Rete Oncologica Veneta
Ricerca, innovazione, assistenza

PDTA del carcinoma dell'Esofago e della Giunzione esofago-gastrica

Vanna Chiarion Sileni

Oncologia Melanoma ed Esofago
IOV-IRCCS, Padova
Vanna.chiarion@ioveneto.it

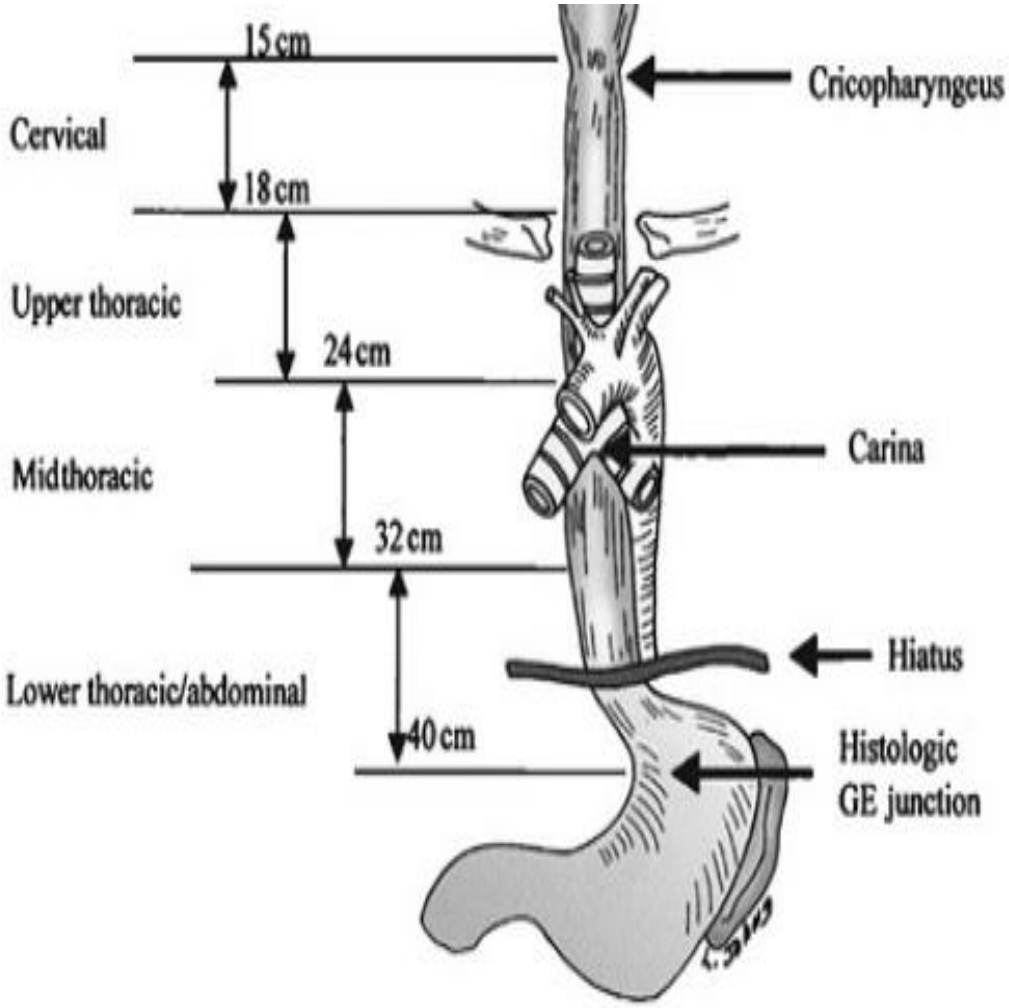
Esophageal Cancer

Cervical = cricoid cartilage to thoracic inlet (15–18 cm from the incisor).

Upper thoracic = thoracic inlet to tracheal bifurcation (18–24 cm).

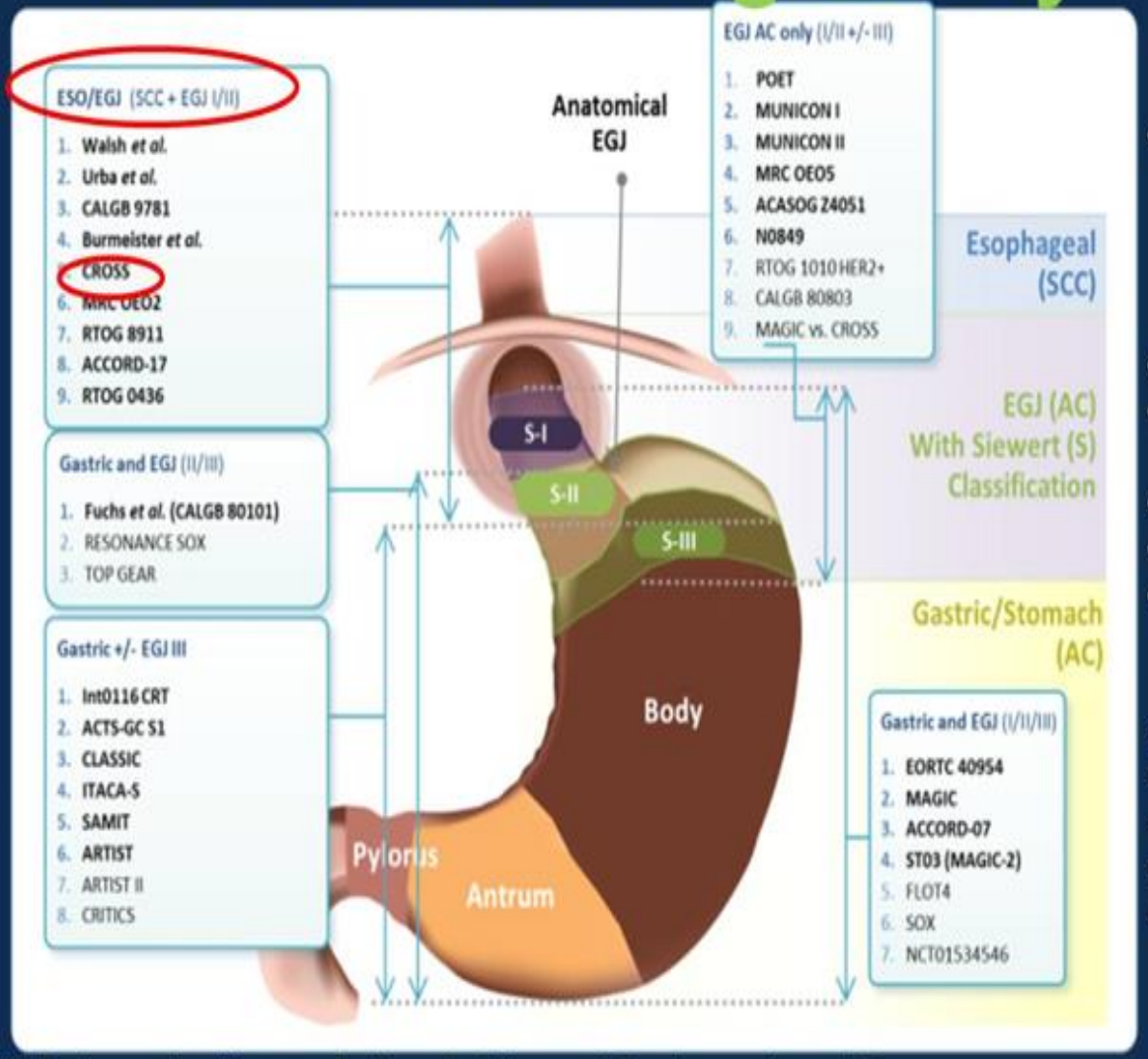
Midthoracic = tracheal bifurcation to just above the GE junction (24–32 cm).

Lower thoracic = GE junction (32–40 cm).



EGA: Heterogeneity

- Anatomy
  proximal/distal
- Etiology
- T,N-stage
- Size/Extent
- Histology
  SCC/AC
  intestinal/diffuse
- Grade
  Well/Mod/PD
  +/- signet rings
- Geography
  Ethnicity
  Treatment practice



- Staging
  - EUS
  - PET
  - Dx Lap and Wash
- D1 vs D2 lymph dissect
- Surgical Quality
- Dosing of Chemo/CRT
- Type of Chemo
- RT Quality
- Chemotherapy before
- Chemotherapy after
- Periop chemotherapy
- CRT before
- CRT after

Sehdev A, Catenacci DVT. Perioperative Therapy for Locally Advanced Gastroesophageal Cancer: Current Controversies and Consensus of Care. *J Hematol Oncol* 2013

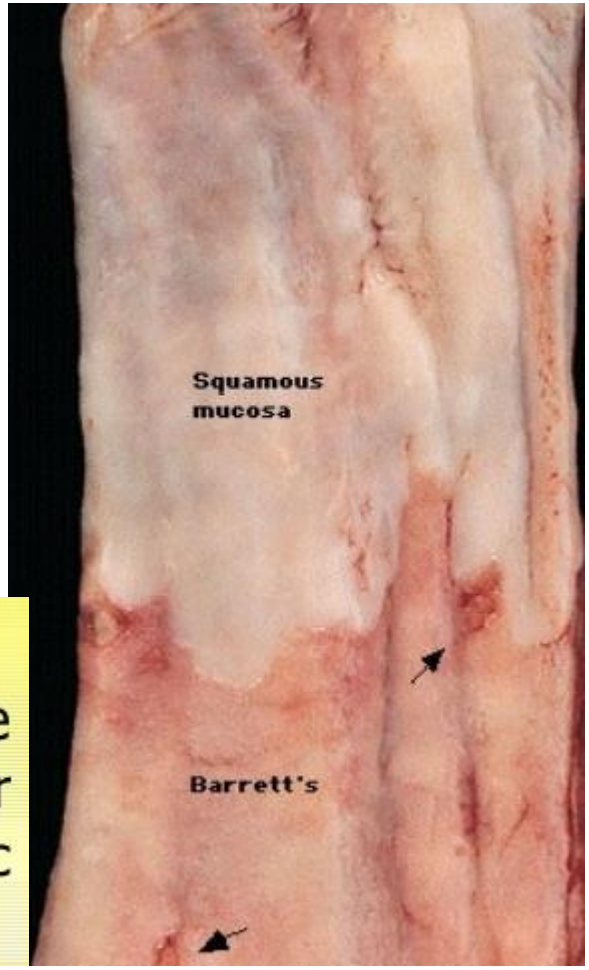
Risk Factors: Adenocarcinoma

Associated with **Barretts's esophagus**, **GERD** & **hiatal** hernia.

Obesity (3 to 4 fold risk)

Smoking (2 to 3 fold risk)

Increased esophageal acid exposure such as Zollinger-Ellison syndrome.



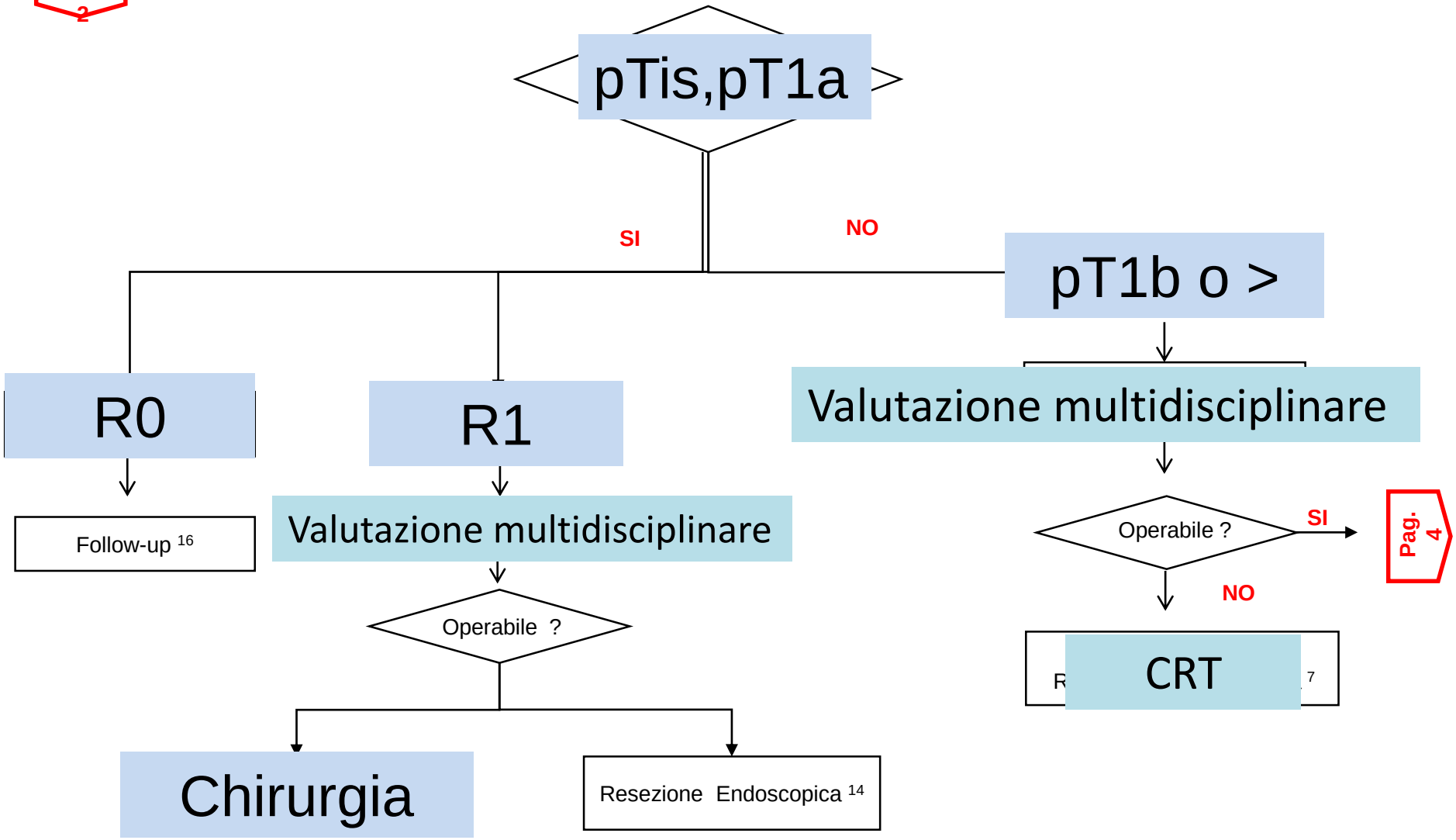
Barrett's esophagus is a metaplasia of the esophageal epithelial lining. The squamous epithelium is replaced by columnar epithelium,with 0.5% annual rate of neoplastic transformation.

Pattern of spread

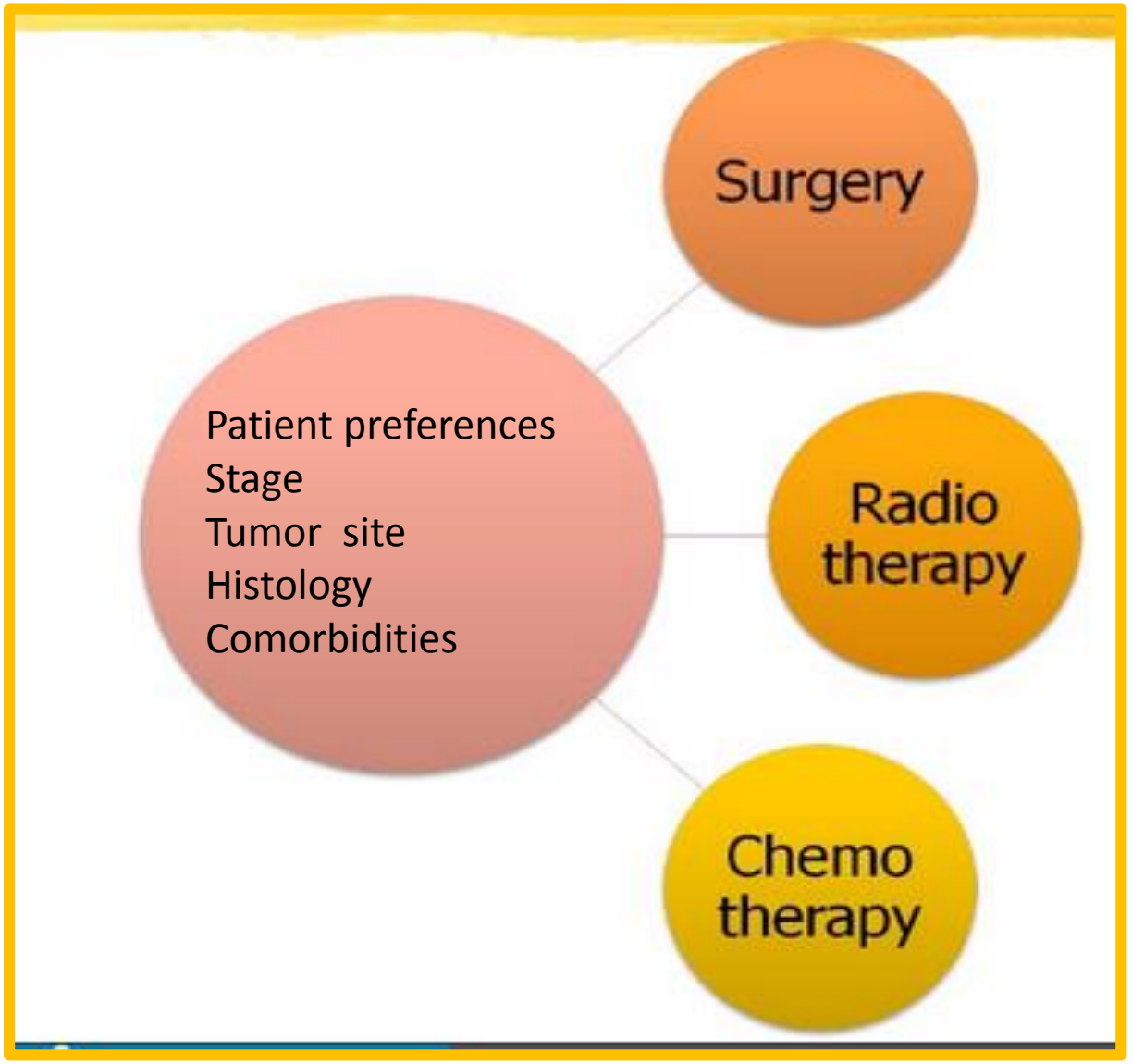
- Commonly spread by lymphatics (70%)
- Lymph node involvement increases with stage
  - ✓ T1: 14 to21%
  - ✓ T2: 38 to 70%
- 25-30% hematogenous metastases at time of presentation
- Most common sites of metasasases are:
  - ✓Lung, liver, pleura, bone, kidney and adrenal gland
- MS with distant metastases - 6 to 12 months

Pag. 2

6. Mappa degli episodi clinici cTis, cT1a-b post resezione endoscopica



Treatment


Patient preferences
Stage
Tumor site
Histology
Comorbidities
Surgery
Radio therapy
Chemo therapy

Platinum doublet is preferred over single agents

Cisplatin plus 5-FU or docetaxel are commonly used combinations

Combinations

Paclitaxel and carboplatin

Cisplatin and 5-FU or capecitabine

Oxaliplatin and 5-FU or capecitabine

Paclitaxel or docetaxel and cisplatin

Carboplatin and 5-FU

Irinotecan and cisplatin

Oxaliplatin, docetaxel and capecitabine

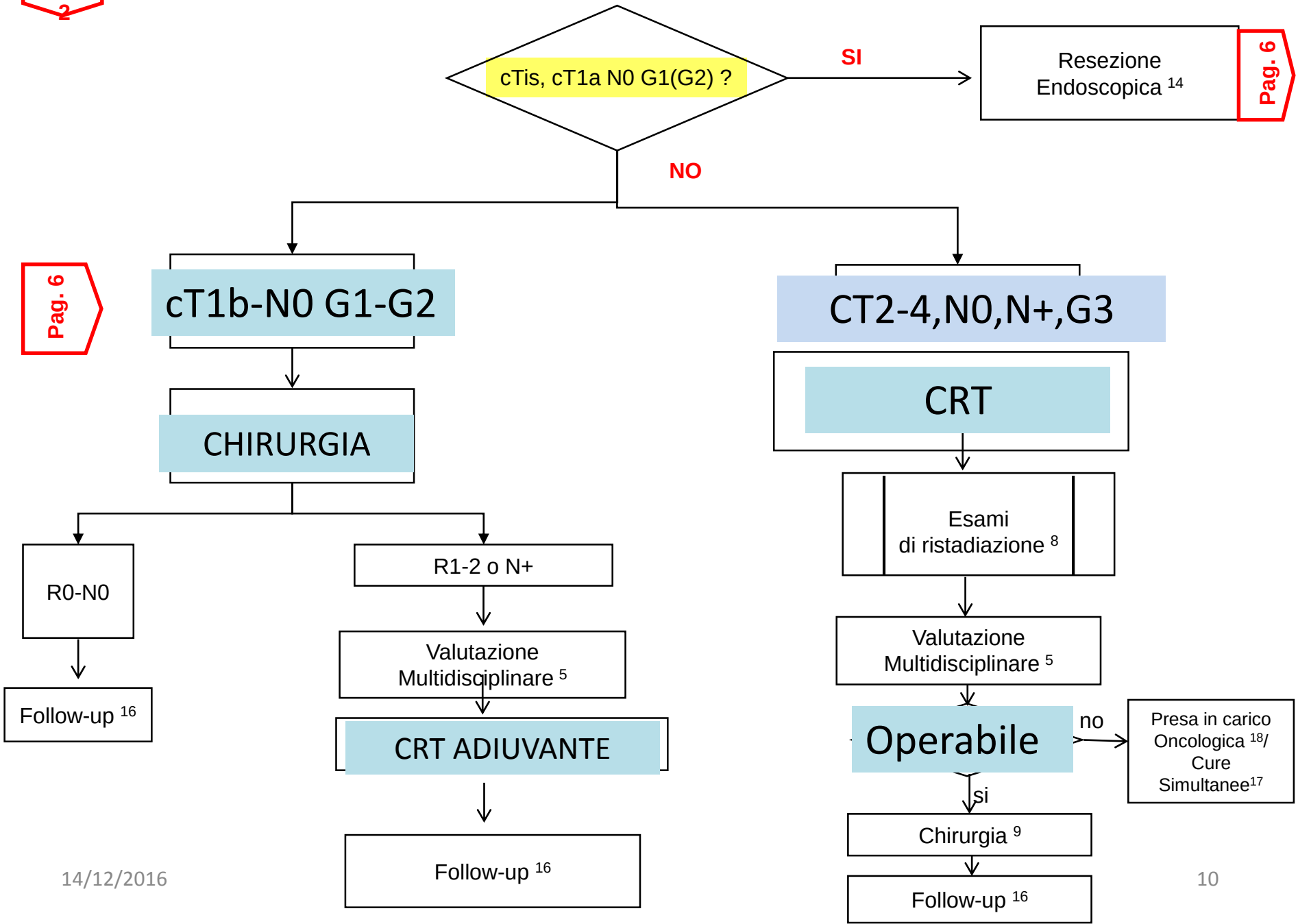
Epirubicin, cisplatin and 5-FU (Only for adenocarcinoma)

Differences in Surgical Epidemiology of pts with SCC and AC of the esophagus

Characteristics	SCC	AC	pValue
Median age	**53.4**	**62.6**	**<.001**
Academics	**20.8 %**	**52.9 %**	**.001**
Blue collar worker	**52.2 %**	**20.2 %**	**.001**
Malnutrition	**24.1 %**	**1.9 %**	**<.001**
Alcohol abuse	**69.7 %**	**51.9 %**	**<.001**
Nicotine abuse	**69.3 %**	**51.9 %**	**<.05**
Cardiovascular risk	**19.5 %**	**34.8 %**	**<0.1**
FEV	**82.5 %**	**93.7 %**	**<.01**
Impaired liver function	**35.3 %**	**24.9 %**	**<.05**

Pag. 2

4. Mappa degli episodi clinici di Valutazione Adenocarcinoma /Trattamento (Siewert Tipo 1-2)



ADENOCARCINOMA DELL' ESOFAGO: *CHIRURGIA O TRATTAMENTO PREOPERATORIO ?*

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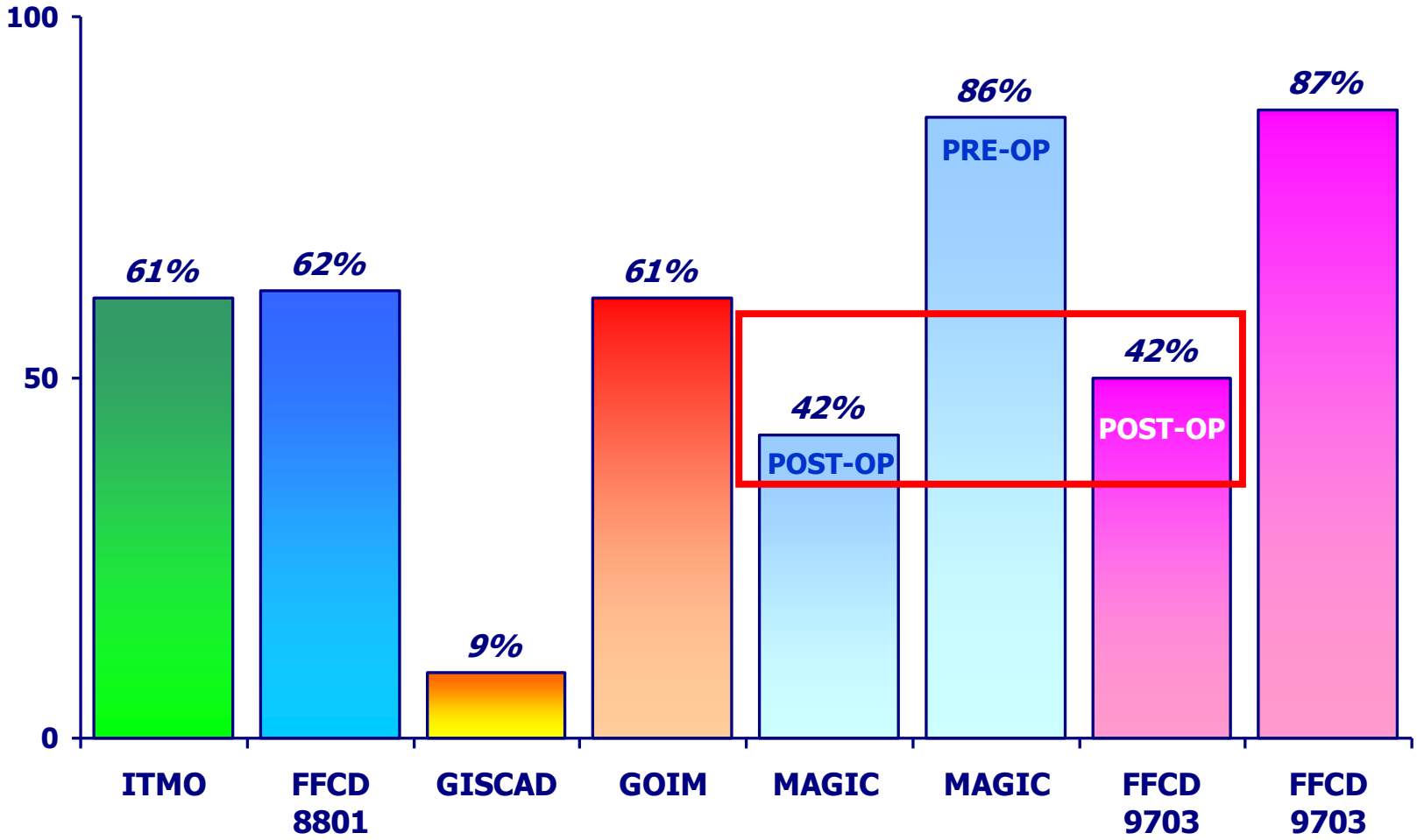

Rate of pts completing post-CT according to the planned dose and timing

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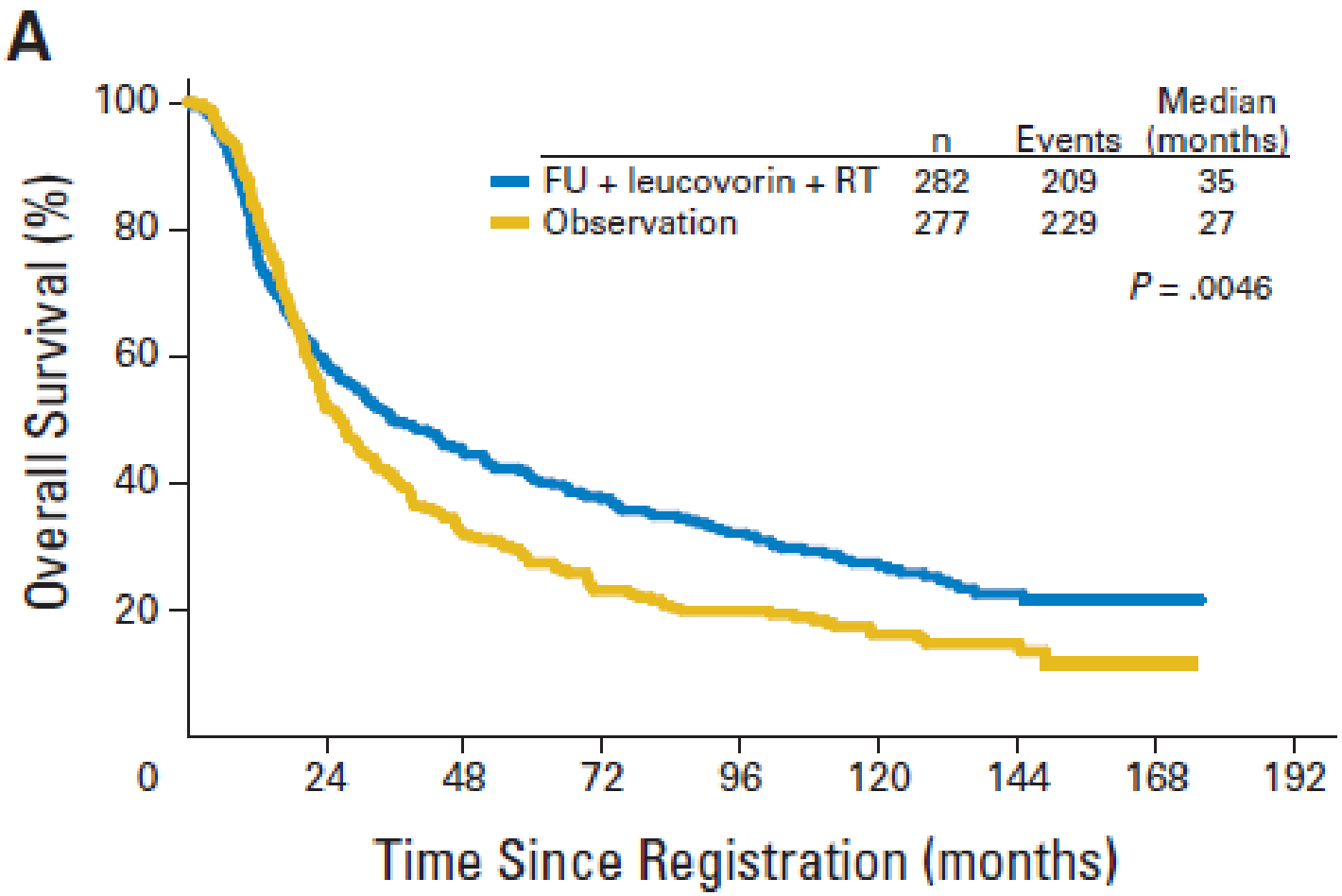
Updated Analysis of SWOG-Directed Intergroup Study 0116: A Phase III Trial of Adjuvant Radiochemotherapy Versus Observation After Curative Gastric Cancer Resection



SR Smalley JCO 2012

ADENOCARCINOMA DELL' ESOFAGO: *CHIRURGIA O TRATTAMENTO PREOPERATORIO ?*

Tassi di RC patologica dopo CT preoperatoria

Studio	Schema	Pazienti (N)	Tasso di resezione R0 (%)	Tasso di RC pat (%)	Tasso di Sopravvivenza (%)
Medical Research Council '02 ADENO-SQUAM	CF → CH	400	60	4	23 (5-ANNI)
	CH	402	54	/	17 (5-ANNI)
MAGIC Trial '06 ADENO	ECF→CH	250	69	0	36.3 (5-ANNI)
	CH	253	66	/	23 (5-ANNI)
RTOG 8911 Intergroup 113 '07 ADENO-SQUAM	CF → CH	213	63	16	23 (3-ANNI)
	CH	227	59	/	26 (3-ANNI)
EORTC 40954 '10 ADENO	CF→CH	72	82	7.1	72.7 (2-ANNI)
	CH	72	67	/	69.9 (2-ANNI)
FFCD 9703 '11 ADENO	CF → CH	109	87	0	38 (5-ANNI)
	CH	110	74	/	24 (5-ANNI)

ADENOCARCINOMA DELL' ESOFAGO: CRT PREOPERATORIA

Tassi di RC patologica dopo CRT preoperatoria

Studio	Schema	Pazienti (N)	Tasso di resezione R0 (%)	Tasso di RCP (%)	Tasso di Sopravvivenza (%)
Walsh '96 ADENO	CF + 40 Gy	58	8	25	32 (3-ANNI)
	CHIRURGIA	55	4	/	6 (3-ANNI)
Urba et '97 ADENO-SQUAM	CFV + 45 Gy	50	45	28	32 (3-ANNI)
	CHIRURGIA	50	45	/	15 (3-ANNI)
Burmeister '05 ADENO-SQUAM	CF + 35 Gy	128	80	16	33 (3-ANNI)
	CHIRURGIA	128	59	/	30 (3-ANNI)
CALGB 9781 '06 ADENO-SQUAM	CF + 50.4 Gy	30	30	40	39 (5-ANNI)
	CHIRURGIA	26	26	/	16 (5-ANNI)
CROSS Gaast et al. 2012 ADENO-SQUAM	C-PTX + 41.1 Gy	188	92.3	32	59 (3-ANNI)
	CHIRURGIA	175	67	/	48 (3-ANNI)

Perioperative ECF vs perioperative FLOT (AIO study)

Primary						
Gastric	59	43,1	68	53,1	127	47,9
AEG I	35	25,5	32	25,0	67	25,3
AEG II	37	27,0	22	17,2	59	22,3
AEG III	6	4,4	6	4,7	12	4,5

Table 4: Pathological Remissions: ITT Population

Pathological Remission	ECF/ECX N=137		FLOT N=128		P value (2-sided)
	no.	%	no.	%	
CR	8	5,8	20	15,6	.015
SR	23	16,8	27	21,1	
CR+SR	31	22,6	47	36,7	.015
PR	28	20,4	23	18,0	
MR	44	32,1	45	35,2	
NR	8	5,8	4	3,1	
Not resectable	26	19,0	9	7,0	

C Pauligk, ASCO 2015

ADENOCARCINOMA ESOFAGO: CRT PREOPERATORIA

VOLUME 27 · NUMBER 6 · FEBRUARY 20 2009

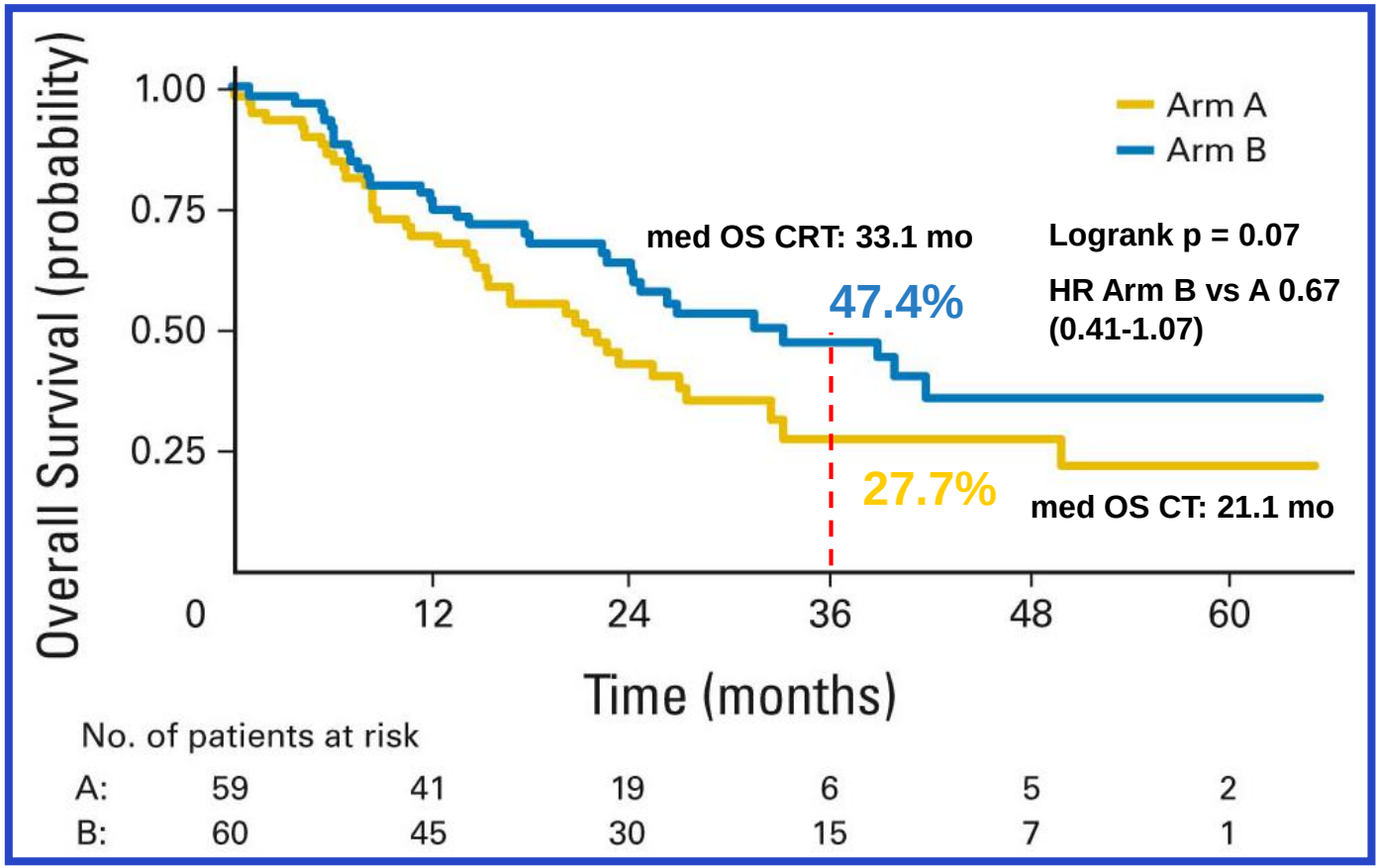
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Phase III Comparison of Preoperative Chemotherapy Compared With Chemoradiotherapy in Patients With Locally Advanced Adenocarcinoma of the Esophagogastric Junction

Michael Stahl, Martin K. Walz, Martin Stuschke, Nils Lehmann, Hans-Joachim Meyer, Jorge Riera-Knorrenschild, Peter Langer, Rita Engenhart-Cabillic, Michael Bitzer, Alfred Königsrainer, Wilfried Budach, and Hansjochen Wilke

Overall survival (med FUP: 45.6 mo)



pathCR
CT: 2.0%
CRT: 15.6%;
P= 0.03

tumor-free lymph nodes (ypN0)
CT 36.7
CRT 64.4%;
P=0.01

Stahl M, JCO 2009

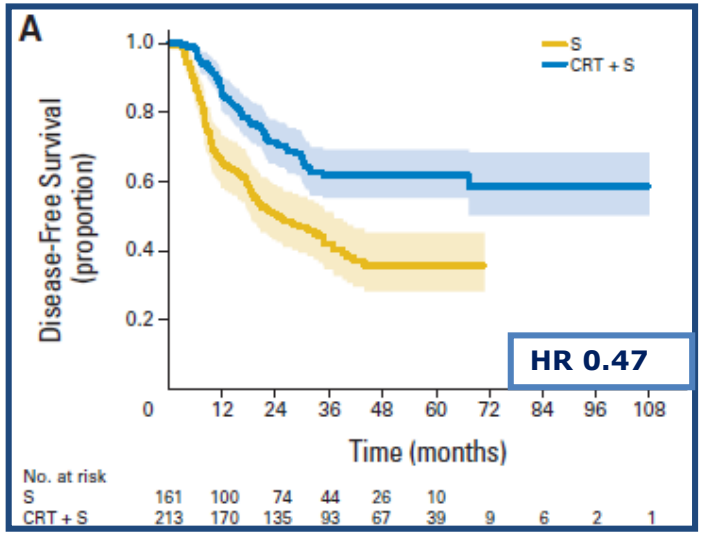
ADENOCA DELL' ESOFAGO: CRT PREOPERATORIA

VOLUME 32 · NUMBER 5 · FEBRUARY 10 2014

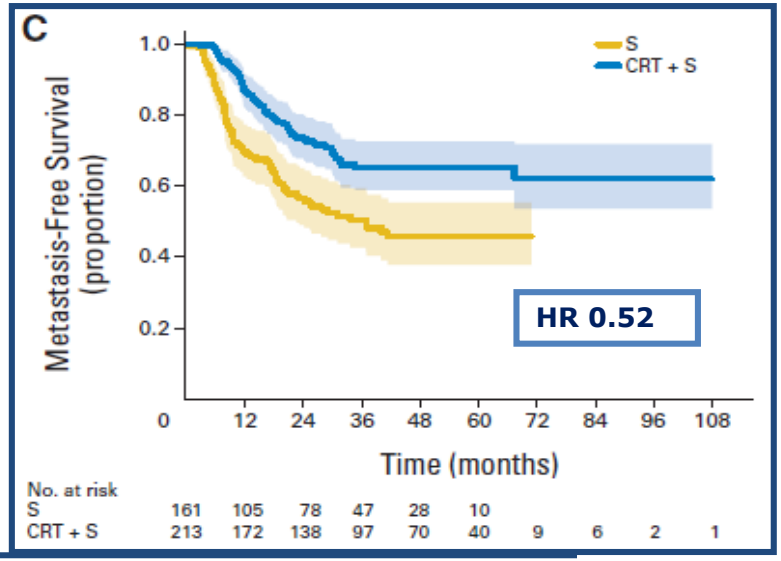
JOURNAL OF CLINICAL ONCOLOGY — ORIGINAL REPORT

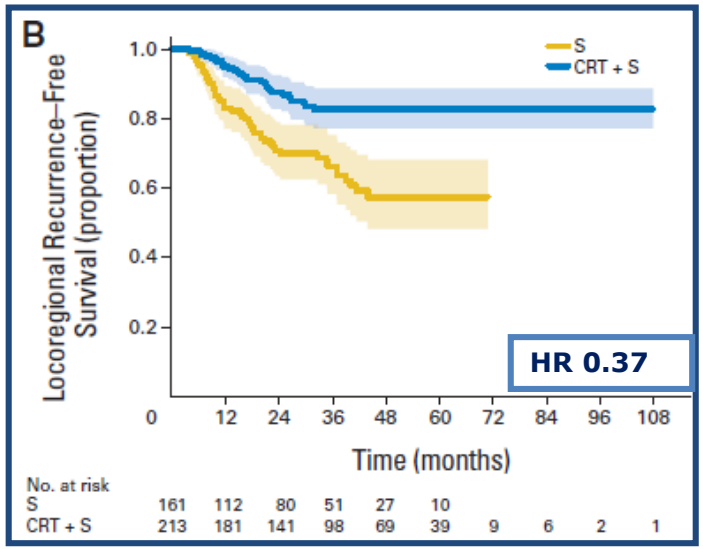
Patterns of Recurrence After Surgery Alone Versus Preoperative Chemoradiotherapy and Surgery in the CROSS Trials

Vera Oppedijk, Ate van der Gaast, Jan J.B. van Lanschot, Pieter van Hagen, Rob van Os, Caroline M. van Rij, Maurice J. van der Sangen, Jannet C. Beukema, Heidi Rütten, Patty H. Spruit, Janny G. Reinders, Dick J. Richel, Mark I. van Berge Henegouwen, and Maarten C.C.M. Hulshof



374 pz
282 adenok
med FUP 45 m





%	CRT	S
Relapse	35	58
LRF	14	34
Peritoneum	14	4
Hematogenous	29	35

Oppedijk V, JCO 2014

ST03

		ECX		ECX+B	
R0		315	(75%)	301	(76%)
R1	Proximal	13	(3%)	9	(2%)
	Distal	6	(1%)	7	(2%)
	Circumferential	42	(10%)	35	(9%)
	Within 1mm of circumferential	30	(7%)	31	(8%)
	Multiple locations	15	(4%)	13	(3%)
Unavailable		26		29	
TOTAL		**447**		**425**	

Proximal ← → Distal

By baseline tumour site

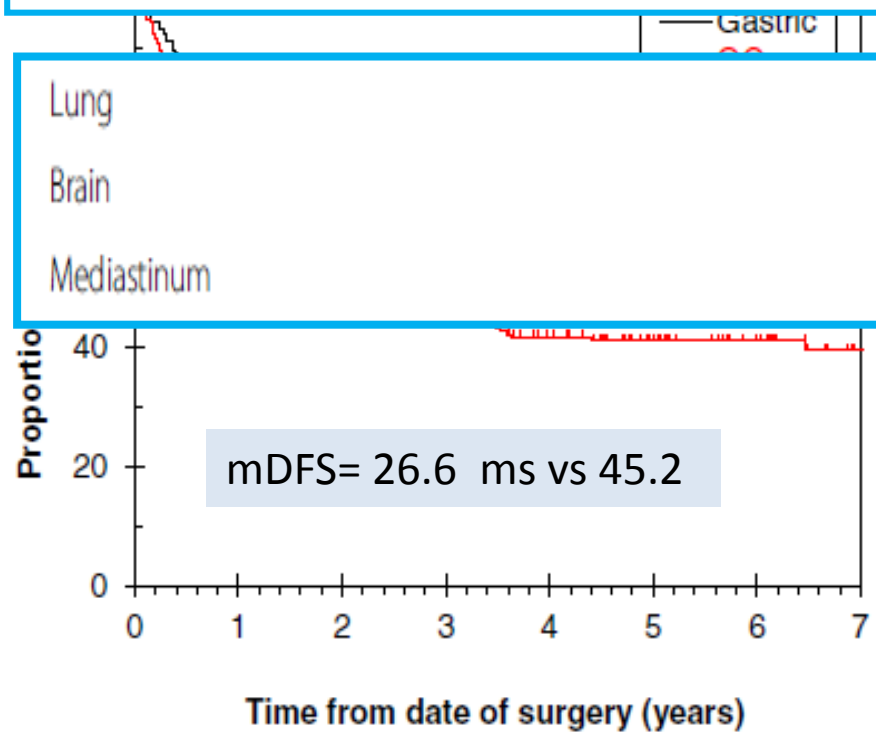
		L. oesophageal		OGJ type I		OGJ type II		OGJ type III		Stomach	
R0		76	(66%)	61	(61%)	104	(71%)	117	(75%)	258	(87%)
R1	Proximal	3	(3%)	0	(0%)	1	(<1%)	7	(4%)	11	(4%)
	Distal	0	(0%)	1	(1%)	0	(0%)	4	(3%)	8	(3%)
	Circumferential	21	(18%)	16	(16%)	20	(14%)	14	(9%)	6	(2%)
	Within 1mm of circumferential	15	(13%)	20	(20%)	12	(8%)	10	(6%)	4	(1%)
	Multiple locations	1	(<1%)	2	(2%)	10	(7%)	5	(3%)	10	(3%)
Unavailable		8		10		10		7		20	
TOTAL		**124**		**110**		**157**		**164**		**317**	

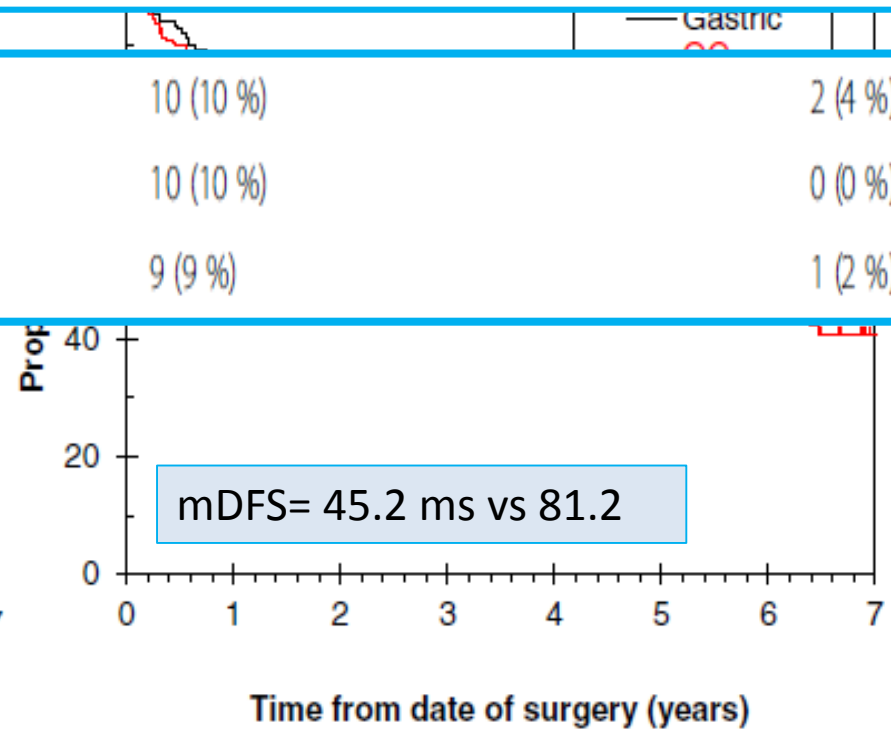
Cunningham *et al*. Peri-operative chemotherapy ± bevacizumab for resectable gastro-oesophageal adenocarcinoma: Results from the UK Medical Research Council randomised ST03 trial (ISRCTN 46020948). *ESMO 2015 Abstr 2201.*

RESEARCH ARTICLE Open Access

Characterising timing and pattern of relapse following surgery for localised oesophagogastric adenocarcinoma: a

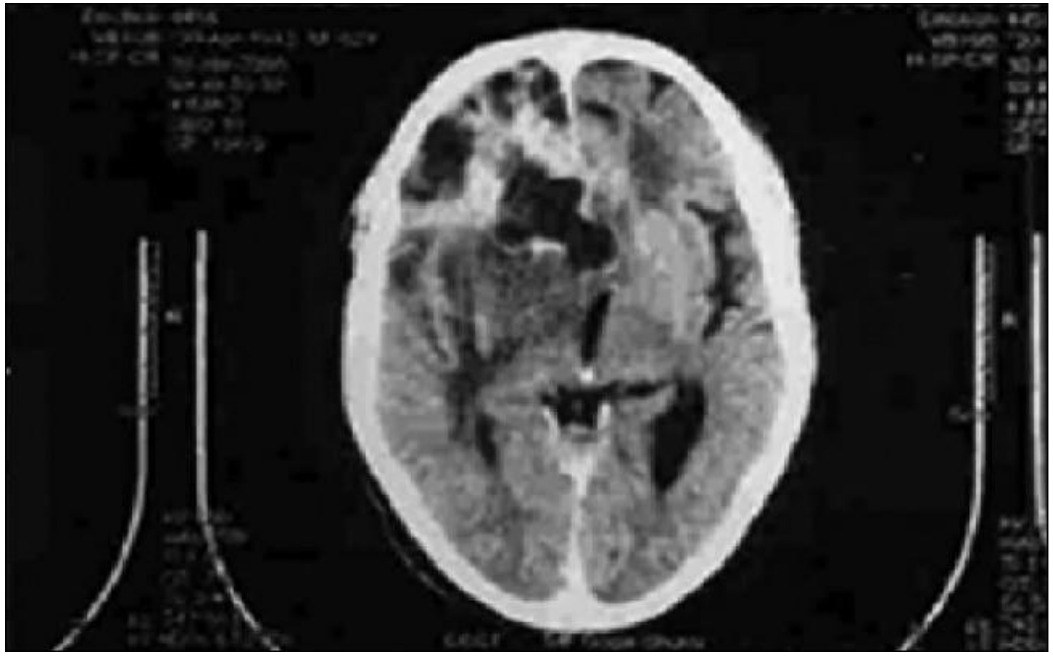
Lymph nodes	52 (52 %)	14 (30 %)
Anastomosis	21 (21 %)	10 (21 %)
Peritoneum	16 (16 %)	18 (38 %)
Lung	10 (10 %)	2 (4 %)
Brain	10 (10 %)	0 (0 %)
Mediastinum	9 (9 %)	1 (2 %)





Brain metastasis from esophageal carcinoma

among 504 cases of EC registered during a 15-year (1990-2005) period, brain metastasis was detected in only 1 case.



Agrawal R. J Cancer Res Ther 2009;5:137-9

RISPOSTA COMPLETA PATOLOGICA SURROGATO DI OS

Multivariable analysis with regard to local progression free survival (LPFS) and overall survival (OS).

Item	LPFS hazard ratio (95%-CI)	LPFS logrank *p*	OS hazard ratio (95%-CI)	OS logrank *p*
Study type Phase III versus II	0.92 (0.58–1.46)	0.72	0.90 (0.56–1.43)	0.64
Resection status R1 versus R0	2.16 (1.11–4.21)	<0.05	2.27 (1.17–4.41)	<0.05
Histologic result Other versus T0N0M0	2.99 (1.61–5.55)	<0.001	3.16 (1.70–5.88)	<0.001

European Journal of Cancer (2012) 48, 2977–2982

Available at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.ejcancer.info

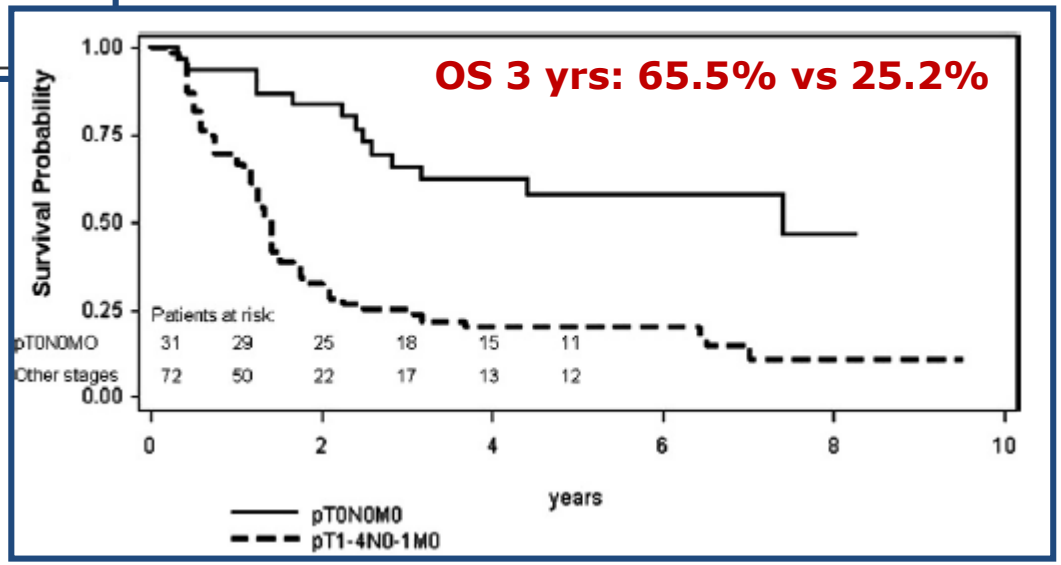
ELSEVIER

EJC

Prediction of prognosis after trimodal therapy in patients with locally advanced squamous cell carcinoma of the oesophagus

Michael Stahl [a,*], Nils Lehmann [b], Martin K. Walz [c], Martin Stuschke [d], Hansjochen Wilke [a]

La RC patologica è un fattore prognostico indipendente



Stahl M, Eur J Cancer2012

RISPOSTA CLINICA ≠ RISPOSTA PATOLOGICA

Preoperative Chemoradiotherapy for Squamous Cell Carcinoma and Adenocarcinoma of the Esophagus*

A Phase II Study

Ferdinando De Vita, MD, PhD; Natale Di Martino, MD; Michele Orditura, MD, PhD; Angelo Cosenza, MD; Gennaro Galizia, MD; Alberto Del Genio, MD; and Giuseppe Catalano, MD, PhD

J Gastrointest Surg (2013) 17:1375–1381
DOI 10.1007/s11605-013-2269-3

ORIGINAL ARTICLE

Complete Clinical Response After Neoadjuvant Chemoradiotherapy for Squamous Cell Cancer of the Thoracic Oesophagus: Is Surgery Always Necessary?

Carlo Castoro · Marco Scarpa · Matteo Cagol · Rita Alfieri · Alberto Ruol · Francesco Cavallin · Silvia Michieletto · Giampietro Zanchettin · Vanna Chiarion-Sileni · Luigi Corti · Ermanno Ancona

ORIGINAL ARTICLES FROM THE ESA PROCEEDINGS

Is There a Role for Surgery for Patients with a Complete Clinical Response after Chemoradiation for Esophageal Cancer?

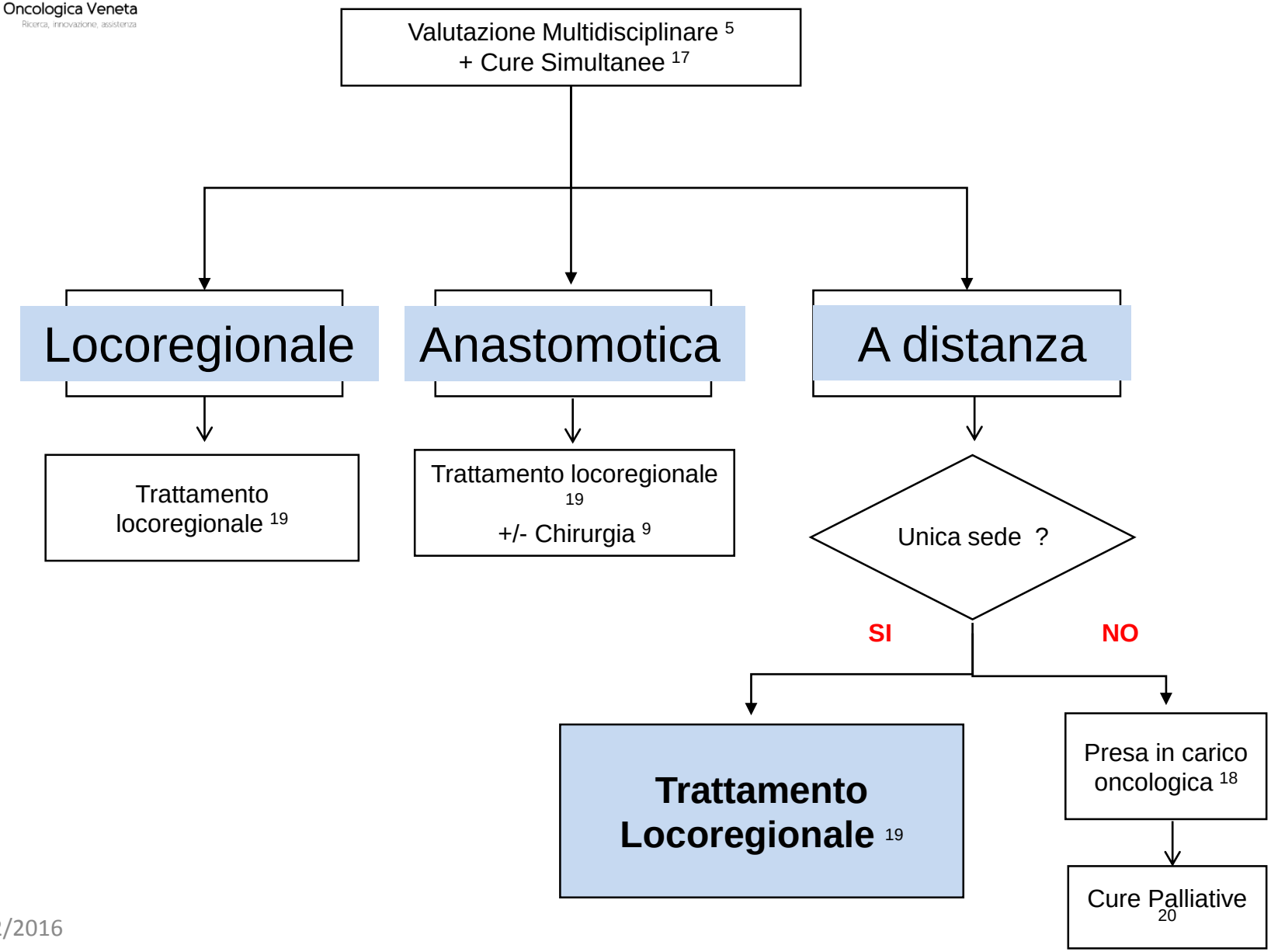
An Intention-to-Treat Case-Control Study

Guillaume Piessen, MD, PhD,†‡ Mathieu Messager, MD,*†‡ Xavier Mirabel, MD,§¶ Nicolas Briez, MD,*† William B. Robb, MD,*† Antoine Adenis, MD,¶ and Christophe Mariette, MD, PhD*†‡*

Residual tumor after preoperative CRT in Clinical Complete Responders pts

Study	Residual tumor
De Vita, *Chest 2002*	41.2%
Castoro, *J Gastrointest Surg 2013*	30.8%
Mariette , *Ann Surg 2013*	34.6%

7. Trattamento della progressione e delle recidive



Salvage radiotherapy in patients with local recurrent esophageal cancer after radical radiochemotherapy

Table 5 | Previous studies on radiotherapy with or without chemotherapy as salvage treatment for patients with postoperative locoregional recurrence of oesophageal squamous cell carcinoma

Study	n	Treatment (n)	ORR	MST (month)	1 year OS	2 year OS	3 year OS
Raoul, J. L., 1995[13]	31[a]	RT + CT	65%	<12	47.1%	17.1%	4.3%
Nemoto, K., 2001[29]	33	RT alone (21)	91%	7	33%	15%	12%
		RT + CT (CF) (12)					
Shioyama, Y., 2007[12]	82	RT alone (52)	78%	7	/	22%	/
		RT + CT (30)					
Nakamura, T., 2008[11]	22	RT + CT	82%	20.3	/	/	26.6%
Lu, J. C., 2010[28]	73	RT alone (42)	76%	9	33.8%	/	0.0%
		CCRT with CF (31)	97%	17	62.5%		10.5%
Maruyama, K., 2011[27]	23	RT + CT	/	13	52%	31%	/
Jingu, K., 2012[26,16]	30	CCRT with three-weekly NF	73.3%	21	60.6%	/	38.4%
Bao, Y., 2012[14]	83	CCRT (3D-CRT)	75.9%	43	/	/	51.8%
Zhang, J., 2012[30]	50	CCRT with four-weekly CF (22)	72.7%	9.8	56%	/	14%
		CCRT with three-weekly TP (28)	71.4%	16.3			
Fakhrian, K., 2012[31]	54[b]	RT alone (18)	/	12	55%	29%	19%
		CCRT (36)					
Ma, D. Y., 2014[24]	98	3D-CRT alone (49)	73.5%	19	69.4%	/	28.6%
		CCRT with weekly cisplatin (49)	91.8%	35	85.7%		46.9%
Kobayashi, R., 2014[15]	42[c]	RT alone (7)	97.6%	24.3	81.2%	51.3%	41.1%
		CCRT with four-weekly regimen (35)					
Current study	27	CCRT with weekly CF (14)	70.4%	26	88.9%	60.2%	/
		CCRT with weekly NF (13)					

Figure 1 Overall survival (OS) curve of NSR group and SR group.

ESOFAGO CERVICALE

RIVALUTAZIONE /FOLLOW UP DOPO CRT ESCLUSIVA

Controllo clinico	Ogni 3 mesi per 2 anni Ogni 6 mesi per altri tre anni
EGDS + BIOPSIE	Dopo 3 mesi Ogni 6 mesi fino ai 2 anni 1 volta all'anno per altri 3 anni
TAC collo-torace-add	Dopo 3 mesi Ogni 6 mesi fino ai 2 anni 1 volta all'anno per altri 3 anni
PET-TAC	Dopo 3 mesi Ogni 6 mesi fino ai 2 anni; 1 volta all'anno per altri 3 anni

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CARCINOMA DELL'ESOFAGO TORACICO E DEL CARDIAS

FOLLOW UP - RACCCOMANDAZIONI

I	
Tis - dopo resezione endoscopica	
EGDS	Ogni 6 mesi per 2 anni 1 volta all'anno per altri 3 anni ulteriori EGDS se presenza di Barrett
TAC torace- addome	raccomandata solo in base ad indicazione clinica

Risk of Second Primary Malignancy After Esophagectomy for SCC of the Thoracic Esophagus

Matsubara T, JCO 2003;21:4336-41

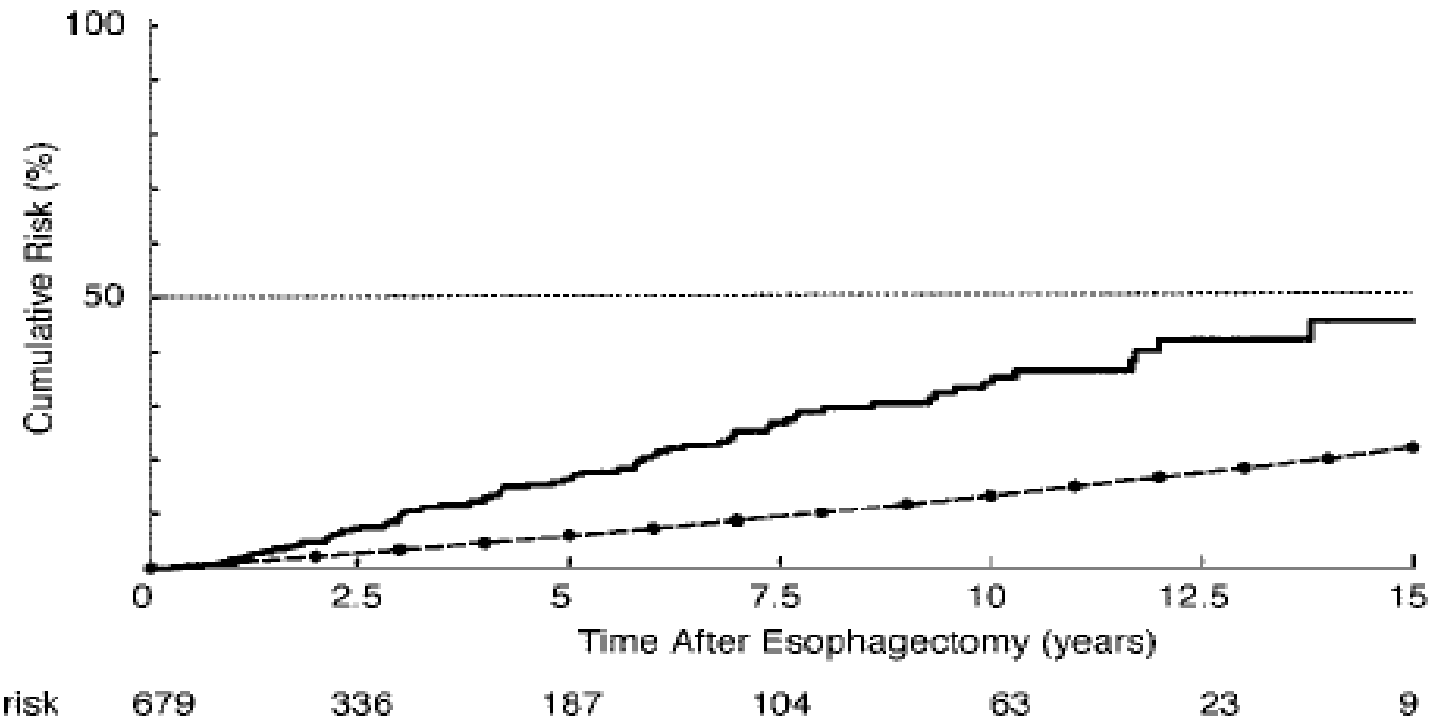
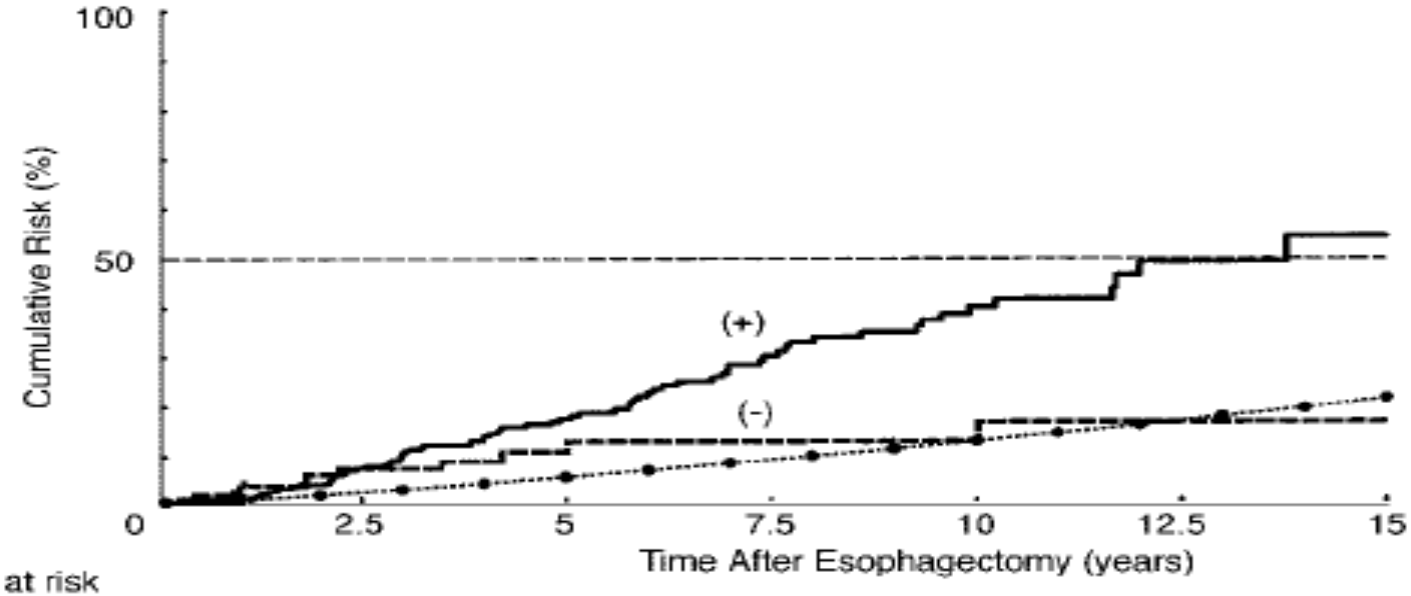


Fig 1. Cumulative risk of developing second malignancy (solid line) after esophagectomy compared with the risk of malignancy in a general population matched for calendar-age and sex (bottom dashed line).

Risk of Second Primary Malignancy After Esophagectomy for SCC of the Thoracic Esophagus

Matsubara T, JCO 2003;21:4336-41



No. at risk

(+)	529	261	144	74	41	15	6
(−)	150	75	43	30	22	8	3

Fig 4. Cumulative risk of developing second malignancy after esophagectomy in patients with (+) and without (−) both smoking and drinking habits. The dotted line indicates the cumulative risk in the general population matched for calendar-age and sex.

Rete Oncologica Veneta
Ricerca, innovazione, assistenza

Terapia palliativa

- **Le cure palliative si occupano in maniera attiva e totale dei pazienti quando la malattia non risponde più a trattamenti specifici e l' inevitabile evoluzione è il decesso.**
- **Criteri di definizione della terminalità:**

✓ *Terapeutico:* esaurimento/assenza o inutilità delle terapie oncologiche per la cura del tumore, o rifiuto da parte del malato.

✓ *Clinico:* presenza di un quadro clinico che comporta limitazioni dell'autonomia e un frequente bisogno di cure mediche, caratterizzato da un Indice di Karnofsky < 50.

✓ *Prognostico*: previsione di sopravvivenza < a 3 mesi.