

Supplementary Tables

Associations between skin rash, treatment outcome, and single nucleotide polymorphisms in head and neck cancer patients receiving the EGFR-inhibitor zalutumumab: Results from the DAHANCA 19 trial

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Supplementary Table 1. SNPs with rs ID and position, minor allele frequency in study (MAF) and from 1000 Genome Project EUR phase 3 (MAF 1000), and test for Hardy-Weinberg equilibrium (HWE) with p-value from Pearson chi2 test.

SNP	Gene	Assumed related to	Chromosome	Cytogenetic band	Reference sequence	Position	Number of patients	Major allele	Minor allele	MAF	MAF 1000	HWE p-value
rs2227983	EGFR	EGFR signaling	7	p11.2	NC_000007.14	55,161,560	293	G	A	0.23	0.28	0.88
rs2293347	EGFR	EGFR signaling	7	p11.2	NC_000007.14	55,201,224	289	C	T	0.11	0.11	0.66
rs4444903	EGF	EGFR signaling	4	q25	NC_000004.12	109,912,952	294	A	G	0.42	0.39	0.48
rs13104811	Near AREG	EGFR signaling	4	q13.3	NC_000004.12	74,529,592	292	A	G	0.41	0.42	0.52
rs9996584	Near AREG	EGFR signaling	4	q13.3	NC_000004.12	74,556,240	293	G	A	0.36	0.38	0.73
rs11942466	Near AREG	EGFR signaling	4	q13.3	NC_000004.12	74,556,360	222	C	A	0.34	0.31	0.69
rs1801274	FCGR2A	ADCC**	1	q23	NC_000001.11	161,509,952	294	G	A	0.49	0.49	0.10
rs396991	FCGR3A	ADCC**	1	q23	NC_000001.11	161,544,752	294	A	C	0.28	n.a.*	0.19
rs9344	CCND1	EGFR signaling	11	q13.3	NC_000011.10	69,648,144	294	G	A	0.41	0.50	0.50

* n.a.: Not available

** ADCC: Antibody-Dependent Cell-mediated Cytotoxicity

Supplementary Table 2. Univariate Cox analysis with moderate to severe skin toxicity, patient, tumor, and treatment characteristics for endpoints loco-regional failure, disease specific survival, and overall survival.

	Loco-regional failure			Disease specific survival			Overall survival		
	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
Skin toxicity (Grade 3-4 vs 0-2)	0.99	(0.55-1.76)	0.96	0.63	(0.29-1.40)	0.26	0.40	(0.19-0.82)	0.013
p16 status* (Pos vs neg)	0.46	(0.29-0.73)	0.0011	0.25	(0.14-0.46)	<0.0001	0.26	(0.16-0.41)	0.013
T stage* (T3-4 vs T1-2)	1.63	(1.04-2.55)	0.035	2.74	(1.58-4.78)	<0.001	2.13	(1.41-3.22)	<0.001
Performance status* (1/2 vs 0)	2.27	(1.40-3.66)	<0.001	3.03	(1.73-5.31)	<0.001	3.09	(2.02-4.72)	<0.001
Smoking history (>10 packyears vs ≤10 packyears)	1.24	(0.73-2.10)	0.43	1.73	(0.87-3.44)	0.12	2.68	(1.46-4.92)	0.0015
Chemotherapy (≥5 series / <5 series / No chemo)	0.95	(0.73-1.23)	0.67	0.80	(0.59-1.09)	0.16	0.70	(0.55-0.88)	0.0027
Site (Oropharynx vs others)	0.67	(0.41-1.07)	0.092	0.35	(0.21-0.61)	<0.001	0.45	(0.29-0.68)	<0.001
Differentiation (Moderate or well vs poor)	1.03	(0.64-1.67)	0.89	1.15	(0.65-2.06)	0.63	1.66	(1.06-2.59)	0.026
Sex (Female vs male)	0.82	(0.45-1.49)	0.52	0.61	(0.27-1.35)	0.22	0.55	(0.29-1.02)	0.060
Age at randomization (Years)	1.00	(0.97-1.03)	0.88	0.98	(0.95-1.02)	0.32	1.01	(0.99-1.04)	0.37
N stage (N+ vs N0)	1.01	(0.56-1.80)	0.98	0.93	(0.47-1.86)	0.84	0.88	(0.53-1.48)	0.64
Disease stage (III-IV vs I-II)	1.04	(0.48-2.26)	0.92	0.79	(0.34-1.85)	0.59	0.92	(0.46-1.84)	0.82
Comorbidity (Yes vs no)	0.71	(0.26-1.94)	0.51	1.09	(0.27-4.49)	0.90	0.94	(0.34-2.55)	0.90

* Included in multivariate analysis

Supplementary Table 3. Univariate logistic regression of SNPs, patient, tumor, and treatment characteristics for endpoint moderate to severe skin toxicity.

	OR	95% CI	p-value
rs2227983	1.11	(0.67-1.83)	0.68
rs2293347	0.98	(0.49-1.96)	0.95
rs4444903	1.05	(0.69-1.61)	0.83
rs13104811	1.51	(0.98-2.32)	0.060
rs9996584	1.55	(0.99-2.43)	0.053
rs11942466	0.74	(0.44-1.25)	0.26
rs1801274	0.93	(0.59-1.47)	0.76
rs396991	0.97	(0.61-1.54)	0.89
rs9344	0.84	(0.54-1.30)	0.42
Performance status (1/2 vs 0)	0.20	(0.06-0.66)	0.0082
Comorbidity (Yes vs no)	0.27	(0.08-0.90)	0.033
Smoking history (>10 packyears vs <10 packyears)	0.41	(0.22-0.77)	0.0058
T stage (T3-4 vs T1-2)	0.45	(0.22-0.90)	0.024
N stage (N+ vs N0)	2.23	(0.84-5.92)	0.11
p16 status (Pos vs neg)	1.66	(0.88-3.15)	0.12
Site (Oropharynx vs others)	1.75	(0.83-3.68)	0.14
Disease stage (III-IV vs I-II)	2.70	(0.62-11.83)	0.19
Differentiation (Moderate or well vs poor)	0.91	(0.47-1.77)	0.78
Chemotherapy (At least 1 series vs no chemo)	1.08	(0.54-2.15)	0.84
Age at randomization (Years)	1.00	(0.96-1.04)	0.85
Sex (Female vs male)	0.96	(0.44-2.13)	0.93

Supplementary Table 4. Univariate Cox analysis with SNPs for endpoints loco-regional failure, disease specific survival, and overall survival.

SNP	Loco-regional failure			Disease specific survival			Overall survival		
	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
rs2227983	0.69	(0.46-1.04)	0.078	0.75	(0.46-1.22)	0.25	0.79	(0.55-1.13)	0.20
rs2293347	1.01	(0.61-1.66)	0.98	0.84	(0.44-1.63)	0.61	0.80	(0.49-1.33)	0.39
rs4444903	1.09	(0.80-1.49)	0.57	0.88	(0.60-1.30)	0.53	0.95	(0.71-1.27)	0.72
rs13104811	0.98	(0.71-1.34)	0.89	0.74	(0.50-1.11)	0.14	0.82	(0.61-1.10)	0.18
rs9996584	0.90	(0.65-1.26)	0.55	0.97	(0.65-1.46)	0.90	0.81	(0.59-1.10)	0.18
rs11942466	1.39	(0.98-1.99)	0.068	1.48	(0.96-2.29)	0.077	1.44	(1.02-2.03)	0.040
rs1801274	0.90	(0.65-1.26)	0.56	1.07	(0.71-1.59)	0.75	0.93	(0.68-1.26)	0.62
rs396991	0.92	(0.65-1.30)	0.63	0.99	(0.66-1.50)	0.97	0.96	(0.70-1.32)	0.79
rs9344	1.03	(0.75-1.42)	0.84	0.94	(0.64-1.39)	0.76	1.01	(0.75-1.36)	0.95