)	9 (4.3)	5 (4.0)	4 (4.9)	.74
AML, n (%)	1 (0.5)	0 (0.0)	1 (1.2)	.40
Waldenström's	1 (0.5)	1 (0.8)	0 (0.0)	>.99
Macroglobulinemia, n (%)				
Colorectal cancer, n (%)	13 (6.3)	9 (7.2)	4 (4.9)	.50
Gastric cancer, n (%)	2 (1.0)	1 (0.8)	1 (1.2)	>.99
Pancreatic cancer, n (%)	2 (1.0)	2 (1.6)	0 (0.0)	.52
Bladder cancer, n (%)	5 (2.4)	4 (3.2)	1 (1.2)	.65
Renal cancer, n (%)	1 (0.5)	1 (0.8)	0 (0.0)	>.99
Lung cancer, n (%)	6 (2.9)	4 (3.2)	2 (2.4)	>.99
Melanoma, n (%)	4 (1.9)	3 (2.4)	1 (1.2)	>.99
Merkel-cell carcinoma, n (%)	2 (1.0)	2 (1.6)	0 (0.0)	.52
Cutaneous adnexal carcinoma, n (%)	1 (0.5)	1 (0.8)	0 (0.0)	>.99
Cutaneous T-cell lymphoma, n (%)	1 (0.5)	0 (0.0)	1 (1.2)	.40
Vulvar carcinoma, n (%)	1 (0.5)	1 (0.8)	0 (0.0)	>.99
Patient characteristics	Total	Non-metastatic	Metastatic	P value
Keratinocyte premalignancies and malignancies, ref n	207	125	82	
Actinic keratosis, n (%)	97 (46.9)	67 (53.6)	30 (36.6)	.02
cSCC <i>in situ</i> , n (%)	53 (25.6)	36 (28.8)	17 (20.7)	.19
Basal cell carcinoma, n (%)	70 (33.8)	53 (42.4)	17 (20.7)	.001
Metatypical carcinoma, n (%)	5 (2.4)	3 (2.4)	2 (2.4)	>.99
Keratoacanthoma, n (%)	12 (5.8)	8 (6.4)	4 (4.9)	.77
Number of pharmaceuticals per patient, ref n	207	125	82	
Mean (SD), n	4.6 (3.2)	4.6 (3.2)	4.7 (3.3)	.78
Median, n	4.0	4.0	4.0	
Range, n	0-16	0-16	0-13	
Pharmaceuticals, ref n	207	125	82	
NSAID (long term), n (%)	9 (4.3)	5 (4.0)	4 (4.9)	.74
Aspirin ^b , n (%)	72 (34.8)	52 (41.6)	20 (24.4)	.01
Warfarin, n (%)	39 (18.8)	22 (17.6)	17 (20.7)	.57
Dipyridamole, n (%)	10 (4.8)	6 (4.8)	4 (4.9)	>.99
Clopidogrel, n (%)	3 (1.4)	2 (1.6)	1 (1.2)	>.99
Thiazide, n (%)	59 (28.5)	30 (24.0)	29 (35.4)	.08
Furosemide, n (%)	37 (17.9)	22 (17.6)	15 (18.3)	.90
Spironolactone, n (%)	5 (2.4)	2 (1.6)	3 (3.7)	.39
ACE inhibitor/ARB, n (%)	76 (36.7)	44 (35.2)	32 (39.0)	.58
Digoxin, n (%)	22 (10.6)	11 (8.8)	11 (13.4)	.29
CCB, n (%)	54 (26.1)	31 (24.8)	23 (28.0)	.60
α1 blocker ^c , n (%)	17 (8.2)	7 (5.6)	10 (12.2)	.09
In males, n (%)	15 (11.9)	6 (8.5)	9 (16.4)	.17
Beta blocker, n (%)	80 (38.6)	46 (36.8)	34 (41.5)	.50
α/β blocker ^d , n (%)	3 (1.4)	3 (2.4)	0 (0.0)	.28

Isosorbide mono-/dinitrate, n (%)	35 (16.9)	28 (22.4)	7 (8.5)	.009
Statin, n (%)	54 (26.1)	37 (29.6)	17 (20.7)	.16
PPI, n (%)	19 (9.2)	11 (8.8)	8 (9.8)	.82
Bisphosphonate, n (%)	15 (7.2)	10 (8.0)	5 (6.1)	.61
Metformin, n (%)	24 (11.6)	15 (12.0)	9 (11.0)	.82
Glitazone, n (%)	3 (1.4)	1 (0.8)	2 (2.4)	.56
Sulfonylurea, n (%)	15 (7.2)	11 (8.8)	4 (4.9)	.29
Gliptin, n (%)	6 (2.9)	2 (1.6)	4 (4.9)	.22
Allopurinol, n (%)	14 (6.8)	7 (5.6)	7 (8.5)	.41
5 α -reductase inhibitor, n (%)	13 (6.3)	4 (3.2)	9 (11.0)	.02
In males, n (%)	13 (10.3)	4 (5.6)	9 (16.4)	.05
Trimethoprim ^e , n (%)	9 (4.3)	4 (3.2)	5 (6.1)	.32
Anticholinergic ^f , n (%)	3 (1.4)	1 (0.8)	2 (2.4)	.56
Oxybutynin, n (%)	3 (1.4)	2 (1.6)	1 (1.2)	>.99
Neuroleptic, n (%)	10 (4.8)	7 (5.6)	3 (3.7)	.74
Tricyclic antidepressant, n (%)	5 (2.4)	4 (3.2)	1 (1.2)	.65
Mirtazapine, n (%)	4 (1.9)	2 (1.6)	2 (2.4)	.65
SSRI/SNRI, n (%)	9 (4.3)	4 (3.2)	5 (6.1)	.32
CBZ/Oxcarbazepine, n (%)	4 (1.9)	2 (1.6)	2 (2.4)	.65
Pramipexole, n (%)	3 (1.4)	0 (0.0)	3 (3.7)	.06
Pentoxifylline, n (%)	3 (1.4)	3 (2.4)	0 (0.0)	.28
Donepezil, n (%)	5 (2.4)	2 (1.6)	3 (3.7)	.39
Memantine, n (%)	3 (1.4)	2 (1.6)	1 (1.2)	>.99
Methotrexate, n (%)	5 (2.4)	3 (2.4)	2 (2.4)	>.99
Sulfasalazine, n (%)	3 (1.4)	1 (0.8)	2 (2.4)	.56
Mesalazine, n (%)	3 (1.4)	3 (2.4)	0 (0.0)	.28
Systemic steroid, n (%)	23 (11.1)	17 (13.6)	6 (7.3)	.16
Ciclosporin, n (%)	9 (4.3)	7 (5.6)	2 (2.4)	.49
Azathioprine, n (%)	13 (6.3)	10 (8.0)	3 (3.7)	.21
Cyclophosphamide, n (%)	3 (1.4)	1 (0.8)	2 (2.4)	.56
Chlorambucil, n (%)	4 (1.9)	3 (2.4)	1 (1.2)	>.99
Leuprorelin/Goserelin, n (%)	3 (1.4)	2 (1.6)	1 (1.2)	>.99
HCQ, n (%)	3 (1.4)	1 (0.8)	2 (2.4)	.56
Acitretin, n (%) ^g	3 (1.4)	1 (0.8)	2 (2.4)	.56

^aFollowing medications were classified as immunosuppressive: mycophenolate, interferone, tacrolimus, chlorambucil, cyclophosphamide, azathioprine, systemic steroid, ciclosporin, thalidomide, methotrexate, sulfasalazine, chloroquine, hydroxychloroquine. ^bLow-dose aspirin (50-250mg daily) usage in cardiovascular protective manner was registered separately and not included under NSAID. ^cPrazosin, alfuzosin and/or tamsulosin. ^dLabetalol and/or carvedilol. ^eUsed in long term prevention. ^fBiperiden and/or solifenacin. ^g40 pharmaceutical agents and 36 comorbidities were excluded from the table since the frequency cohorts combined was less than 3.

ACE inhibitor: angiotensin-converting-enzyme inhibitor; AF: atrial fibrillation; AFL: atrial flutter; AML: acute myeloid leukemia; ARB: angiotensin II receptor blocker; Aspirin: low-dose aspirin (50-250 mg per day); CBZ: carbamazepine; CCB: calcium channel blocker; CLL: chronic lymphocytic leukemia; COPD: chronic obstructive pulmonary disease; HIV: Human immunodeficiency virus positive; HNSCC: head and neck squamous-cell carcinoma; HZQ: hydroxychloroquine; IQR: interquartile range; MCC: coronary artery disease; NSAID: nonsteroidal anti-inflammatory drugs; PPI: proton-pump inhibitor; ref n: reference number; SNRI: serotonin-norepinephrine reuptake inhibitor; SOTR: solid organ transplant recipient; SSRI: selective serotonin reuptake inhibitor; T2DM: diabetes mellitus type 2.