RARE TUMOURS OF THE FEMALE GENITAL SYSTEM

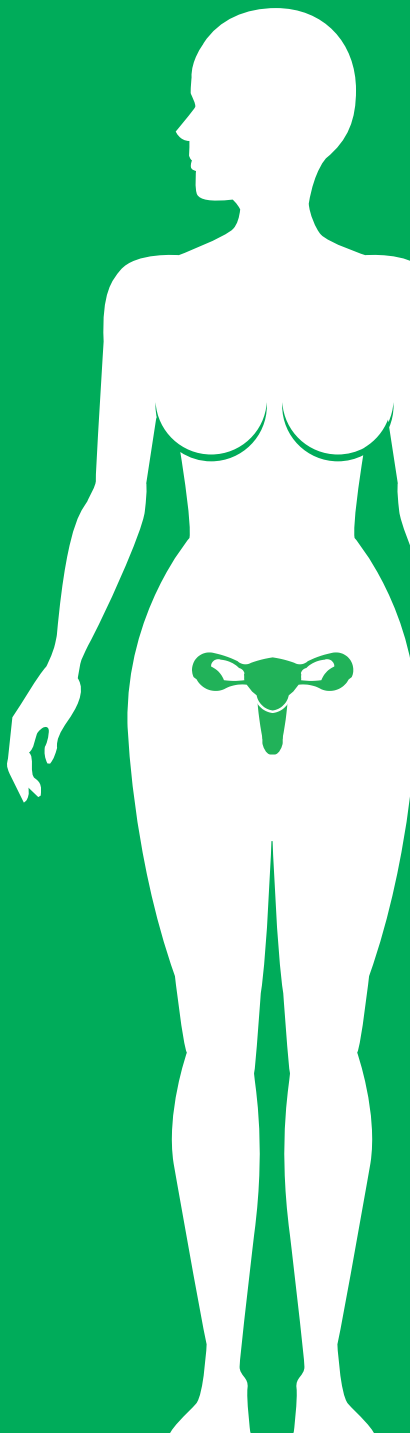
17%
OF FEMALE GENITAL SYSTEM TUMOURS ARE RARE

INCIDENCE

11 970
ESTIMATED NEW CASES
ITALY, 2015

3 093	RARE EPITHELIAL TUMOURS OF BREAST	6
553	RARE EPITHELIAL TUMOURS OF CORPUS UTERI	7
2 499	EPITHELIAL TUMOURS OF CERVIX UTERI	90
4 283	EPITHELIAL TUMOURS OF OVARY AND FALLOPPIAN TUBE	65
115	NON EPITHELIAL TUMOURS OF OVARY	2
1 414	EPITHELIAL TUMOURS OF VULVA AND VAGINA	95
12	TROPHOBLASTIC TUMOURS OF PLACENTA	82
246	EPITHELIAL TUMOURS OF MALE BREAST	100

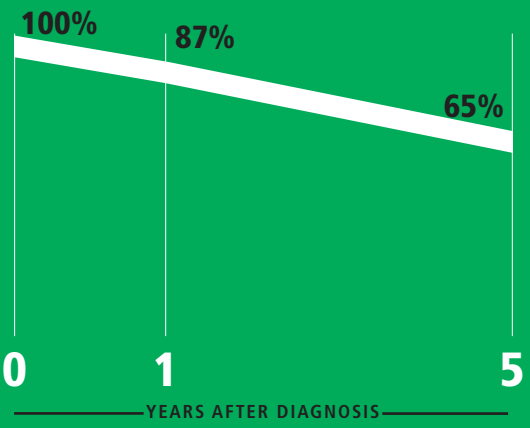
% **OF RARE TUMOURS OUT OF ALL TUMOURS IN EACH SITE**



PREVALENCE

154 397
ESTIMATED PREVALENT CASES
ITALY, 2010

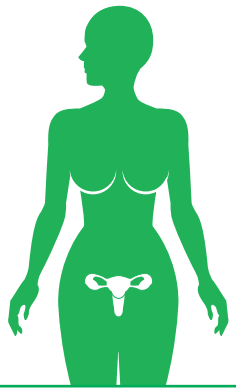
SURVIVAL



SOURCE: AIRTUM. ITALIAN CANCER FIGURES–REPORT 2015

RARE TUMOURS OF THE FEMALE GENITAL SYSTEM

INCIDENCE

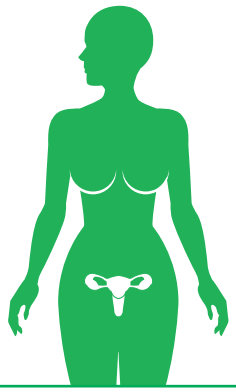


RARE TUMOURS OF THE FEMALE GENITAL SYSTEM. Crude incidence (rate per 100,000/year) and 95% confidence interval (95% CI), observed cases and proportion of rare cancers on all (common + rare) cancers by site. Rates with 95% CI by sex and age. Estimated new cases at 2015 in Italy.

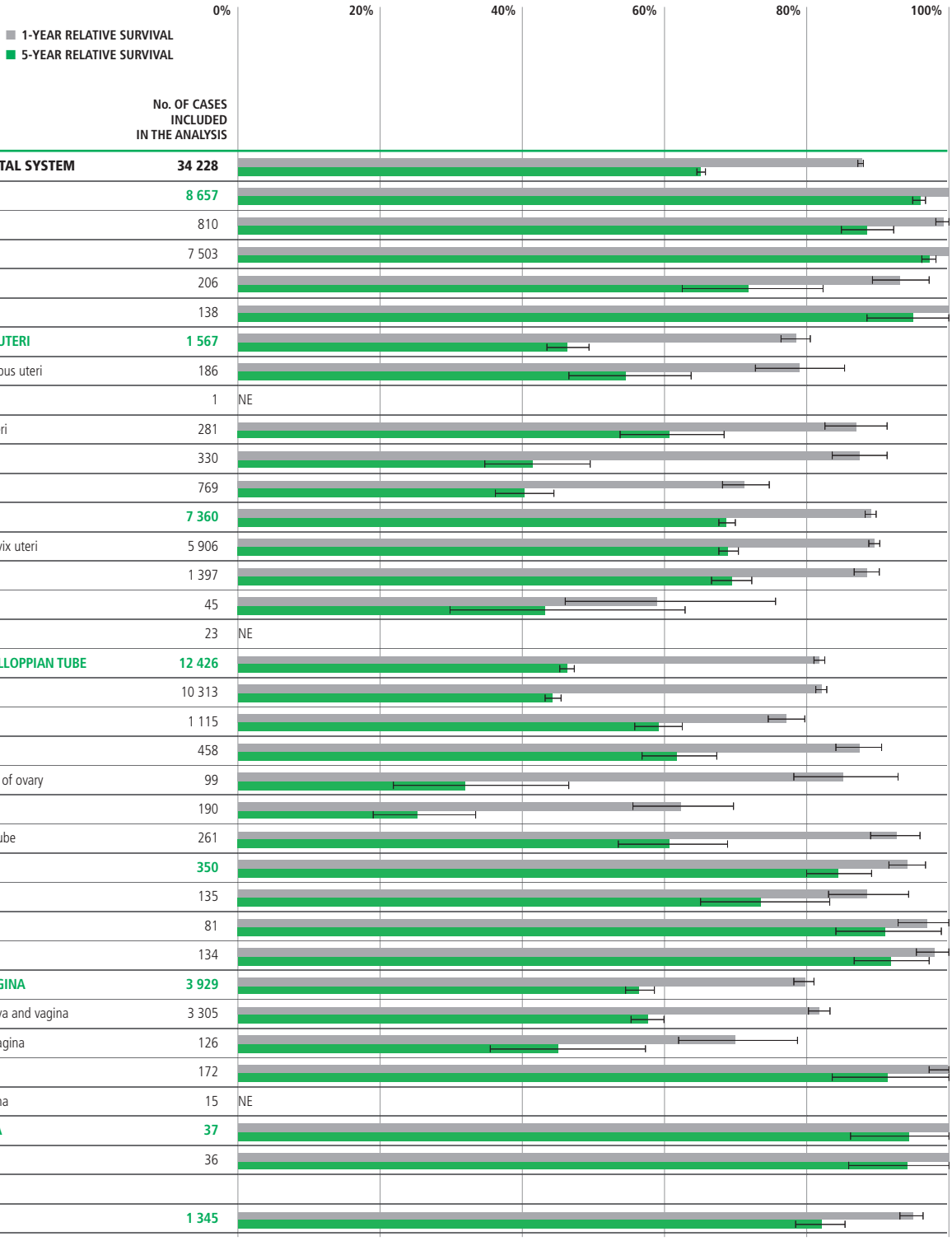
	AIRTUM POOL (period of diagnosis 2000-2010)														ITALY
					SEX				AGE						
					MALE		FEMALE		0-54 yrs		55-64 yrs		65+ yrs		
	RATE	95% CI	OBSERVED CASES (No.)	RARE CANCERS BY SITE (%)	RATE	95% CI	RATE	95% CI	RATE	95% CI	RATE	95% CI	RATE	95% CI	ESTIMATED NEW CASES 2015
RARE TUMOURS OF THE FEMALE GENITAL SYSTEM	**18.55**	**18.37-18.73**	**41 141**	**17%**	**0.08**	**0.07-0.10**	**35.86**	**35.52-36.21**	**8.12**	**7.98-8.27**	**30.77**	**30.12-31.44**	**46.70**	**46.06-47.34**	**11 970**
RARE EPITHELIAL TUMOURS OF BREAST	**4.75**	**4.65-4.84**	**10 522**	**6%**	**0.08**	**0.06-0.10**	**9.12**	**8.94-9.29**	**1.94**	**1.87-2.01**	**7.77**	**7.45-8.11**	**12.47**	**12.14-12.80**	**3 093**
Mammary Paget's disease of breast	0.43	0.41-0.46	963		0.01	0.01-0.02	0.83	0.78-0.88	0.16	0.14-0.18	0.72	0.63-0.83	1.21	1.11-1.32	283
Special types of adenocarcinoma of breast	4.12	4.04-4.21	9 138		0.06	0.05-0.08	7.92	7.76-8.09	1.70	1.64-1.77	6.75	6.44-7.06	10.77	10.47-11.09	2 687
Metaplastic carcinoma of breast	0.12	0.10-0.13	256		0.00	0.00-0.01	0.22	0.20-0.25	0.05	0.04-0.06	0.17	0.12-0.23	0.30	0.25-0.36	75
Salivary gland type tumours of breast	0.07	0.06-0.09	165		0.00	0.00-0.01	0.14	0.12-0.17	0.03	0.02-0.04	0.14	0.10-0.19	0.18	0.14-0.22	48
RARE EPITHELIAL TUMOURS OF CORPUS UTERI	**0.86**	**0.82-0.90**	**1 907**	**7%**			**1.67**	**1.59-1.74**	**0.11**	**0.10-0.13**	**1.65**	**1.50-1.81**	**2.93**	**2.77-3.10**	**553**
Squamous cell carcinoma with variants of corpus uteri	0.10	0.09-0.11	222				0.19	0.17-0.22	0.03	0.02-0.04	0.22	0.16-0.28	0.27	0.23-0.33	65
Adenoid cystic carcinoma of corpus uteri	<0.01	0.00-0.01	1				NE	–	NE	–	NE	–	NE	–	0
Clear cell adenocarcinoma, NOS of corpus uteri	0.15	0.13-0.16	327				0.29	0.26-0.32	0.02	0.02-0.03	0.23	0.18-0.30	0.51	0.45-0.59	94
Serous (papillary) carcinoma of corpus uteri	0.20	0.18-0.22	447				0.39	0.36-0.43	0.01	0.01-0.02	0.43	0.35-0.51	0.72	0.64-0.80	129
Mullerian mixed tumours of corpus uteri	0.41	0.38-0.44	910				0.79	0.74-0.85	0.05	0.04-0.06	0.77	0.67-0.89	1.42	1.31-1.54	264
EPITHELIAL TUMOURS OF CERVIX UTERI	**3.94**	**3.85-4.02**	**8 726**	**90%**			**7.62**	**7.46-7.78**	**2.80**	**2.72-2.89**	**5.88**	**5.59-6.17**	**6.61**	**6.37-6.85**	**2 499**
Squamous cell carcinoma with variants of cervix uteri	3.13	3.05-3.20	6 932				6.06	5.91-6.20	2.24	2.16-2.32	4.68	4.42-4.94	5.20	4.99-5.42	1 987
Adenocarcinoma with variants of cervix uteri	0.78	0.74-0.81	1 721				1.50	1.43-1.58	0.55	0.51-0.59	1.17	1.04-1.30	1.31	1.20-1.42	491
Undifferentiated carcinoma of cervix uteri	0.02	0.02-0.03	47				0.04	0.03-0.05	0.01	0.01-0.02	0.03	0.01-0.06	0.05	0.03-0.08	14
Mullerian mixed tumours of cervix uteri	0.01	0.01-0.02	26				0.02	0.01-0.03	<0.01	0.00-0.01	<0.01	0.00-0.02	0.05	0.03-0.07	8
EPITHELIAL TUMOURS OF OVARY AND FALLOPPIAN TUBE	**6.68**	**6.58-6.79**	**14 819**	**65%**			**12.94**	**12.74-13.15**	**2.78**	**2.69-2.86**	**13.28**	**12.85-13.72**	**15.97**	**15.60-16.35**	**4 283**
Adenocarcinoma with variants of ovary	5.53	5.43-5.63	12 261				10.71	10.52-10.90	2.25	2.17-2.32	11.11	10.72-11.52	13.30	12.96-13.65	3 550
Mucinous adenocarcinoma of ovary	0.60	0.57-0.63	1 326				1.16	1.10-1.22	0.31	0.28-0.34	0.94	0.83-1.07	1.37	1.26-1.48	380
Clear cell adenocarcinoma of ovary	0.25	0.23-0.28	565				0.49	0.45-0.54	0.14	0.13-0.16	0.61	0.52-0.71	0.41	0.36-0.48	163
Primary peritoneal serous/papillary carcinoma of ovary	0.05	0.04-0.06	115				0.10	0.08-0.12	0.02	0.01-0.02	0.08	0.05-0.13	0.16	0.13-0.20	33
Mullerian mixed tumours of ovary	0.10	0.09-0.12	231				0.20	0.18-0.23	0.02	0.01-0.03	0.23	0.18-0.30	0.32	0.27-0.38	66
Adenocarcinoma with variants of falloppian tube	0.14	0.13-0.16	321				0.28	0.25-0.31	0.04	0.03-0.05	0.30	0.24-0.37	0.40	0.35-0.47	91
NON EPITHELIAL TUMOURS OF OVARY	**0.19**	**0.17-0.21**	**424**	**2%**			**0.37**	**0.34-0.41**	**0.21**	**0.19-0.24**	**0.17**	**0.12-0.22**	**0.14**	**0.11-0.18**	**115**
Sex cord tumours of ovary	0.07	0.06-0.08	155				0.14	0.11-0.16	0.05	0.04-0.06	0.14	0.10-0.19	0.10	0.07-0.14	45
Malignant/Immature teratomas of ovary	0.05	0.04-0.05	100				0.09	0.07-0.11	0.06	0.05-0.07	0.01	0.00-0.04	0.02	0.01-0.04	26
Germ cell tumours of ovary	0.08	0.07-0.09	169				0.15	0.13-0.17	0.11	0.09-0.12	0.01	0.00-0.03	0.01	0.01-0.03	44
EPITHELIAL TUMOURS OF VULVA AND VAGINA	**2.12**	**2.06-2.18**	**4 697**	**95%**			**4.10**	**3.99-4.22**	**0.25**	**0.22-0.27**	**2.03**	**1.86-2.20**	**8.59**	**8.31-8.86**	**1 414**
Squamous cell carcinoma with variants of vulva and vagina	1.77	1.71-1.82	3 921				3.43	3.32-3.53	0.19	0.17-0.22	1.63	1.48-1.79	7.24	6.99-7.50	1 176
Adenocarcinoma with variants of vulva and vagina	0.06	0.05-0.08	142				0.12	0.10-0.15	0.02	0.01-0.03	0.08	0.05-0.13	0.21	0.17-0.25	42
Paget's disease of vulva and vagina	0.09	0.08-0.10	202				0.18	0.15-0.20	0.01	0.01-0.02	0.15	0.10-0.20	0.33	0.27-0.38	58
Undifferentiated carcinoma of vulva and vagina	0.01	0.00-0.01	16				0.01	0.01-0.02	<0.01	0.00-0.00	0.01	0.00-0.03	0.03	0.02-0.05	5
TROPHOBLASTIC TUMOURS OF PLACENTA	**0.02**	**0.02-0.03**	**46**	**82%**			**0.04**	**0.03-0.05**	**0.03**	**0.02-0.04**	**<0.01**	**0.00-0.02**	**<0.01**	**0.00-0.01**	**12**
Choriocarcinoma of placenta	0.02	0.01-0.03	45				0.04	0.03-0.05	0.03	0.02-0.04	<0.01	0.00-0.02	<0.01	0.00-0.01	12
EPITHELIAL TUMOURS OF MALE BREAST			**1 604**	**100%**	**1.50**	**1.42-1.57**			**0.31**	**0.27-0.35**	**2.63**	**2.36-2.93**	**5.65**	**5.31-6.00**	**246**

NE: not estimable because 15 or less incident cases were observed **NOS:** not otherwise specified

SURVIVAL



RARE TUMOURS OF THE FEMALE GENITAL SYSTEM. One and 5-year relative survival. Error bars are 95% confidence interval. Cohort approach (complete analysis), period of diagnosis 2000-2008.

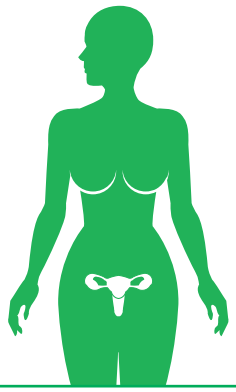


	No. OF CASES INCLUDED IN THE ANALYSIS
RARE TUMOURS OF THE FEMALE GENITAL SYSTEM	**34 228**
RARE EPITHELIAL TUMOURS OF BREAST	**8 657**
Mammary Paget's disease of breast	810
Special types of adenocarcinoma of breast	7 503
Metaplastic carcinoma of breast	206
Salivary gland type tumours of breast	138
RARE EPITHELIAL TUMOURS OF CORPUS UTERI	**1 567**
Squamous cell carcinoma with variants of corpus uteri	186
Adenoid cystic carcinoma of corpus uteri	1
Clear cell adenocarcinoma, NOS of corpus uteri	281
Serous (papillary) carcinoma of corpus uteri	330
Mullerian mixed tumours of corpus uteri	769
EPITHELIAL TUMOURS OF CERVIX UTERI	**7 360**
Squamous cell carcinoma with variants of cervix uteri	5 906
Adenocarcinoma with variants of cervix uteri	1 397
Undifferentiated carcinoma of cervix uteri	45
Mullerian mixed tumours of cervix uteri	23
EPITHELIAL TUMOURS OF OVARY AND FALLOPPIAN TUBE	**12 426**
Adenocarcinoma with variants of ovary	10 313
Mucinous adenocarcinoma of ovary	1 115
Clear cell adenocarcinoma of ovary	458
Primary peritoneal serous/papillary carcinoma of ovary	99
Mullerian mixed tumours of ovary	190
Adenocarcinoma with variants of falloppian tube	261
NON EPITHELIAL TUMOURS OF OVARY	**350**
Sex cord tumours of ovary	135
Malignant/Immature teratomas of ovary	81
Germ cell tumours of ovary	134
EPITHELIAL TUMOURS OF VULVA AND VAGINA	**3 929**
Squamous cell carcinoma with variants of vulva and vagina	3 305
Adenocarcinoma with variants of vulva and vagina	126
Paget's disease of vulva and vagina	172
Undifferentiated carcinoma of vulva and vagina	15
TROPHOBLASTIC TUMOURS OF PLACENTA	**37**
Choriocarcinoma of placenta	36
EPITHELIAL TUMOURS OF MALE BREAST	**1 345**

NE

NE: not estimable because 30 or less incident cases were observed **NOS:** not otherwise specified

PREVALENCE



RARE TUMOURS OF THE FEMALE GENITAL SYSTEM. Observed prevalence (proportion per 100,00 and 95% confidence interval - 95% CI) by duration (≤2, 2-5, ≤15 years) prior to prevalence date (1st January 2007), and complete prevalence. Estimated prevalent cases in 2010 in Italy.

	AIRTUM POOL								ITALY
	OBSERVED PREVALENCE BY DURATION						COMPLETE PREVALENCE		
	≤2 YEARS		2-5 YEARS		≤15 YEARS				ESTIMATED PREVALENT CASES 2010
	PROPORTION	95% CI	PROPORTION	95% CI	PROPORTION	95% CI	PROPORTION	95% CI	
RARE TUMOURS OF THE FEMALE GENITAL SYSTEM	**34.26**	**33.04-35.51**	**39.74**	**38.42-41.08**	**161.23**	**158.58-163.92**	**264.54**	**259.45-269.62**	**154 397**
RARE EPITHELIAL TUMOURS OF BREAST	**10.58**	**9.90-11.28**	**14.46**	**13.67-15.28**	**58.22**	**56.63-59.84**	**80.24**	**77.60-82.89**	**46 858**
Mammary Paget's disease of breast	0.94	0.75-1.17	1.25	1.03-1.51	4.78	4.33-5.26	6.81	6.14-7.49	3 961
Special types of adenocarcinoma of breast	9.29	8.66-9.95	12.84	12.10-13.62	51.48	49.98-53.01	70.99	68.46-73.52	41 472
Metaplastic carcinoma of breast	0.23	0.14-0.35	0.20	0.11-0.31	0.74	0.57-0.95	1.02	0.76-1.27	595
Salivary gland type tumours of breast	0.11	0.06-0.21	0.17	0.10-0.28	1.22	1.00-1.47	1.42	1.14-1.71	830
RARE EPITHELIAL TUMOURS OF CORPUS UTERI	**1.63**	**1.37-1.92**	**1.25**	**1.03-1.51**	**4.92**	**4.47-5.41**	**6.45**	**5.78-7.12**	**3 742**
Squamous cell carcinoma with variants of corpus uteri	0.13	0.06-0.23	0.18	0.11-0.30	0.67	0.51-0.86	1.12	0.82-1.42	643
Adenoid cystic carcinoma of corpus uteri	NE	–	NE	–	0.01	0.00-0.06	0.08	0.00-0.33	46
Clear cell adenocarcinoma, NOS of corpus uteri	0.36	0.24-0.51	0.30	0.20-0.44	1.11	0.90-1.36	1.38	1.10-1.65	821
Serous (papillary) carcinoma of corpus uteri	0.31	0.20-0.45	0.29	0.19-0.42	0.77	0.59-0.97	0.80	0.61-1.00	460
Mullerian mixed tumours of corpus uteri	0.84	0.65-1.05	0.48	0.35-0.65	2.36	2.05-2.71	3.07	2.64-3.50	1 772
EPITHELIAL TUMOURS OF CERVIX UTERI	**6.98**	**6.43-7.55**	**8.59**	**7.99-9.23**	**40.14**	**38.82-41.50**	**92.32**	**88.80-95.84**	**53 952**
Squamous cell carcinoma with variants of cervix uteri	5.52	5.04-6.04	7.16	6.61-7.74	33.33	32.13-34.57	76.94	73.72-80.16	44 975
Adenocarcinoma with variants of cervix uteri	1.43	1.19-1.71	1.43	1.19-1.71	6.77	6.24-7.34	15.12	13.71-16.53	8 819
Undifferentiated carcinoma of cervix uteri	NE	–	0.02	0.00-0.08	0.07	0.03-0.16	0.20	0.04-0.37	117
Mullerian mixed tumours of cervix uteri	0.02	0.00-0.08	0.01	0.00-0.06	0.05	0.01-0.12	0.06	0.00-0.12	41
EPITHELIAL TUMOURS OF OVARY AND FALLOPPIAN TUBE	**11.56**	**10.86-12.30**	**11.39**	**10.69-12.12**	**42.61**	**41.25-44.01**	**61.30**	**59.24-63.36**	**35 633**
Adenocarcinoma with variants of ovary	9.50	8.86-10.17	9.20	8.58-9.86	33.32	32.12-34.56	45.94	44.21-47.66	26 690
Mucinous adenocarcinoma of ovary	1.08	0.87-1.32	1.09	0.88-1.33	5.68	5.19-6.21	10.56	9.57-11.55	6 157
Clear cell adenocarcinoma of ovary	0.39	0.27-0.55	0.54	0.40-0.72	1.94	1.66-2.25	2.59	2.19-2.99	1 497
Primary peritoneal serous/papillary carcinoma of ovary	0.11	0.06-0.21	0.13	0.06-0.23	0.26	0.17-0.40	0.27	0.16-0.38	159
Mullerian mixed tumours of ovary	0.17	0.10-0.28	0.16	0.09-0.27	0.42	0.30-0.58	0.62	0.41-0.82	357
Adenocarcinoma with variants of falloppian tube	0.31	0.20-0.45	0.28	0.18-0.41	0.99	0.79-1.22	1.34	1.05-1.62	774
NON EPITHELIAL TUMOURS OF OVARY	**0.44**	**0.31-0.60**	**0.45**	**0.32-0.61**	**2.38**	**2.06-2.72**	**5.04**	**4.31-5.77**	**2 970**
Sex cord tumours of ovary	0.21	0.12-0.33	0.17	0.10-0.28	0.95	0.76-1.18	1.32	1.03-1.61	787
Malignant/Immature teratomas of ovary	0.08	0.03-0.17	0.10	0.05-0.20	0.40	0.28-0.56	0.98	0.61-1.35	590
Germ cell tumours of ovary	0.15	0.08-0.25	0.17	0.10-0.28	1.02	0.82-1.26	2.74	1.92-3.56	1 595
EPITHELIAL TUMOURS OF VULVA AND VAGINA	**3.13**	**2.76-3.52**	**3.63**	**3.24-4.05**	**13.27**	**12.52-14.06**	**18.62**	**17.54-19.70**	**10 906**
Squamous cell carcinoma with variants of vulva and vagina	2.77	2.43-3.14	3.18	2.82-3.58	11.38	10.69-12.11	16.44	15.41-17.47	9 645
Adenocarcinoma with variants of vulva and vagina	0.05	0.01-0.12	0.09	0.04-0.18	0.41	0.28-0.57	0.56	0.37-0.74	329
Paget's disease of vulva and vagina	0.15	0.08-0.26	0.20	0.11-0.31	0.83	0.65-1.04	0.95	0.72-1.17	546
Undifferentiated carcinoma of vulva and vagina	NE	–	NE	–	0.01	0.00-0.06	0.01	0.00-0.04	8
TROPHOBLASTIC TUMOURS OF PLACENTA	**0.02**	**0.00-0.08**	**0.09**	**0.04-0.18**	**0.26**	**0.17-0.40**	**0.56**	**0.28-0.83**	**335**
Choriocarcinoma of placenta	0.02	0.00-0.08	0.09	0.04-0.18	0.26	0.17-0.40	0.56	0.28-0.83	335
EPITHELIAL TUMOURS OF MALE BREAST	**3.11**	**2.60-3.69**	**3.58**	**3.03-4.20**	**12.94**	**11.87-14.07**	**15.41**	**14.11-16.71**	**4 334**

NE: not estimable in observed prevalence if no cases were observed within ≤2, 2-5, ≤15 years prior to prevalence date, in complete prevalence if the 15-year prevalence is NE

NOS: not otherwise specified

This group includes heterogeneous invasive cancers with different behaviour and prognosis:

- **rare epithelial breast cancers of females** (mammary Paget's disease, special types of adenocarcinoma of breast, metaplastic carcinoma of breast, salivary gland type tumours of breast);
- **epithelial breast cancers of males** (all histotypes are rare, including ductal and lobular carcinomas);
- **rare epithelial tumours of corpus and cervix uteri** (squamous cell carcinoma of cervix and corpus uteri; Mullerian mixed tumour of cervix and corpus uteri; clear cell adenocarcinoma; NOS of corpus uteri; serous/papillary carcinoma of corpus uteri; adenoid cystic carcinoma of corpus uteri; adenocarcinoma with variants of cervix uteri and undifferentiated carcinoma of cervix uteri);
- **epithelial tumours of ovary and falloppian tubes** (adenocarcinoma with variants of ovary, mucinous adenocarcinoma of ovary, clear cell adenocarcinoma of ovary, primary peritoneal serous/papillary carcinoma of ovary, MMMT of ovary, and adenocarcinoma with variants of the fallopian tubes);
- **non epithelial tumours of ovary and falloppian tubes** (sex cord, germ cell tumours, and immature teratomas);
- **epithelial tumours of vulva and vagina** (squamous cell carcinoma with variants of vulva and vagina, adenocarcinoma with variants of vulva and vagina, and Paget's disease of vulva and vagina);
- **trophoblastic placenta tumours**.

With a number of 41,141 incident cases (in the period 2000-2010), rare cancers represent 17% of all female genital system cancers, corresponding to about 12,000 new cases per year in Italy (incidence table, p. 57). It must be noted that, as reported in the «Materials and methods» chapter (pp. 14-21), rates are provided for both sexes with the exception of male breast cancer. In any case, sex-specific incidence rates are provided in the incidence table.

RARE EPITHELIAL BREAST CANCERS

WHAT DO WE KNOW ABOUT THESE CANCERS?

Mammary Paget's disease (PD) occurs almost exclusively in women. The typical pathologic finding is represented by Paget cells within the epidermis of the nipple.[1]

Special types of adenocarcinoma of the breast are a mixture of different types (tubular, mucinous, medullary, papillary, secretory, glycogen-rich clear cell, lipid-rich and oncocytic carcinoma).

Metaplastic carcinoma of the breast: part or all of the carcinomatous epithelium is transformed into a nonglandular (metaplastic) growing tissue; these tumours are often clinically palpable, large, and appear well circumscribed. Metaplastic carcinomas are mainly negative for oestrogen and progesterone receptors and for HER2/neu overexpression.[2]

Salivary gland type tumour of the breast is a very rare histological type including adenoid cystic carcinoma, mucoepidermoid carcinoma, acinic cell carcinoma, and polymorphous low-grade adenocarcinoma; a high percentage of triple negative breast cancer is reported, too.

THE EPIDEMIOLOGICAL DATA IN ITALY

Incidence

Rare epithelial breast cancers (10,522 cases) account for 26% of rare cancers of the female genital system, but only 6% of breast cancer. Special types of adenocarcinoma are the most common (87%), followed by mammary PD (9%), metaplastic carcinoma (2%), and salivary gland type tumours (2%). Distribution of the different types is similar to that observed in the European data from RARECAREnet (www.rarecarenet.eu), except for special types of adenocarcinoma, showing a slightly higher rate in Italy than in Europe (4% vs. 3%, respectively). More than 50% (5,425) of cases involves subjects aged over 65 years, with the highest rate in the 80-84 age class (24.5 per 100,000, data not shown).

In males, all breast tumours are rare and have a sex-specific IR of 1.5 per 100,000. The age trend is similar to that observed for females (see table p. 57). Approximately 3,500 Italians were estimated to be diagnosed with a rare cancer of the breast in 2015; of these 250 were males.

Survival

Five-year relative survival (RS) for rare female breast cancer is relatively high and varies from 88% for mammary PD to 72% for metaplastic carcinoma (survival figure, p. 58). Lower prognosis of metaplastic carcinoma is due to more advanced stage at diagnosis and the high percentage of "triple negative" subtypes.[3] One-year RS is similar to 5-year RS except for mammary PD and metaplastic tumours. Rare epithelial cancers of the breast have a similar prognosis to the more common ductal and lobular invasive carcinomas of the breast (85% at 5 years in European RARECAREnet data). Prognosis is worse in males than in females, probably because of the different biological patterns in males compared to females.[4] This result highlights the need for new treatment protocols for these specific cancers.

Prevalence

Around 47,000 persons were estimated to be alive in 2010 with a past diagnosis of one of these rare epithelial tumours of the breast in Italy.

RARE EPITHELIAL TUMOURS OF CORPUS AND CERVIX UTERI

WHAT DO WE KNOW ABOUT THESE CANCERS?

Squamous cell carcinoma with variants of corpus and cervix uteri include different types of cancers (papillary squamous cell carcinoma, squamous cell carcinoma NOS, keratinizing and nonkeratinizing squamous cell carcinoma, spindle cell squamous cell carcinoma, lymphoepithelial carcinoma) and is more frequent in the cervix than in the corpus uteri. Based on histopathology, molecular profile and clinical course of endometrial cancers are divided into two categories.

Uterine clear-cell carcinoma (UCC) is a type II endometrial cancer (not hormone dependent and usually grade III endometrioid adenocarcinomas, papillary serous and clear cell carcinomas and carcinosarcomas, or malignant mixed Mullerian tumours) and it typically occurs in older patients, as it is not hormone dependent. These tumours are generally more aggressive and have a

worse prognosis than type I endometrial cancer (typically low-grade (I-II) adenocarcinomas that are usually oestrogen related, diagnosed early, and with a favourable prognosis) and usually display p53 mutations.[5]

Serous (papillary) carcinoma of corpus uteri (USC) is characterised by nipple-shaped structures (papillae) with fibrovascular cores, marked nuclear atypia, psammoma bodies, and cilia. It has been associated with women of African-American ethnicity, tamoxifen use, and BRCA gene mutations.[6] About 60% of USCs overexpress the HER2/neu protein, showing some benefits with trastuzumab (Herceptin) treatment.[7]

Malignant mixed Mullerian tumour (MMMT) of the uterine corpus and cervix is an extremely rare and aggressive malignancy with a dedifferentiated or metaplastic form containing both carcinomatous and sarcomatous components, affecting postmenopausal women. Risk factors for the development of MMMT are similar to those of endometrial carcinoma and include nulliparity, advanced age, obesity, exposure to exogenous estrogens, pelvic irradiation, and long-term use of tamoxifen.[4]

Adenocarcinoma of the cervix is a mixture of different cancer types (adenocarcinoma NOS, adenocarcinoma with squamous metaplasia, mucinous, clear cell, or endometrioid adenocarcinoma, serous cystadenocarcinoma, signet ring cell, mesonephroma, villous, intestinal type and mixed cell adenocarcinoma) showing an incidence increase over time, probably attributable to cervix screening implementation. The causal role of human papillomavirus (HPV) in all cancers of the uterine cervix has been firmly established both biologically and epidemiologically. The status of current tobacco smoking is associated with an increased risk of squamous cell adenocarcinoma but not of adenocarcinoma in the cervix. No differences between the two most common histological types of invasive cervical cancer with respect to the role of number of sexual partners, age at first intercourse, age at first birth, body mass index, or use of oral contraceptives were observed.[9]

THE EPIDEMIOLOGICAL DATA IN ITALY

Incidence

In the **cervix**, squamous carcinoma represents 79% of epithelial tumours, followed by adenocarcinoma (20%) (see table p. 57). The other histotypes are very rare. In the **corpus uteri**, MMMT are the most common (48%) followed by USC (23%), UCC (17%), and squamous cell carcinoma (12%). The other histotypes are very rare. The same distribution is reported in the European RARECAREnet data. Rare epithelial cancers of corpus uteri are typical of elderly, with the highest incidence rate in the 80-84 age class (3.6 per 100,000, data not shown). Epithelial cancers of cervix uteri show a bimodal distribution with two peaks: one in the perimenopausal age group 45-49 years (6.1 per 100,000, data not shown) and the other in the 80-84-year age group (8.1 per 100,000, data not shown). Approximately 3,000 Italians were estimated to be diagnosed with rare cancers of the uterus in 2015.

Survival

One-year and 5-year RS of cervix uteri cancer are 89% and 69%, respectively. These results are mainly due to squamous cell carcinoma and adenocarcinoma of cervix uteri (see figure p. 58). The RS of undifferentiated carcinomas is much lower at both 1 and 5 years after diagnosis: 59% and 43%, respectively (based on 45 cases). It is not possible to provide an RS of MMMT because of the few cases available for analysis. However, in RARECAREnet data, 5-year RS is 34%. The RS of corpus uteri cancer is 78% at 1 year, but goes down to 46% at 5 years. This pattern is constant for all histotypes. After 5 years from diagnosis the RS is highest for UCC (61%), followed by squamous cell carcinoma (54%), USC, and MMMT (40%) (see figure p. 58). The results are coherent with European RARECAREnet data. Adenoid cystic carcinoma of the corpus uteri is so rare that no data are available in Italy and Europe. The availability of improved genetic and/or pathological characterisation by specialized laboratories could improve the prognosis of these rare tumours, enabling the development of specific therapeutic protocols.

Prevalence

Around 54,000 persons were estimated to be alive in 2010 with a past diagnosis of epithelial tumours of the cervix (43% survived more than 15 years from diagnosis) and around 4,000 with a diagnosis of rare epithelial tumours of the corpus uteri (76% survived more than 15 years from diagnosis).

EPITHELIAL TUMOURS OF OVARY AN FALLOPPIAN TUBES AND NON EPITHELIAL TUMOURS OF OVARY

The list of rare cancers separate epithelial and non epithelial tumours. Thus, this group includes epithelial tumours of the ovary and fallopian tubes and non epithelial tumours of the ovary.

WHAT DO WE KNOW ABOUT THESE CANCERS?

Epithelial ovarian cancers (EOC) are a heterogeneous group of tumours. To explain this heterogeneity a new classification is used distinguishing type I and type II ovarian carcinoma. Type I includes low-grade carcinomas, frequently diagnosed in early stages, with indolent behaviour. Type II includes high-grade carcinomas, diagnosed in advanced stages, and characterised by genomic instability. Recent evidence suggests that the different histotypes of epithelial ovarian cancers originate from three different sites (fimbria, endometrial tissue, and tubal-mesothelium junction), while serous ovarian cancer originates from the fallopian tubes.[10] New promising molecular targeted drugs are bevacizumab (monoclonal antibody directed against VEGF) and PARP inhibitor.[11]

MMMT of the ovary is an exceedingly rare cancer, accounting for 1% to 3% of ovarian malignancies. These tumours are carcinosarcoma characterised by malignant epithelial and stromal elements. MMMTs are very aggressive tumours usually diagnosed at an older age and at advanced stages.[12] MMMT diagnosis is difficult; there are no useful biochemical markers and diagnostic imaging methods do not provide specific data.[13]

Sex cord tumours of the ovary include malignant granulosa cell tumour, Sertoli-Leydig cell tumour, poorly differentiated and malignant steroid cell tumour, which show areas with unequivocal gonadal stromal differentiation.[14]

Ovarian germ cell tumours (OGCT) include several types of cancer (dysgerminoma/seminoma, yolk sac tumour, mixed germ cell tumour, embryonal adenocarcinoma, choriocarcinoma, and

polyembryoma). Most OGCTs are benign, unilateral with the exception of dysgerminomas, are usually diagnosed at stage I, and are responsive to chemotherapy. Several reports suggest a genetic susceptibility.[15]

THE EPIDEMIOLOGICAL DATA IN ITALY

Incidence

The risk for **EOCs** increases with age: the highest incidence rate (IR) occurs in postmenopausal women, with 47% of all cases diagnosed in patients older than 65 years (data not shown). Adenocarcinoma of the ovary is the most common histotype, with 12,261 incident cases in the period 2000-2010, followed by mucinous adenocarcinoma, clear cell adenocarcinoma, and MMMT (see table p. 57). Primary peritoneal serous/papillary carcinoma of the ovary is very rare (115 cases in 11 years). The relative frequency of histological variants observed in the Italian database is similar to the one documented by RARECAREnet. Fallopian tube includes all rare cancers and it is rare per se.

Non EOCs typically affect young people, with a peak of incidence in the 15-19 age group (0.47 per 100,000 data not shown). OGCT represents the most frequent subtype (40%), although European RARECAREnet data showed a higher frequency of sex cord tumours of the ovary (50%) compared to OGCT. Around 4,500 Italians were estimated to be diagnosed with rare cancers of the ovary in 2015.

Survival

EOC 1- and 5-year RS is 82% and 46%. All epithelial tumours of the ovary have a poor prognosis, with a 5-year RS ranging from 62% for clear cell adenocarcinoma to 25% for MMMT. This is probably due to the fact that the majority of these tumours are aggressive and become symptomatic at advanced stage. The Italian database shows better RS for EOC than European RARECAREnet data (70% and 37% at 1 and 5 years, respectively).

Non EOC has better prognosis than EOC, probably attributable to young age and early-stage at diagnosis and to the fact that the majority of these tumours are germ cell tumours, which are among the most curable diseases (see figure p. 58).

Prevalence

Around 35,000 persons were estimated to be alive in 2010 with a past diagnosis of **EOC**; 30% survived more than 15 years from diagnosis. Most prevalent cases were adenocarcinomas, mainly because of their relatively higher incidence compared to the other histotypes.

Around 3,000 persons were estimated to be alive with a diagnosis of **Non EOC**; 53% survived more than 15 years from diagnosis, coherently with young age at diagnosis and prognosis (prevalence table, p. 59).

EPITHELIAL TUMOURS OF VULVA AND VAGINA

WHAT DO WE KNOW ABOUT THESE CANCERS?

Squamous cell carcinoma originates from epidermal squamous cells.

Vulvar adenocarcinoma most often originates from cells of the Bartholin glands, although it is often very difficult to identify the site of origin.[16]

Vaginal adenocarcinoma arises from the glandular (secretory) cells in the lining of the vagina. Clear cell adenocarcinoma is associated with in utero exposure to diethylstilbestrol (DES). The peak of incidence of DES-associated adenocarcinoma is at young ages (less than 30 years), otherwise these tumours occur primarily in post menopause. Human papillomavirus (HPV) infection in associated to development of vulvar and vaginal cancers.[17]

Paget's disease of vulva and vagina is an uncommon cancer characterised by a chronic eczema-like rash of the skin around the anogenital regions. It microscopically looks like mammary Paget's disease and is predominantly an intraepithelial lesion, even though it may be associated with an underlying invasive adenocarcinoma.[18]

THE EPIDEMIOLOGICAL DATA IN ITALY

Incidence

Vulvar and vaginal cancers most commonly occur in people over 65 years old, with adenocarcinomas occurring a decade earlier than squamous cancers (see table p. 57). Squamous cell carcinomas are the most common histotype in Italy (83%) and Europe (RARECAREnet database 85%). Paget's disease is typical of older people (>70 years of age) (data not shown). About 1,500 rare epithelial tumours of the vulva and vagina are estimated to occur during 2015 in Italy; few cases (4%) are Paget's disease (see table p. 57).

Survival

One- and 5-year RS is 79% and 56%, respectively. Adenocarcinoma has the worse outcomes (67% and 45% RS at 1 and 5 years, respectively) (see figure p. 58). The number of cases of undifferentiated carcinomas is too low to estimate survival; however, according to the RARECAREnet data, 5-year RS is 26% (based on 85 cases). Five-year RS of Paget's disease is very good (91%), most likely because it is not aggressive. Italian and European RARECAREnet data are the same.

Prevalence

In Italy, around 11,000 persons were estimated to be alive in 2010 with a past diagnosis of epithelial tumours of vulva and vagina, and 72% were still alive more than 15 years after diagnosis. The most prevalent were squamous cell carcinomas because of the relatively high incidence and survival (see table p. 59).

TROPHOBLASTIC TUMOURS OF PLACENTA

Trophoblastic tumours of placenta (TTP) are very rare. There were only 46 cases in 11 years (2000-2010) in Italy (see table p. 57). These tumours are highly curable malignancies arising in relation to pregnancy. Treatment of TTP is a success story in medical oncology. When treated by surgery alone, the cure rate is only 40%.[19] With the use of chemotherapeutic agents, outcome becomes excellent for more than 98% of women.[20] Survival in Italy is 94% (based on 34 cases), whereas according to RARECAREnet, which has a higher number of cases to base an estimate on, it is 89%.

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