Radioterapia w raku żołądka – kiedy i jak; ewolucja rekomendacji w kontekście europejskich, amerykańskich i azjatyckich badań klinicznych

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Zakład Radioterapii Centrum Onkologii-Instytut im. M.Skłodowskiej-Curie, Oddział w Gliwicach

Rak żołądka

rok	zachorowania	zgony
2000	5842	6036
2004	5436	5716
2008	5103	5673
2010	5276	5364
2011	5368	5239
2012	5441	5317

Rak żołądka

kraj	zachorowania	zgony	wsp. zach./zg.
Polska (2012)	5441	5317	1,02
USA (2013)	21600	10990	1,97

EUROCARE-3

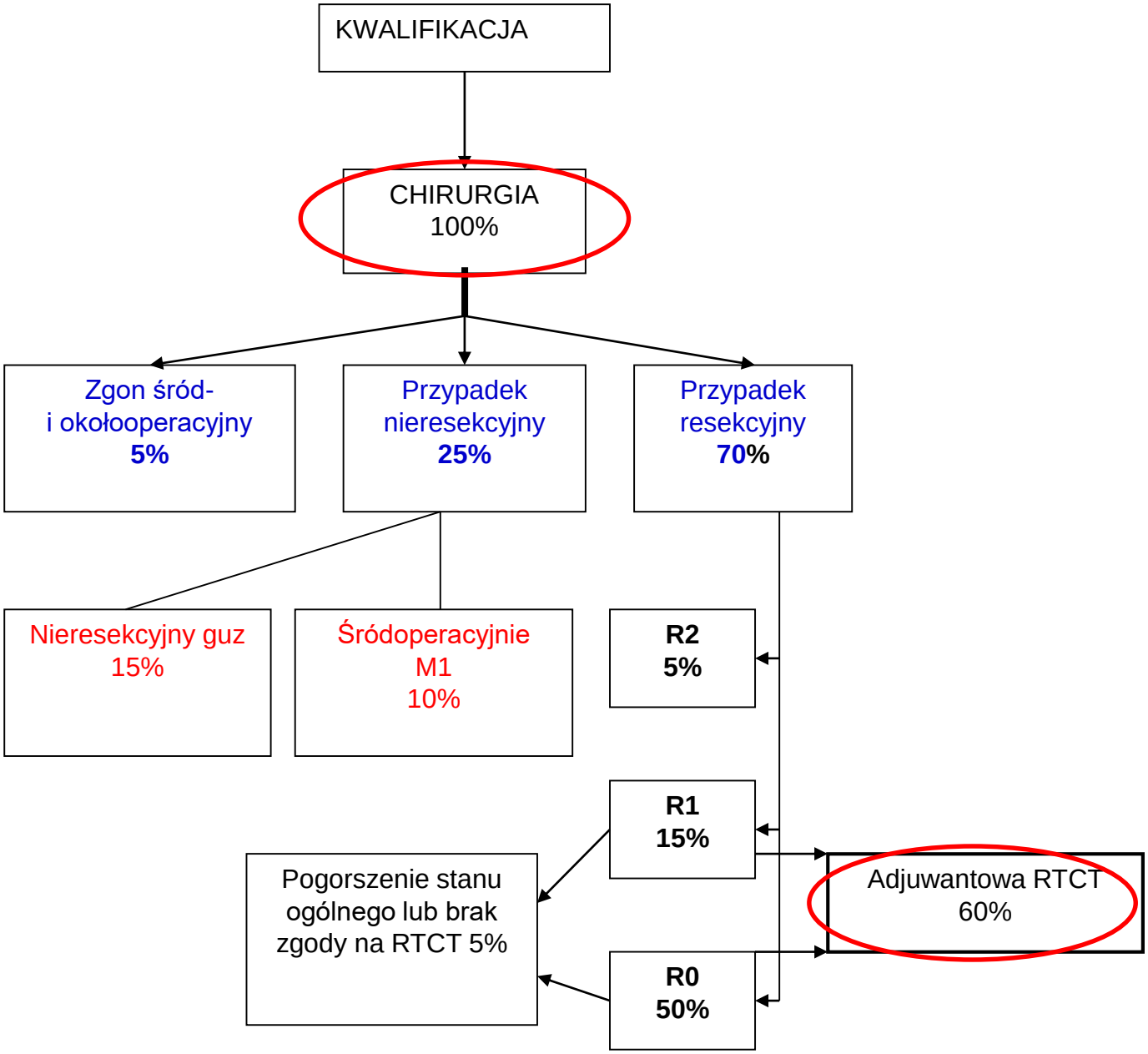
Państwo	1-rok	2-lata	5-lat
Polska	29%	15%	12%
Czechy	33%	20%	17%
Anglia	30%	16%	14%
Niemcy	46%	32%	29%
Szwajcaria	51%	32%	30%

Zagadnienia

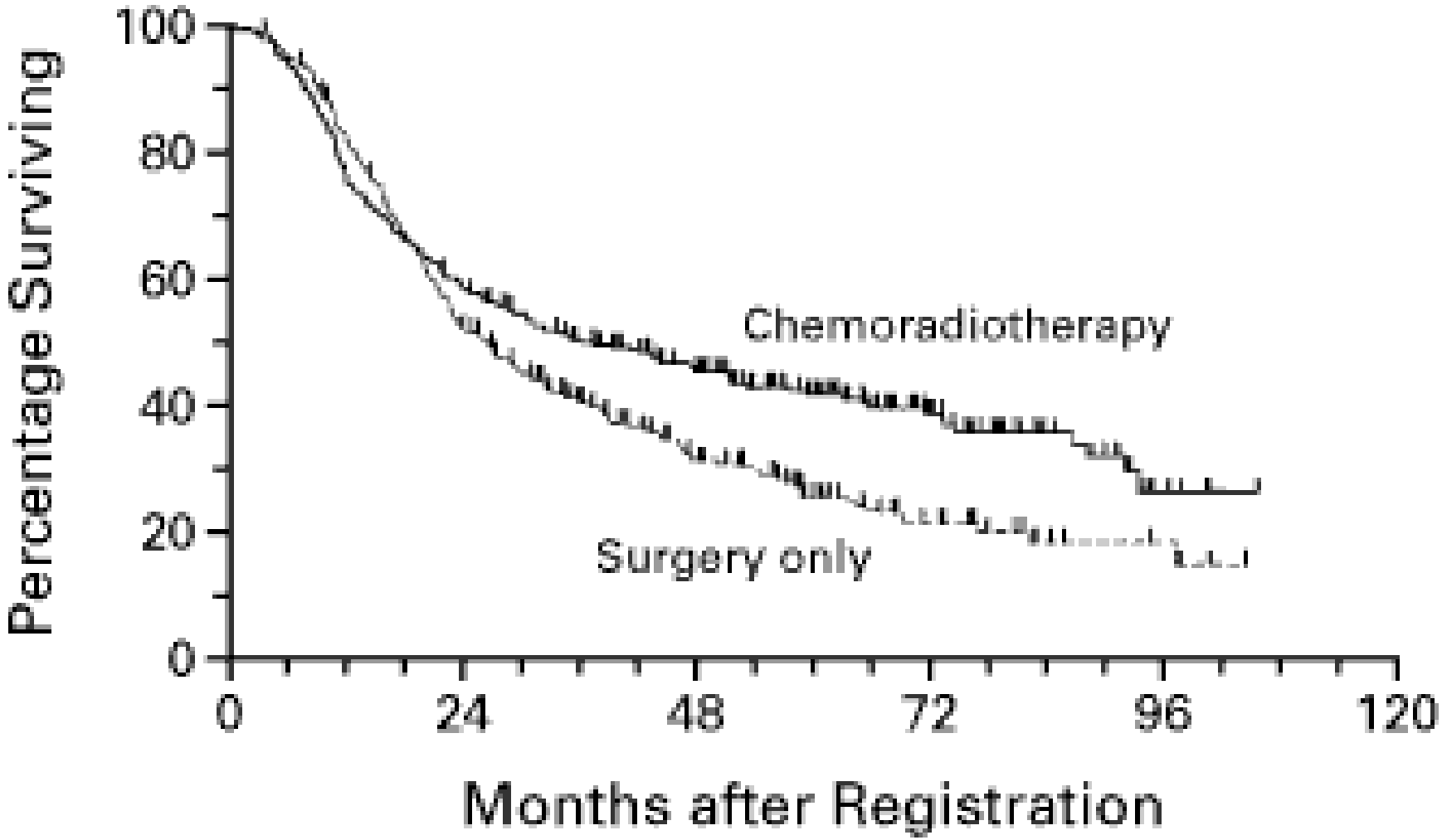
- 1. pooperacyjna radiochemioterapia
- 2. radio(chemio)terapia przedoperacyjna
- 3. radykalna radio(chemio)terapia
- 4. paliatywna radioterapia

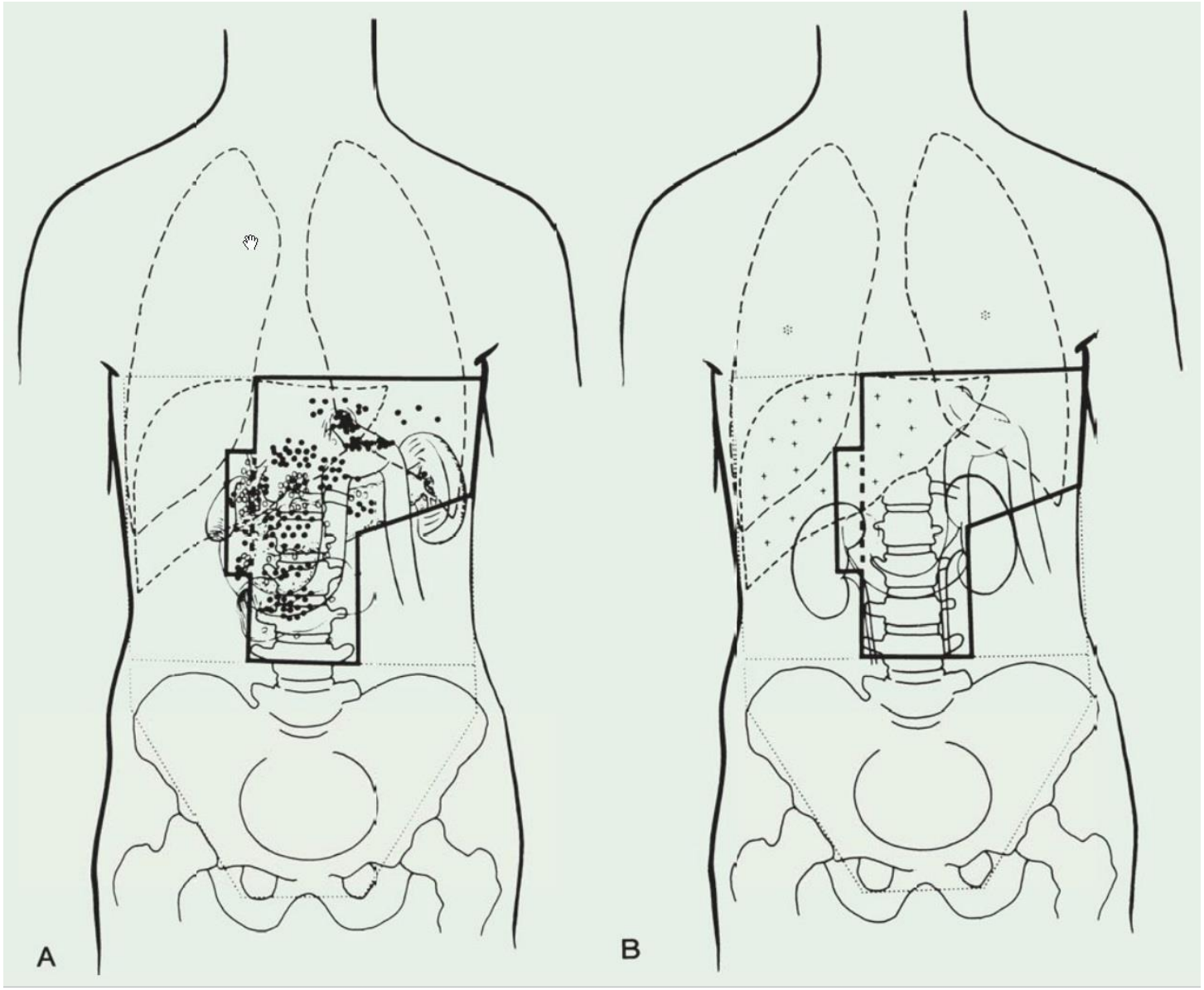
Zagadnienia

- **1. pooperacyjna radiochemioterapia**
- 2. radio(chemio)terapia przedoperacyjna
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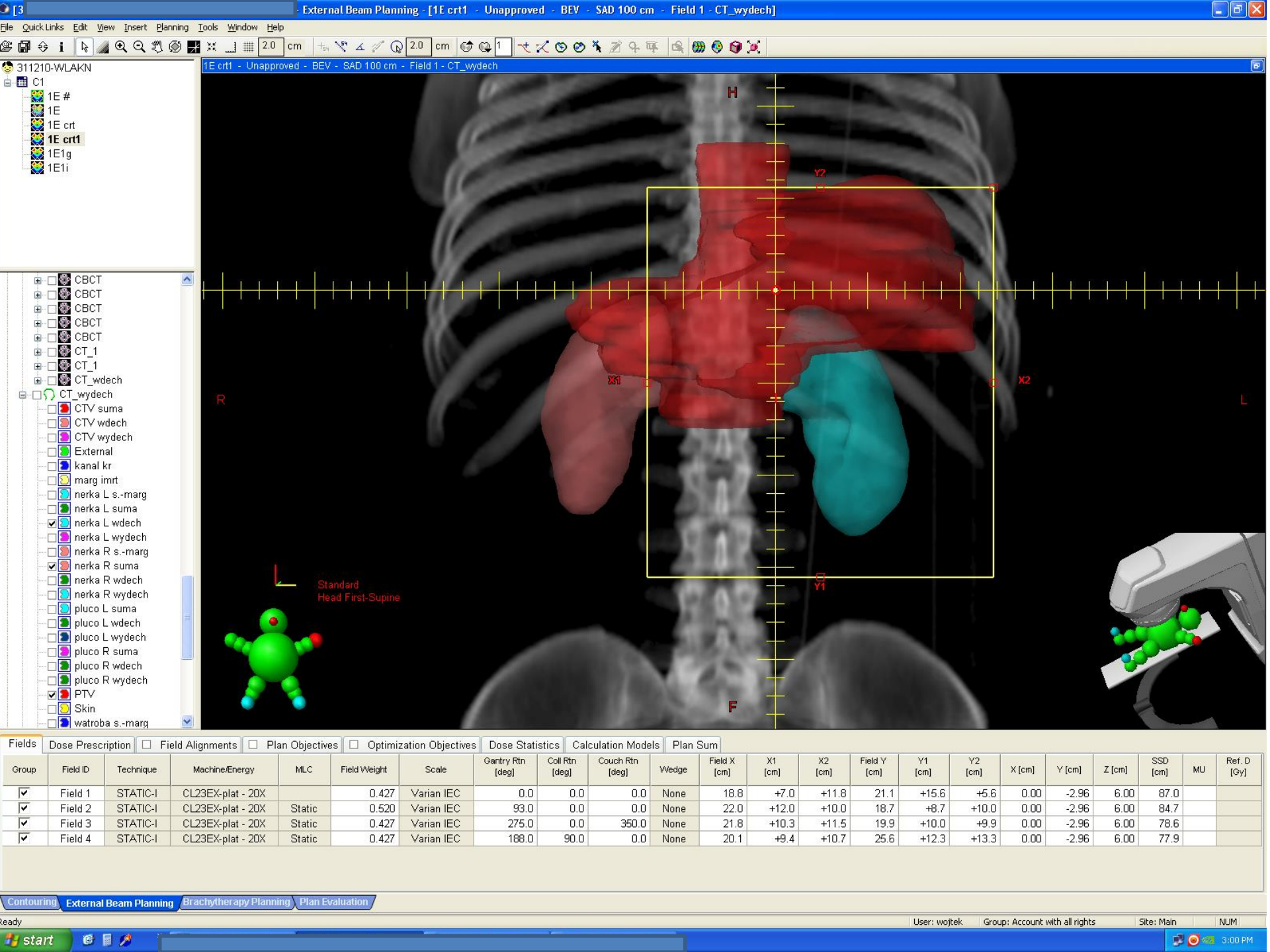

KWALIFIKACJA
CHIRURGIA
100%
Zgon śród-
i okołooperacyjny
5%
Przypadek
nieresekcyjny
25%
Przypadek
resekcyjny
70%
Nieresekcyjny guz
15%
Śródoperacyjnie
M1
10%
R2
5%
R1
15%
Pogorszenie stanu
ogólnego lub brak
zgody na RTCT 5%
Adjuwantowa RTCT
60%
R0
50%

INT-0116


Percentage Surviving
100
80
60
40
20
0
0
24
48
72
96
120
Months after Registration
Chemoradiotherapy
Surgery only



Gunderson LL, Sosin H. Adenocarcinoma of the stomach: areas of failure in a re-operation series (second or symptomatic look) clinicopathologic correlation and implications for adjuvant therapy. Int J Radiat Oncol Biol Phys. 1982 Jan;8(1):1-11.



Group	Field ID	Technique	Machine/Energy	MLC	Field Weight	Scale	Gantry Rtn [deg]	Coll Rtn [deg]	Couch Rtn [deg]	Wedge	Field X [cm]	X1 [cm]	X2 [cm]	Field Y [cm]	Y1 [cm]	Y2 [cm]	X [cm]	Y [cm]	Z [cm]	SSD [cm]	MU	Ref. D [Gy]
☑	Field 1	STATIC-I	CL23EX-plat - 20X		0.427	Varian IEC	0.0	0.0	0.0	None	18.8	+7.0	+11.8	21.1	+15.6	+5.6	0.00	-2.96	6.00	87.0		
☑	Field 2	STATIC-I	CL23EX-plat - 20X	Static	0.520	Varian IEC	93.0	0.0	0.0	None	22.0	+12.0	+10.0	18.7	+8.7	+10.0	0.00	-2.96	6.00	84.7		
☑	Field 3	STATIC-I	CL23EX-plat - 20X	Static	0.427	Varian IEC	275.0	0.0	350.0	None	21.8	+10.3	+11.5	19.9	+10.0	+9.9	0.00	-2.96	6.00	78.6		
☑	Field 4	STATIC-I	CL23EX-plat - 20X	Static	0.427	Varian IEC	188.0	90.0	0.0	None	20.1	+9.4	+10.7	25.6	+12.3	+13.3	0.00	-2.96	6.00	77.9		

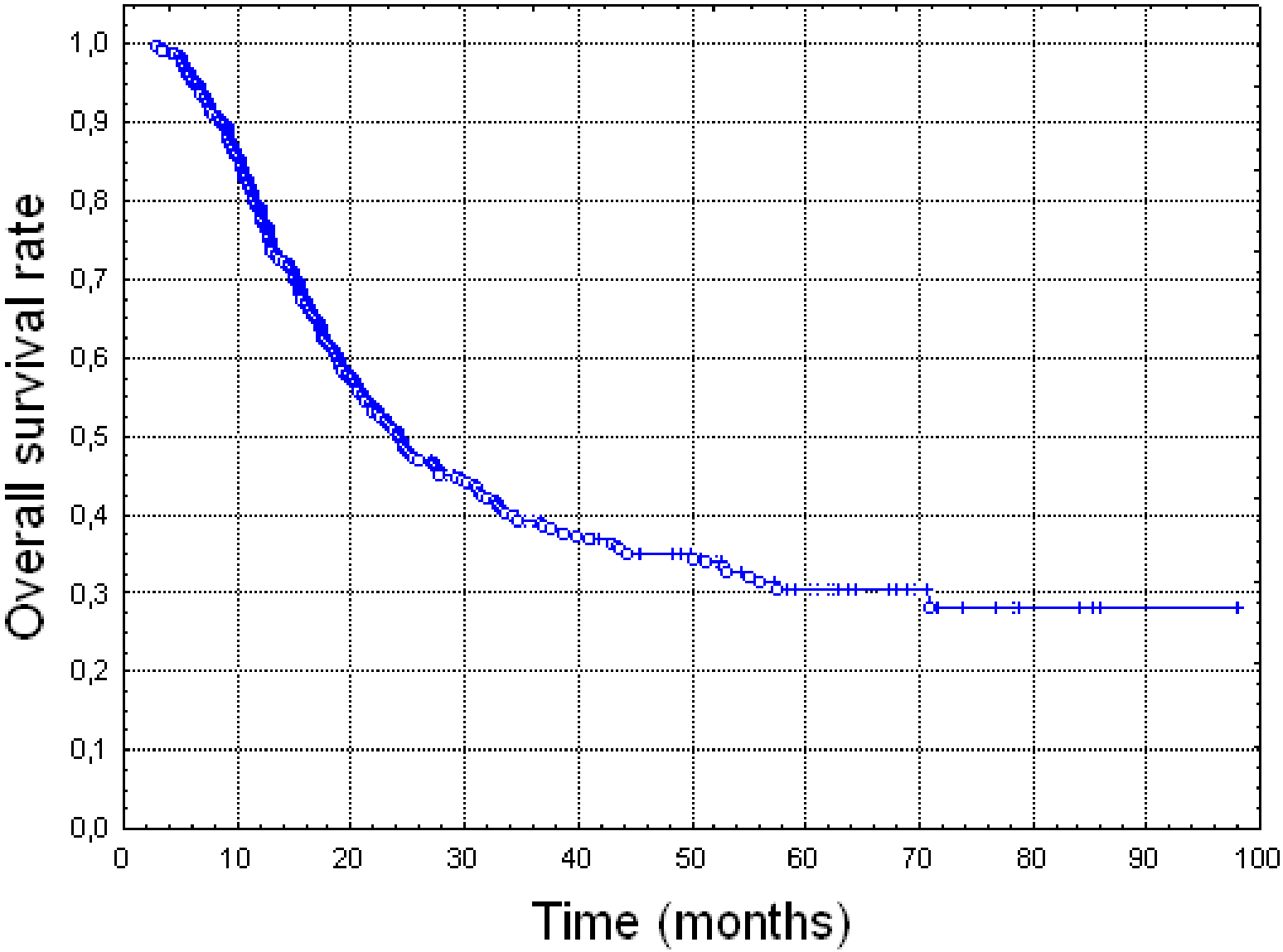
TABLE 3. MAJOR TOXIC EFFECTS OF CHEMORADIOTHERAPY.*

TYPE OF TOXIC EFFECT	NO. OF PATIENTS (%)
Hematologic	148 (54)
Gastrointestinal	89 (33)
Influenza-like	25 (9)
Infection	16 (6)
Neurologic	12 (4)
Cardiovascular	11 (4)
Pain	9 (3)
Metabolic	5 (2)
Hepatic	4 (1)
Lung-related	3 (1)
Death†	3 (1)

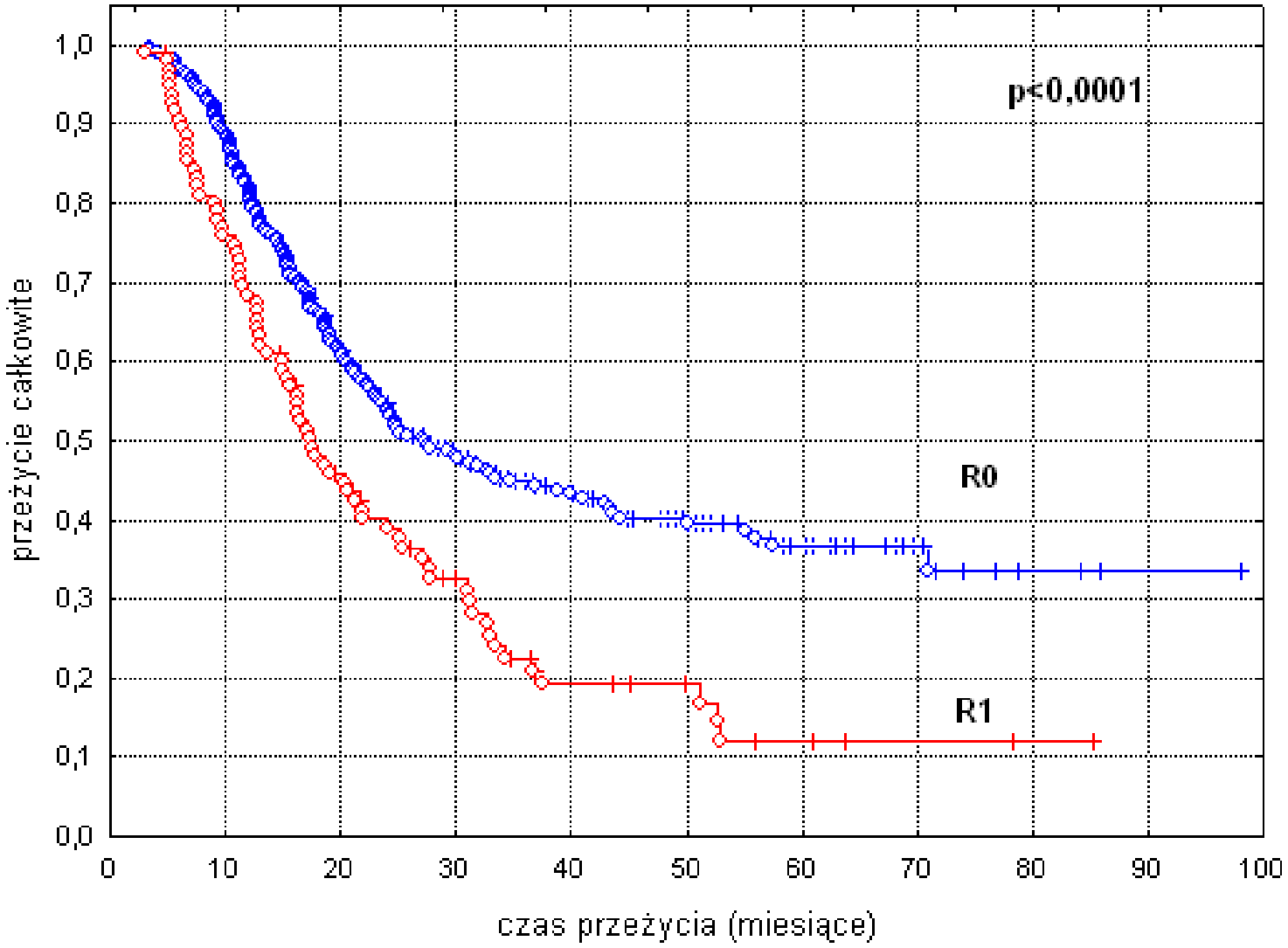
*Major toxic effects were defined as those of grade 3 or higher. Data are for the 273 patients who received chemoradiotherapy.

†One patient died from a cardiac event, one from sepsis complicating myelosuppression, and one from pulmonary fibrosis.

386 chorych po RTCT



R0 vs. R1

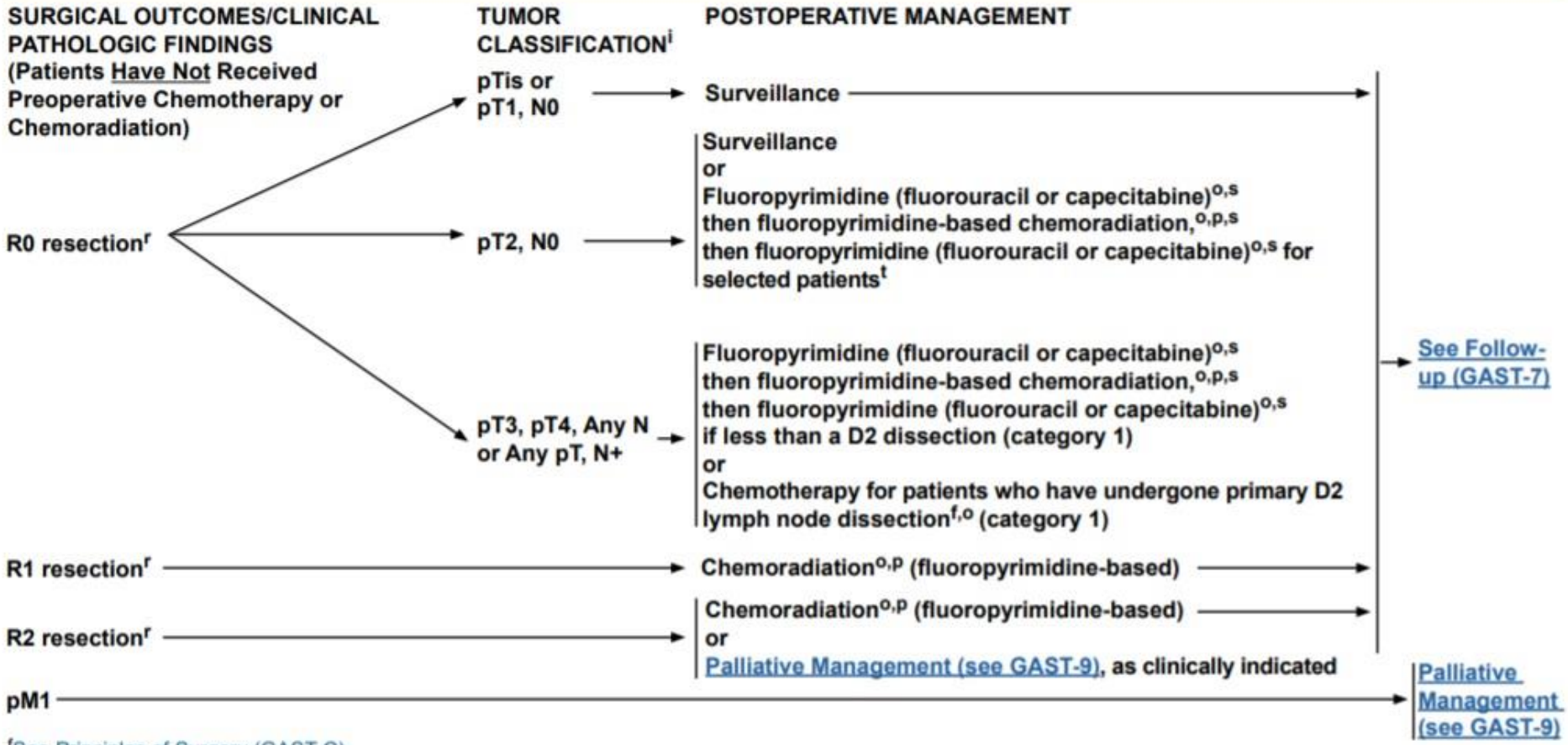

p<0,0001
R0
R1
przeżycie całkowite
czas przeżycia (miesiące)
1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
0
10
20
30
40
50
60
70
80
90
100

Kryteria kwalifikacji do RTCHT

- T2-4N0
- T1-4N1-3
- R1, R2

NCCN Guidelines Version 2.2018
Gastric Cancer

NCCN Guidelines Index
Table of Contents
Discussion



[f] See Principles of Surgery (GAST-C).
[i] See Staging (ST-1) for tumor classification.
[o] See Principles of Systemic Therapy (GAST-F).
[p] See Principles of Radiation Therapy (GAST-G).

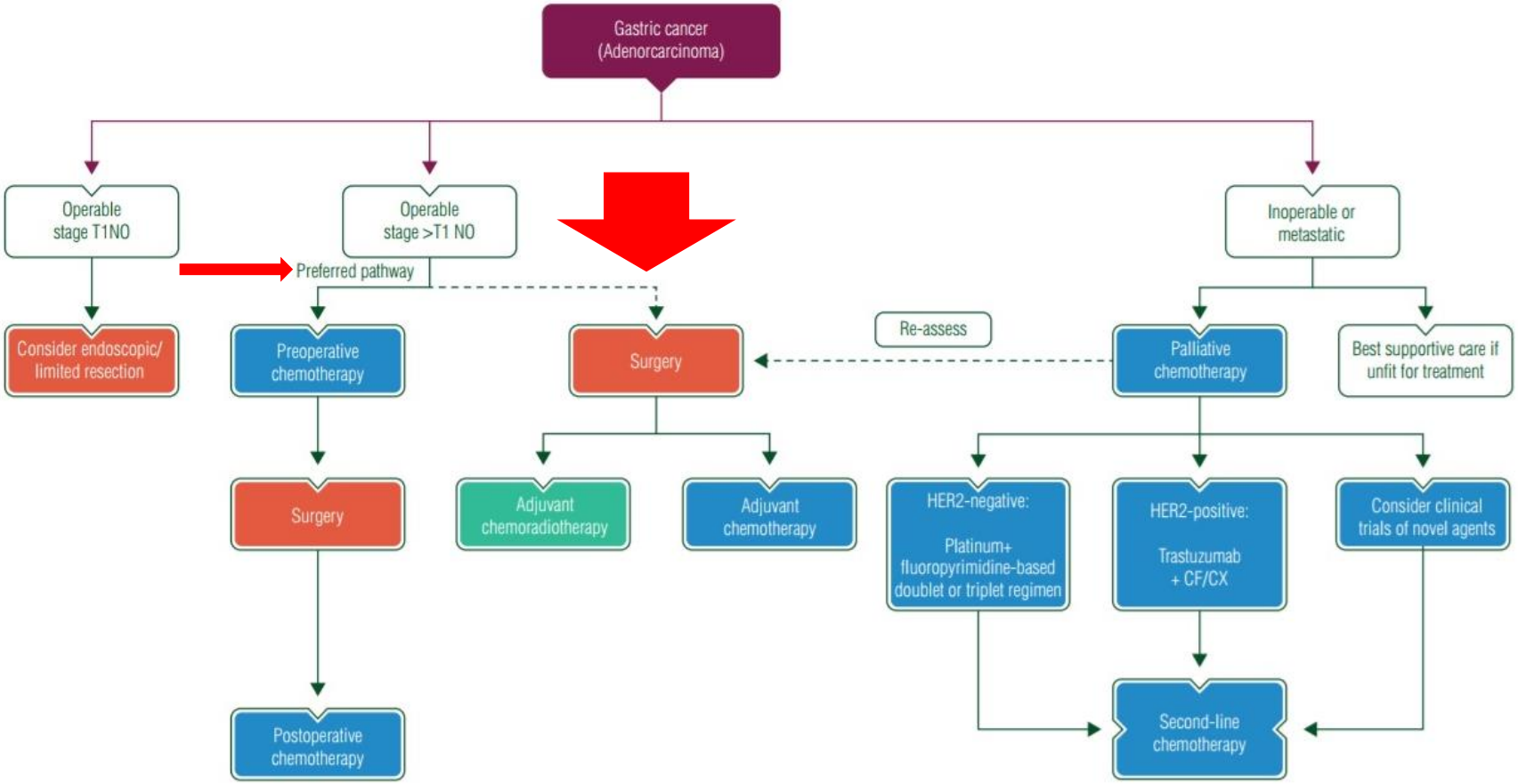


Figure 1. Gastric cancer treatment algorithm.

HER2, human epidermal growth factor receptor 2; CF, cisplatin and 5-fluorouracil; CX, cisplatin and capecitabine

Zagadnienia

- 1. pooperacyjna radiochemioterapia
- **2. radio(chemio)terapia przedoperacyjna**
- 3. radykalna radio(chemio)terapia
- 4. paliatywna radioterapia

Założenia teoretyczne:

⇨ 1. Wielkości guza ⇩

⇨ 2. Resekcyjność ⇧

⇨ 3. R0 ⇧

⇨ 4. Wznowa ⇩

Założenia teoretyczne:

⇨ 5.Rozsiew

⇨ 6.Rozsiew wewnątrzotrzewnowy

⇨ 7.Skuteczność miejscowa

aspekty radiobiologiczne

⇨ 8.Planowanie RT

Metody leczenia:

1. Chemioterapia
2. Radioterapia
3. Terapia celowana, immunoterapia
4. Leczenie skojarzone

Neo-adjuvant chemotherapy for operable gastric cancer: long term results of the Dutch randomised FAMTX trial

H.H. Hartgrink[a,*], C.J.H. van de Velde[a], H. Putter[b], I. Songun[a,c], M.E.T. Tesselaar[d], E. Klein Kranenbarg[a], J.E. de Vries[e], J.A. Wils[f], J. van der Bijl[g], J.H.J.M. van Krieken[h], for the Cooperating Investigators of the Dutch Gastric Cancer Group[1]

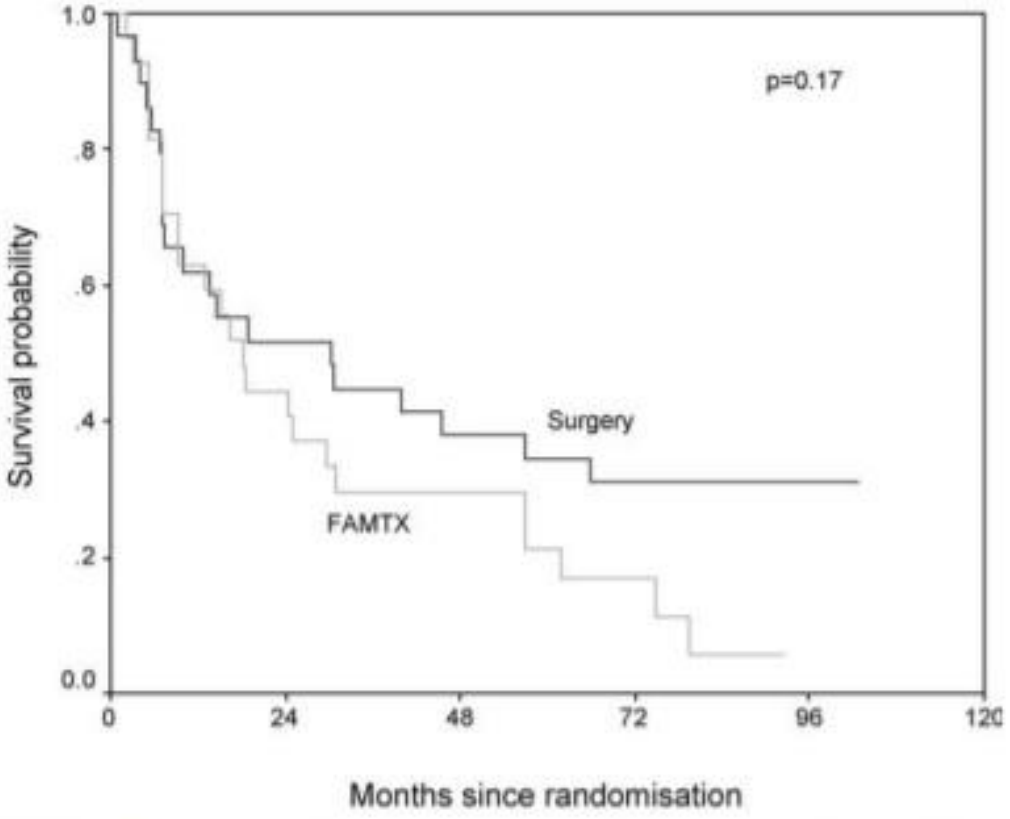


Figure 2 Overall survival of eligible patients ($n = 56$).

CHEMIOTERAPIA

Badanie	Liczba chorych	Schemat	Resekcyjność	R0	Guz-CR	N0
MAGIC	250	ECF/CH/ECF	87%	69%	0%	31%
	253	**Ch**	94%	66%	0%	27%
ACCORD07	113	DDP+FU/Ch/ DDP+FU	94%	87%	3%	33%
	111	**Ch**	90%	74%	0%	20%

CHEMIOTERAPIA

Badanie	LR	LRR	DM	5-letnie przeżycie	Mediana przeżycia (mies.)
MAGIC	14%	b.d.	24%	36%	25
	21%	b.d.	37%	23%	20
ACCORD07	24%	b.d.	42%	38%	32
	26%	b.d.	56%	24%	22

Table 3. Surgical and Pathological Results.

Variable	Perioperative-Chemotherapy Group (N=250)	Surgery Group (N=253)
	number of patients/total number (percent)	
Extent of resection according to surgeon		
Curative	169/244 (69.3)	166/250 (66.4)
Palliative	44/244 (18.0)	70/250 (28.0)
Opinion not specified	16/244 (6.6)	8/250 (3.2)
No surgery	15/244 (6.1)	6/250 (2.4)
Surgical status unknown	6/250 (2.4)	3/253 (1.2)
Operation performed*		
Esophagogastrectomy	58/219 (26.5)	52/238 (21.8)
D1 distal resection	19/219 (8.7)	30/238 (12.6)
D1 total resection	20/219 (9.1)	20/238 (8.4)
D2 distal resection	32/219 (14.6)	24/238 (10.1)
D2 total resection	61/219 (27.9)	72/238 (30.3)
Nonresectional surgery	29/219 (13.2)	40/238 (16.8)
Unknown	10/229 (4.4)	6/244 (2.5)
Pathology reports		
Tumor stage (all patients)		
T1	27/172 (15.7)	16/193 (8.3)
T2	62/172 (36.0)	55/193 (28.5)
T3	75/172 (43.6)	106/193 (54.9)
T4	8/172 (4.7)	16/193 (8.3)
Nodal status (patients with gastric cancer)		
N0	42/135 (31.1)	42/156 (26.9)
N1 (<7 nodes involved)	72/135 (53.3)	68/156 (43.6)
N2 (7–14 nodes involved)	19/135 (14.1)	34/156 (21.8)
N3 (>14 nodes involved)	2/135 (1.5)	12/156 (7.7)



* D1 denotes limited lymph-node dissection, and D2 extended lymph-node dissection.

Badania kliniczne vs praktyka kliniczna

Table 1. Pretreatment Characteristics of the Patients.*

Characteristic	Perioperative-Chemotherapy Group (N=250)	Surgery-Only Group (N=253)
Age		
<60 yr — no. (%)	108 (43.2)	104 (41.1)
60–69 yr — no. (%)	91 (36.4)	95 (37.5)
≥70 yr — no. (%)	51 (20.4)	54 (21.3)
Median — yr	62	62
Range — yr	29–85	23–81
Sex — no. (%)		
Male	205 (82.0)	191 (75.5)
Female	45 (18.0)	62 (24.5)
WHO performance status — no. (%)†		
0	169 (67.6)	173 (68.4)
1	81 (32.4)	80 (31.6)
Site of tumor — no. (%)		
Stomach	185 (74.0)	187 (73.9)
Lower esophagus	37 (14.8)	36 (14.2)
Esophagogastric junction	28 (11.2)	30 (11.9)
Maximum tumor diameter		
0.0–3.9 cm — no. (%)‡	50 (30.9)	61 (33.3)
4.0–7.9 cm — no. (%)‡	79 (48.8)	87 (47.5)
8.0–11.9 cm — no. (%)‡	29 (17.9)	24 (13.1)
12.0–15.9 cm — no. (%)‡	2 (1.2)	8 (4.4)
>16.0 cm — no. (%)‡	2 (1.2)	3 (1.6)
Unknown — no. (%)	88 (35.2)	70 (27.7)
Median — cm	5.0	5.0
Interquartile range — cm	3.0–7.0	3.0–7.0

Badania kliniczne vs praktyka kliniczna

Żródło	3 cykle + CH + 3 cykle
MAGIC	**44%**
Kanhere i wsp.	**32%**

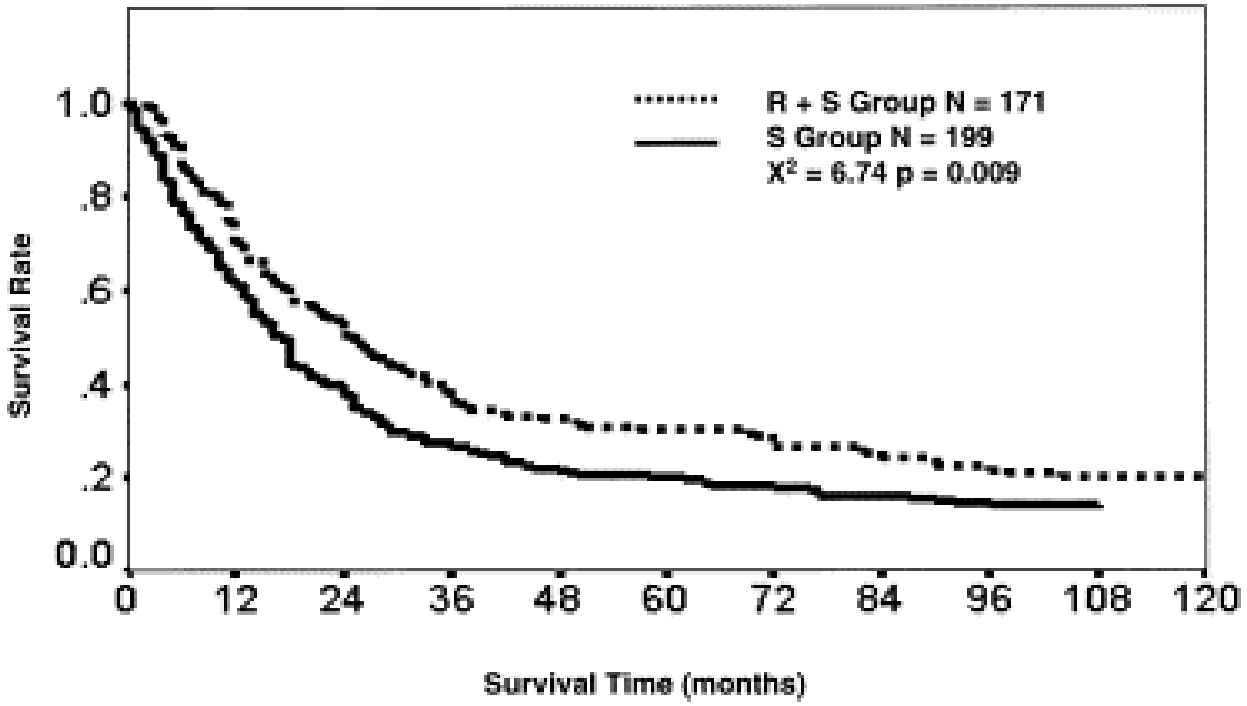
Metody leczenia:

1. Chemioterapia
2. Radioterapia
3. Terapia celowana, immunoterapia
4. Leczenie skojarzone

RADIOTERAPIA

Study	Number of pts.	Schedule	Resectability	R0	CR-tumor	pN0
Zhang	171	40Gy+Ch	90%	85%	0%	36%
	199	Ch	79%	75%	0%	15%

Zhang


R + S Group N = 171
S Group N = 199
X² = 6.74 p = 0.009
Survival Rate
1.0
.8
.6
.4
.2
0.0
0
12
24
36
48
60
72
84
96
108
120
Survival Time (months)

Metody leczenia:

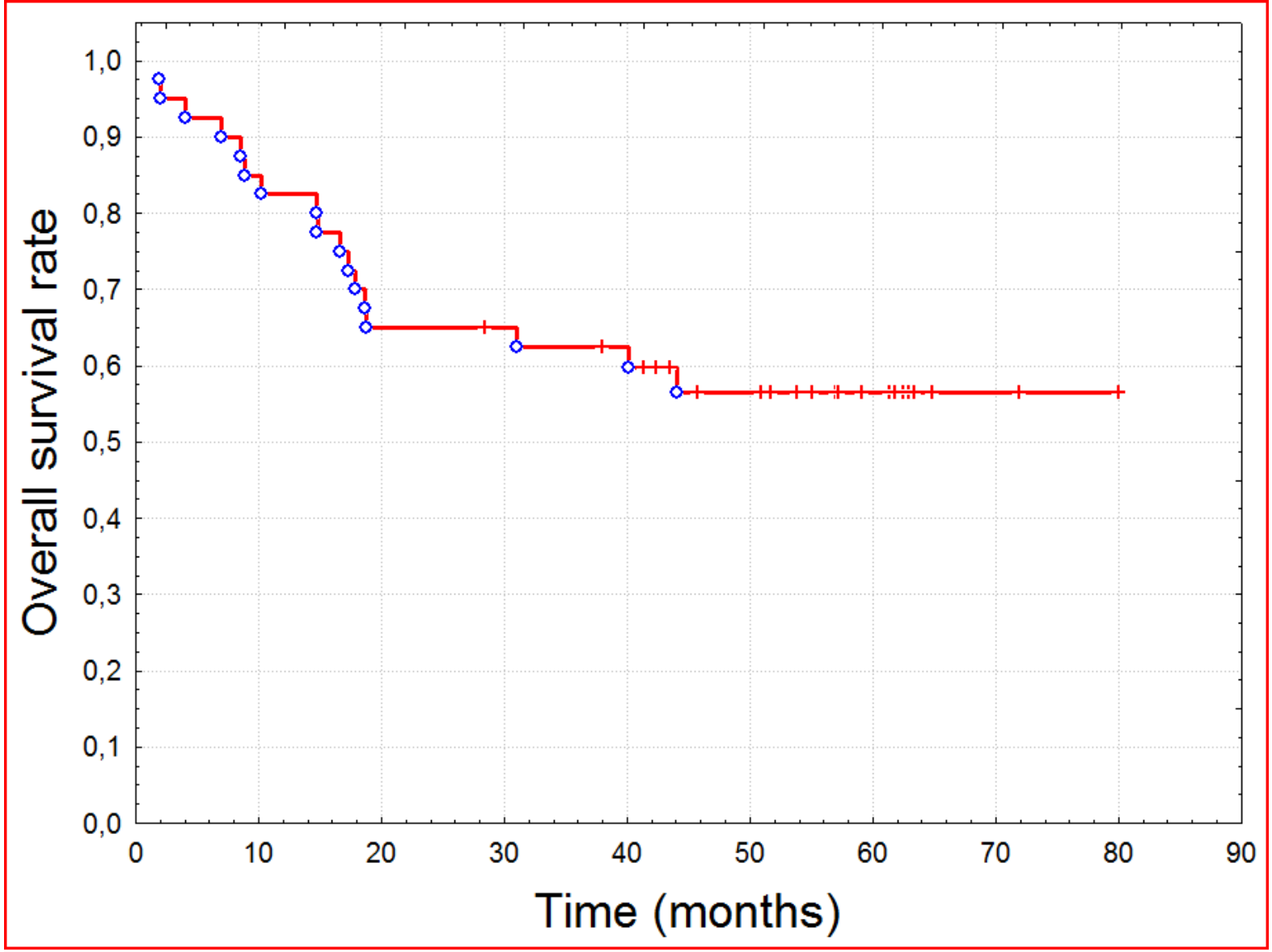
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Metody leczenia:

1. Chemioterapia
2. Radioterapia
3. Terapia celowana, immunoterapia
4. Leczenie skojarzone

RADIOCHEMIOTERAPIA
badania II fazy

Study	Number of pts.	Schedule	Resectability	R0	CR-tumor
Lowy	24	45Gy+CT	79%	94%	10%
Ajani	34	45Gy+CT	82%	82%	35%
Balandraud	42	45Gy+CT	90%	89%	14%
Allal	19	31,2-45,6Gy +CT	100%	81%	5%
Ajani	41	45Gy+CT	98%	78%	20%
Ajani	49/43	45Gy+CT	83%	77%	26%
Wydmański	40	45Gy+CT	80%	94%	18%

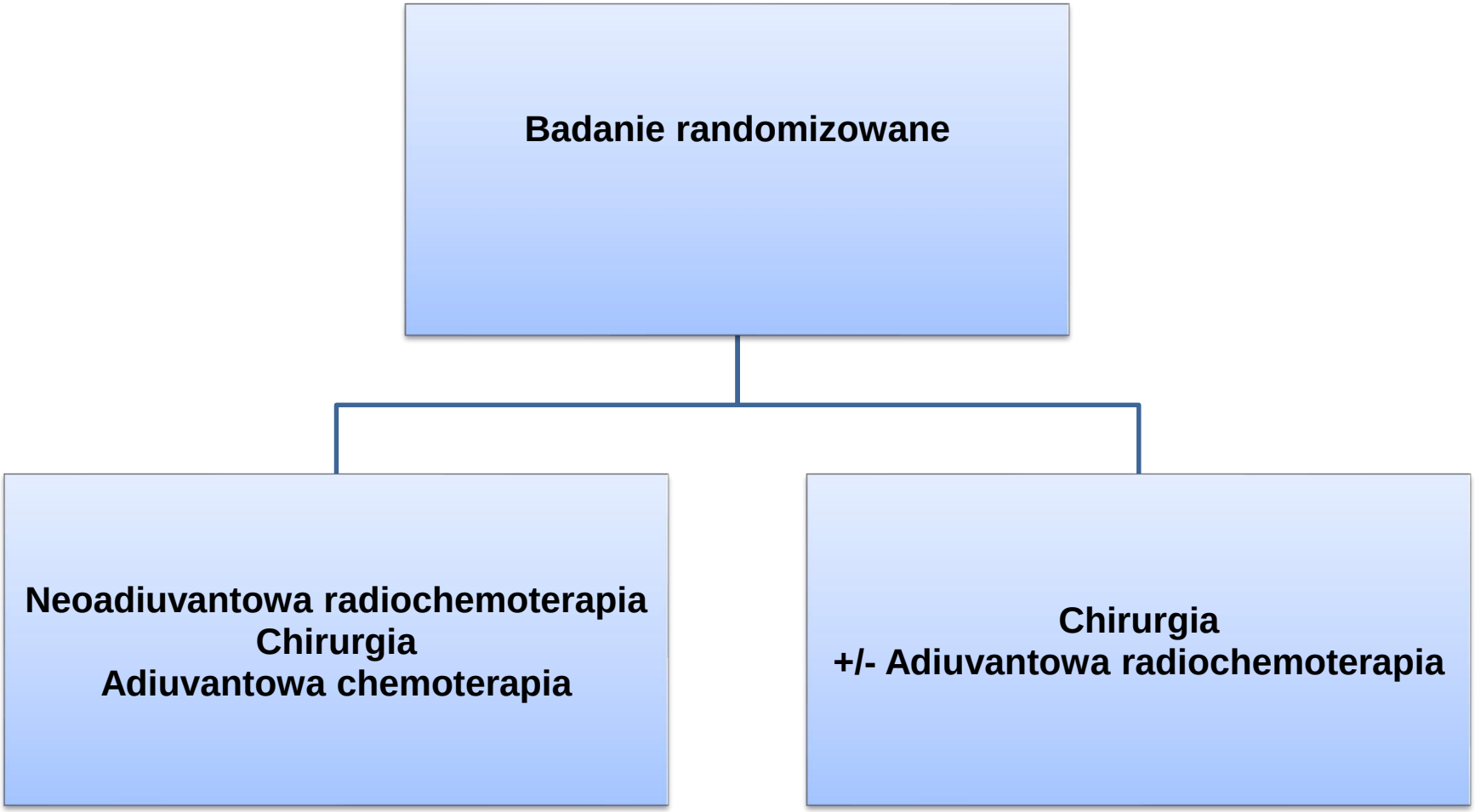


The tolerance and efficacy of preoperative chemoradiotherapy followed by gastrectomy in operable gastric cancer, a phase II study

Jerzy Wydmański[a,b,*], Rafal Suwinski[b], Stanislaw Poltorak[c], Bogusław Maka[c], Leszek Miszczyk[b], Edyta Wolny[b], Grzegorz Bielaczyc[d], Aleksander Zajusz[b]

Radiotherapy and Oncology 82 (2007) 132–136
www.thegreenjournal.com

Gliwice-2006



Schemat leczenia

1. Neoadiuvantowa radiochemioterapia

   RT 45Gy/1.8Gy

   CT 5-Fu 325mg/m2 d1-5 i d29-33

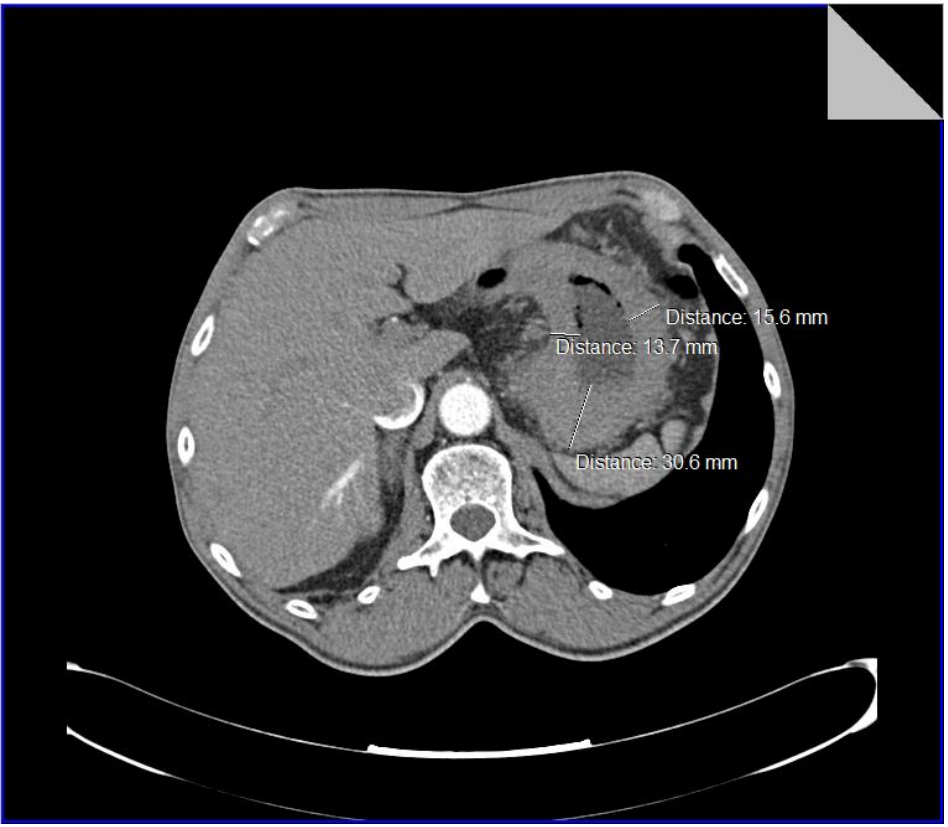
2. Chirurgia

3. Adiuvantowa chemoterapia LF1

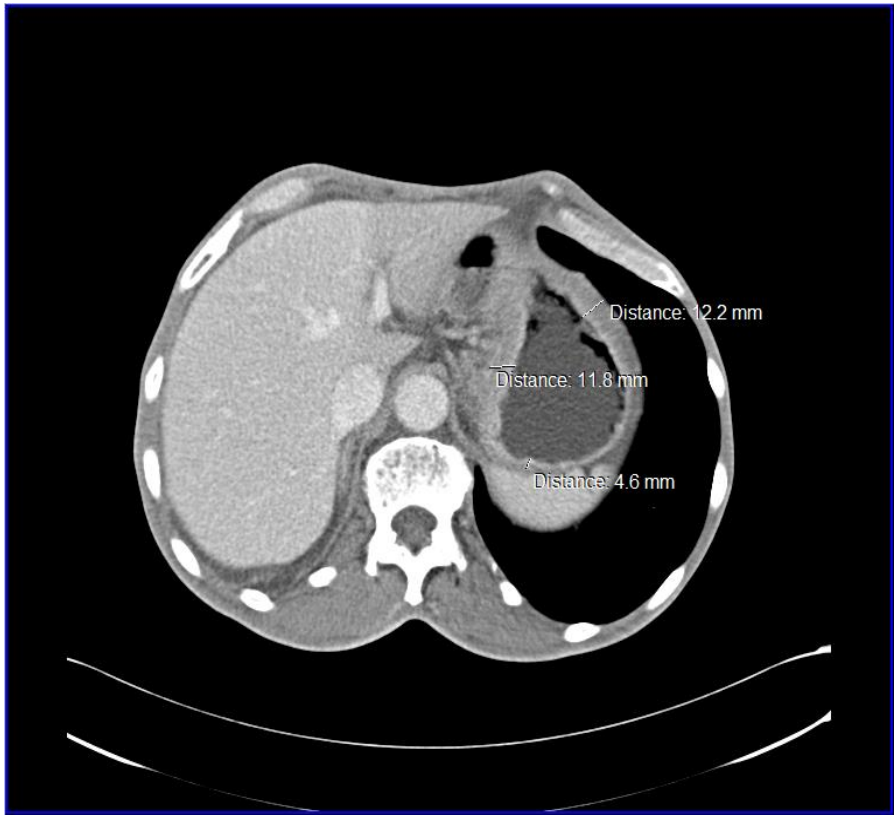
Tolerancja RTCT

Skutki uboczne	A	B
Wymioty		
0	40%	77%
1 lub 2	53%	23%
3 lub 4	7%	0%
Biegunka		
0	68%	31%
1 lub 2	30%	62%
3 lub 4	2%	7%
Leukopenia		
0	35%	31%
1 lub 2	60%	62%
3 lub 4	5%	7%

Przed RTCT



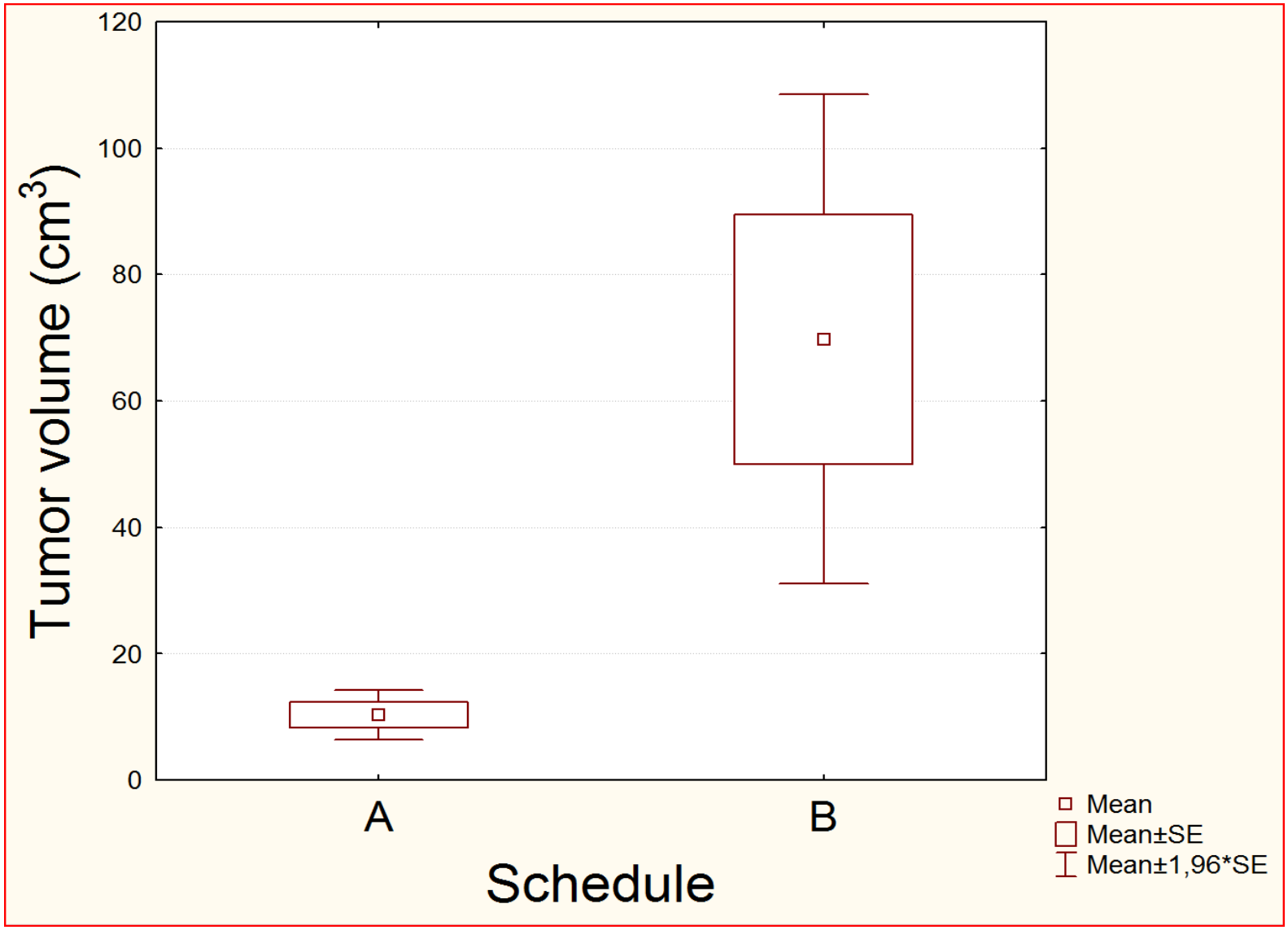
Po RTCT



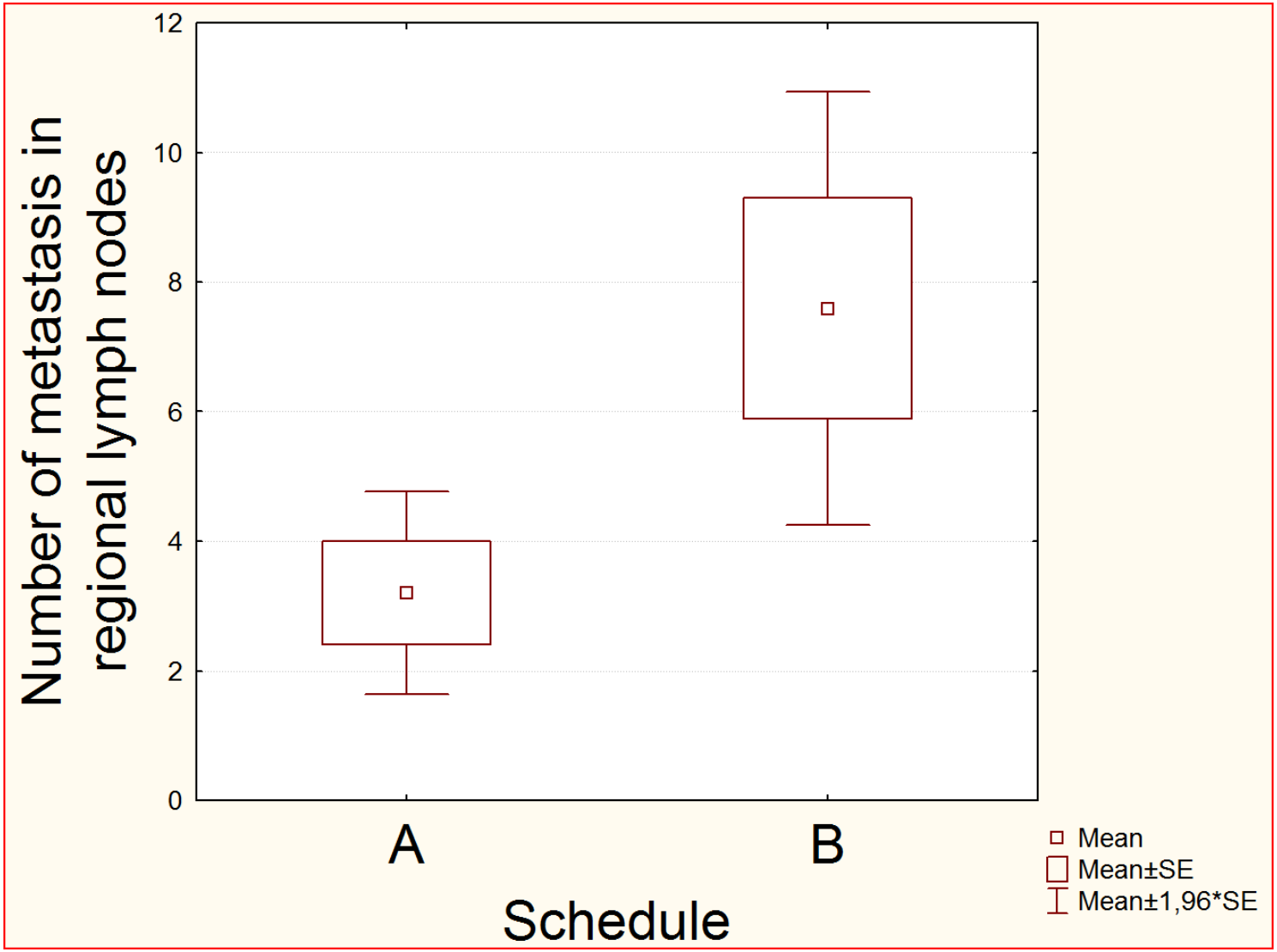
Leczenie chirurgiczne

	A	B
Resekcyjność	88%	73%
R0	84%	64%
R1	4%	4.5%
R2	0%	4.5%

Objętość guza w badaniu H-P

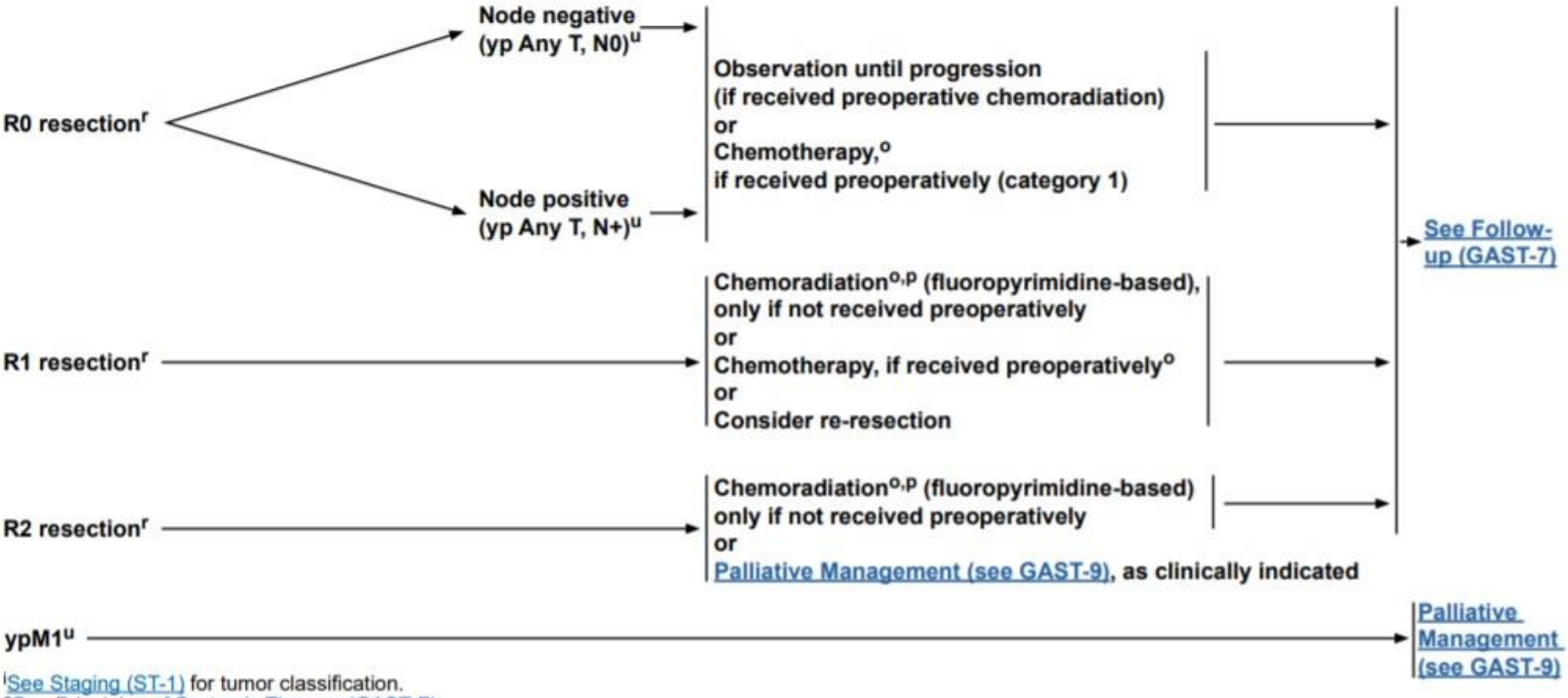


Liczba przerzutowych węzłów chłonnych



RADIOCHEMIOTERAPIA
badania III fazy

Badanie	Liczba chorych	Schemat	3-lata	5-lat
POET	119	CHT	26,1%	24,4%
		30 Gy+CHT	46,7%	39,5%



[i] See Staging (ST-1) for tumor classification.
[o] See Principles of Systemic Therapy (GAST-F).
[p] See Principles of Radiation Therapy (GAST-G).
[R0 = No cancer at resection margins, R1 = Microscopic residual cancer, R2 = Macroscopic residual cancer or M1

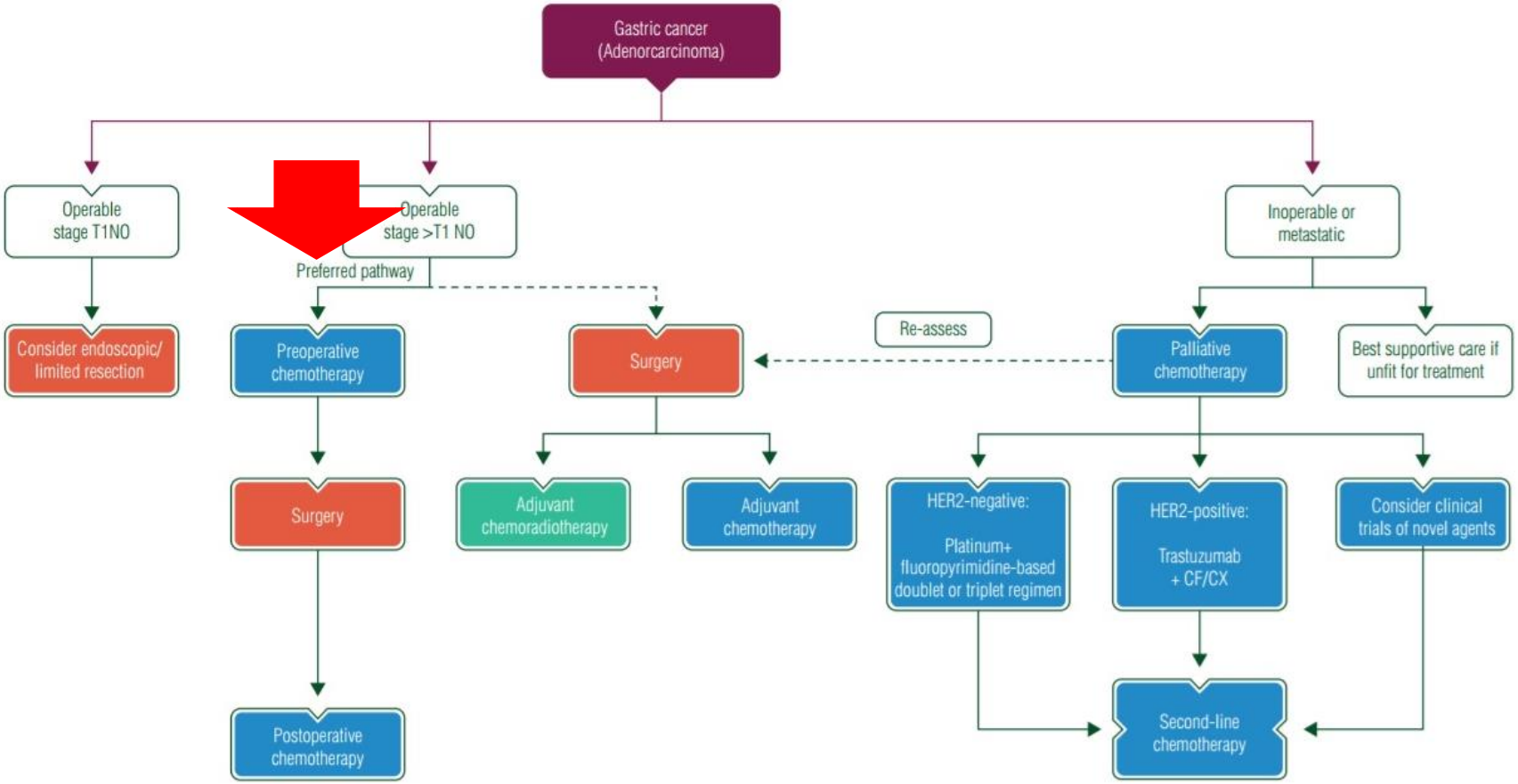


Figure 1. Gastric cancer treatment algorithm.

HER2, human epidermal growth factor receptor 2; CF, cisplatin and 5-fluorouracil; CX, cisplatin and capecitabine

Zagadnienia

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- 2. radio(chemio)terapia przedoperacyjna
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- 4. paliatywna radioterapia

Nieresekcyjny rak żołądka , M0



Nieresekcyjny/nieoperacyjny rak żołądka , M0

- Zaawansowanie miejscowe – po laparotomii zwiadowczej
- Zaawansowanie miejscowe – na podstawie CT/MR
- Operacyjny guz – p/wskazania internistyczne do znieczulenia
- Operacyjny guz – brak zgody chorego na leczenie operacyjne
- Zaawansowanie miejscowe – na podstawie CT/MR – granicznie operacyjny rak
- Nieoperacyjne/nieresekcyjne wznowy miejscowe

clinical practice guidelines

Annals of Oncology 24 (Supplement 6): vi57–vi63, 2013
doi:10.1093/annonc/mdt344

Gastric cancer†: ESMO–ESSO–ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up

T. Waddell[1], M. Verheij[2], W. Allum[3], D. Cunningham[4], A. Cervantes[5] & D. Arnold[6*]

[1]GI Clinical Trials Unit, Royal Marsden Hospital, Sutton, UK; [2]Department of Radiation Oncology and Division of Biological Stress Response, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands; [3]Department of Surgery, Royal Marsden Hospital, London; [4]Department of Medicine, Royal Marsden Hospital, Sutton, UK; [5]Department of Hematology and Medical Oncology, INCLIVA, University of Valencia, Valencia, Spain; [6]Department of Medical Oncology, Tumor Biology Center, Freiburg, Germany

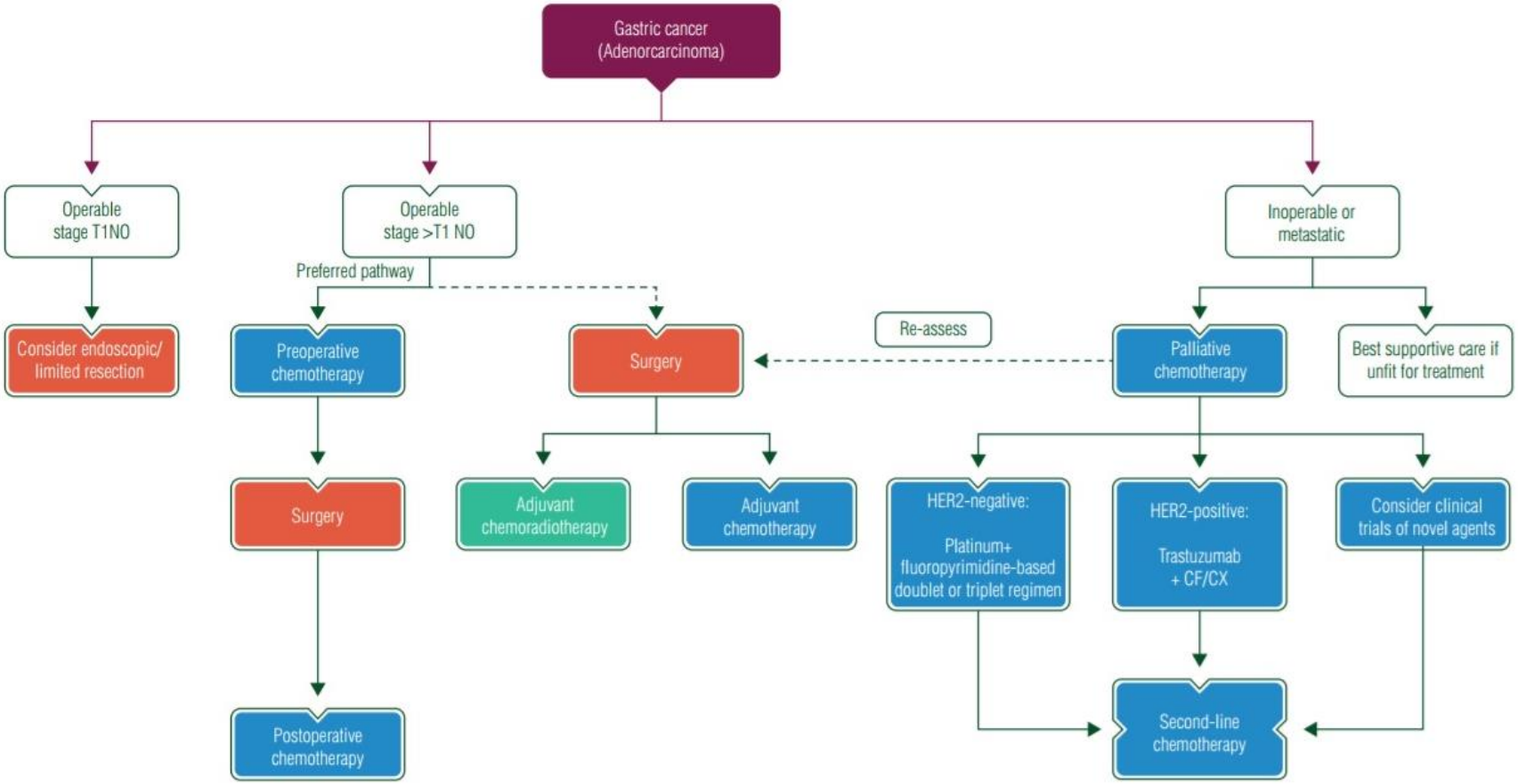


Figure 1. Gastric cancer treatment algorithm.
HER2, human epidermal growth factor receptor 2; CF, cisplatin and 5-fluorouracil; CX, cisplatin and capecitabine

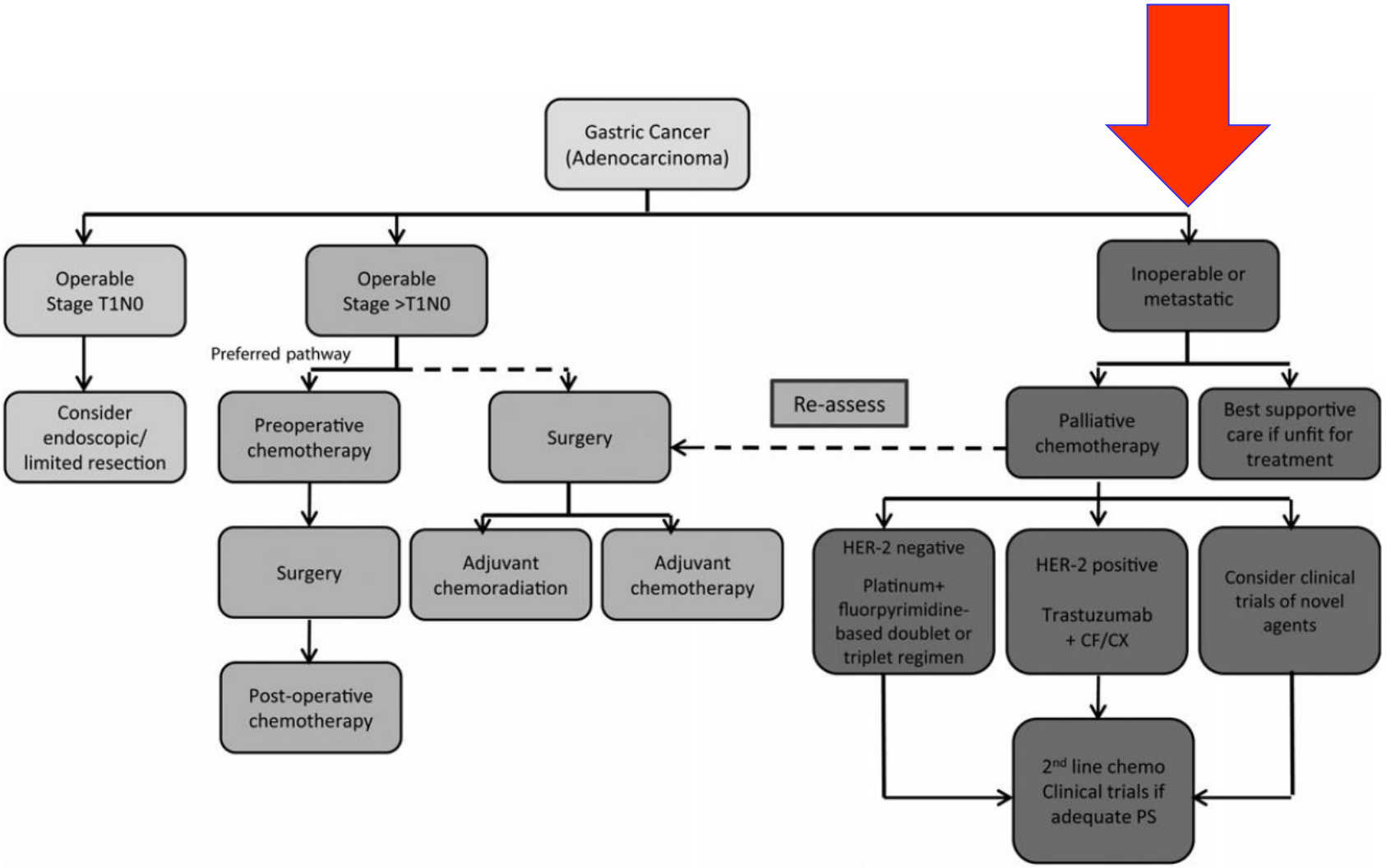
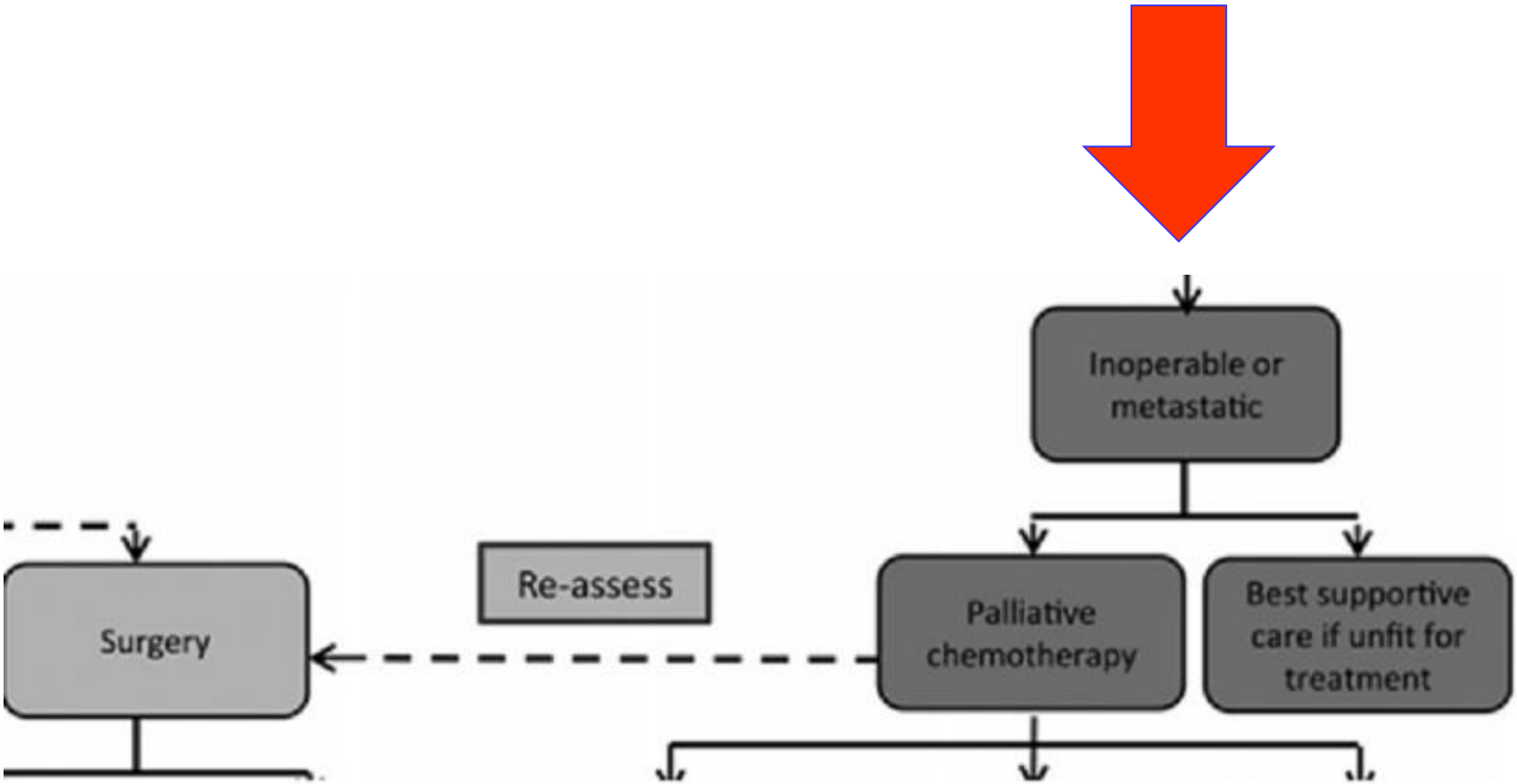
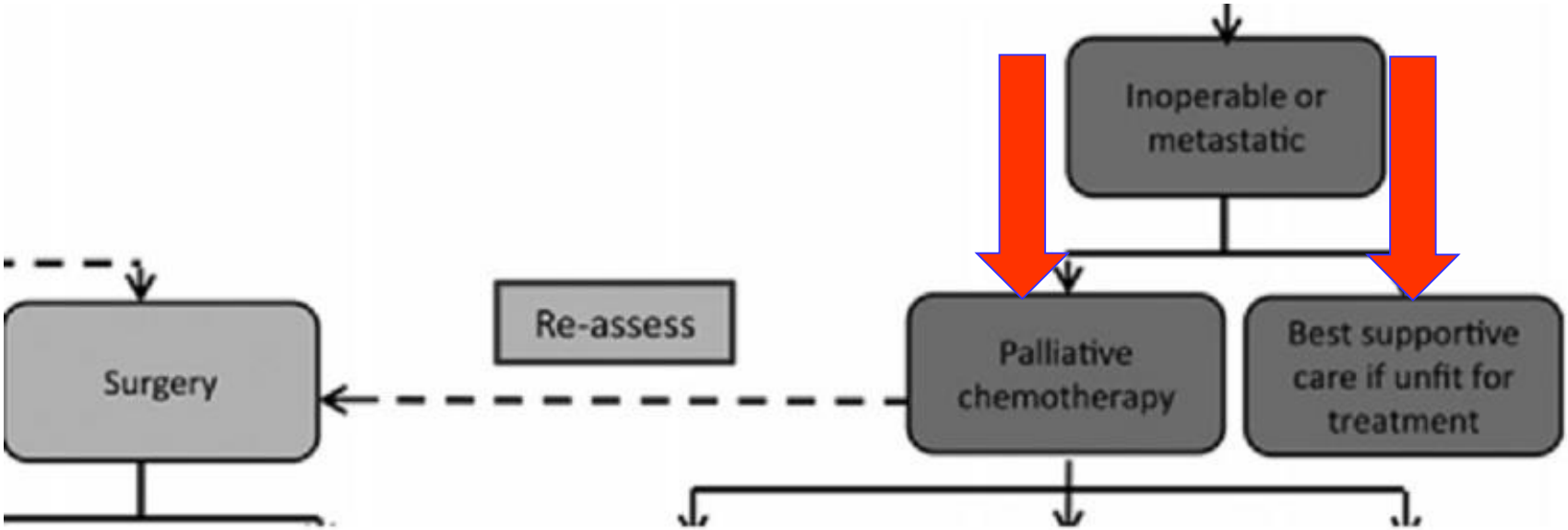


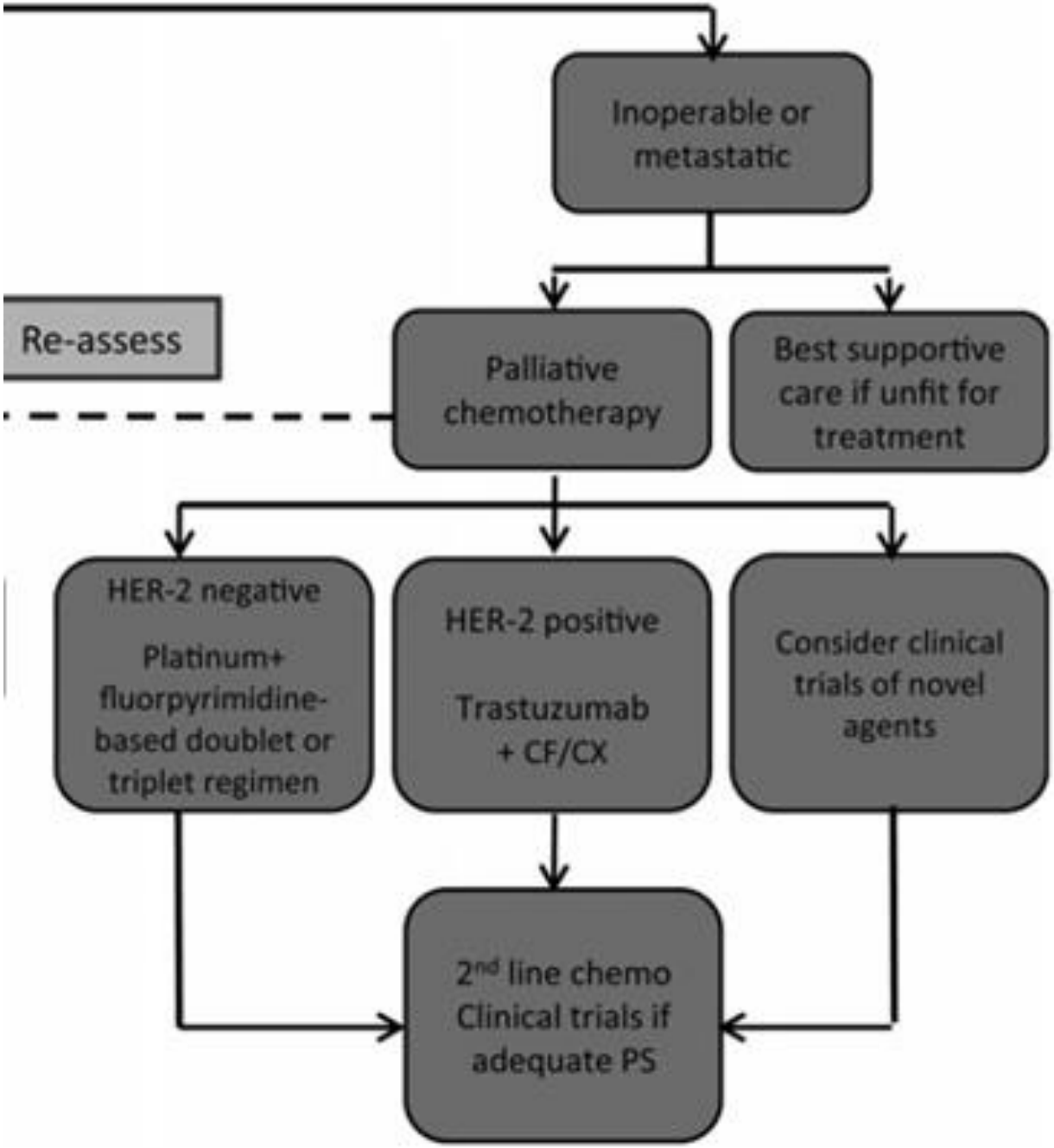
Figure 1. Algorithm for the management of gastric cancer.

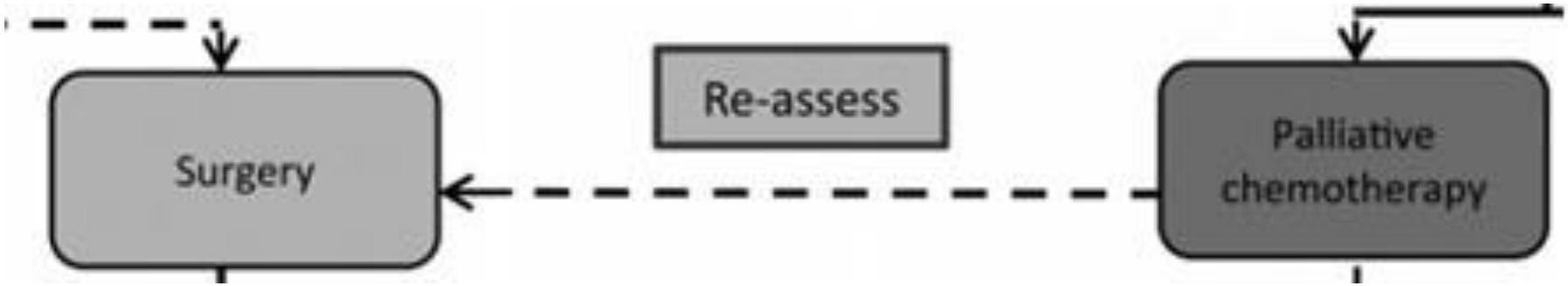

Inoperable or metastatic
Palliative chemotherapy
Best supportive care if unfit for treatment
Re-assess
Surgery


Inoperable or metastatic
Re-assess
Surgery
Palliative chemotherapy
Best supportive care if unfit for treatment

Best **S**upportive **C**are




Inoperable or metastatic
Re-assess
Palliative chemotherapy
Best supportive care if unfit for treatment
HER-2 negative
Platinum+ fluorpyrimidine-based doublet or triplet regimen
HER-2 positive
Trastuzumab + CF/CX
Consider clinical trials of novel agents
2nd line chemo
Clinical trials if adequate PS


Surgery
Re-assess
Palliative chemotherapy

BSC vs CHT

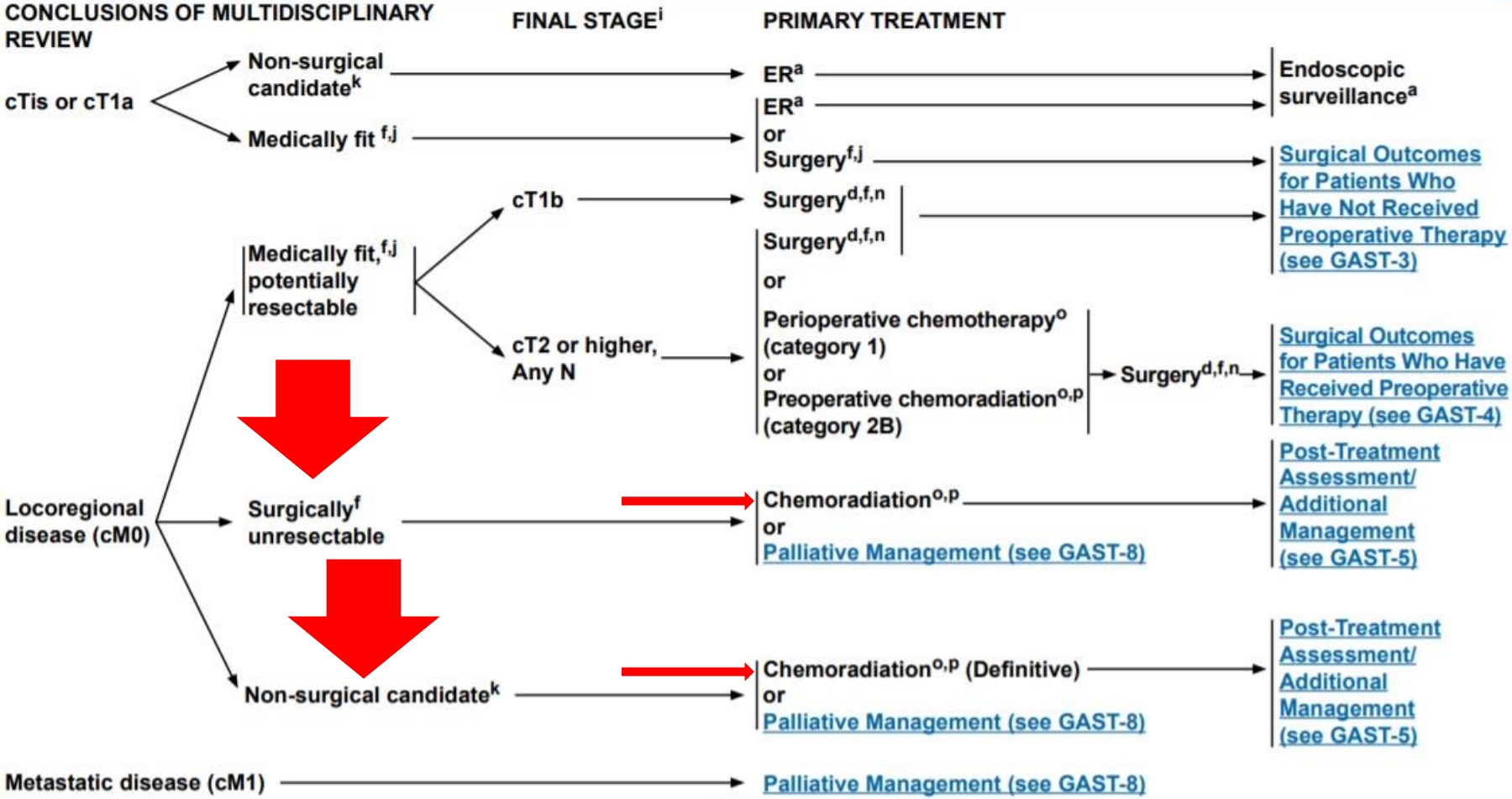
Schemat CHT	Liczba chorych	Mediana przeżycia (mies.)
FAMTX BSC	30 10	10 3
FAMTX BSC	17 19	12 3
ELF BSC	10 8	10 3

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National Comprehensive Cancer Network®

NCCN Guidelines Version 5.2017
Gastric Cancer
NCCN Evidence Blocks™

NCCN Guidelines Index
Table of Contents
Discussion



[a]See Principles of Endoscopic Staging and Therapy (GAST-A).
[d]See Principles of Pathologic Review and HER2 Testing (GAST-B).
[f]See Principles of Surgery (GAST-C).

[k]Medically unable to tolerate major surgery or medically fit patients who decline surgery.
[n]Surgery as primary therapy is appropriate for ≥T1b cancer or actively bleeding cancer, or when postoperative therapy is preferred.

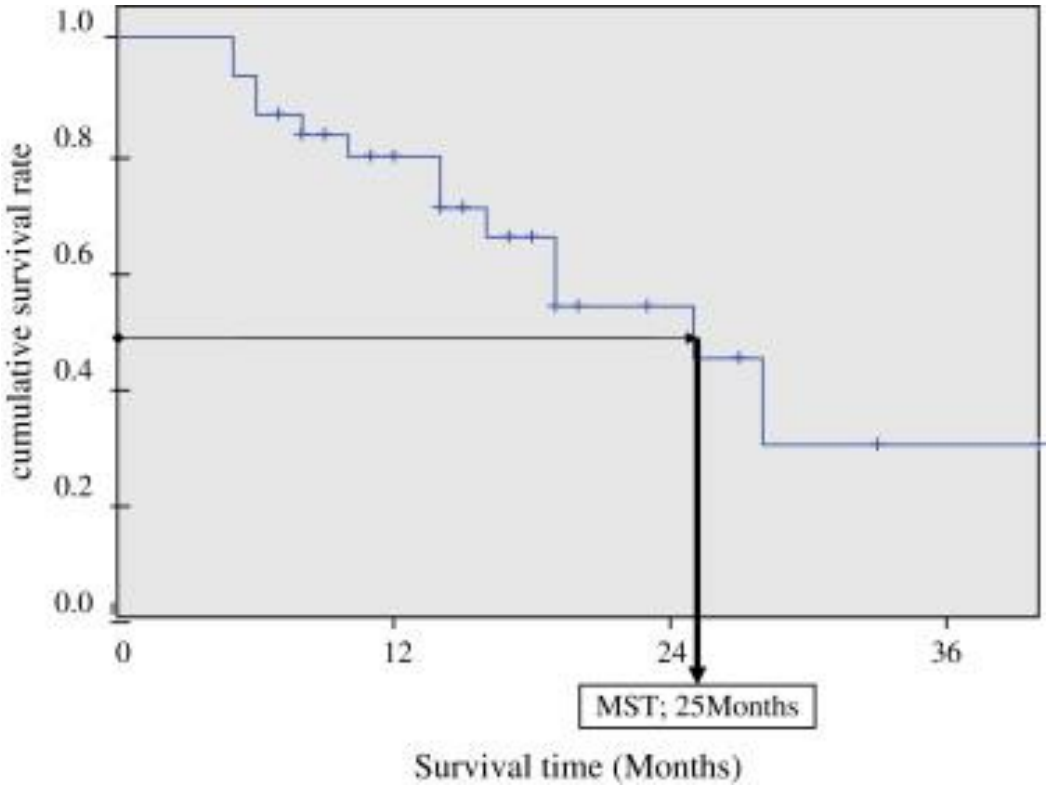
Przypadki nieresekcyjne/nieoperacyjne

- **Radio(chemio)terapia radykalna?**

PHASE II STUDY OF CHEMORADIOTHERAPY WITH S-1 AND LOW-DOSE CISPLATIN FOR INOPERABLE ADVANCED GASTRIC CANCER

YOSHIRO SAIKAWA, M.D., PH.D.,* TETSURO KUBOTA, M.D., PH.D.,† KOSHI KUMAGAI, M.D.,* RIEKO NAKAMURA, M.D.,* KOICHIRO KUMAI, M.D., PH.D.,‡ NAOYUKI SHIGEMATSU, M.D., PH.D.,§ ATSUSHI KUBO, M.D., PH.D.,§ MASAKI KITAJIMA, M.D., PH.D.,* AND YUKO KITAGAWA, M.D., PH.D.*

Int. J. Radiation Oncology Biol. Phys., Vol. 71, No. 1, pp. 173–179, 2008



National Cancer Database 2004-2015

Schemat leczenia	Liczba chorych	2-letnie przeżycie
chemioterapia	3316	21,5%
radiochemioterapia	1479	28,3%

Chemoradiation Improves Survival Compared With Chemotherapy Alone in Unresected Nonmetastatic Gastric Cancer

Richard Li, MD[a], Wei-Hsien Hou, MD, PhD[a], Joseph Chao, MD[b], Yanghee Woo, MD[c], Scott Glaser, MD[a], Arya Amini, MD[a], Rebecca A. Nelson, PhD[d] and Yi-Jen Chen, MD, PhD[a]

Schemat leczenia

1. Radykalna radio(chemio)terapia

   RT 45Gy/1.8Gy

   CT 5-Fu 325mg/m2 d1-5 i d29-33

Przed RTCT

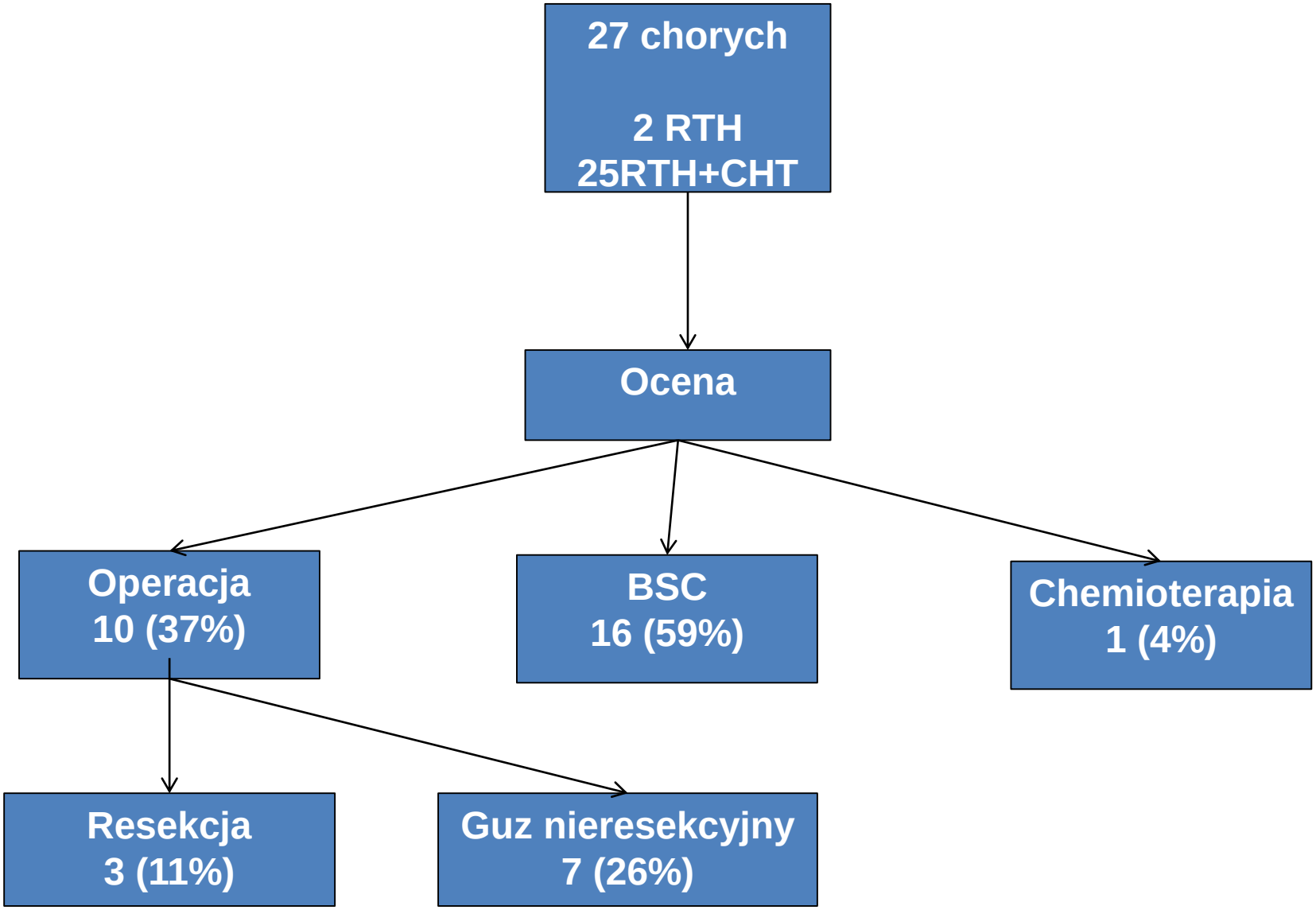


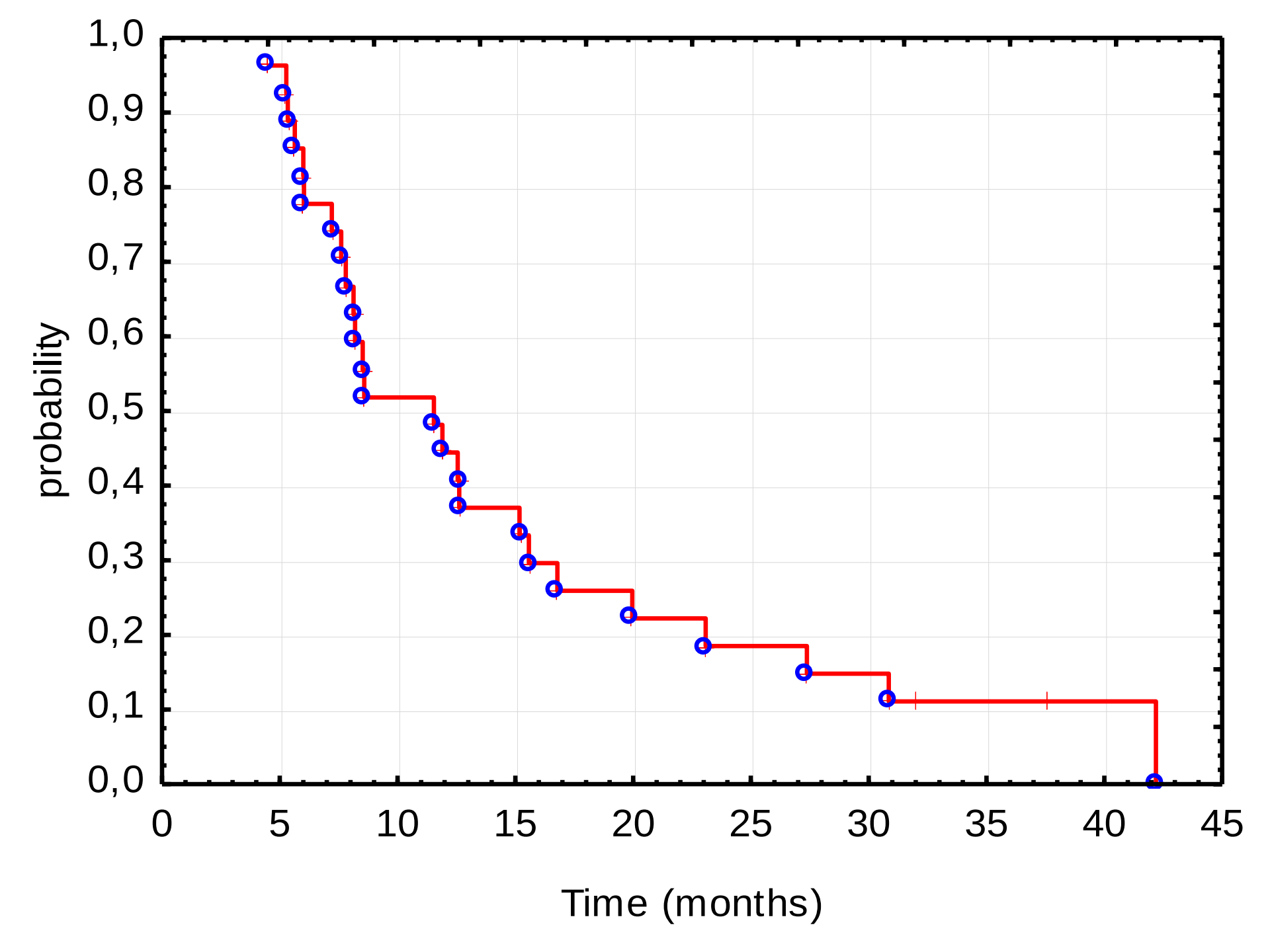
Po RTCT



TK po 6-8 tyg.

regresja	Liczba chorych	%
CR	1	3.7
PR	5	18.5
SD	7	25.9
PD	11	40.8
Brak danych	3	11.1


27 chorych
2 RTH
25RTH+CHT
Ocena
Operacja
10 (37%)
BSC
16 (59%)
Chemioterapia
1 (4%)
Resekcja
3 (11%)
Guz nieresekcyjny
7 (26%)


1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
probability
0
5
10
15
20
25
30
35
40
45
Time (months)

Nieresekcyjny/nieoperacyjny rak żołądka , M0

- Zaawansowanie miejscowe – po laparotomii zwiadowczej
- Zaawansowanie miejscowe – na podstawie CT/MR
- **Operacyjny guz – p/wskazania internistyczne do znieczulenia**
- **Operacyjny guz – brak zgody chorego na leczenie operacyjne**
- Zaawansowanie miejscowe – na podstawie CT/MR – granicznie operacyjny rak

Schemat leczenia

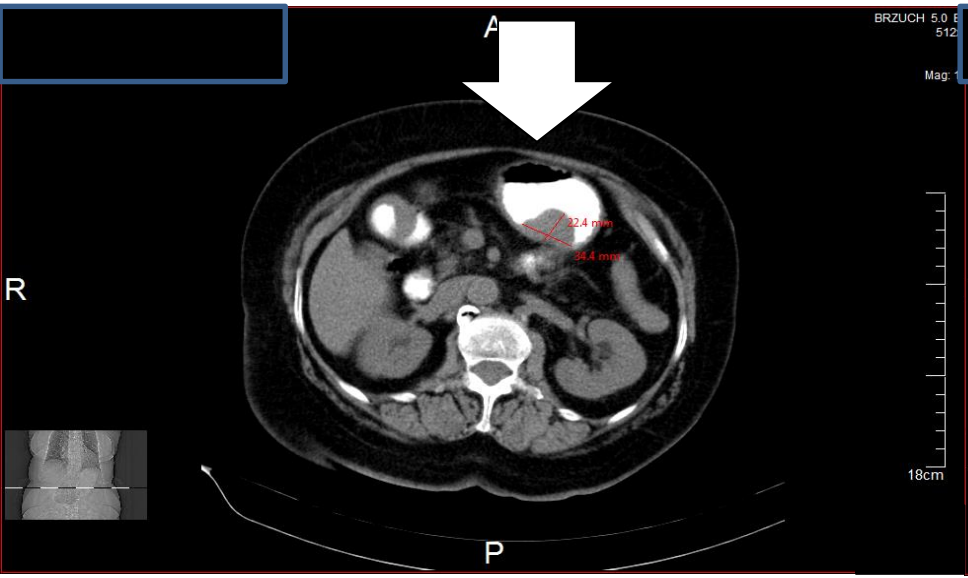
1. Radykalna radio(chemio)terapia

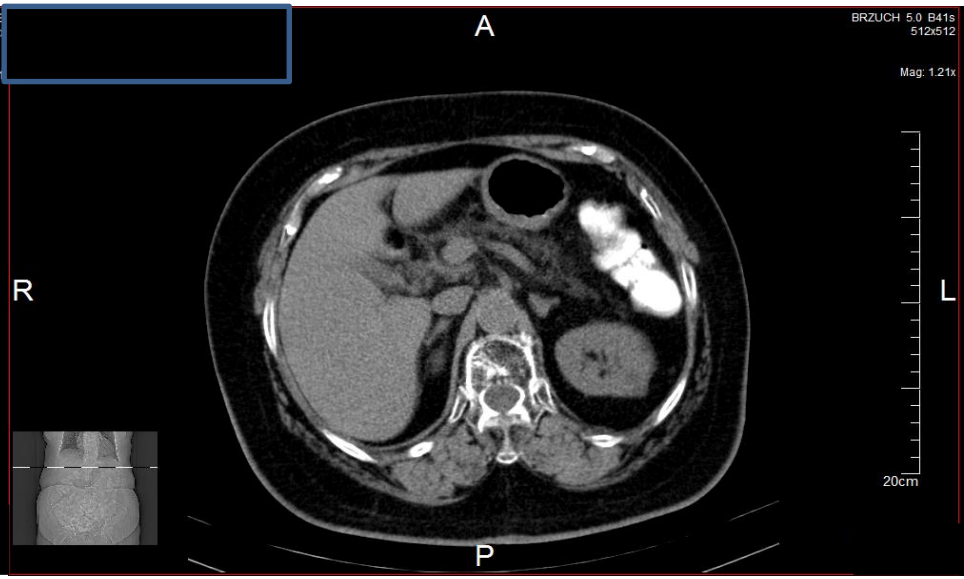
   RT 45Gy/1.8Gy

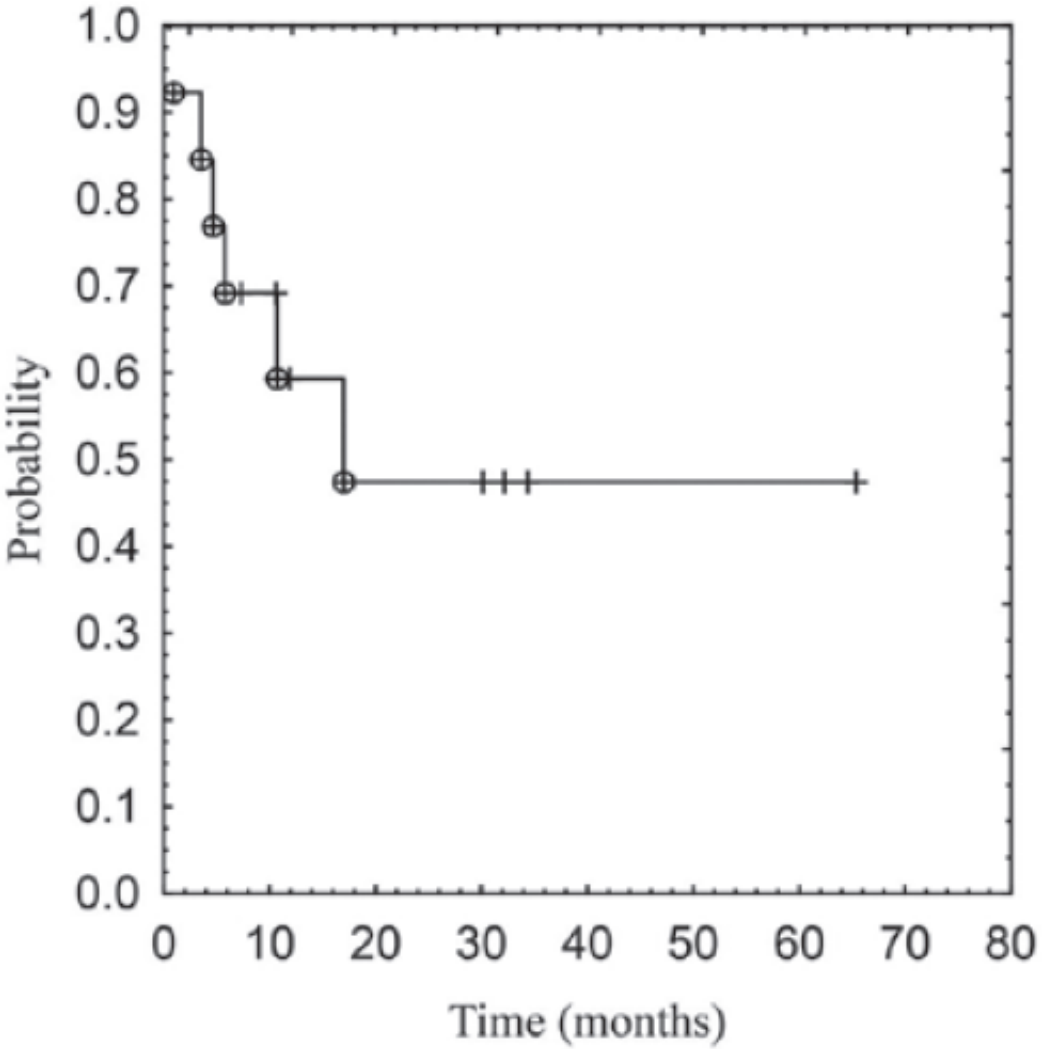
   CT 5-Fu 325mg/m2 d1-5 i d29-33

przed

po





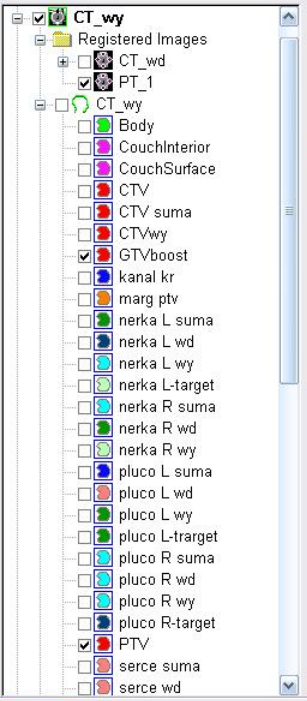

1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Probability
0
10
20
30
40
50
60
70
80
Time (months)

Kliszcz, Ryszard (170113-WLPPO), (55080614175) - External Beam Planning - [1E_TB - Completed Early - CT_wy - Blended with registered image: PT_1]

File Quick Links Edit View Insert Planning Tools Window Help









Fields | Dose Prescription | Field Alignments | Plan Objectives | Optimization Objectives | Dose Statistics | Calculation Models | Plan Sum

Group	Field ID	Technique	Machine/Energy	MLC	Field Weight	Scale	Gantry Rtn [deg]	Coll Rtn [deg]	Couch Rtn [deg]	Wedge	Field X [cm]	X1 [cm]	X2 [cm]	Field Y [cm]	Y1 [cm]	Y2 [cm]	X [cm]	Y [cm]	Z [cm]	SSD [cm]	MU	Ref. D [Gy]
☑	B	STATIC-I	TrueBeam1_BLUE - 6X		0.000	Varian IEC	270.0	0.0	0.0	None	12.0	+6.0	+6.0	12.0	+6.0	+6.0	2.10	-1.66	6.44	80.7		
☑	A	STATIC-I	TrueBeam1_BLUE - 6X		0.000	Varian IEC	0.0	0.0	0.0	None	12.0	+6.0	+6.0	12.0	+6.0	+6.0	2.10	-1.66	6.44	87.4		
☑	cbct	STATIC-I	TrueBeam1_BLUE - 6X		0.000	Varian IEC	0.0	0.0	0.0	None	10.0	+5.0	+5.0	10.0	+5.0	+5.0	2.10	-1.66	6.44	87.4		
☑	2	ARC-I	TrueBeam1_BLUE - 6X	VMAT	1.278	Varian IEC	179.0	350.0	357.0	None	22.1	+10.7	+11.4	33.2	+16.0	+17.2	2.10	-1.66	6.44	80.8	278	
☑	1	ARC-I	TrueBeam1_BLUE - 6X	VMAT	1.276	Varian IEC	181.0	10.0	3.0	None	22.1	+11.3	+10.7	32.2	+15.5	+16.7	2.10	-1.66	6.44	80.8	277	

Contouring | External Beam Planning | Brachytherapy Planning | Plan Evaluation

Ready | User: wojtek | Group: Account with all rights | Site: Main | NUM

start | Calculator | Kliszcz, Ryszard (170... | untitled - Paint | 10:54 AM

Zagadnienia

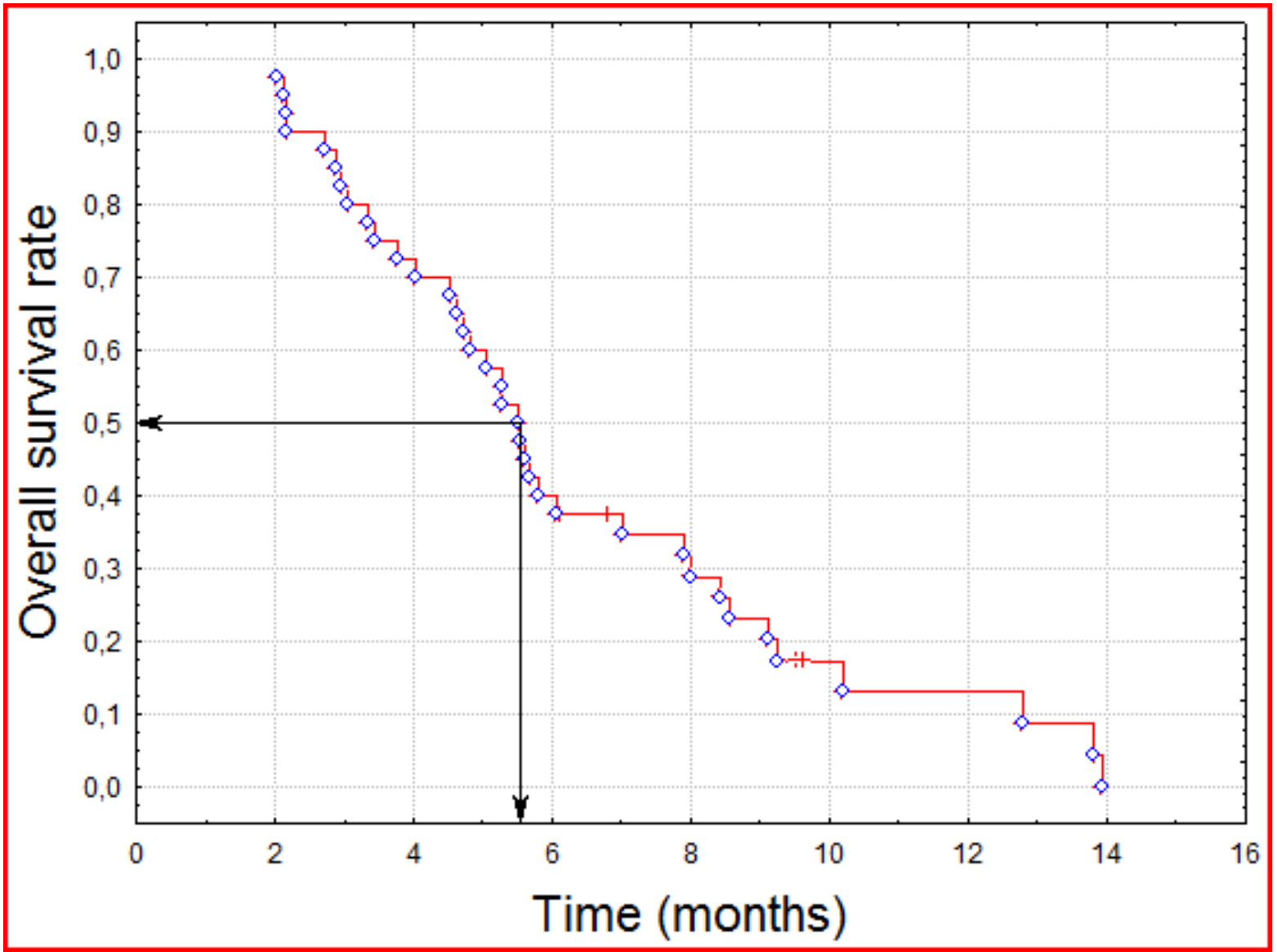
- 1. pooperacyjna radiochemioterapia
- 2. radio(chemio)terapia przedoperacyjna
- 3. radykalna radio(chemio)terapia
- **4. paliatywna radioterapia**



Table 2: Symptomatic response to palliative radiotherapy for gastric cancer

Author/ year	Radiotherapy (dose/fraction size/treatment period	Index symptom	Response	Survival (months)	Duration (months)	BED correlation
Kim MM 2008[6]	Median 35Gy (25-36Gy), 24/37 patients had concurrent chemotherapy)	Gastric bleeding, pain , obstruction	Bleeding 70%(14/20), pain 86% (6/7), obstruction 81% (13/16)	5.2	Bleeding (11.4), pain (NR), obstruction (6.2)	BED 41 Gy10 conferred better local control of symptoms but not overall survival
Hashimoto 2009[12]	Median 40Gy (2-50Gy in 1.8-3Gy / fr) (4/19 patients had CRT)	Gastric bleeding	Bleeding 68% (13/19)	3.4	1.5	BED 50 Gy10 conferred higher success rate of haemostasis compared to those received BED <50 Gy10
Lee JA 2009[13]	30 Gy / 10 fr (12/30 patients had CRT)	Gastric bleeding	Bleeding 91% (21/23)	4	4	NR
Asakura 2011[14]	30 Gy / 10 fr (12/30 patients had concurrent chemotherapy)	Gastric bleeding	Bleeding 73% (22/30)	3.6	3.3	BED 39 Gy10, conferred a response rate comparable to higher BED (50 Gy10 or more)
Chaw 2014[5]	8Gy single fr 20Gy / 5 fr	Gastric bleeding	Bleeding 50% (22/44, 8 patients unevaluable)	5.3	NR	BED 28 Gy10, conferred a similar response rate compared to other studies
Tey 2014[15]	8-40Gy	Bleeding, pain , obstruction	Bleeding 80.6%(83/103), pain 45.5% (5/11), obstruction 51.2% (9/17)	2.8	Bleeding (3.3), pain (7.8), obstruction (3.2)	Trend for poorer local control for BED ≤39 Gy10
Kondoh 2015[16]	Median 30Gy (30-40Gy in 2-3Gy / fr) (5/15 patients had CRT)	Bleeding	Bleeding 80.6%(11/15- RT:7/15 CRT: 4/15)	2.1	NR	NR

Paliatywna radioterapia



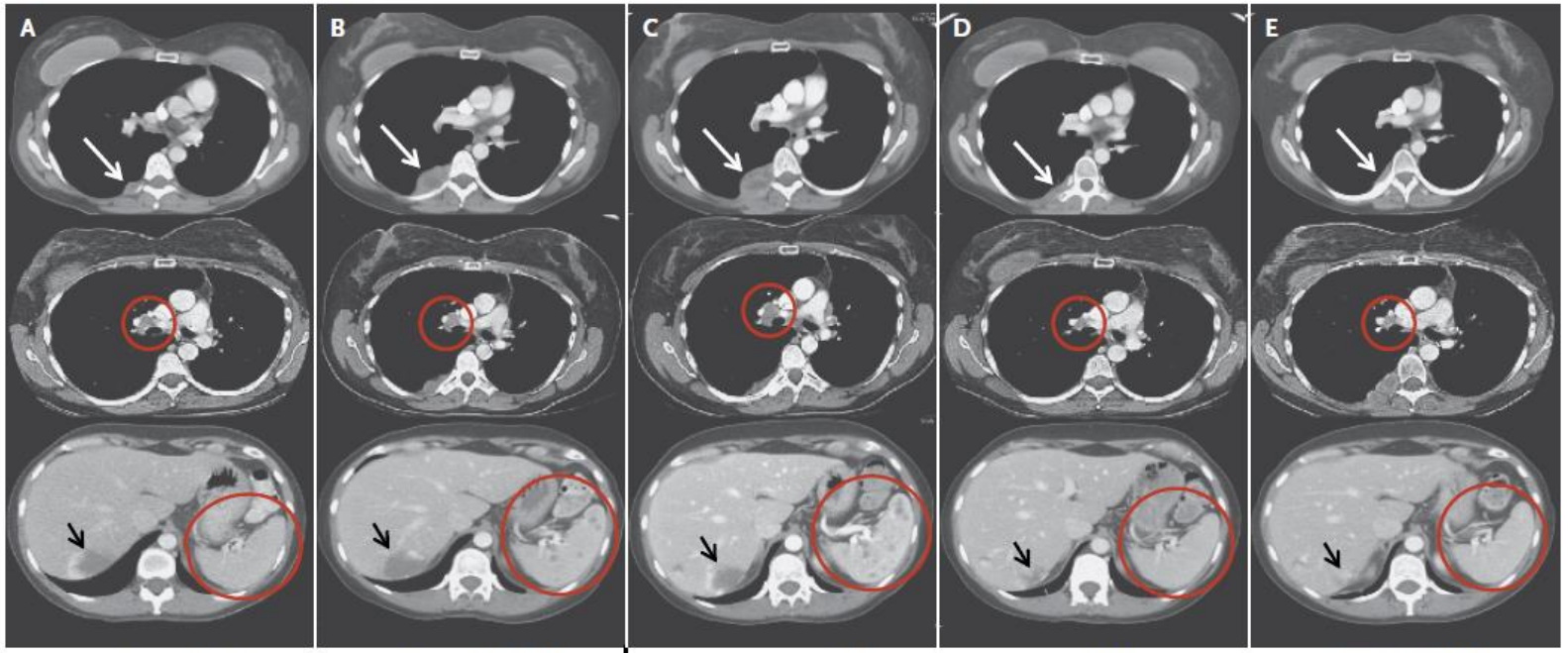
Efekt abskopalny

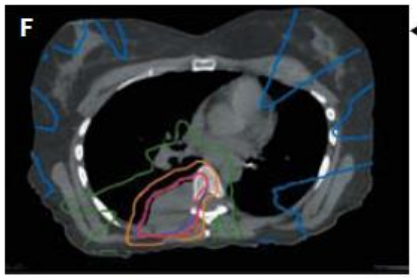
The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

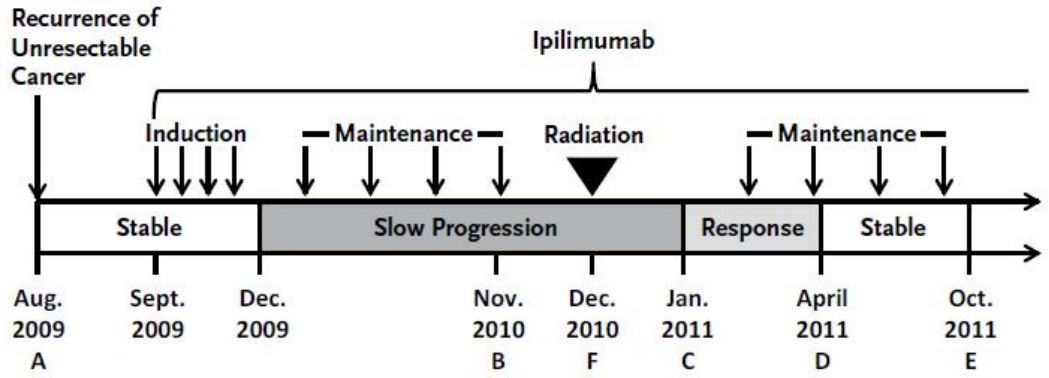
Immunologic Correlates of the Abscopal Effect in a Patient with Melanoma

Michael A. Postow, M.D., Margaret K. Callahan, M.D., Ph.D., Christopher A. Barker, M.D., Yoshiya Yamada, M.D., Jianda Yuan, M.D., Ph.D., Shigehisa Kitano, M.D., Ph.D., Zhenyu Mu, M.D., Teresa Rasalan, B.S., Matthew Adamow, B.S., Erika Ritter, B.S., Christine Sedrak, B.S., Achim A. Jungbluth, M.D., Ramon Chua, B.S., Arvin S. Yang, M.D., Ph.D., Ruth-Ann Roman, R.N., Samuel Rosner, Brenna Benson, James P. Allison, Ph.D., Alexander M. Lesokhin, M.D., Sacha Gnjatic, Ph.D., and Jedd D. Wolchok, M.D., Ph.D.





December 2010



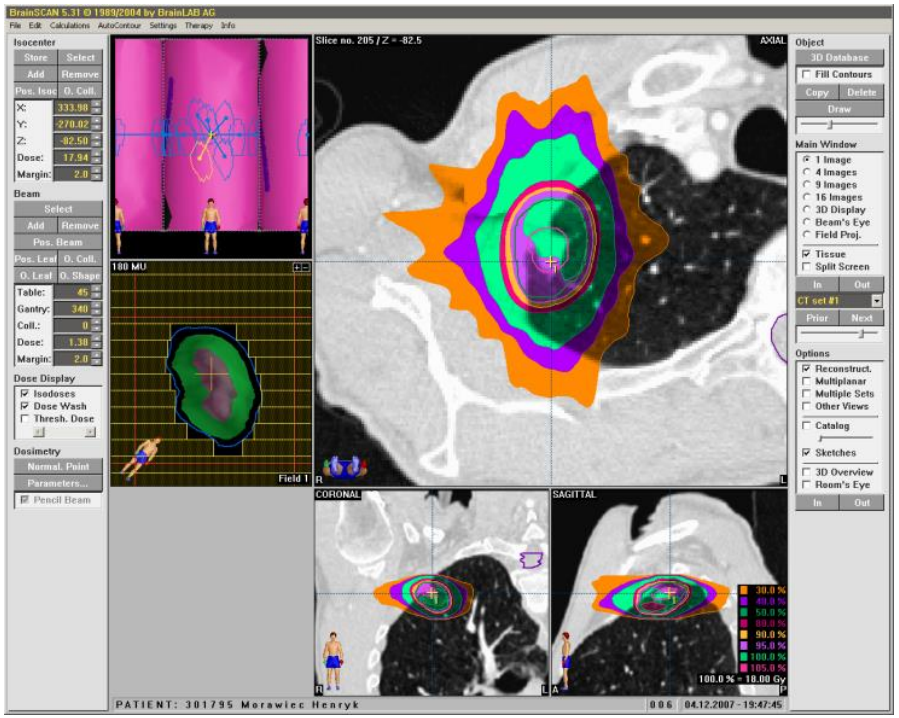
The NEW ENGLAND JOURNAL of MEDICINE

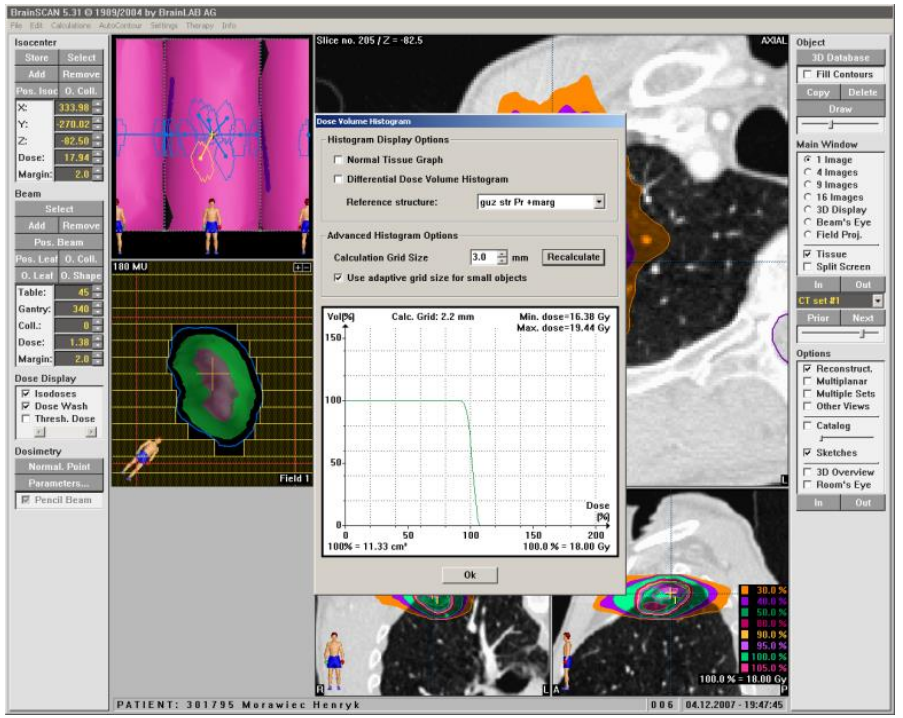
BRIEF REPORT

Immunologic Correlates of the Abscopal Effect in a Patient with Melanoma

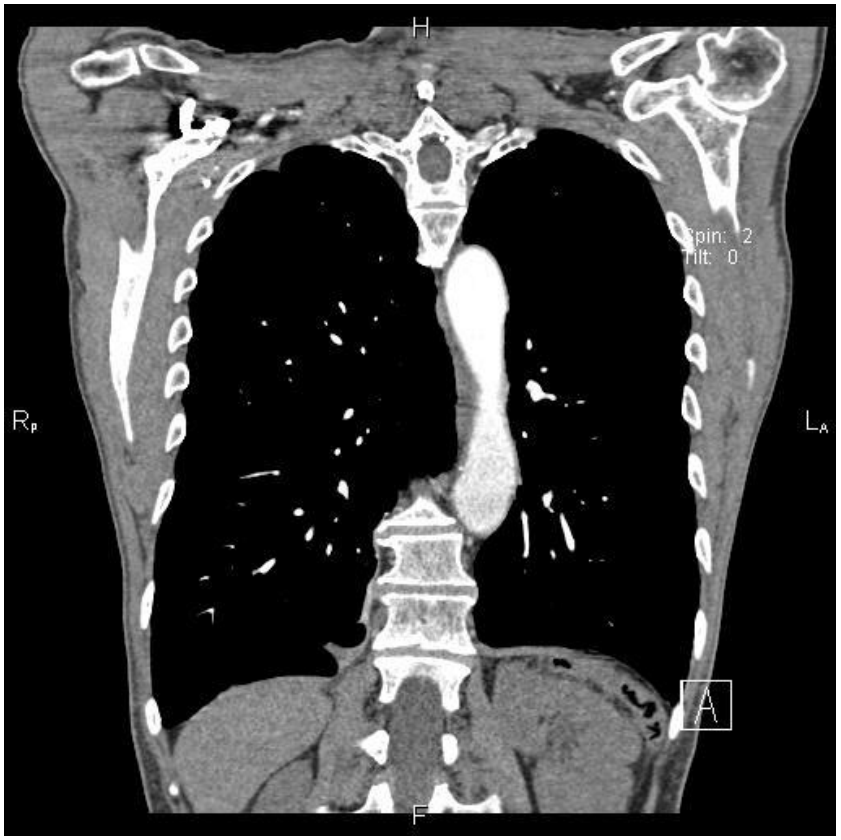
Michael A. Postow, M.D., Margaret K. Callahan, M.D., Ph.D., Christopher A. Barker, M.D., Yoshiya Yamada, M.D., Jianda Yuan, M.D., Ph.D., Shigehisa Kitano, M.D., Ph.D., Zhenyu Mu, M.D., Teresa Rasalan, B.S., Matthew Adamow, B.S., Erika Ritter, B.S., Christine Sedrak, B.S., Achim A. Jungbluth, M.D., Ramon Chua, B.S., Arvin S. Yang, M.D., Ph.D., Ruth-Ann Roman, R.N., Samuel Rosner, Brenna Benson, James P. Allison, Ph.D., Alexander M. Lesokhin, M.D., Sacha Gnjatic, Ph.D., and Jedd D. Wolchok, M.D., Ph.D.

- Radioterapia stereotaktyczna 54Gy w III frakcjach





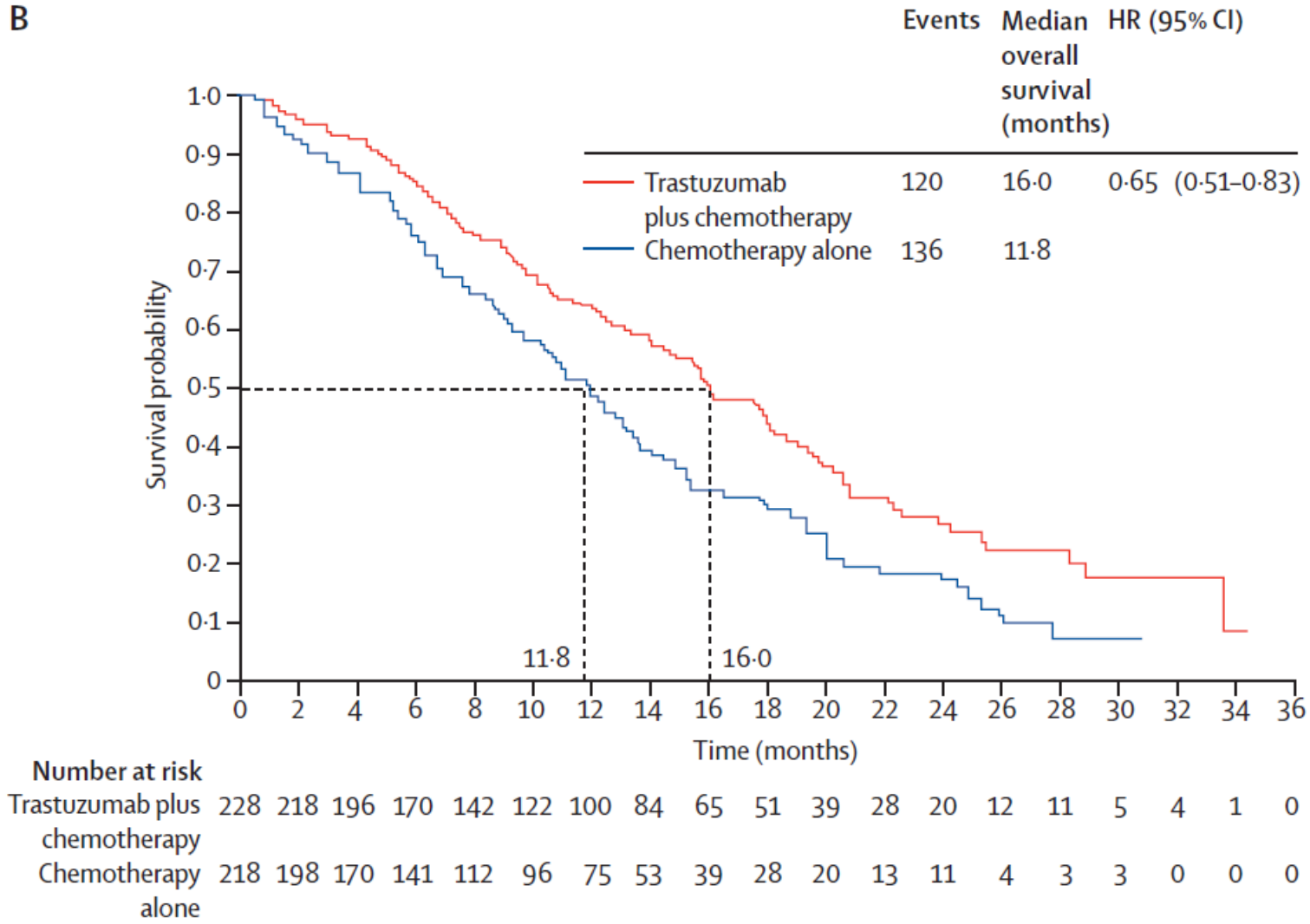
5 lat po leczeniu





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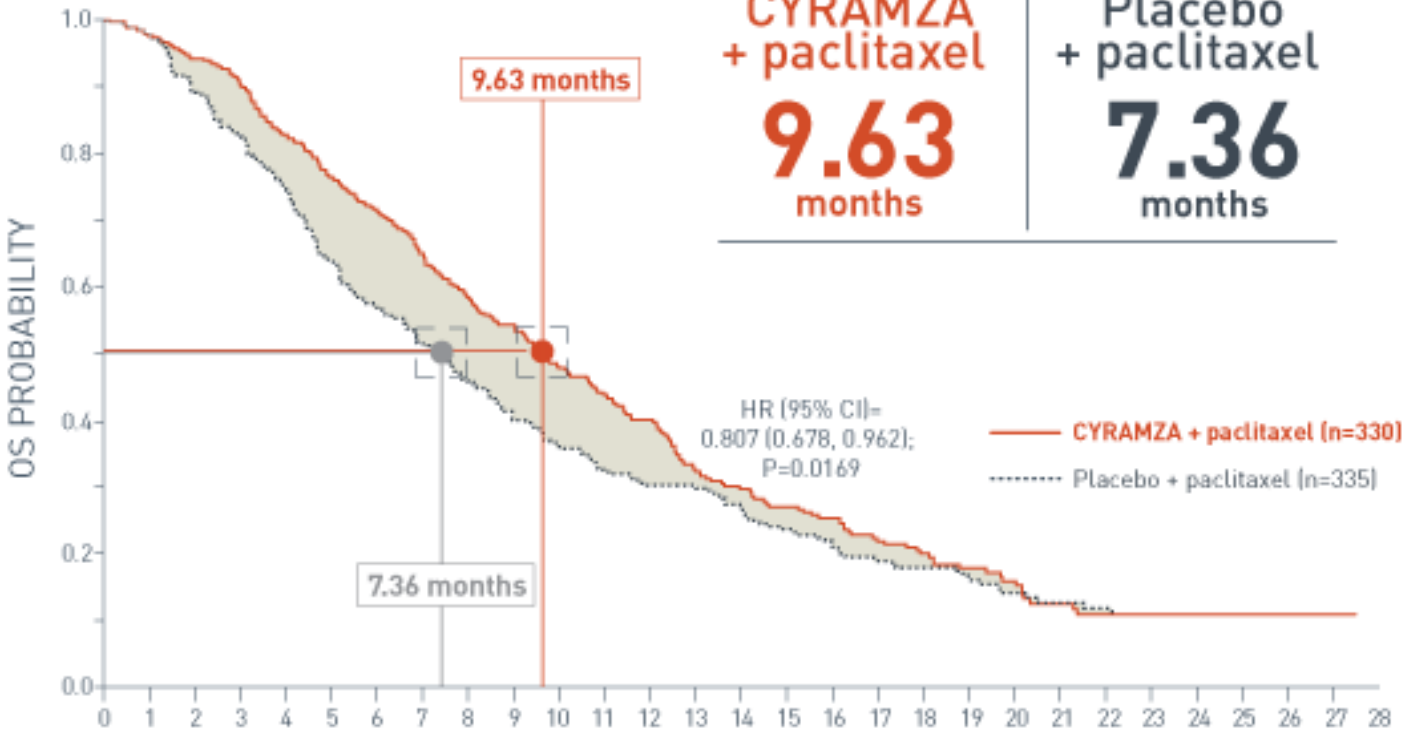
ToGA (Trastuzumab for Gastric Cancer)



Yung-Jue Bang,* Eric Van Cutsem,* Andrea Feyereislova, Hyun C Chung, Lin Shen, Akira Sawaki, Florian Lordick, Atsushi Ohtsu, Yasushi Omuro, Taroh Satoh, Giuseppe Aprile, Evgeny Kulikov, Julie Hill, Michaela Lehle, Josef Rüschoff , Yoon-Koo Kang, for the ToGA Trial Investigators† Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positiveadvanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet 2010; 376: 687–97

OVERALL SURVIVAL: MEDIAN - MONTHS [95% CI][1]

PRIMARY EFFICACY OUTCOME



Number at Risk

CYRAMZA + paclitaxel	330	308	267	228	185	148	116	78	60	41	24	13	6	1	0
Placebo + paclitaxel	335	294	241	180	143	109	81	64	47	30	22	13	5	2	0

2.3 months INCREASE IN MEDIAN OS

CI=confidence interval.

Data from Reference 1

Table 2 Phase II and III studies of bevacizumab combined with chemotherapy for advanced GC in a first-line setting

Author/type of study	N	Bevacizumab + chemotherapy	% RR	TTP months	OS months	Grade 3–4 toxicity (%)
Shah et al[10] Phase II	47	Cisplatin/irinotecan	65	8.3	12.3	HT: 28, TEE: 25 GIP: 6, MI: 2
Shah et al[11] Phase II	44	Docetaxel/cisplatin/5-FU	67	12	16.2	NTP: 50, Fatigue: 5 TEE: 39, ⊥Other: <10
Enzinger et al[12,◊] Phase II	26	Docetaxel/cisplatin/irinotecan	24	NA	NA	NTP: 22, Diarrhea: 28 Nausea: 6, TEE: 9
El-Reyes et al[13] Phase II	38	Oxaliplatin/docetaxel	59	66	11.1	NTP: 34 GIP: 8
Cohenuram and Lacy[14] Retrospective	16	FOLFOX	63	7	8.9	TEE: 0, GIP: 0
Ohtsu et al[15,*]	387	Bevacizumab + cisplatin/capecitabine	46[θ]	6.7[§]	12.1[Π]	TEE: 7, GIP: 2
Phase III	387	Placebo + cisplatin/capecitabine	37.4	5.3	10.1	TEE: 7, GIP: 2

Notes: *AVAGAST; [θ]$P = 0.0315$; [§]PFS $P = 0.0037$; [Π]$P = 0.1002$; [◊]tumor partial responses were 63% and stable disease 30%; ⊥other includes gastrointestinal toxicity, neuropathy, and febrile neutropenia.

Abbreviations: RR, response rate; TTP, time to progression; OS, overall survival; PFS, progression free survival; NA, data is not available; HT, hypertension; TEE, thromboembolic events; MI, myocardial infarction; GIP, gastrointestinal perforation.

Meza-Junco J, Sawyer MB. Metastatic gastric cancer - focus on targeted therapies. Biologics. 2012;6:137-46. doi: 10.2147/BTT.S23917. Epub 2012 Jun 20.

Table 3 Anti EGFR therapy for advanced gastric cancer

Study/phase	Treatment	N	% RR	TTP months	OS months	Grade 3–4 toxicity (%)
CALGB 80403/ ECOG 1206[36]	ECF + cetuximab	67	57.8	5.9	11.5	Hem: 51, nonHem: 60
	IC + cetuximab	71	45.6	5	8.9	Hem: 56, nonHem: 70
	FOLFOX + cetuximab	72	53.6	6.7	12.4	Hem: 45, nonHem: 64
MATRIX[41]	ECX	36	58	7.1	12.2	NTP: 33, SD: 33
Phase II	ECX + matuzumab	35	31	4.8	9.4	NTP: 37, SD: 66
REAL III	EOX	NA	NA	NA	NA	NA
	EOX + chemotherapy					
Phase II[42]	Irinotecan	40	NA	73 days*	293 days	NA
second-line	Irinotecan + nimotuzumab	42		85 days*	227 days	
ToGA[51]	Capecitabine/5-FU + cisplatin + trastuzumab	298	NA	6.7*	13.5	Overall: 68, CE: 6
Phase II	Capecitabine/5-FU + cisplatin	296		5.5*	11.1	Overall: 68, CE: 6
TYTAN[56,a]	Paclitaxel + lapatinib	NA	NA	NA	NA	NA
Phase III	Paclitaxel					
LOGiC[57]	Capecitabine + oxaliplatin + lapatinib	NA	NA	NA	NA	NA
	Capecitabine + oxaliplatin + placebo					

Notes: *Progression free survival; [a]second line of treatment.

Abbreviations: Hem, hematological toxicity; NTP, neutropenia; OS, overall survival; SD, skin disorders; CE, cardiac events; RR, reported response rates; TTP, time to progression.

Meza-Junco J, Sawyer MB. Metastatic gastric cancer - focus on targeted therapies. Biologics. 2012;6:137-46. doi: 10.2147/BTT.S23917. Epub 2012 Jun 20.