

## Vulvar Cancer in Germany: Increase in Incidence and Change in Tumour Biological Characteristics from 1974-2013

Supplementary Table 1: Characteristics of patients with invasive vulvar cancer (ICD-9: 184.1-184.4, ICD-10: C51) from Saarland diagnosed between 1989 and 2013 (analysis based on data with missing values).

	1989-1993		1994-1998		1999-2003		2004-2008		2009-2013	
	N	%	N	%	N	%	N	%	N	%
Overall	91		88		123		295		325	
Median age at diagnosis	72 yrs		76.5 yrs		75 yrs		70 yrs		69 yrs	
Lower and upper quartile of age at diagnosis	65; 83		67; 85		64; 83		58; 79		55; 79	
<= 54 years	10	11	3	9	12	10	63	21	76	23
55-74 years	41	45	8	34	48	39	121	41	134	41
>=75 years	40	44	30	57	63	51	111	38	115	35
Death certificate only notified	2	2	0	0	5	4	3	1	1	0
Tumour size available	50	55	57	65	87	71	244	83	259	80
T1 <sup>1</sup>	15	30	19	33	32	37	119	49	211	81
T2 <sup>1</sup>	22	44	27	47	47	54	112	46	37	14
T3/4 <sup>1</sup>	13	26	11	19	8	9	13	5	11	4
Clinical stage <sup>3</sup> available	40	44	30	34	53	43	111	38	139	43
Clinical stage I <sup>1,3</sup>	8	20	9	30	15	28	35	32	68	49
Clinical stage II <sup>1,3</sup>	2	5	3	10	14	26	21	19	6	4
Clinical stage III <sup>1,3</sup>	15	38	9	30	13	25	35	32	38	27
Clinical stage IV <sup>1,3</sup>	15	38	9	30	11	21	20	18	27	19
Microscopically verified	89	98	85	97	117	95	289	98	322	99
Squamous cell carcinoma <sup>1,2</sup>	73	82	67	79	87	74	258	89	286	89

Adenocarcinoma <sup>1,2</sup>	1	1	2	2	1	1	2	1	2	1
Malignant melanoma <sup>1,2</sup>	2	2	3	4	5	4	4	1	7	2
Basal cell carcinoma <sup>1,2</sup>	6	7	1	1	13	11	16	6	13	4
Paget disease <sup>1,2</sup>	2	2	4	5	4	3	7	2	7	2
Other/unspecified tumors <sup>1,2</sup>	5	6	6	7	7	6	2	1	7	2
Histopathologic grade available	65	71	66	75	89	72	257	87	280	86
G1 <sup>1</sup>	10	15	19	29	9	10	16	6	16	6
G2 <sup>1</sup>	40	62	35	53	53	60	168	65	186	66
G3/4 <sup>1</sup>	15	23	12	18	27	30	73	28	78	28

<sup>1</sup>Numbers of cases and percentages based on observations with available information. <sup>2</sup>Squamous cell carcinoma (ICD-O-3 codes [first 3/4 digits]: 805-808), basal cell carcinoma (809-811), adenocarcinoma (814-838), Paget disease (8542), malignant melanoma (872-879), and other/unspecified (remaining codes). <sup>3</sup>Clinical stage according to the International Federation of Gynecology and Obstetrics (FIGO) based on the sixth edition of the TNM [22].

Supplementary Table 2: Characteristics of patients with invasive vulvar cancer (ICD-9: 184.1-184.4, ICD-10: C51) from Saarland diagnosed between 1989 and 2013 (analysis based on 15 multiply imputed datasets).

	1989-1993		1994-1998		1999-2003		2004-2008		2009-2013		<i>P</i> value <sup>1</sup>
	N	%	N	%	N	%	N	%	N	%	
Overall	91		88		123		295		325		
Median age at diagnosis	72 yrs		76.5 yrs		75 yrs		70 yrs		69 yrs		0.007
Lower and upper quartile of age at diagnosis	65; 83		67; 85		64; 83		58; 79		55; 79		
<= 54 years	10	11	3	9	12	10	63	21	76	23	< 0.001
55-74 years	41	45	8	34	48	39	121	41	134	41	
>= 75 years	40	44	30	57	63	51	111	38	115	35	
T1 <sup>2</sup>	31	34	33	38	52	42	146	49	257	79	< 0.001
T2 <sup>2</sup>	40	44	38	43	55	44	127	43	46	14	
T3/4 <sup>2</sup>	20	22	17	20	17	14	22	8	22	7	
Clinical stage I <sup>2,4</sup>	28	31	28	32	49	40	113	38	170	52	0.001
Clinical stage II <sup>2,4</sup>	7	8	16	18	24	20	52	18	17	5	
Clinical stage III <sup>2,4</sup>	36	39	33	38	37	30	105	36	105	32	
Clinical stage IV <sup>2,4</sup>	20	21	11	12	13	11	25	8	33	10	
Squamous cell carcinoma <sup>2,3</sup>	74	81	69	78	90	73	261	88	287	88	0.002
Other invasive cancers <sup>2,3</sup>	17	19	19	22	33	27	34	12	38	12	
- Basal cell carcinoma <sup>2,3</sup>	6	7	1	1	13	11	17	6	13	4	
- Adenocarcinoma <sup>2,3</sup>	1	1	3	3	1	1	2	1	2	1	
- Paget disease <sup>2,3</sup>	2	2	4	5	4	3	7	2	7	2	
- Malignant melanoma <sup>2,3</sup>	2	2	3	3	5	4	4	1	7	2	
- Other/unspecified tumors <sup>2,3</sup>	6	7	9	10	10	8	4	1	9	3	
G1 <sup>2</sup>	15	16	27	31	10	8	24	8	24	7	< 0.001
G2 <sup>2</sup>	56	61	39	44	63	51	183	62	215	66	
G3/4 <sup>2</sup>	20	22	22	25	49	40	88	30	87	27	

<sup>1</sup>Mood's test (H0: no trend in median age at diagnosis over time) and chi-squared test (H0: no differences in the distribution of patient or tumour characteristics across different calendar periods; for testing whether the proportion of squamous cell carcinoma changed over time, all other invasive cancers were combined). <sup>2</sup>Rounded numbers of cases and percentages based on 15 multiply imputed datasets. <sup>3</sup>Squamous cell carcinoma (ICD-O-3 codes [first 3/4 digits]: 805-808), basal cell carcinoma (809-811), adenocarcinoma (814-838), Paget disease (8542), malignant melanoma (872-879), and other/unspecified (remaining codes). <sup>4</sup> Clinical stage according to the International Federation of Gynecology and Obstetrics (FIGO) based on the sixth edition of the TNM [22].

Supplementary Table 3: Truncated age-standardised incidence rates of invasive vulvar cancer (ICD-9: 184.1-184.4, ICD-10: C51) according to tumour size, clinical stage, tumour morphology and histopathologic grade in Saarland between 1989 and 2013 and distribution of tumour characteristics of patients diagnosed in 2009-13 across age groups

	Age <= 54 years							Age 55-74 years							Age >= 75 years							P value <sup>1</sup>
	1989-1993	1994-1998	1999-2003	2004-2008	2009-2013			1989-1993	1994-1998	1999-2003	2004-2008	2009-2013			1989-1993	1994-1998	1999-2003	2004-2008	2009-2013			
	N	N	N	N	N			N	N	N	N	N			N	N	N	N	N			
Overall	10	8	12	63	76			41	30	48	121	134			40	50	63	111	115			
	TASR	TASR	TASR	TASR	TASR	N	%	TASR	TASR	TASR	TASR	TASR	N	%	TASR	TASR	TASR	TASR	TASR	N	%	
Overall	0.5	0.4	0.6	2.8	3.8			5.9	4.0	6.9	17.0	19.7			16.0	19.0	21.3	35.6	34.0			
Crude rate <sup>2</sup>	0.5	0.4	0.7	3.7	4.8			6.3	4.3	7.3	18.5	20.1			15.7	19.6	21.6	35.7	34.5			
T1 <sup>3</sup>	0.5	0.1	0.3	2.0	3.6	70	92	1.8	1.4	3.3	9.6	16.3	109	82	3.3	8.0	7.3	11.1	23.0	78	68	0.008
T2 <sup>3</sup>	0.0	0.2	0.2	0.6	0.2	4	6	2.9	1.8	2.9	6.5	2.7	19	14	8.4	7.8	10.2	21.0	7.0	23	20	
T3/4 <sup>3</sup>	0.0	0.1	0.0	0.2	0.0	1	2	1.2	0.8	0.6	0.9	0.7	6	4	4.3	3.2	3.8	3.4	4.1	14	12	
Clinical stage I <sup>3</sup>	0.4	0.1	0.3	1.4	2.6	50	66	1.8	1.3	3.2	7.5	10.6	70	52	3.2	6.6	7.0	8.8	14.9	50	44	
Clinical stage II <sup>3</sup>	0.0	0.2	0.0	0.1	0.0	1	1	0.7	1.0	1.6	2.9	0.9	7	5	1.3	1.8	4.4	9.5	2.8	9	8	0.141
Clinical stage III <sup>3</sup>	0.1	0.1	0.1	1.0	1.1	23	31	2.5	1.3	1.8	5.1	5.8	40	30	6.9	8.1	6.7	14.4	12.4	42	37	
Clinical stage IV <sup>3</sup>	0.0	0.1	0.1	0.2	0.1	2	3	1.0	0.4	0.3	1.6	2.3	17	13	4.6	2.6	3.2	2.9	4.0	13	12	
Squamous cell carcinoma <sup>3</sup>	0.3	0.2	0.4	2.4	3.4	67	88	5.1	3.3	4.9	15.8	18.2	124	92	13.2	15.5	16.0	30.3	29.0	97	84	0.375
Other invasive cancers <sup>3</sup>	0.2	0.2	0.1	0.3	0.5	9	12	0.7	0.7	1.9	1.1	1.4	10	8	2.8	3.6	5.3	5.2	5.0	18	16	
- Basal cell carcinoma <sup>3</sup>	0.0	0.0	0.0	0.2	0.1	2	3	0.4	0.0	1.0	0.2	0.6	4	3	1.1	0.4	2.0	3.1	1.9	7	6	
- Adenocarcinoma <sup>3</sup>	0.0	0.0	0.0	0.0	0.0	0	0	0.1	0.0	0.0	0.2	0.0	0	0	0.0	0.9	0.3	0.0	0.5	2	2	
- Paget disease <sup>3</sup>	0.1	0.0	0.0	0.0	0.1	2	3	0.0	0.2	0.1	0.4	0.5	3	2	0.0	0.7	1.0	1.2	0.6	2	2	1.000
- Malignant melanoma <sup>3</sup>	0.0	0.0	0.1	0.1	0.2	3	4	0.1	0.2	0.1	0.1	0.0	9	0	0.5	0.3	0.4	0.3	1.0	4	4	
- Other/unspecified <sup>3</sup>	0.1	0.2	0.0	0.0	0.1	2	3	0.1	0.3	0.7	0.2	0.3	3	2	1.3	1.3	1.6	0.6	1.0	3	3	
G1 <sup>3</sup>	0.0	0.1	0.1	0.3	0.2	4	5	1.4	1.2	0.4	0.9	1.2	8	6	2.4	6.7	1.9	3.2	3.4	12	10	
G2 <sup>3</sup>	0.4	0.2	0.2	1.7	2.7	52	68	2.9	2.2	3.3	10.7	14.0	93	69	10.5	7.4	12.2	21.5	20.7	70	61	
G3/4 <sup>3</sup>	0.1	0.1	0.3	0.8	1.0	21	27	1.7	0.7	3.2	5.3	4.5	33	25	3.2	5.0	7.2	10.9	9.9	33	29	

TASR: truncated age-standardised rate. <sup>1</sup>Chi-squared test for homogeneity (H0: no differences in the distribution of tumour characteristics between patients aged  $\leq 54$ , 55-74, and  $\geq 75$  years in 2009-13; for testing whether the proportion of squamous cell carcinoma changed across age groups, all other invasive cancers were combined. <sup>2</sup>No adjustment for age. <sup>3</sup>TASRs, rounded numbers of cases, and percentages based on 15 multiply imputed datasets. <sup>4</sup>Clinical stage according to the International Federation of Gynecology and Obstetrics (FIGO) based on the sixth edition of the TNM [22].