Supplementary Table 1. Clinical characteristics of FA SCCs*

FA sample	Sex	Age, y	Site	Therapy	Primary tumor	Recurrence	Age at AML, y	Age at BMT, y	GvHD	Disease-free interval (mo)	Follow-up interval (mo)	Vital status
Fa1_t	F	26	BOT	SURGRT	T2N0	SPT	-	-	-	62	62	DD Fa1_g
Fa1_g	F	31	Gingiva	SURG	T4N0	LOC	-	-	-	13	15	DD
Fa3	F	34	Lip	SURG	T2N1	LOC	-	12	No	8	12	DD
Fa4	F	30	Buccal mucosa	SURG	T1N0	-	30	-	-	1	1	DC
Fa5	F	36	Anus	SURG	CIS	SPT	-	-	-	17	76	Alive
Fa6_e	F	39	Esophagus	SURG	T3N1	DM	-	-	-	2	4	DD
Fa6_v	F	37	Vulva	SURG	CIS	SPT	-	-	-	3	34	DD Fa6_e
Fa8	M	22	Mouth	SURG	T4N?	LOC	-	13	Yes	5	20	DD
Fa9	F	30	Esophagus	SURG	U	U	-	-	-	U	U	U
Fa10	F	13	Tongue	SURG	T1N0	SPT	-	11	No	13	39	Alive
Fa11	F	24	Mouth	SURG	U	LOC	-	-	-	12	49	DOC
Fa12	M	29	Hypopharynx	Laser/RT	U	U	-	12	U	1	9	DD
Fa13	F	28	Vulva	SURG	T1N0	LOC	-	-	-	12	60	DD
Fa14	F	25	Tongue	SURGRT	U	-	-	9	Yes	31	31	Alive
Fa15	F	44	Soft palate	SURG	T1N0	SPT	-	-	-	39	115	Alive
Fa16	F	25	Tongue	SURG	T1N2b	SPT	-	9	No	10	10	DD
Fa17	M	16	Tongue	SURG	T1N0	-	-	4	Yes	24	24	DOC
Fa18	F	56	Epiglottis	SURG	T?N0	-	-	-	-	1	1	Alive
Fa19	F	26	Tongue	SURG	T1N0	LOC	-	7	Yes	5	10	DD
Fa20	M	21	Palatum	SURG	T1N0	SPT	-	11	No	5	7	Alive
Fa21	F	25	Oral cavity	SURG	T1N0	REG	-	9	U	6	91	DD

*Specimens and clinical information were obtained for three patients from The Netherlands, four from Spain, one from Sweden, four from Germany, four from France, one from Ireland, and two from the United States. Fa1_t and Fa1_g are two primary SCCs from the same patient; Fa6_e and Fa6_v are two primary SCCs from the same patient. Multiple tumors from the same patient were included in the study only when their relative location (> 2 cm apart) or time interval between their diagnoses (> 3 years) clearly indicated that they were independent. Age (y) at which the first primary tumor was diagnosed is indicated. Tumor stage is given for the primary tumor, according to International Union Against Cancer (12). In some cases, a lymph node metastasis or recurrence rather than the primary tumor was analyzed. The disease-free interval was calculated from the date of histological diagnosis of the primary tumor to the date of recurrence or diagnosis of a second primary tumor, the last contact date, or date of death, whichever came first. DOC = death from other causes; DD = death from disease. M = Male; F = Female; BOT = base of tongue; U = unknown; CIS = carcinoma-in-situ; SPT = second primary tumor; LOC = local recurrence; DM = distant metastasis; REG = regional recurrence; BMT = bone marrow transplanted; SURG = surgery; RT = radiotherapy; GvHD = graft versus host disease.

Supplementary Table 2. Data summary for all SSC FA samples*

		Genetic analysis			Immunohistochemistry		HPV detection	
Sample	BMT	freq LOH	T-Source	*TP53* mutation	p16	p53	GP5+/6+	HPV type
Fa1_t	-	9/14 (64%)		ND	-	+	-	none
Fa1_g	-	11/18 (61%)		WT	-	-	-	none
Fa3	+	18/18 (100%)	OoT: patient	R273L (G→T)	-	+	-	none
Fa4	-	13/16 (81%)		WT	-	-	-	none
Fa5	-	3/17 (18%)		WT	+	-	+	HPV 16
Fa6_e	-	11/22 (50%)		R248W (C→T)	-	+	-	none
Fa6_v	-	12/22 (55%)		R213* (C→T)	+	+	-	none
Fa8	+	13/19 (68%)	OoT: patient	R282W (C→T)	-	-	-	none
Fa9	-	15/19 (79%)		WT	-	-	-	none
Fa10	+	NE	OoT: patient	Del TG codon 215	+	-	-	none
Fa11	-	13/20 (65%)		R175K (G→A)	+	+	-	none
Fa12	+	NE	OoT: not conclusive	Del AC codon 208	-	-	-	none
Fa13	-	1/14 (7%)		WT	+	-	+	HPV 33
Fa14	+	NE	OoT NA	WT, not dissected	NA	NA	-	none
Fa15	-	11/17 (65%)		R273H (G→A)	-	+	-	none
Fa16	+	NE	OoT: patient	del CC codon 127	-	-	-	none
Fa17	+	13/17 (76%)	OoT: patient	WT	-	+	-	none
Fa18	-	4/15 (27%)		WT	-	-	-	none
Fa19	+	NE	OoT: patient	NA	NA	NA	-	none
Fa20	+	NE	OoT: not conclusive	NA	NA	NA	-	none
Fa21	+	NE	OoT: patient	Y234H (T→C)	-	+	-	none

* Available material was either paraffin blocks, frozen biopsies or paraffin sections in a vial. In some cases we only received DNA material from the tumor directly. BMT status of patients is indicated. The frequency of allelic loss is defined as the number of allelic losses per informative marker, with the percentage between brackets. Patterns of allelic loss are depicted in Table 2. OoT: Origin of tumor was determined on microsatellite markers of both patient and donor as explained in Supplementary Figure 2. NE= not evaluable. Due to donor contamination, reliable profiles could not always be established; only assignment of tumor origin could be evaluated in these cases. NA = Not analyzed due to lack of material. *TP53* mutation analysis was performed on exons 5–9. WT = wild-type. Fa1_t could not be analyzed due to lack of primary tumor material. In Fa19 and Fa20, too many donor-derived tumor-infiltrating lymphocytes were present in the tumor sample to establish a reliable profile. Immunostaining for p16 and p53 was performed on paraffin-embedded or frozen sections of tumor material, and the staining result is indicated. HPV DNA detection was performed on all tumors by GP5+/6+ PCR, and the HPV type and viral load were determined for HPV DNA–positive tumors.