Gastric Cancer

Incontri Bresciani di Radioterapia Oncologica – Edizione 2014
Brescia Meetings in Radiation Oncology – 2014 Edition
NORTHWEST PASSAGE:
KEY-FUNCTIONS PRESERVATION
IN ONCOLOGY
Brescia – September 25th/26th, 2014

Surgery/Radiotherapy/Chemotherapy

interactions and treatment damage:

a Radiation Oncologist's point of view

D. Genovesi

www.radioterapia.unich.it

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EJSO
the Journal of Cancer Surgery
EJSO 40 (2014) 584–591
www.ejso.com

Gastric cancer: ESMO–ESSO–ESTRO clinical practice guidelines for diagnosis, treatment and follow-up☆,☆☆

T. Waddell [a], M. Verheij [b], W. Allum [c], D. Cunningham [d], A. Cervantes [e], D. Arnold [f,*]

- Surgery is the main treatment for gastric cancer
  Gastrectomy; subtotal gastrectomy if 5-8 cm margin can be achieved

- D2 lymphadenectomy: benefit debated on OS and DFS;
  current consensus in the West (I,B) (Dikken JL 2013)
  ≥ 15 lymph nodes removed

- >50% of patients relapse after complete resection, therefore there's a need for Integrated treatments aimed at decrease local and distant relapse for ≥ Stage IB

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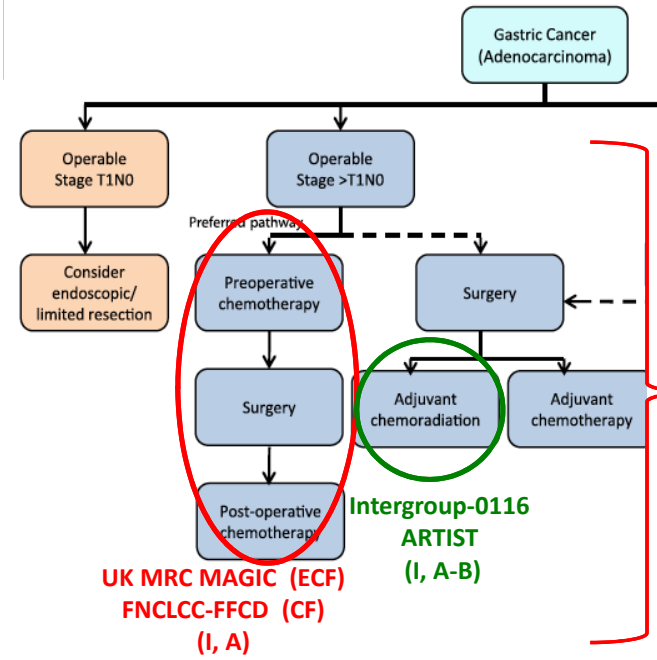


UK MRC MAGIC (ECF)
FNCLCC-FFCD (CF)
(I, A)

Intergroup-0116
ARTIST
(I, A-B)

Adjuvant setting
Chemotherapy vs Chemoradiotherapy
?
Waiting ongoing randomised phase III
CRITICS trial

Ongoing..

Neo-adjuvant chemotherapy followed by surgery and chemotherapy or by surgery and chemoradiotherapy for patients with resectable gastric cancer (CRITICS)

Johan L Dikken[1,2], Johanna W van Sandick[3], HA Maurits Swellengrebel[3], Pehr A Lind[4], Hein Putter[5], Edwin PM Jansen[2], Henk Boot[6], Nicole CT van Grieken[7], Cornelis JH van de Velde[1], Marcel Verheij[2] and Annemieke Cats[8*]

BMC Cancer

ECC x 3 → Surgery → ECC x 3 + RT
→ ECC

Locoregional failure are quite high. This trial could strengthen the need for radiotherapy as integral part of the treatment

Ongoing...

2001

EMORADIOTHERAPY AFTER SURGERY COMPARED WITH SURGERY ALONE FOR ADENOCARCINOMA OF THE STOMACH OR GASTROESOPHAGEAL JUNCTION

JOHN S. MACDONALD, M.D., STEPHEN R. SMALLEY, M.D., JACQUELINE BENEDETTI, PH.D., SCOTT A. HUNDAHL, M.D., NORMAN C. ESTES, M.D., GRANT N. STEMMERMANN, M.D., DANIEL G. HALLER, M.D., JAFFER A. AJANI, M.D., LEONARD L. GUNDERSON, M.D., J. MILBURN JESSUP, M.D., AND JAMES A. MARTENSON, M.D.

N Engl J Med, Vol. 345, No. 10 · September 6, 2001 · www.nejm.org

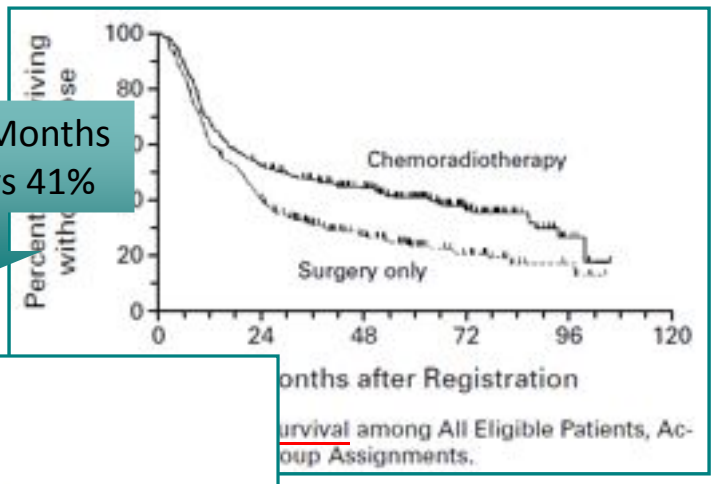
556 Patients → Surgery → None / CHRT

1,8 Gy/25 fr. Total dose: 45 Gy

Fluoruracil 425 mg/mq/die + Leucovorin 20 mg/mq/die i.c. 5d

- **Local relapse: 19% vs 29%!**

OS: 36 vs 27 Months
OS 3y: 50% vs 41%



urvival among All Eligible Patients, Ac-
oup Assignments.

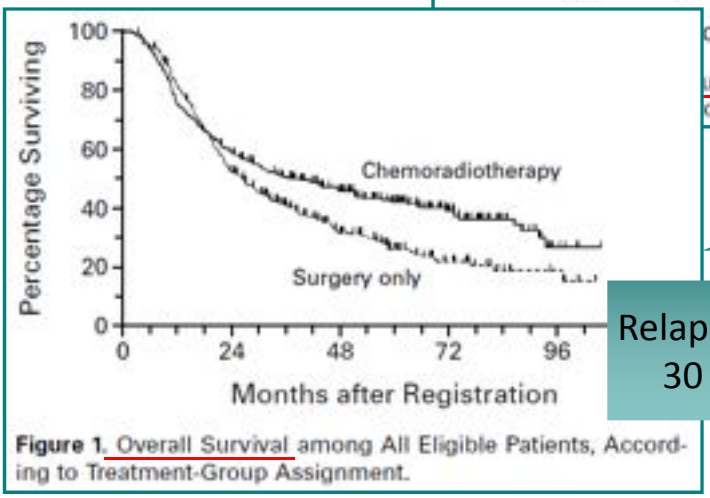


Figure 1. Overall Survival among All Eligible Patients, According to Treatment-Group Assignment.

Relapse-free survival:
30 vs 16 Months

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BUT

Only 10% pts underwent D2 resection

Haematological toxicity Grade 3-4 : 54%
GI toxicity Grade 3-4: 33%
Compliance to treatment: 64%

Subsequent studies have tried to evaluate the effectiveness of RT after D2 resection

Study	Stage	Group	Patient number	Treatment RT/CTx	Survival	P-value
Kim et al.(27)	II~IVA	Control	446	-	MS 63 mo	0.02
		CCRT	544	45 Gy/FL	95 mo	
Dikken et al.(28)	-	Control	325	-	2-yr LRR 13%	0.84
		CCRT	25	45 Gy/FL, XP	12%	
ARTIST(14)	IB~IVA	CTx	228	XP	3-yr DFS 74.2%	0.08
		CCRT	230	45 Gy/XP	78.2%	
Zhu et al.(29)	IB~IVA	CTx	175	FL	MS 48 mo	0.12
		CCRT	205	45 Gy/FL	58 mo	

Level IB EBM

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Radiotherapy and Oncology 92 (2009) 176–183

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Systematic review

Survival after rac
and meta-analys

Vincenzo Valentini
Giuseppe D'Agostino
Giuseppe La Torre

Study [Reference]	Hematological toxicity (%)	Gastrointestinal toxicity (%)	Global toxicity (%)
Skoropard et al. [30]	n.r.	13.56	25.42
	n.r.	34	35.85
Moertel et al. [31]	56.41	56.41	76.92
	n.r.	n.r.	n.r.
Takahashi and Abe [32]	n.r.	n.r.	n.r.
	n.r.	n.r.	n.r.
Macdonald et al. [10]	52.67	31.67	97.15
	n.r.	n.r.	n.r.
Allum et al. [33]	1.31	27.45	64.05
	n.r.	n.r.	n.r.
Zhang et al. [34]	n.r.	n.r.	n.r.
	n.r.	n.r.	n.r.
Skoropard et al. [13]	2.6	13	37.66
	5.33	21.33	33.33
Shchepotin et al. [35]	n.r.	n.r.	n.r.
	n.r.	n.r.	n.r.
Dent et al. [36]	77.14	n.r.	77.14
	29.03	n.r.	29.03

Journal of Medical Imaging and Radiation Oncology 58 (2014) 483–496

RADIATION ONCOLOGY—REVIEW ARTICLE

Postoperative chemo-radiotherapy versus chemotherapy for resected gastric cancer: A systematic review and meta-analysis

Yu Yang Soon,[1] Cheng Nang Leong,[1] Jeremy Chee Seong Tey,[1] Ivan Weng Keong Tham[1] and Jiade Jay Lu[2]

[1]Department of Radiation Oncology, National University Cancer Institute, Singapore, National University Health System, National University of Singapore, Singapore and [2]Department of Radiation Oncology, Shanghai Cancer Centre, Fudan University,Shanghai, China

Surgery/Radiotherapy/Chemotherapy interactions and Toxicity

Heterogeneous methods of reporting precluded statistical pooling of toxicity data

Four trials used common terminology criteria for adverse events to grade toxicity *(Kwon HC 2010; ARTIST trial 2012; Yu CH 2012;Zhu WG 2012)*

Two trials did not report the toxicity scales used *(Bamias A. 2010; Kim TH 2012)*

Quality of life data was not available while could be pivotal in decision making for treatments with similar efficacy

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Surgery/Radiotherapy/Chemotherapy interactions and Toxicity

No significant differences in G3-G4 toxicities between CT-RT vs Chemo alone in 5/6 trials reviewed

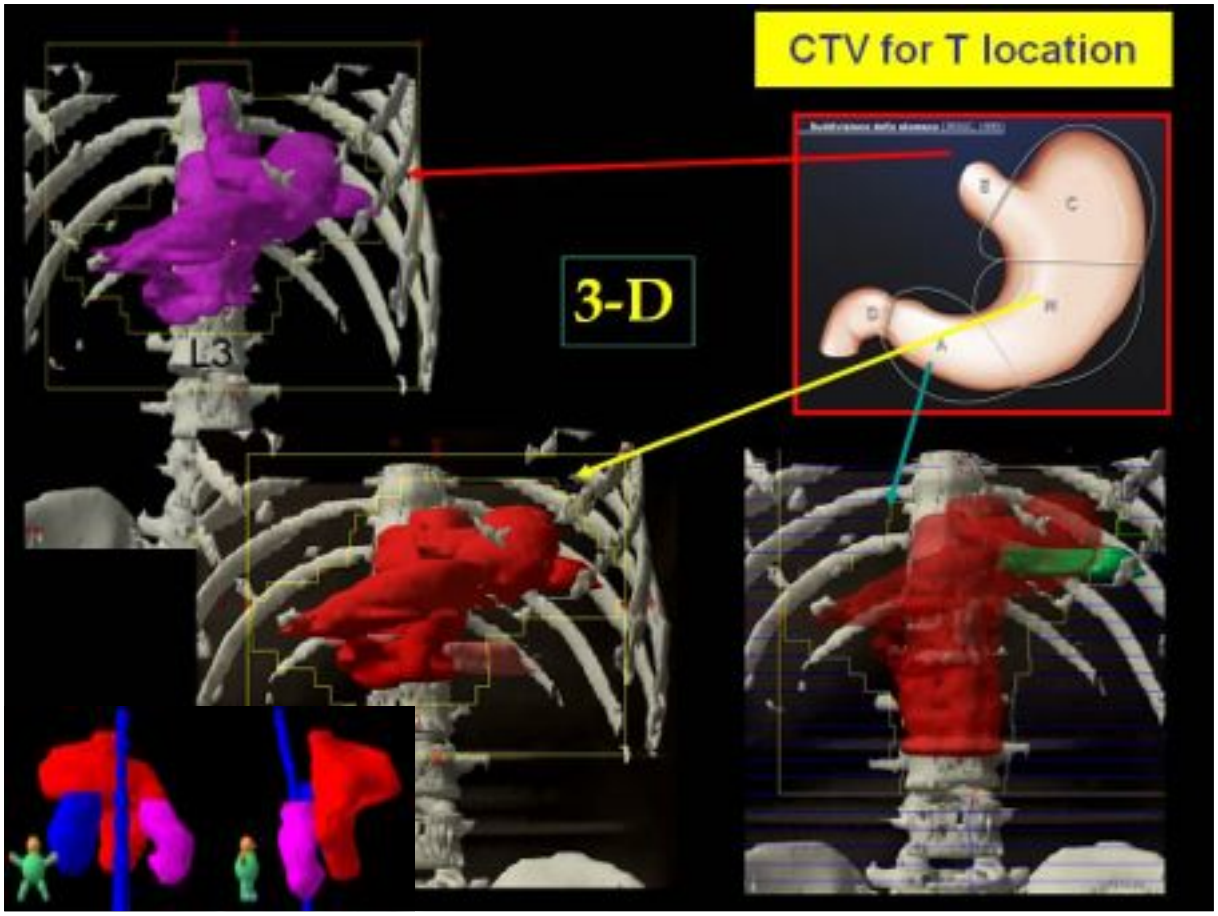
Bamias 2010 Lee 2012 **ARTIST trial**

Kim 2012 Yu 2012

Zhu 2012

Only one trial reported a higher rate of G3-G4 neutropenia for postop CT-RT (48.4%) vs Chemo alone (16.7%)

Kwon 2010



AIRO Update Guideline **2014**: CTV/N in post-operative Gastric Cancer

1/3 superior

7-8-9-10-11 if N+12-19; if N+ 16 a2; if N Ratio >25% 16 a1

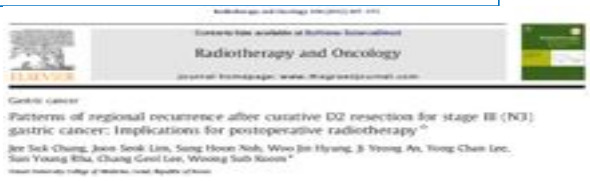
1/3 medium

7-8-9-10-11-12-13-14 if N+ 17 and 16 a2; if N+ N Ratio >25% 16b1

1/3 inferior

7-8-9-11-12-13-14-16a2 if N+ 17 and if N+ N Ratio >25%

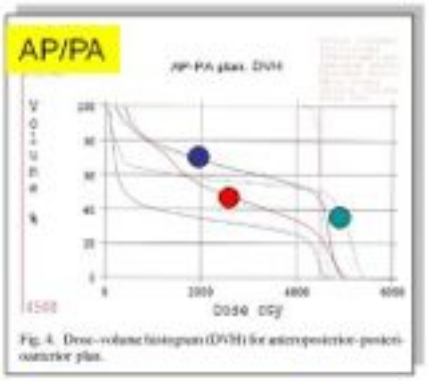
Perigastric nodal 1-4,5,6, in case of total gastrectomy not be included.
For subtotal gastrectomy should be included only to the level corresponding to the remnant stomach

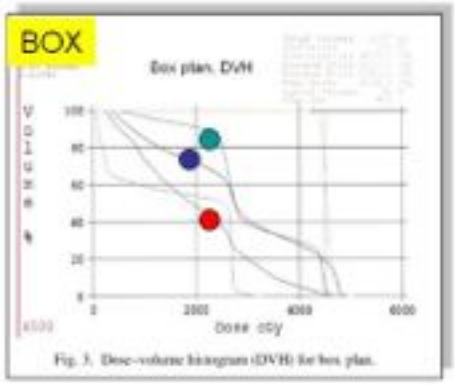


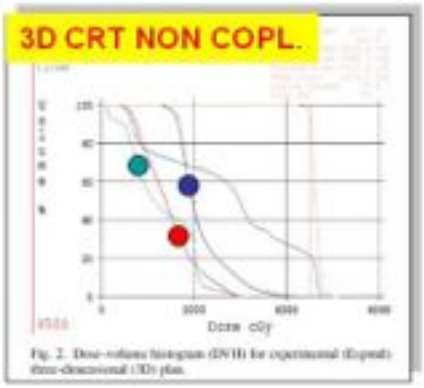
AP/PA vs 3D CRT non coplanar

Soyfer IJROBP 2007

- Right kidney
- Left kidney
- Liver





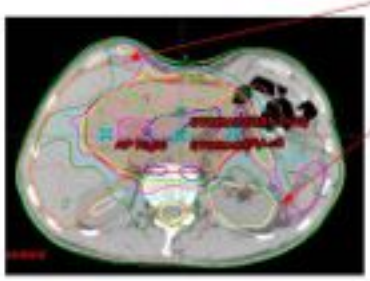


3DCRT vs IMRT in Gastric Cancer

Sophisticated 3D CRT: gold standard

IMRT improves OARs sparing , particularly the kidneys
Reduction of late toxicity

IMRT requires expertise: be careful to hot spots!!!!



OARs Dose Constraints

Spinal Cord	Dmax 45 Gy	
Heart	V30 < 46% Dose Media: < 26 Gy (32) V40 < 30% V25 < 50% (24)	Pericardio Whole organ. Long-term cardiac mortality
Kidneys	V28 < 20% V23 < 30% V20 < 32% V12 < 55% Dose media < 18 Gy (33)	Bilateral whole kidney
Liver	Dose Media < 30-32 Gy (34) V30 ≤ 30% (24)	Whole liver minus GTV
Lung	V20 ≤ 30% Dose media: 20-23 Gy (35)	Whole organ. For combined lung
Small bowel	V15 <120 cc V45 < 195 cc (36)	Individual small bowel loops Entire peritoneal potential space of bowel

Clinical status of the patient: malnutrition

- Recommended anti-emetic and anti-acid drugs as a prophylaxis prior to therapy and anti-diarrheal drugs as needed
- Individualized nutritional support: advisable
- **Adequate nutritional support: effective for the treatment compliance**
- Weight loss and caloric intake < 1.500 Kcal/day should be considered enteral nutritional support (jejunostomy) or parenteral
- Supplementation of Calcium, B12 vitamin and iron: to take into account

AIRO GI Study Group

National Survey 2006

Compliance RT-CT/CT

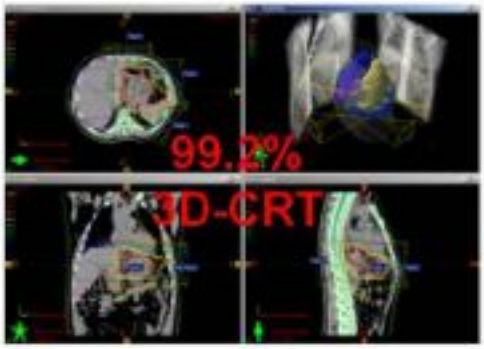
Completion of adjuvant therapy 74.13%

CT suspension: 23.5%

RT-CT suspension: 4.5%

RT break <3 gg: 15.8%

RT break >3gg: 9.1%



Acute toxicity ≥G2 RT-CT/CT

Haematological 9.1% (3.7% RT-CT)

Intestinal 10% (4% RT-CT)

AIRO GI Study Group
National Survey 2012

Take home messages

- Adjuvant CHRT is a standard of care
- Standard dose RT (45 Gy): safe and well tolerated
- Intensified RT(RT dose and/or Chemo periop): safe
  - *Accurate and appropriate Target Volume & OARs delineation*
  - *Technique: Advanced 3D-CRT; IMRT/IGRT*
  - *Assessment patient clinical status and application of supportive care: Be careful !!*
- Clinical data (outcome & tox) reporting and analysis !!!