Topics

- Head & Neck
- Prostate
- **Lung**
- Breast
- Rectum

Lung Topics 2008

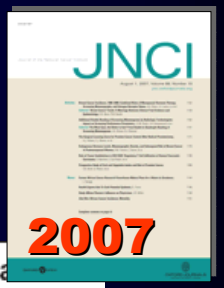
Induction Treatment

Definitive irradiation

Post-operative RT

PCI

Mediastinal ypN0 status significantly predicts greater 5-year survival



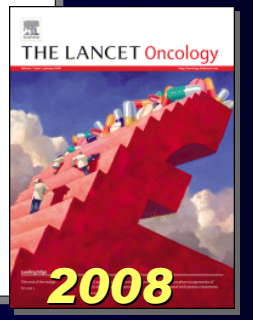
Subgroup	N	Median OS, months (95% CI)	5-year OS, %	*P*, Univariate analysis	*P*, Multiva analysis
Extent of resection				.009	.03
(Bi-)lobectomy	58	25.4 (17.7 to 48.9)	27		
Pneumonectomy	72	13.4 (11.1 to 19.5)	12		
Mediastinal status				<.001	.04
ypN0–1	64	22.7 (17.6 to 42.7)	29		
ypN2	86	14.9 (11.2 to 18.5)	7		
Type of resection				<.001	.01
Complete	77	24.1 (16.7 to 42.4)	27		
Incomplete	76	12.1 (9.5 to 17.1)	7		

EORTC 08941

Is there a preferred preoperative approach in locally advanced NSCLC ?

Effect of preoperative chemoradiation in addition to preoperative chemotherapy: a randomised trial in stage III non-small-cell lung cancer

Michael Thomas, Christian Rübe, Petra Hoffknecht, Hans N Macha, Lutz Freitag, Albert Linder, Norman Willich, Michael Hamm, Gerhard W Sybrecht, Dieter Ukena, Karl-Matthias Deppermann, Cornelia Dröge, Dorothea Riesenbeck, Achim Heinecke, Cristina Sauerland, Klaus Junker, Wolfgang E Berdel*, Michael Semik*, for the German Lung Cancer Cooperative Group**



Random ***(524 pts.)***

iCT x 3 → **Surgery** → 54 (+/- 14) Gy

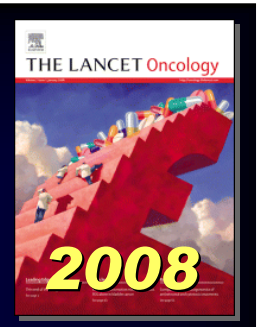
iCT x 3 → 45Gy(BID)+CT → +/- 24 Gy (BID)

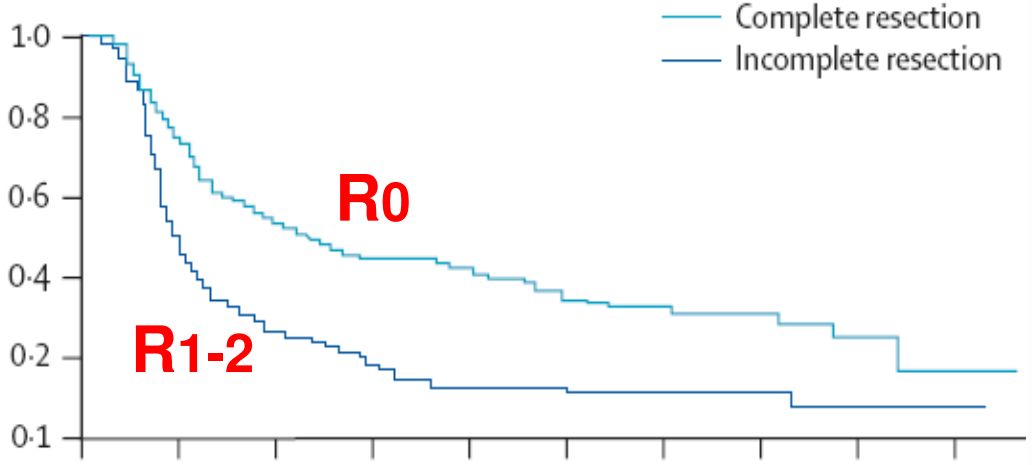
Improvement on

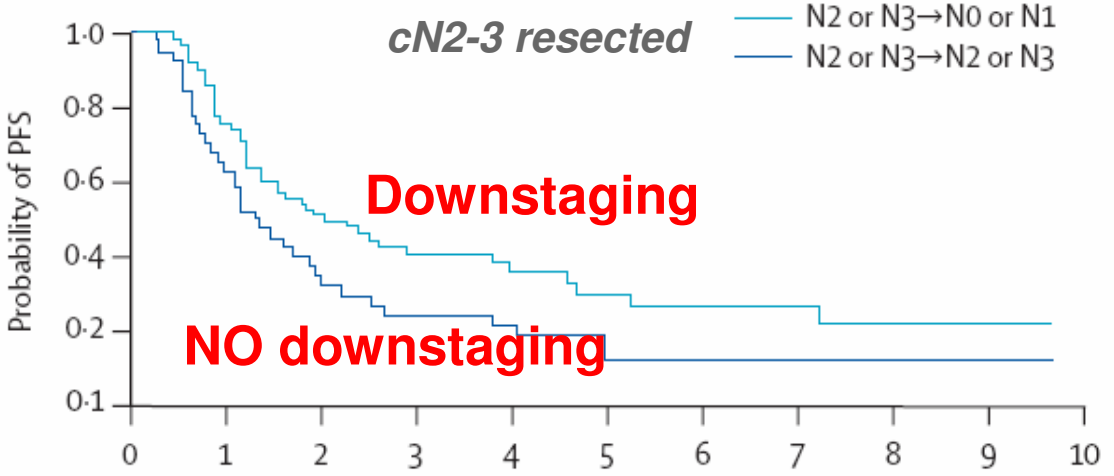
✓ **complete resections**

✓ **mediastinal downstaging**

furthermore...

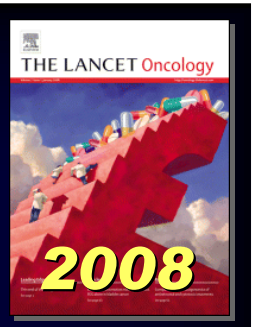


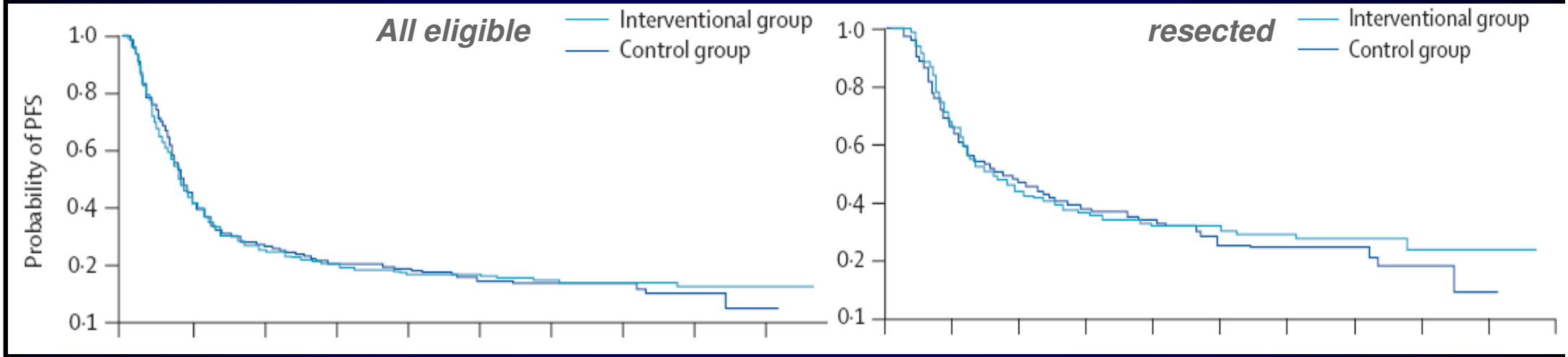




Complete resection and mediastinal downstaging as prognostic factors for PFS

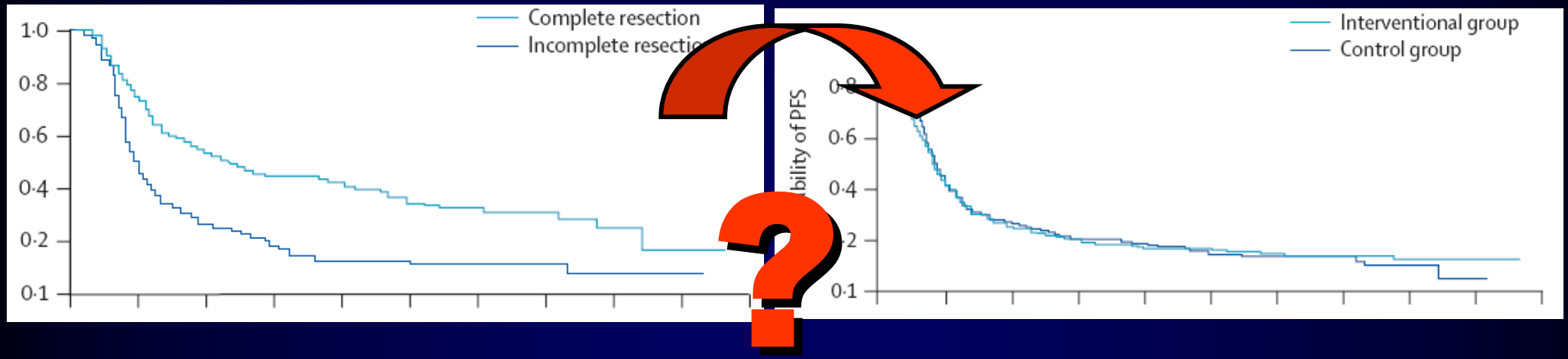
... nevertheless ...





"...no significant differences in PFS and OS between groups..."

"...no significant differences in PFS and OS between groups..."

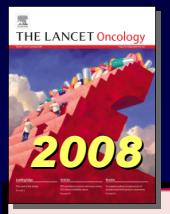


Statistics ? ← *complete resections: 182/524 (35%)*

Post-op RT as confounding factor

Surgical delay (2 months) in RT+CT group

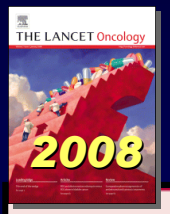
Last but not least … toxicity



	GLCCG (stage IIIA or IIIB)		EORTC 08941[13] (stage IIIA; N2)	INT 0139[14] (stage IIIA; N2)
	Randomisation; CT, CT/RT, surgery	Randomisation; CT, surgery, RT	CT, response, randomisation, surgery vs RT	Randomisation, CT/RT vs CT/RT, surgery, CT
Surgical mortality, %				
Total	9·2	4·5	4	7·9
After lobectomy or bilobectomy	7·5	2·4	0	1
After pneumonectomy	14·0	5·5	7	26

Trimodality approach not optimal when a pneumonectomy is required

Last but not least … toxicity



	GLCCG (stage IIIA or IIIB)		EORTC 08941[13] (stage IIIA; N2)	INT 0139[14] (stage IIIA; N2)
	Randomisation; CT, CT/RT, surgery	Randomisation; CT, surgery, RT	CT, response, randomisation, surgery vs RT	Randomisation, CT/RT vs CT/RT, surgery, CT
Surgical mortality, %				
Total	9·2	4·5	4	7·9
After lobectomy or bilobectomy	7·5	2·4	0	1
After pneumonectomy	14·0	5·5	7	26

At present, there's no evidence of superiority of preoperative CT+RT over CT alone

Lung Topics 2008

Induction Treatment

Definitive irradiation

Post-operative RT

PCI

"What is the standard for stage IIIA NSCLC ?"

Evidence teaches us that the superiority in outcome of concomitant over sequential approach may be counterbalanced in excess of toxicity

"Optimization of chemo-radiotherapy integration has the best perspective to improve the outcome and to become the novel standard..."

Van Meerbeck et al

Optimization = intensification !

Randomized Phase II Trial of Induction Chemotherapy Followed by Concurrent Chemotherapy and Dose-Escalated Thoracic Conformal Radiotherapy (74 Gy) in Stage III Non–Small-Cell Lung Cancer: CALGB 30105

Mark A. Socinski, A. William Blackstock, Jeffrey A. Bogart, Xiaofei Wang, Michael Munley, Julian Rosenman, Lin Gu, Gregory A. Masters, Peter Ungaro, Arthur Sleeper, Mark Green, Antonius A. Miller, and Everett E. Vokes

69 pts.

- **CBDCA/PTX x 2 →** **3D-RT** **+ weekly low dose CBDCA/PTX**
- **CBDCA/Gem x 2 →** **74 Gy** **+ twice weekly low dose Gem**

End-points: overall survival (i.e. MST => 18 months)

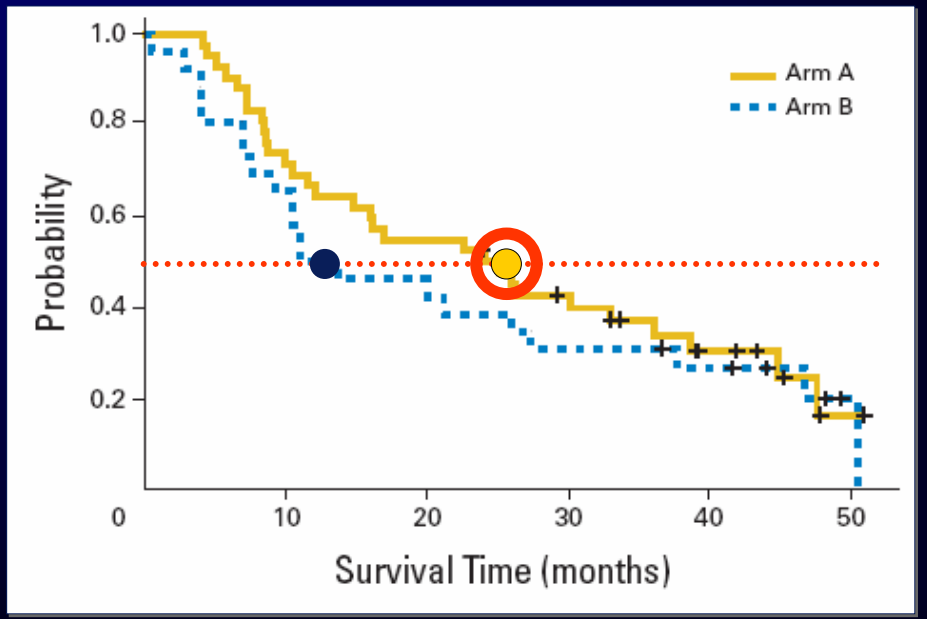
Intensification = toxicity !

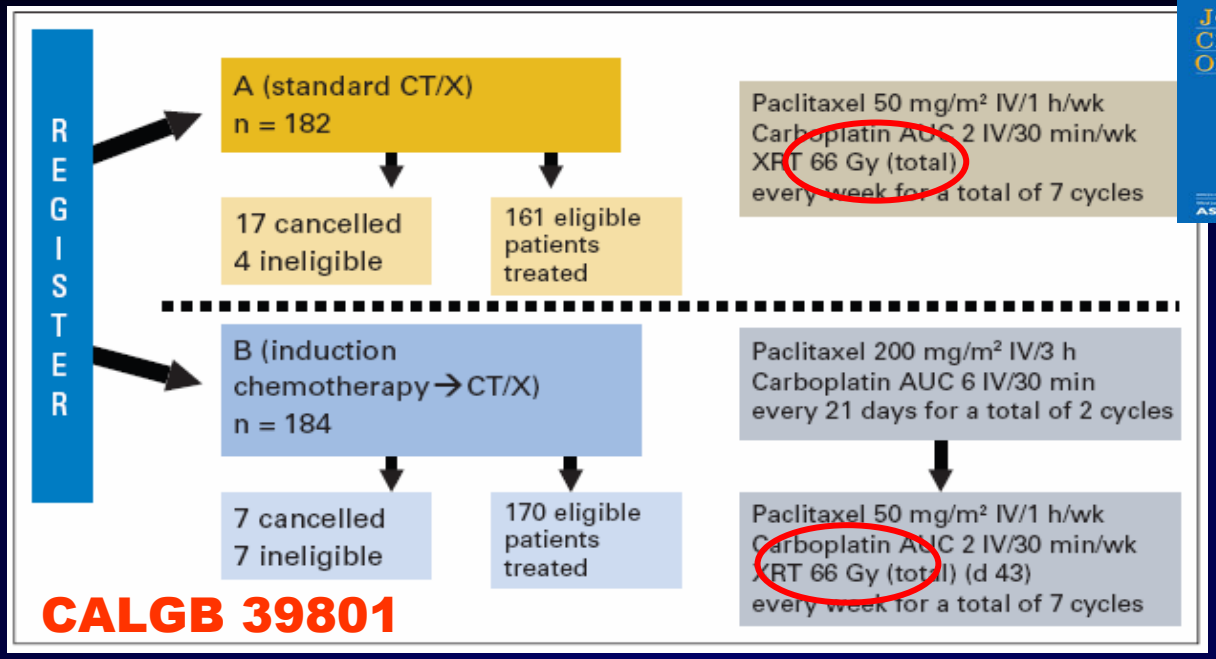
Summary of Grade 3, 4, and 5 Toxicities During Concurrent Chemoradiation

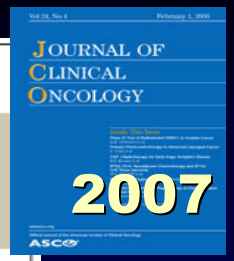
	CBDCA/PTX Arm A (n = 37)						**CBDCA/Gem** Arm B (n = 23)					
	Grade 3		Grade 4		Grade 5		Grade 3		Grade 4		Grade 5	
Toxicity	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Esophagitis	6	16	0	0	0	0	9	39	0	0	0 ()	0
Nausea	3	8	0	0	0	0	1	4	0	0	0	0
Vomiting	2	5	0	0	0	0	0	0	0	0	0	0
Dehydration	2	5	0	0	0	0	3	13	0	0	0	0
Weight loss	2	6	0	0	0	0	2	9	0	0	0	0
Fatigue	3	8	1	3	0	0	8	35	0	0	0	0
Infection without neutropenia	3	8	0	0	0	0	3	13	0	0	0	0
Pulmonary	4	11	2	5	0	0	5	21	2	9	2	8
Cardiac	0	0	0	0	1	3	1	4	0	0	0	0

Grade 3-5: 16% vs. 37%

Arm A	**Arm B**
MST: 24.3 mth	**vs. 12.5 mth**
3yOS: 37.1%	**vs. 30.8%**







- **Induction chemotherapy added to RT+CT does not lead to a significant increase in survival in unresectable stage III NSCLC**
- ***Survival on both study arms disappointing (MST ~ 14 mth)***

… So far, dose-escalation with 3-D planning should be tested in RCTs of integrated treatments !

16.30-18.00

Sala Rossa

• SESSIONE 18

WORKSHOP

Highlights in oncologia toracica

MODERATORI: ***E. Emiliani*** *(Ravenna)*, ***G. Silvano*** *(Taranto)*

NSCLC localmente avanzato: come migliorare il controllo di malattia?
L. Trodella *(Roma)*

Ruolo delle tecniche stereotassiche nel NSCLC
F. Casamassima *(Firenze)*

Quale spazio per la brachiterapia in oncologia polmonare?
G. Gava *(Treviso)*

Lung Topics 2008

Induction Treatments

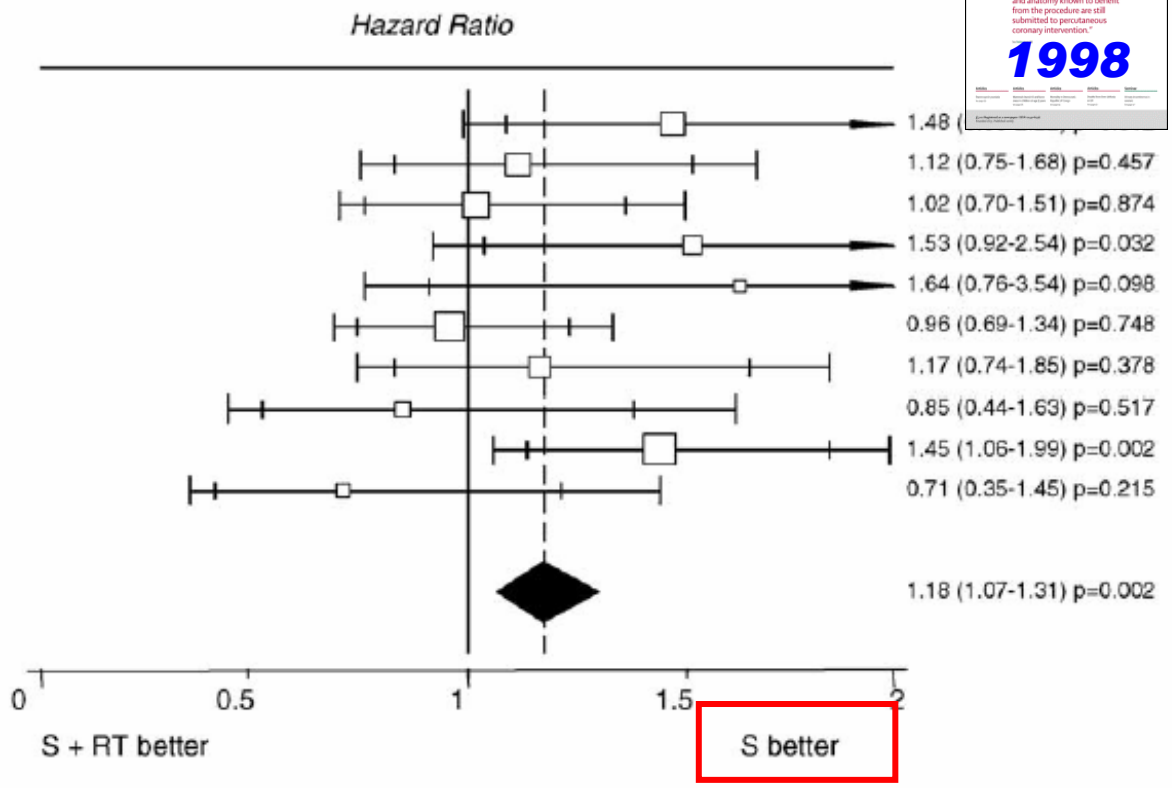
Definitive irradiation

Post-operative RT

PCI

current evidence

	(no. events/no. entered) S + RT	S
Belgium	88/98	80/104
LCSG 773	84/110	81/120
CAMS	83/153	100/164
Lille	59/81	45/82
EORTC 08861	26/52	20/54
MRC LU11	116/154	123/154
GETCB 04CB86	69/99	59/90
Slovenia	30/35	33/39
GETCB 05CB88	152/274	120/265
Italy (3)	23/51	30/53
Total	730/1107	691/1125



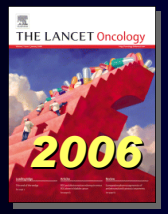
HR=1.18 (95% CI 1.07-1.31) $\chi^2_{(1)}$=9.88, p=0.002; Het $\chi^2_{(9)}$=16.62, p=0.06

2005

"...post-op RT is detrimental in completely resected...
...the role in N2 is not clear... further research..."

IMPACT OF POSTOPERATIVE RADIATION THERAPY ON SURVIVAL IN PATIENTS WITH COMPLETE RESECTION AND STAGE I, II, OR IIIA NON–SMALL-CELL LUNG CANCER TREATED WITH ADJUVANT CHEMOTHERAPY: THE ADJUVANT NAVELBINE INTERNATIONAL TRIALIST ASSOCIATION (ANITA) RANDOMIZED TRIAL

JEAN-YVES DOUILLARD, M.D., PH.D.,* RAFAEL ROSELL, M.D.,† MARIO DE LENA, M.D.,‡ MARCELLO RIGGI, M.D.,§ PATRICK HURTELOUP, M.D.,§ AND MARC-ANDRE MAHE, M.D., PH.D
ON BEHALF OF THE ADJUVANT NAVELBINE INTERNATIONAL TRIALIST ASSOCIATION

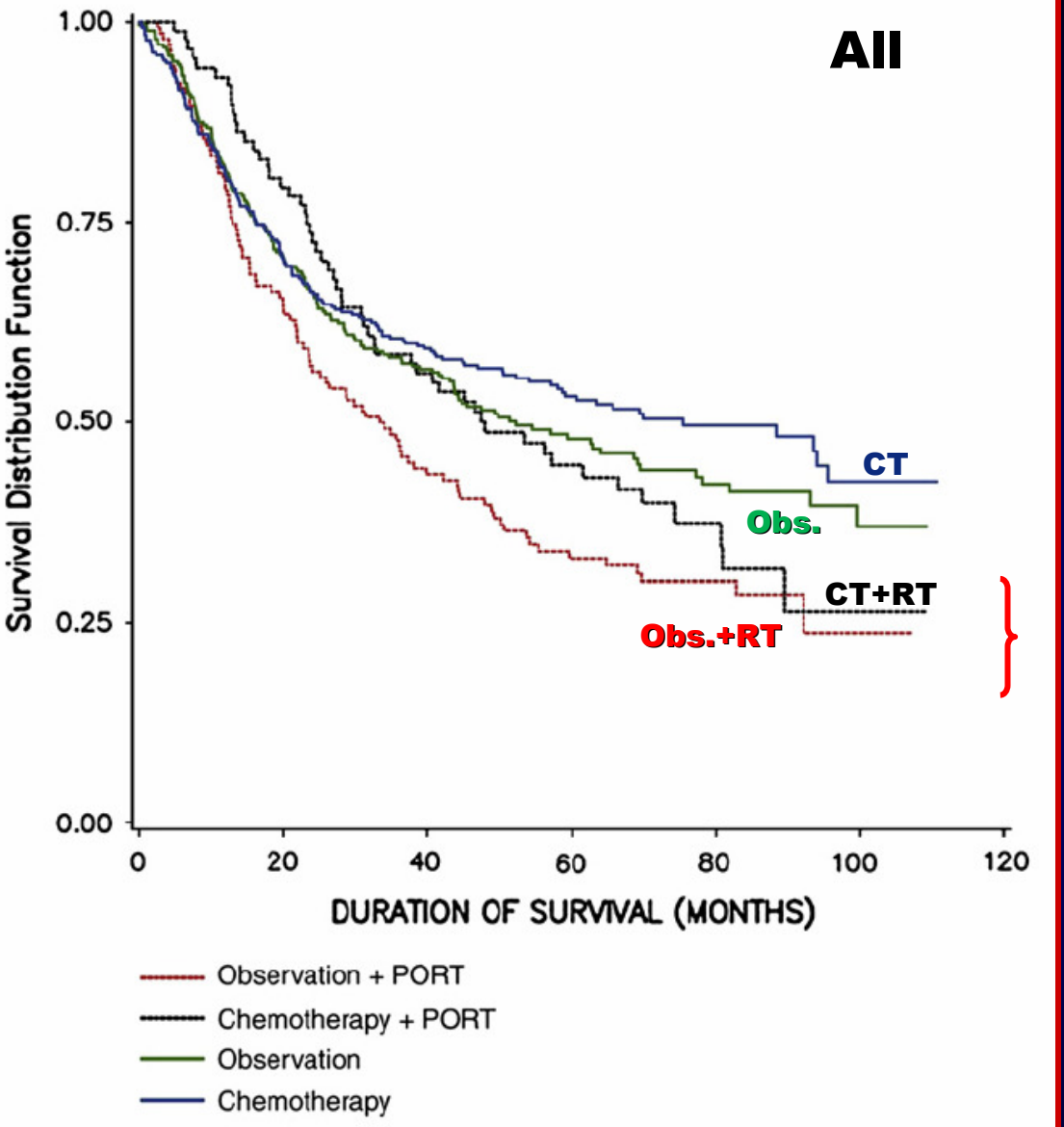


Surgery → *Random* → **CDDP+VNR +/- RT (N+)**

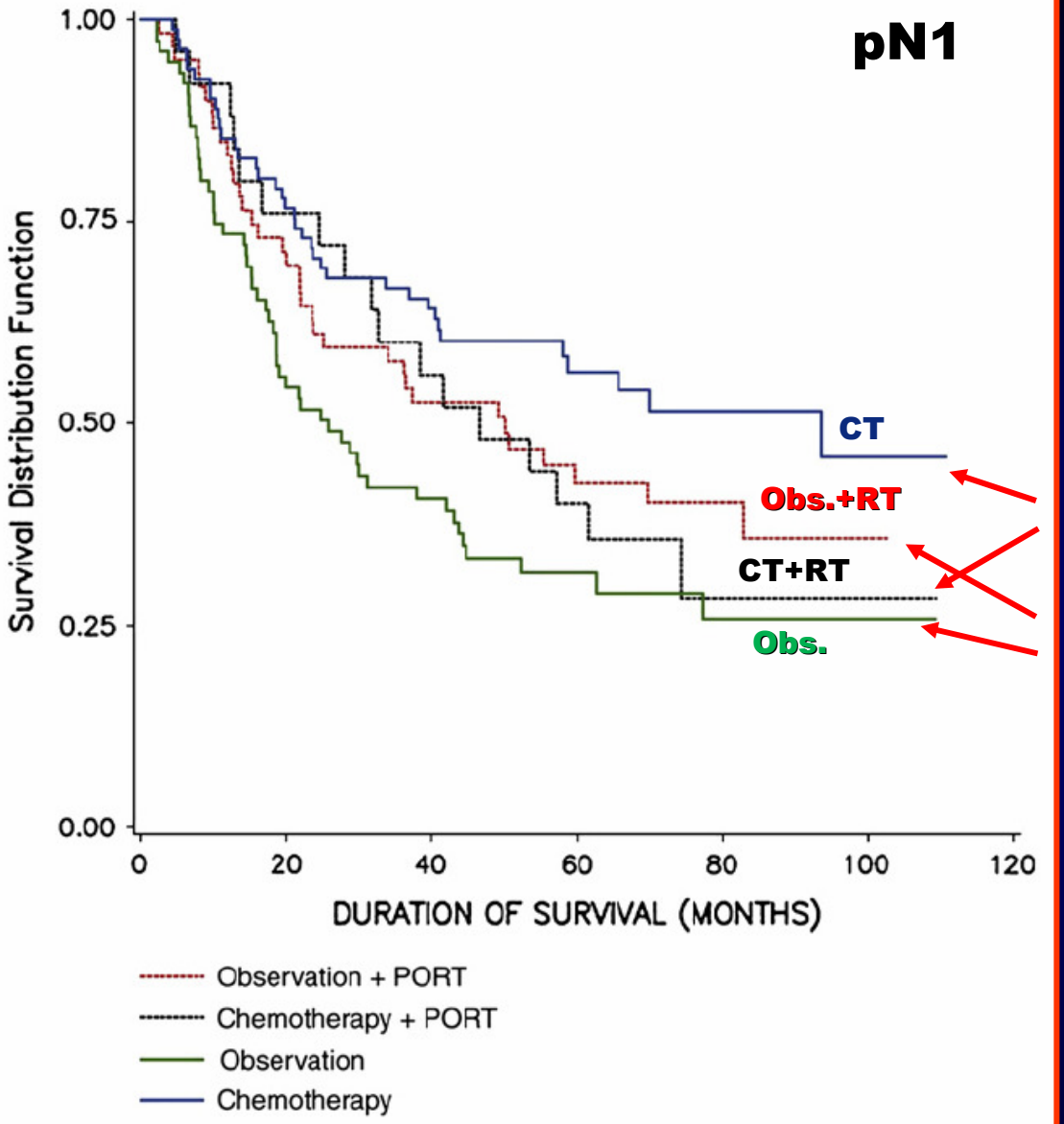
Observation +/- RT (N+)

840 Stage I-IIIA

	Observation			Cisplatin + vinorelbine			
	pN0	pN1	pN2	pN0	pN1	pN2	Total
Total population	188	136	106	179	107	118	840*
PORT population	16	60	68	15	25	48	232
% PORT	8.5	44.1	64.5	8.4	23.3	40.6	27.6

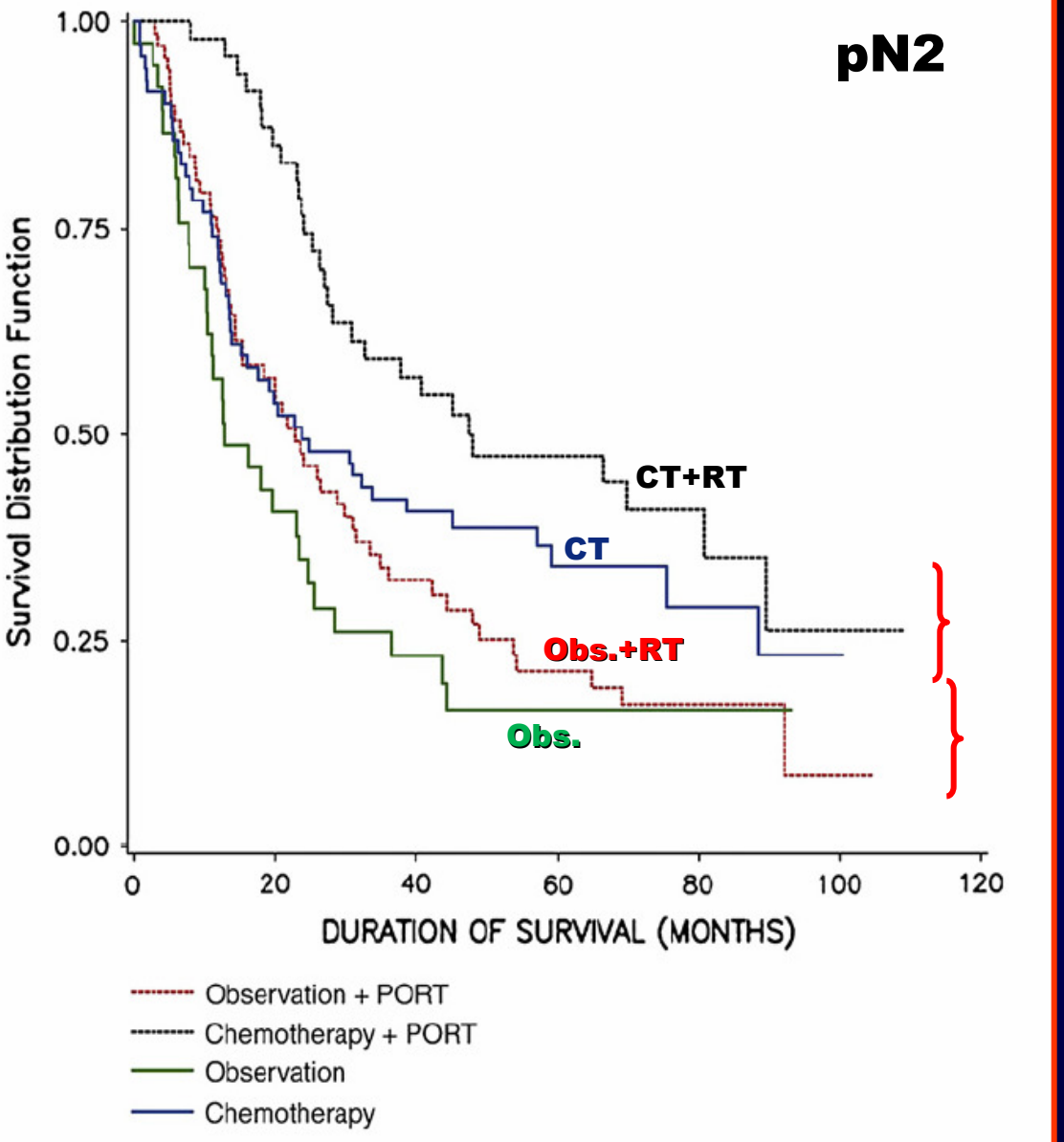


PORT detrimental !!



CT group: PORT detrimental

Obs. group: PORT beneficial



CT group: PORT+ CT better than CT alone

Obs. group: PORT beneficial

Is it enough to change the evidence ?

.....?

Cancer Care Ontario and American Society of Clinical Oncology Adjuvant Chemotherapy and Adjuvant Radiation Therapy for Stages I-IIIA Resectable Non–Small-Cell Lung Cancer Guideline

Katherine M.W. Pisters, William K. Evans, Christopher G. Azzoli, Mark G. Kris, Christopher A. Smith, Christopher E. Desch,† Mark R. Somerfield, Melissa C. Brouwers, Gail Darling, Peter M. Ellis, Laurie E. Gaspar, Harvey I. Pass, David R. Spigel, John R. Strawn, Yee C. Ung, and Frances A. Shepherd

Dec '07

Reference	Median Follow-Up (years)	Intervention	No. of Patients Randomly Assigned	Survival		Local Recurrence Rate (%)
				Median (years)	5-Year Rate (%)	
Mayer et al, 1997[43]	3.6	Surgery + RT	83	NR	29.7	**6.0**
		Surgery	72	NR	20.4	**23.6**
Dautzenberg et al, 1999[44]	5.7	Surgery + RT	373	**2.3**	**30.0***	22.5†
		Surgery	355	**3.5**	**43.0**	28.5
Feng et al, 2000[45]	NR	Surgery + RT	134‡	NR	43.4	**12.7§**
		Surgery	162‡	NR	40.5	**33.2§**

Published after PORT Meta-anaysis

NO survival benefit !

Need for a New Trial to Evaluate Adjuvant Postoperative Radiotherapy in Non–Small-Cell Lung Cancer Patients With N2 Mediastinal Involvement

Cecile Le Péchoux, Ariane Dunant, and Jean-Pierre Pignon

Departments of Radiotherapy and Biostatistics, Institut Gustave Roussy, Villejuif, France

Dirk De Ruysscher

Academic Hospital Maastricht/GROW/MAASTRO Clinic, Maastricht, the Netherlands

Lung Topics 2008

Induction Treatments

Definitive irradiation

Post-operative RT

PCI

PCI improves survival in responsive SCLC

... not only in Limited Disease !!

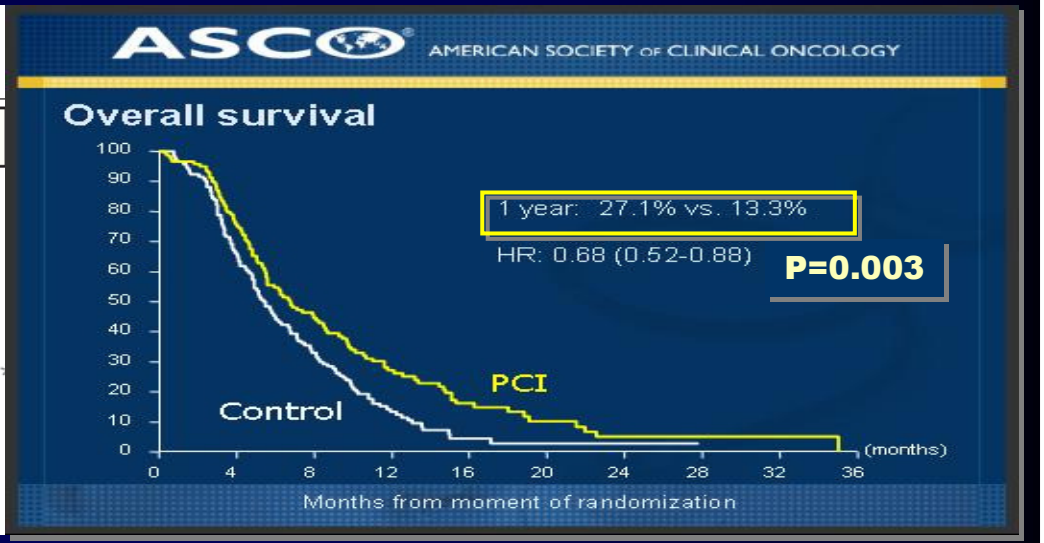
The NEW ENGLAND JOURNAL of MEDICINE

August 2007

ORIGINAL ARTICLE

Prophylactic Cranial Irradiation in Extensive Small-Cell Lung Cancer

Ben Slotman, M.D., Ph.D., Corinne Faivre-Finn, M.D., Ph.D., Gijs Kramer, M.D.,
Elaine Rankin, M.D., Michael Snee, D.M., Matthew Hatton, F.R.C.R.,
Pieter Postmus, M.D., Ph.D., Laurence Collette, Ph.D., Elena Musat, M.D.,
and Suresh Senan, Ph.D., F.R.C.R., for the EORTC Radiation Oncology Group
and Lung Cancer Group†



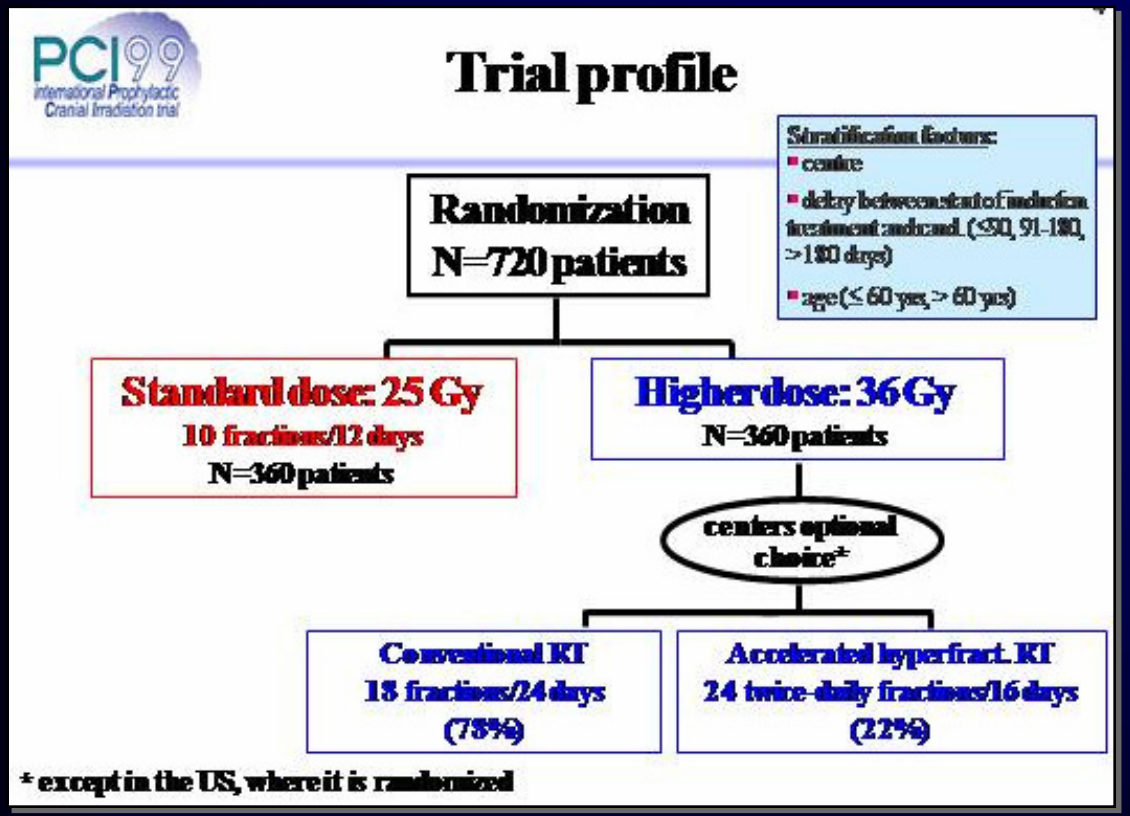
- **The optimal PCI dose is not well defined**

...meta-analysis suggested that brain metastases incidence might be reduced at higher doses...

Randomized Trial of Standard Dose to a Higher Dose PCI in LS-SCLC Complete Responders: Primary Endpoint Analysis

C. Le Pechoux, et al

ASCO 2008



End-points: BM incidence

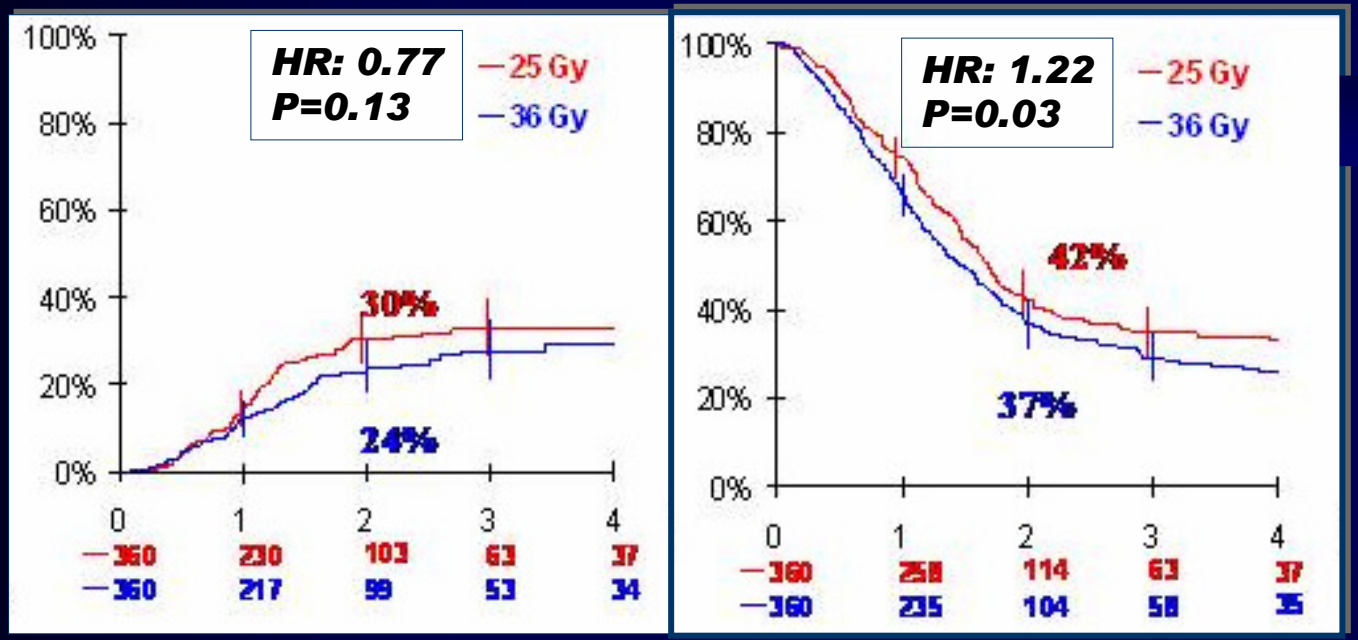
(decrease of 15% at 2 yrs)

Overall survival

QoL

Late sequelae

Results



Lower OS

Non-significant reduction in BM incidence

PCI at 25 Gy remains the standard for LD-SCLC

Is there a role for PCI in NSCLC ?

Prophylactic Cranial Irradiation in Operable Stage IIIA Non–Small-Cell Lung Cancer Treated With Neoadjuvant Chemoradiotherapy: Results From a German Multicenter Randomized Trial

Christoph Pöttgen, Wilfried Eberhardt, Andreas Grannass, Soenke Korfee, Georg Stüben, Helmut Teschler, Georgios Stamatis, Horst Wagner, Bernward Passlick, Volker Petersen, Volker Budach, Hans Wilhelm, Isabel Wanke, Herbert Hirche, Hans-Jochen Wilke, and Martin Stuschke

Random *(106 pts.)*

- **Surgery → post-op RT (50 Gy)**
- **CE x 3 → RT (45Gy BID) + CE → PCI (30Gy/15 frs) → Surgery**

End-points: ***Overall survival***
BM incidence

- ✓ ***No systemic treatment in control arm***
- ✓ ***Too many variables in experimental arm***

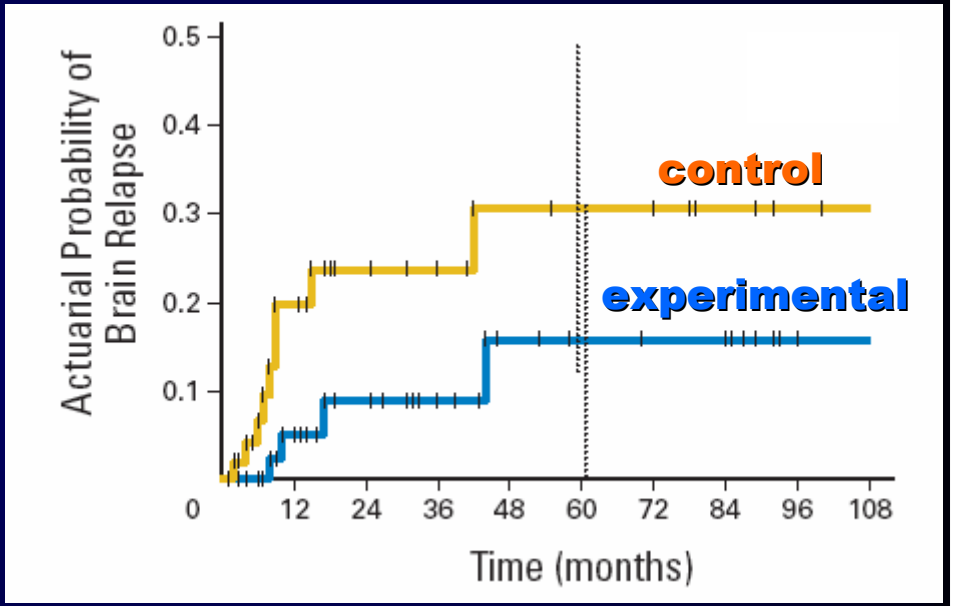
Is there a role for PCI in NSCLC ?

- **Significant reduction of BM incidence**

  (30.7% vs. 15.8% after 5 years)

- **NO DIFFERENCE in survival**

  5y-OS: 18% vs. 16% (*P* 0.15)



No evidence for PCI in NSCLC
Need for RCTs (RTOG ?)

Domenica 16 Novembre 2008

9.00-10.00
Sala Rossa

• SESSIONE 4

CONTROVERSIE IN RADIOTERAPIA

L'irradiazione profilattica dell'encefalo

Pro e Contro

MODERATORI: ***R. Santoni*** *(Roma)*, ***L. Pirtoli*** *(Siena)*

Pro
U. Ricardi *(Torino)*

Contro
E. Maranzano *(Terni)*

Replica
U. Ricardi *(Torino)*

Replica
E. Maranzano *(Terni)*

Topics

- Head & Neck
- Prostate
- Lung
- **Breast**
- Rectum

Breast Topics 2008

Hypofractionation

Partial Breast Irradiation

Carcinoma in situ

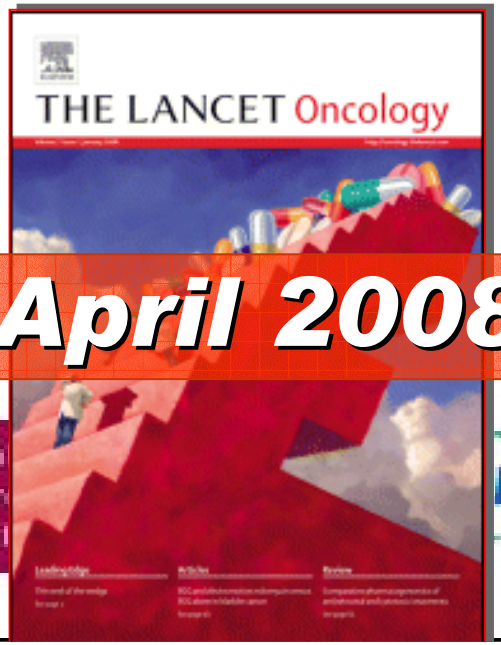
NCRI
National Cancer Research Institute

START

The Institute of Cancer Research
ICR-CTSU

Hypofractionation for early breast cancer: First results of the UK standardisation of breast radiotherapy (START) trials

March 2008



April 2008

CANCER RESEARC

MRC Medica Resear Council

Department of Health

START Trials: design and endpoints

BCS + mastectomy

Women with completely excised invasive breast cancer, T1-3 N0-1 M0

Trial A (ST-A)
N=2236

- 50Gy in 25 # (2.0Gy) 5 wks N=749
- 39.0Gy in 13 # (3.0Gy) 5 wks N=750
- 41.6Gy in 13 # (3.2Gy) 5 wks N=737

standard | **Hypofractionation**

Trial B (ST-B)
N=2215

- 50Gy in 25 # (2.0Gy) 5 wks N=1105
- 40Gy in 15 # (2.67Gy) 3 wks N=1110

Primary endpoint:
- local-regional relapse

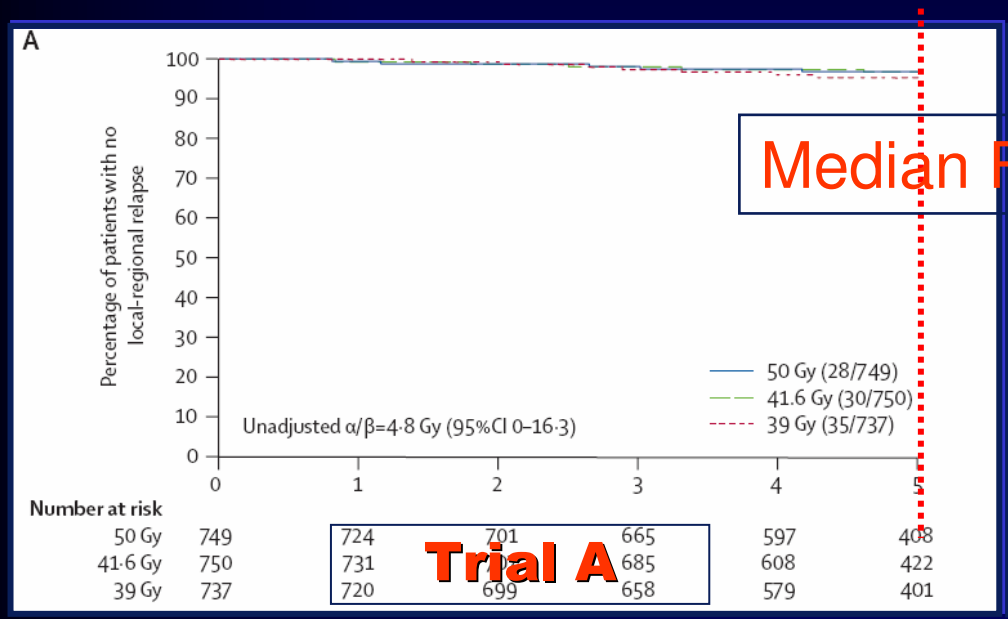
Secondary endpoints:
- normal tissue effects (NTEs)

Additional endpoints:
- disease-free survival
- overall survival

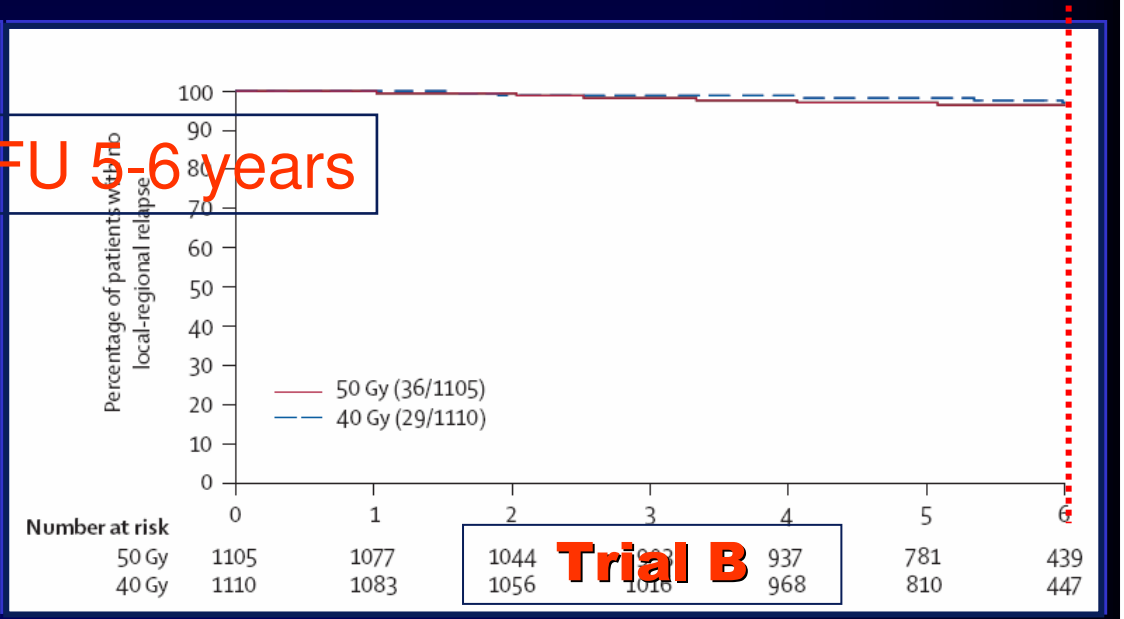
	Number of patients Trial A	Trial B
	2236	2215
-annual physician assessments of induration, shrinkage, oedema	2236	2215
-photographs (baseline, 2y & 5y)	1291	1094
quality of life EORTC Breast, body image, HADS (baseline, 6m, 1y, 2y, 5y)	1129	1079
	2236	2215

Recruitment from 35 UK centres between Jan 1999 & Oct 2002

No differences in local-regional relapse



Median FU 5-6 years



Trial A

Trial B

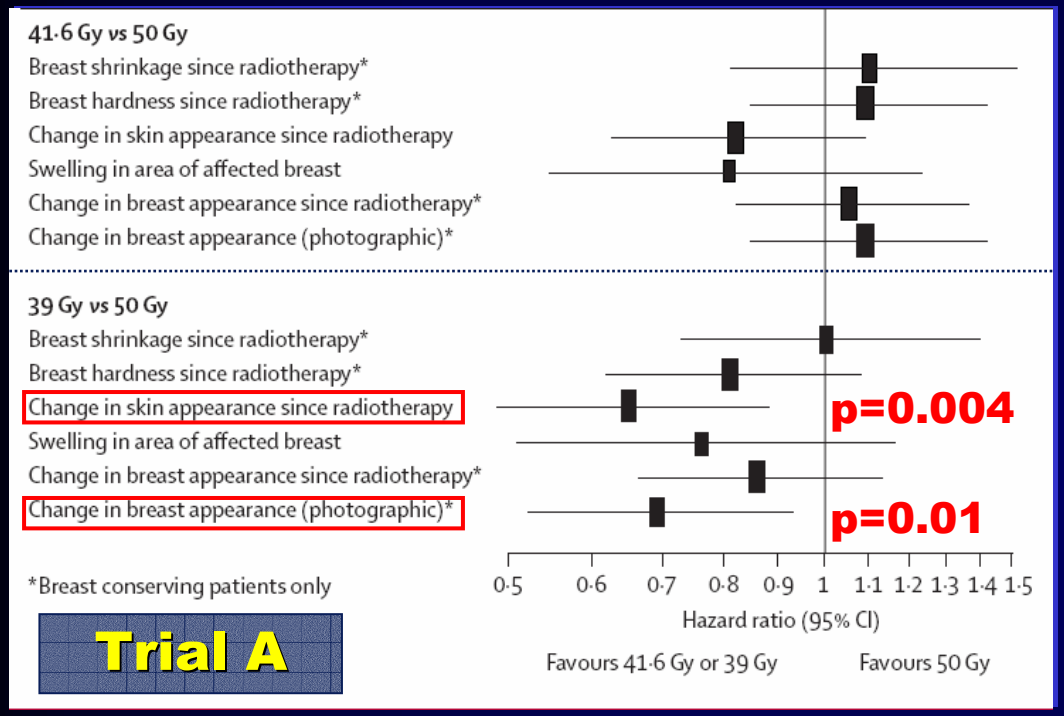
Local-regional relapse		% at 5 yrs	crude HR (95% CI)	p value
50 Gy	28/749 (3·7)	3·6 (2·2–5·1)	1	–
41·6 Gy	30/750 (4·0)	3·5 (2·1–4·3)	1·05 (0·63–1·75)	0·86
39 Gy	35/737 (4·7)	5·2 (3·5–6·9)	1·26 (0·77–2·08)	0·35

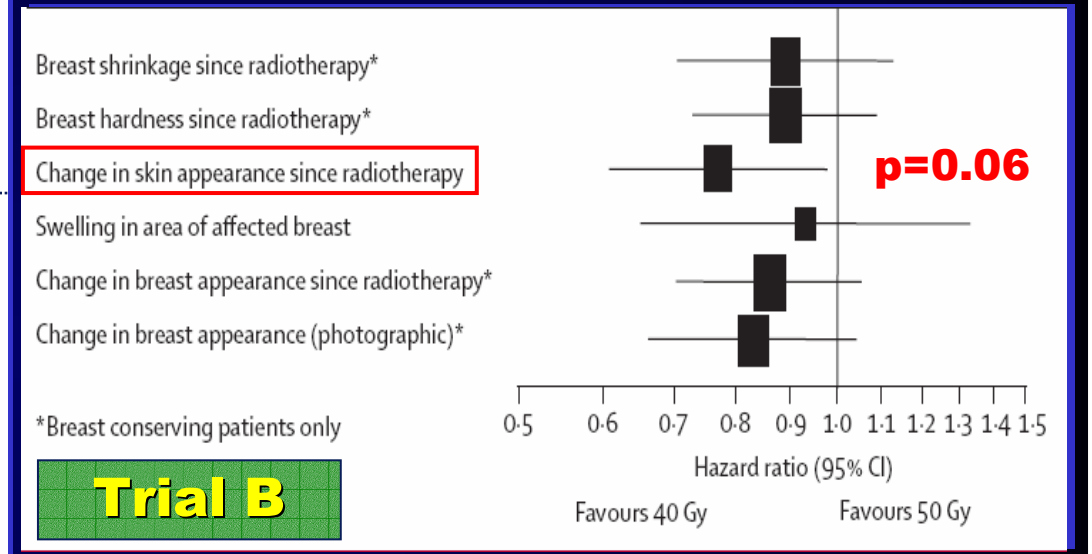
p: n.s.

Local-regional relapse		% at 5 yrs	crude HR (95% CI)	p value
50 Gy	36/1105 (3·2)	3·3 (2·2–4·5)	1	
40 Gy	29/1110 (2·6)	2·2 (1·3–3·1)	0·79 (0·48–1·29)	0·35

p: n.s.

No toxicity increase with hypofractionation





... hypofractionated could offer rates of tumor control and normal tissue damage as least as favourable as standard schedule...

Is there enough evidence to change?

No

Comments on
the START -trials
Dr. LJ Boersma, MAASTRO
clinic, Maastricht, The Netherlands

ESTRO
European Society for Therapeutic Radiology and Oncology
#68 Summer 2008

	% without any systemic treatment	# Fractions	Fraction size (Gy)	Total dose (Gy)	NTD2 (Gy)	NTD3,4 (Gy)	Breast changes (HR)	NTD10 (Gy)	NTD4,6 (Gy)	5 yr LRR (%)
					NTD for normal tissue			NTD for tumour		
START-A-B		25	2	50,00	50,00	50,00	1	50,00	50,00	3,3-3,6
START-A	7,7%	13	3	39,00	48,75	46,22	0,69	42,25	44,91	5,2
START-A	7,7%	13	3,2	41,60	54,08	50,84	1,09	45,76	49,16	3,5
START-B	3%	15	2,67	40,05	46,76	45,02	0,83	42,29	44,12	2,2
Bartelink	70%	25	2	50,00	50,00	50,00		50,00	50,00	7,3
Bartelink	70%	33	2	66,00	66,00	66,00		66,00	66,00	4,3

Similar LC despite different dose

→ different risk?

- **Age (younger in EORTC)**
- **Resection margin**
- **Surgery**

Syst. tr: EORTC 30%, START 90%

Is there enough evidence to change?

No

Comments on
the START -trials
Dr. LJ Boersma, MAASTRO
clinic, Maastricht, The Netherlands

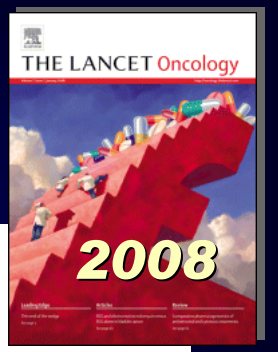
	% without any systemic treatment	# Fractions	Fraction size (Gy)	Total dose (Gy)	NTD2 (Gy)	NTD3,4 (Gy)	Breast changes (HR)	NTD10 (Gy)	NTD4,6 (Gy)	5 yr LRR (%)
					NTD for normal tissue			NTD for tumour		
START-A-B		25	2	50,00	50,00	50,00	1	50,00	50,00	3,3-3,6
START-A	7,7%	13	3	39,00	48,75	46,22	0,69	42,25	44,91	5,2
START-A	7,7%	13	3,2	41,60	54,08	50,84	1,09	45,76	49,16	3,5
START-B	3%	15	2,67	40,05	46,76	45,02	0,83	42,29	44,12	2,2
Bartelink	70%	25	2	50,00	50,00	50,00		50,00	50,00	7,3
Bartelink	70%	33	2	66,00	66,00	66,00		66,00	66,00	4,3

Low NTD for normal tissues

… but short FU!

Is there enough evidence to change?

No



Comment *Harry Bartelink, Rodrigo Arriagada

Hypofractionation in radiotherapy for breast cancer

Balanced ?

Mixed population :	*Trial A*	*Trial B*
Mastectomy	*15%*	*8%*
Boost	*61%*	*43%*
Tamoxifen	*79%*	*87%*
Chemotherapy	*35%*	*22%*
Oestrogen receptors	*?*	*?*

"… hypofractionation is convenient… nevertheless we have to wait for longer FU before final conclusions."

Is there enough evidence to change?

Yes

"There are now long-term data from randomized trials to support the concept that modest hypofractionation can be used to treat the whole breast after breast conserving surgery with similar rates of local control and morbidity as seen with conventional fractionation."

Whelan TJ et al.

Study	Patients	Fractionation Schedule	Follow-up (yrs)	Locoregional Recurrence (%)	Breast Appearance (% excellent/good or no change)
Whelan et al, 2002[26]	1234 Node −ve	50 Gy/25 fractions/ 5 weeks 42.5 Gy/ 16 fractions/3 weeks	5, 5	3.0, 2.8*	77, 77†
Yarnold et al,[28] Owen et al, 2006[29]	1410 Node −ve and +ve	50 Gy/25 fractions/ 5 weeks 42.9 Gy/ 13 fractions/5 weeks 39 Gy/13 fractions/5 weeks	10, 10, 10	12.1, 9.1, 14.8	47, 42, 44‡, 72.3
START A[30]	2236 Node −ve and +ve	50 Gy/25 fractions/ 5 weeks 41.6 Gy/ 13 fractions/5 weeks 39 Gy/13 fractions/5 weeks	5, 5, 5	3.6, 3.5, 5.2	59, 59, 70‡
START B[31]	2215 Node −ve and +ve	50 Gy/25 fractions/ 5 weeks 40 Gy/ 15 fractions/5 weeks	5, 5	3.3, 2.2	57, 64‡

50th ANNUAL MEETING
50 YEARS OF LEARNING, CARING AND COLLABORATION IN THE TREATMENT OF CANCER PATIENTS
BOSTON • SEPTEMBER 21-25, 2008
ASTRO
AMERICAN SOCIETY FOR THERAPEUTIC RADIOLOGY AND ONCOLOGY

10-years FU	Standard	Hypo
LR risk	6.7%	6.2%
cosmesis > good	71%	70%
skin morbidity > moderate	3%	6%

XVIII Congresso Nazionale AIRO
15-18 novembre 2008

Breast Topics 2008

Hypofractionation

Partial Breast Irradiation

Carcinoma in situ

Key question: is less more?

Changing Concepts in Radiation Therapy for Early Breast Cancer

By Krystyna Kiel, MD

ASCO 2008

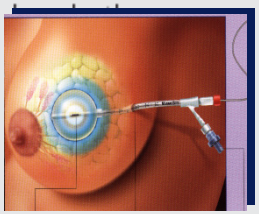
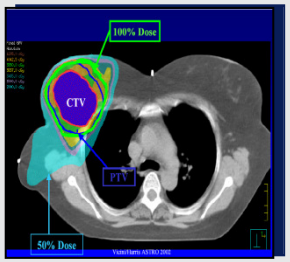
*"… Accelerated PBI may be an alternative to conventional irradiation for **some** patients…*

*… many studies suggest that, for **selected** patients, this approach is safe and effective."*

Overview of Accelerated Partia Breast Irradiation 2008

Todd A. Swanson, MD, PhD, and Frank A. Vicini, MD

CURRENT Oncology reports

APBI technique	Study/Institution	Patients, *n*	Median follow-up, *mo*	Recurrence rate, %	Good or excellent cosmesis, %
MIB 	King et al. [20] Oschner Clinic (New Orleans, LA)	84	84	2.5	75
	Vicini et al. [21] William Beaumont Hospital (Royal Oak, MI)	199	65	2	99
	Kuske et al. [23] RTOG 95-17 (multi-institutional)	99	45	3	NR
Phase III	Polgár et al. [34••]	258	66	MIB: 4.7% WBI: 3.4%	MBI: 77; WBI: 63
MammoSite® breast 	Keisch et al. [25]	70	60		86
	Benitez (personal communication)				
	Zannis et al. [18••] ASBS registry trial	1403	15	0.1	98
	Benitez et al. [25•]	100	9.5	2	98
3D-CRT 	Vicini et al. [29••] RTOG 03-19 (multi-institutional)	46	NR	NR	NR
	William Beaumont Hospital (personal communication)	91	24	0	91
	Wernicke et al. [28] New York University (New York, NY)	78	28	0	92

... but who's to be treated!

CURRENT Oncology reports

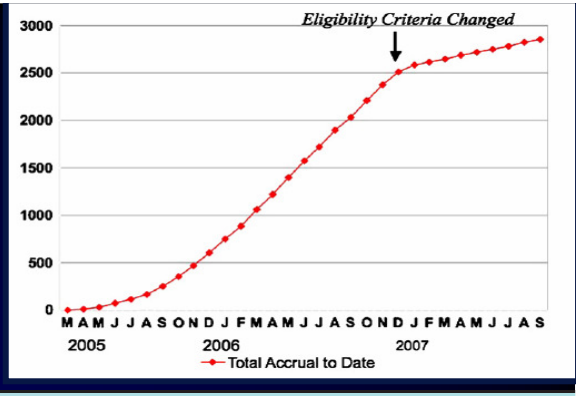
Organization	Participant age, *y*	Tumor size, *cm*	Histology	Lymph node status	Margin status
ABS	≥ 50	≤ 3	Invasive ductal carcinoma	Negative (by sentinel lymph node or axillary dissection)	Negative (at inked margin)
ASBS	≥ 45	≤ 3	Invasive ductal carcinoma and ductal carcinoma in situ	Negative (by sentinel lymph node or axillary dissection)	Negative (> 2 mm)
NSABP B-39 RTOG 0413	≥ 18	≤ 3	Invasive ductal carcinoma and ductal carcinoma in situ	Allows for 0–3 nodes (with negative sentinel lymph node or > 6 nodes sampled)	Negative (at inked margin)

LOW RISK

Shifting from a "careful" selection to a more realistic PBI investigation in clinical practice

... are we ready for it ?

NSABP B-39 / RTOG 0413



Inclusion of Low risk pts. finished after 2547 pts

Current eligibility criteria

- Women < 50 with DCIS or invasive breast cancer (with an index lesion < 3 cm and ≤ 3 positive lymph nodes)
- Women > 50 with an index lesion < 3 cm and either hormone receptor–negative disease or 1–3 positive lymph nodes

Randomize

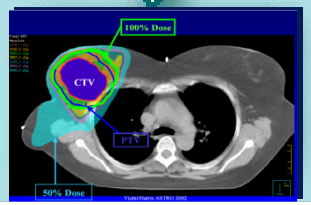
Whole breast irradiation

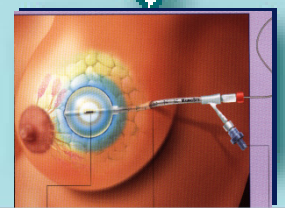
- 45–50 Gy to whole breast with boost to 60 Gy after chemotherapy if necessary
- Treatment daily, 5 days/wk × 5–7 wk

Accelerated partial breast irradiation

- 34 Gy to the index quadrant before chemotherapy if necessary
- Treatment twice daily × 5 days ≥ 6 hours between treatments

Physician/patient choice





CLINICAL OUTCOME ANALYSIS IN "HIGH-RISK" VERSUS "LOW-RISK" PATIENTS ELIGIBLE FOR NATIONAL SURGICAL ADJUVANT BREAST AND BOWEL B-39/ RADIATION THERAPY ONCOLOGY GROUP 0413 TRIAL: FIVE-YEAR RESULTS

RAKESH R. PATEL, M.D., MICHAEL E. CHRISTENSEN, B.S., C. WESLEY HODGE, M.D., JARROD B. ADKISON, M.D., AND RUPAK K. DAS, PH.D.

Purpose: to compare the clinical outcome of a retrospective PBI population, whose elegibility criteria were the same as NSABP/RTOG trial

CLINICAL OUTCOME ANALYSIS IN "HIGH-RISK" VERSUS "LOW-RISK" PATIENTS ELIGIBLE FOR NATIONAL SURGICAL ADJUVANT BREAST AND BOWEL B-39/ RADIATION THERAPY ONCOLOGY GROUP 0413 TRIAL: FIVE-YEAR RESULTS

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Characteristic	Low-risk group	High-risk group
Patient/tumor related		
Patients *(n)*	183	90
Median age (y)	63	47
Median pathologic size (mm)	11	14
Patients <50 y	0 (0)	70 (78)
Positive lymph nodes	0 (0)	16 (18)
Estrogen receptor negative	0 (0)	21 (23)
DCIS	28 (15)	8 (9)
Treatment related		
Multicatheter brachytherapy	162 (89)	85 (94)
MammoSite	21 (11)	5 (6)
Chemotherapy	20 (11)	48 (53)
Hormonal therapy	104 (57)	45 (50)
Outcome related		
Median follow-up (mo)	47.9	49.7
Crude ipsilateral breast recurrence	4 (2.2)	4 (4.4)
Death from any cause	8 (4.4)	5 (5.6)

… no difference in outcome… →

Support the inclusion of High risk pts !

Breast Topics 2008

Hypofractionation

Partial Breast Irradiation

Carcinoma in situ

Key question: should post-op RT be offered to any patient with DCIS?

- Are there patient groups where RT is more or less effective?

VOLUME 24 · NUMBER 7 · MARCH 1 2006

JOURNAL OF CLINICAL ONCOLOGY

EDITORIAL

Is Excision Alone Adequate Treatment for Low-Risk Ductal Carcinoma-in-Situ of the Breast?

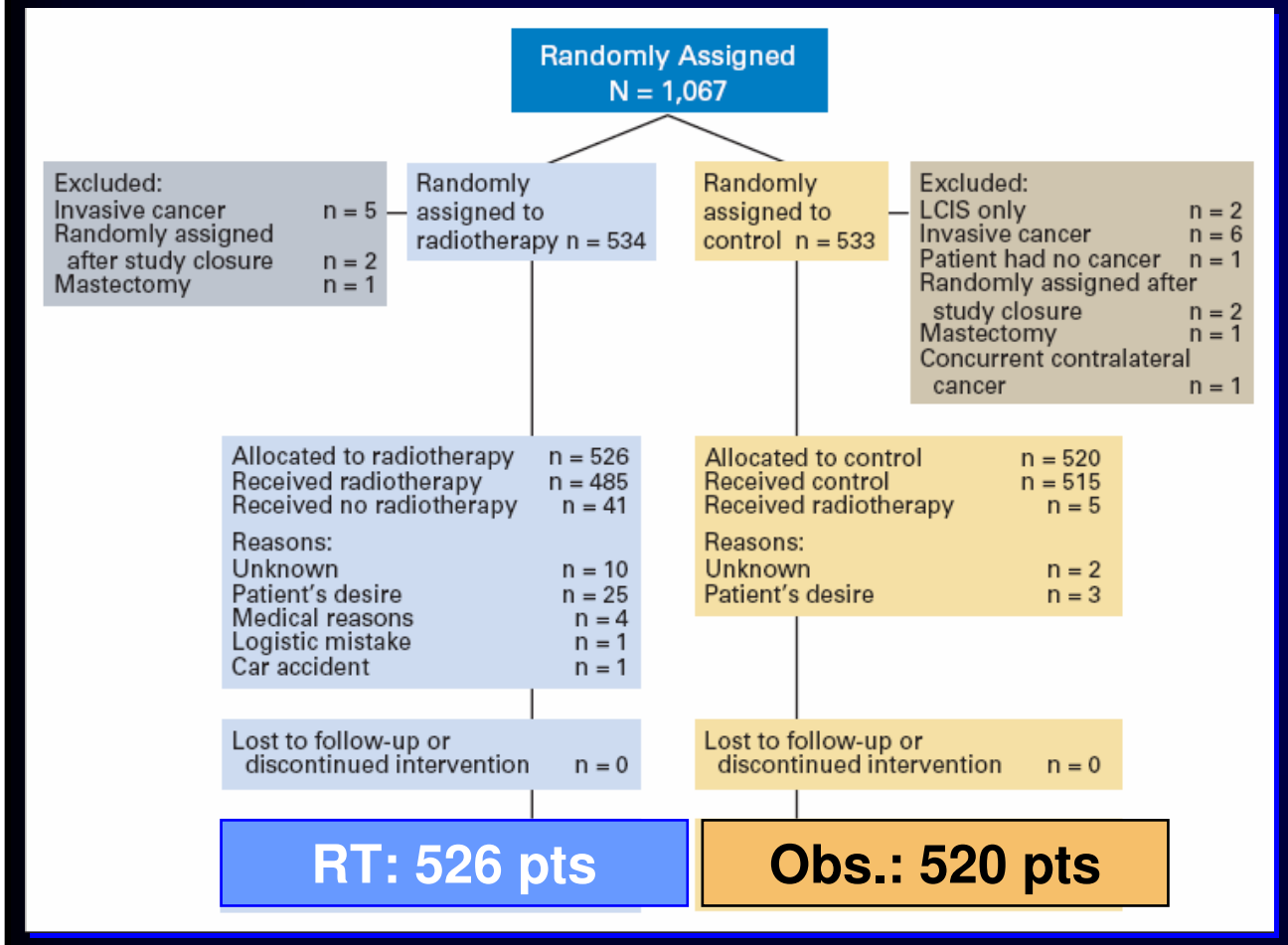
Lawrence J. Solin, *University of Pennsylvania, Philadelphia, PA*

The diagnosis of ductal carcinoma-in-situ (DCIS; intraductal carcinoma) of the breast presents a dilemma for both the patient and the treating physician. DCIS is a nonobligate precursor of invasive carcinoma and occupies a position on the spectrum of neoplasia between benign and malignant.[1] Some patients with

It is noteworthy that the study by Wong et al[2] failed to identify prospectively a low-risk cohort of patients suitable for treatment with excision alone. Given the small total number of patients in this study, many subsets contained too few patients for meaningful analysis. As a result, the study provides no substantive clues to

Absolute Risk Reductions for Local Recurrence After Postoperative Radiotherapy After Sector Resection for Ductal Carcinoma In Situ of the Breast

Lars Holmberg, Hans Garmo, Bengt Granstrand, Anita Ringberg, Lars-Gunnar Arnesson, Kerstin Sandelin, Per Karlsson, Harald Anderson, and Stefan Emdin

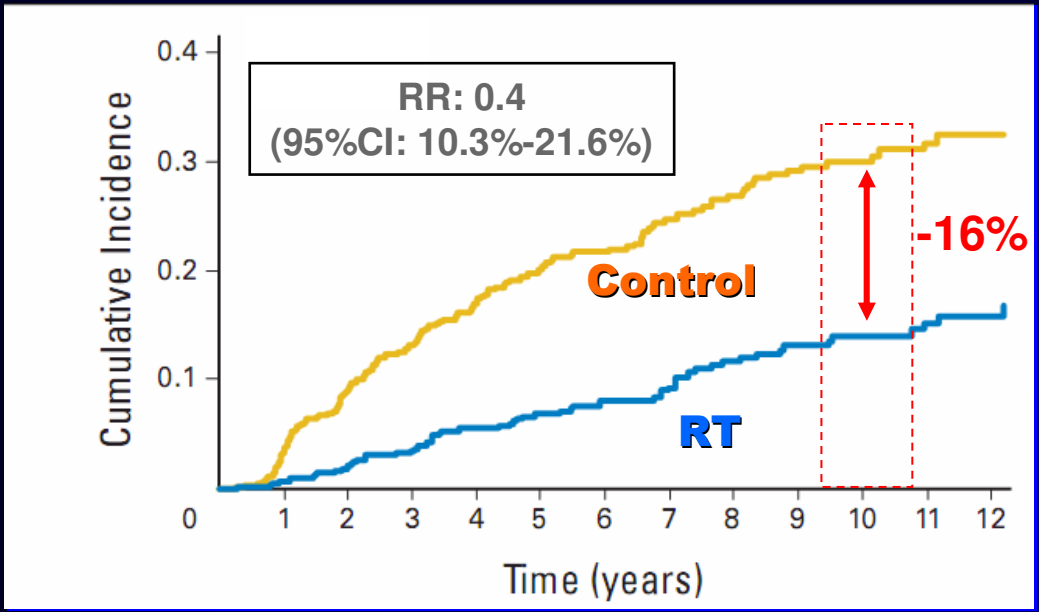


End-points:

Absolute risk reduction of Local recurrence incidence

Mean FU: 8.4 years

Risk reduction with RT



Increasing RT effect with age

Characteristic		No. of Ipsilateral Events		Stratified Univariate Model		Stratified Multivariate Model	
		RT Arm	Control Arm	RR (RT *v* control)	95% CI	RR (RT *v* control)	95% CI
Age, years							
< 50	<50	27	32	0.74	0.45 to 1.23	0.73	0.43 to 1.24
50-57	>50	15	38	0.36	0.20 to 0.66	0.36	0.19 to 0.65
58-64	>50	11	40	0.25	0.13 to 0.48	0.26	0.13 to 0.50
65+	>50	11	31	0.29	0.15 to 0.58	0.27	0.14 to 0.54

current evidence

- **Young age as indipendent factor for local relapse**

	Trial	Age
	NSABP B-17	≤ 49aa *(Trend)*
	EORTC 10853	≤ 40aa p = 0.0021
	Solin J et al.	≤ 39aa p = 0.0006

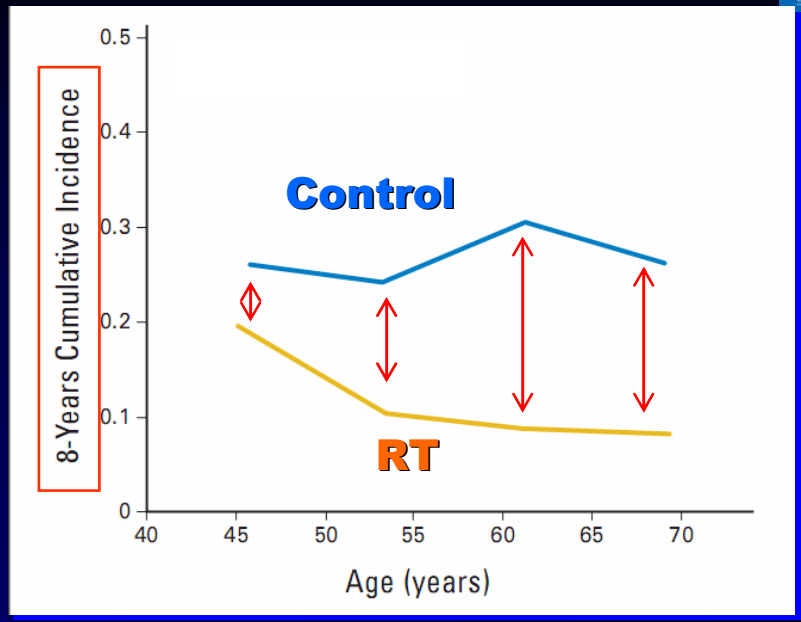
- **Older patients still benefit from adjuvant RT**

  (5-year risk of recurrence up to 13.6% without RT in 3409 pts of ≥ 66)

Smith et al.

modest risk reduction in younger (6%)

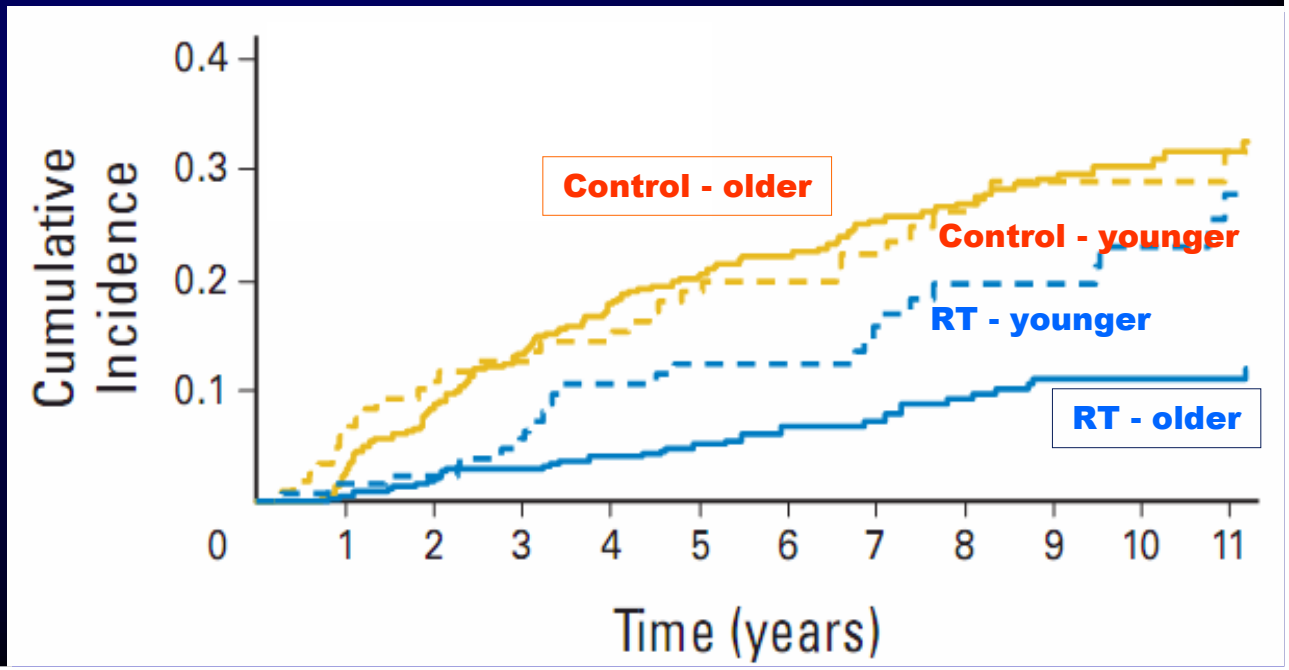
significant reduction in older (18%)



Does age effect result in low risk group?

Younger
Similar difference in RT vs. Control group

Older
RT reduces the risk during FU



modest risk reduction in younger (6%)

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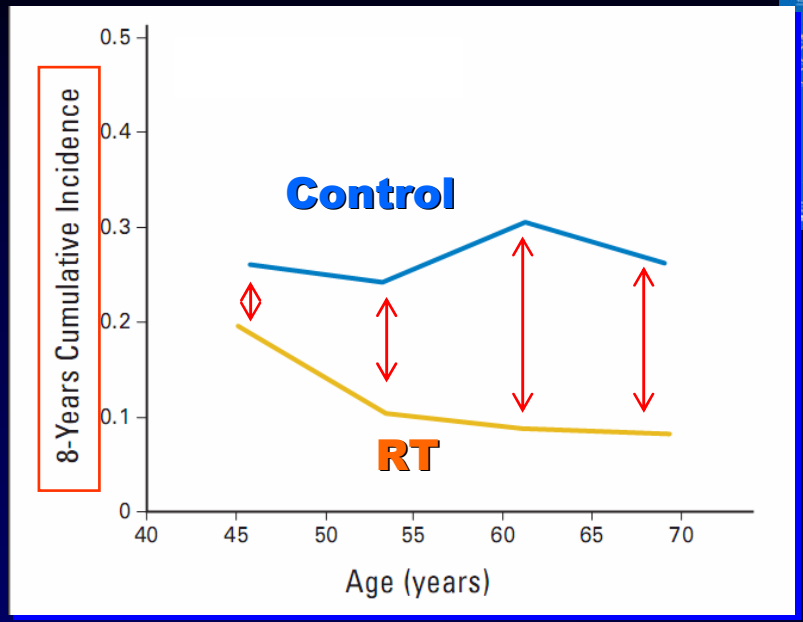
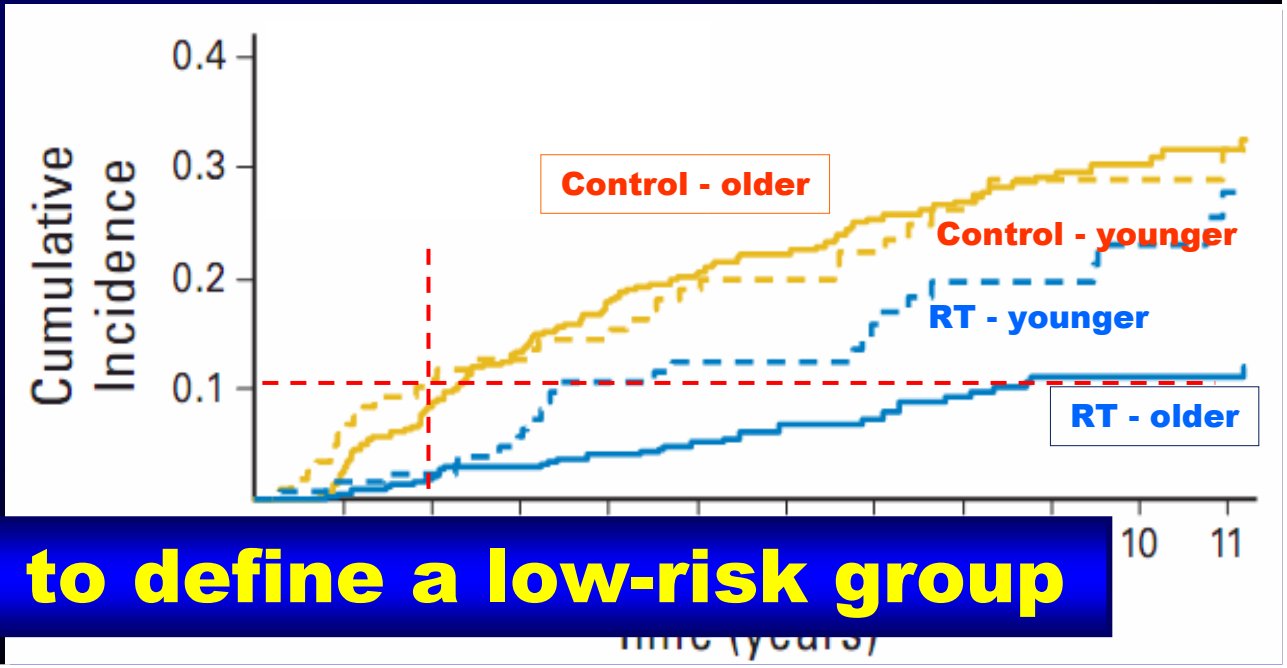


Does age effect result in low risk group?

2-year Incidence > 10% in Controls



Not possible to define a low-risk group

Should post-op RT be offered to any patient with DCIS?

XVIII Congresso Nazionale

Lunedì 17 Novembre 2008

8.00-8.40
Sala Rossa

• SESSIONE 13

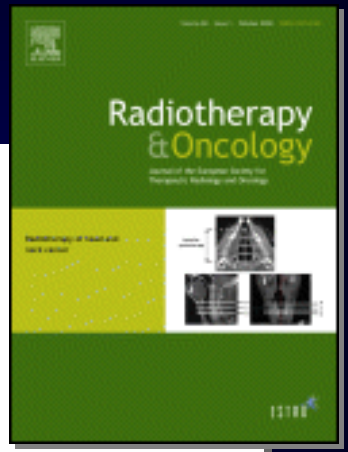
"Meet The Professor"
LEZIONE DI AGGIORNAMENTO
Il carcinoma in situ della mammella
RELATORE: ***C. Aristei*** *(Perugia)*

Shooter: ***L. Livi*** *(Firenze)*

Topics

- Head & Neck
- Prostate
- Lung
- Breast
- **Rectum**

Radiotherapy and Oncology 87 (2008) 449—474
www.thegreenjournal.com



Educational review

Evidence and research in rectal cancer

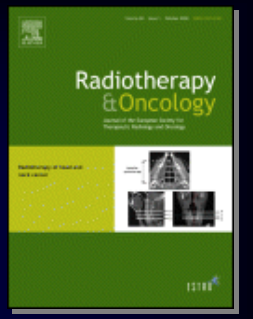
Vincenzo Valentini[a,*], Regina Beets-Tan[b], Josep M. Borras[c], Zoran Krivokapić[d], Jan Willem Leer[e], Lars Påhlman[f], Claus Rödel[g], Hans Joachim Schmoll[h], Nigel Scott[i], Cornelius Van de Velde[j], Christine Verfaillie[k]

[a]Department of Radiation Oncology, Università Cattolica S.Cuore, Rome, Italy, [b]Department of Radiology, University Hospital Maastricht, The Netherlands, [c]IDIBELL-Cancer Plan, Department of Health, Barcelona, Spain, [d]Institute for Digestive Diseases, Clinical Center of Serbia, Belgrade, Serbia, [e]Department of Radiation Oncology, Radboud University Nijmegen Medical Center, The Netherlands, [f]Department of Surgery, Uppsala University Hospital, Uppsala, Sweden, [g]Department of Radiation Oncology, University of Frankfurt, Germany, [h]Department of Medical Oncology, Martin Luther University Halle-Wittenberg, Germany, [i]Department of Pathology, St. James's University Hospital, Leeds, UK, [j]Department of Surgery, Leiden University Medical Center, The Netherlands, [k]ESTRO Office, Brussels, Belgium

Rectum Topics 2008

Resectable disease

Unresectable disease



High evidence of better local control with short-course preoperative RT in resectable disease

Less evidence for Survival benefit
(systematic review on 25.000 pts →10% gain - Acta Oncol 2003)

- ***Has anything changed?***
- ***What role does chemotherapy play?***

ANNALS OF SURGERY

Peeters et al. 2007

FU: 6 years

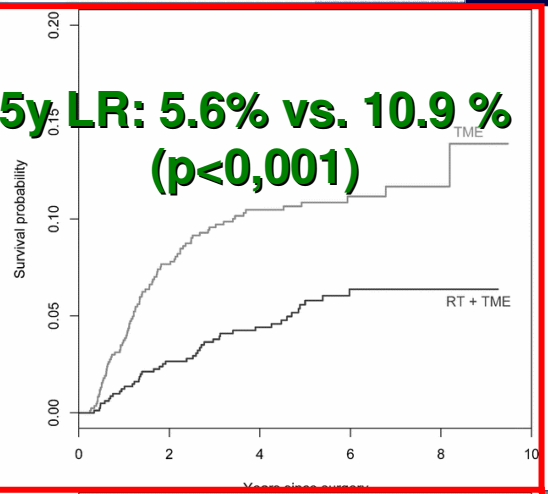
The New England Journal of Medicine

2001

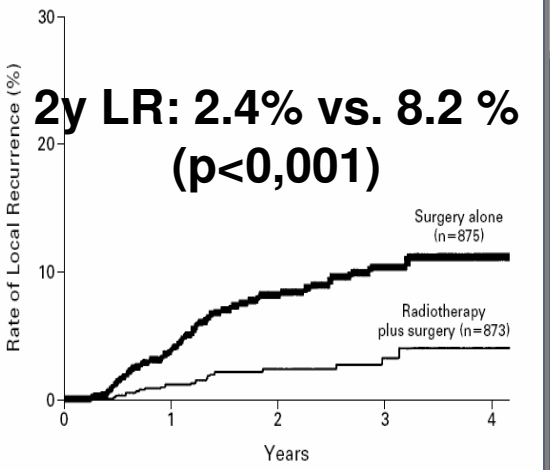
PREOPERATIVE RADIOTHERAPY COMBINED WITH TOTAL MESORECTAL EXCISION FOR RESECTABLE RECTAL CANCER

ELLEN KAPITEIJN, M.D., CORRIE A.M. MARIJNEN, M.D., IRIS D. NAGTEGAAL, M.D., HEIN PUTTER, PH.D., WILLEM H. STEUP, M.D., PH.D., THEO WIGGERS, M.D., PH.D., HARM J.T. RUTTEN, M.D., PH.D., LARS PAHLMAN, M.D., PH.D., BENGT GLIMELIUS, M.D., PH.D., J. HAN J.M. VAN KRIEKEN, M.D., PH.D., JAN W.H. LEER, M.D., PH.D., AND CORNELIS J.H. VAN DE VELDE, M.D., PH.D., FOR THE DUTCH COLORECTAL CANCER GROUP*

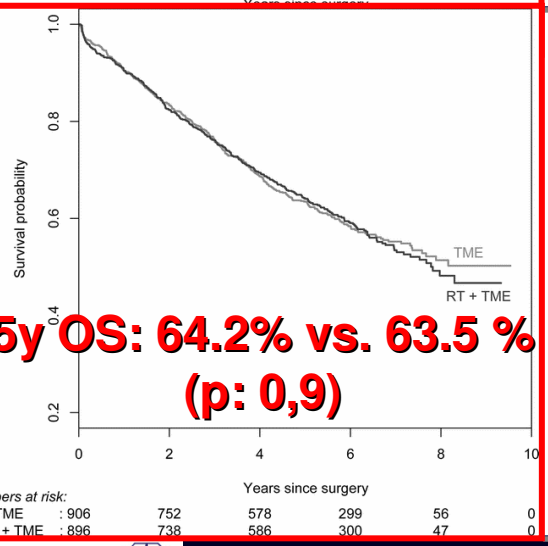
5y LR: 5.6% vs. 10.9 %
(p<0,001)



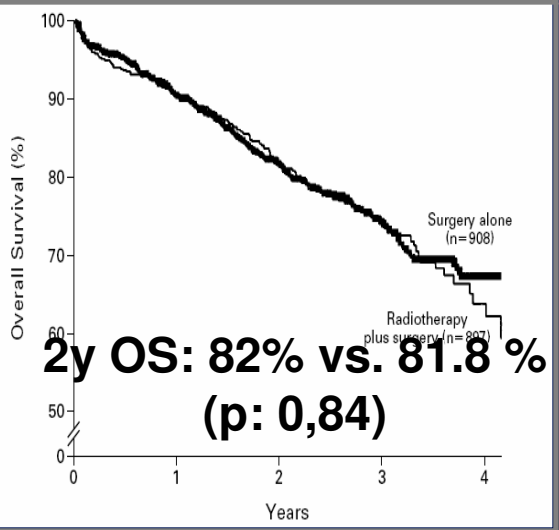
2y LR: 2.4% vs. 8.2 %
(p<0,001)



5y OS: 64.2% vs. 63.5 %
(p: 0,9)



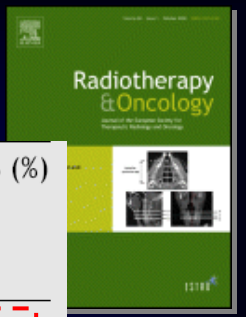
2y OS: 82% vs. 81.8 %
(p: 0,84)



Major advantage:

- ✓ **Node-positive disease**
- ✓ **Non-low seated tumors**
- ✓ ***CRM* negative**

Chemotherapy

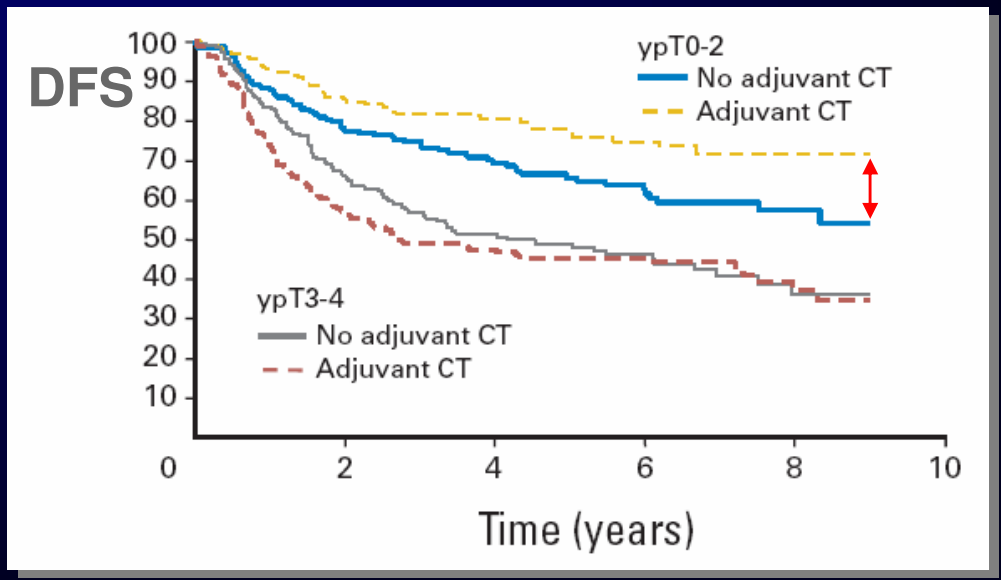


Benefit on resectability and LC
No impact on Survival

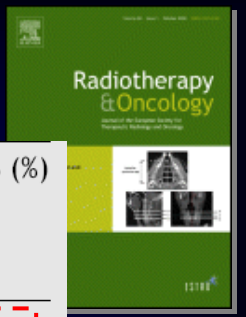
Author	Regimen Preop Postop		Patients	pCR (%)	Spincter preservation (%)	Local failure (%)	5 y DFS (%)	5 y OS (%)
Bosset EORTC '06	RT RT						] 54	] 65
	RT/5-FU RT/5-FU	5-FU/FA	1011	] 14 *p* = 0.0001	] 52.8	8.7 7.6 *p* = 0.002	] 56	] 66
Gerard FFCD '06	RT RT/5-FU	5-FU/FA 5-FU/FA	733	3.6 11.4 *p* = 0.0001	52 53	16.5 8.1 *p* = 0.003	56 59	66 67
Bujko Polish '07	RT (5 × 5 Gy) RT/5-FU		312	0.7 15.2 *p* = 0.0001	61 58	9 14	58° 55°	67° 66°

Patients With Curative Resection of cT3-4 Rectal Cancer After Preoperative Radiotherapy or Radiochemotherapy: Does Anybody Benefit From Adjuvant Fluorouracil-Based Chemotherapy? A Trial of the European Organisation for Research and Treatment of Cancer Radiation Oncology Group

Laurence Collette, Jean-Francois Bosset, Marcel den Dulk, France Nguyen, Laurent Mineur, Philippe Maingon, Ljiljana Radosevic-Jelic, Marianne Piérart, and Gilles Calais



Chemotherapy

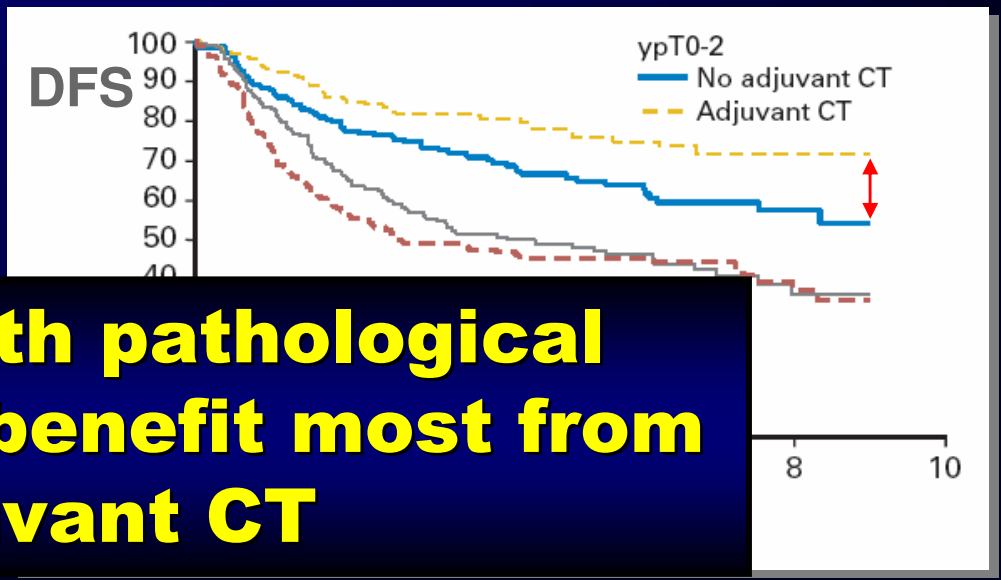


Author	Regimen		Patients	pCR (%)	Spincter preservation (%)	Local failure (%)	5 y DFS (%)	5 y OS (%)
	Preop Postop							
Bosset EORTC '06	RT RT						] 54	] 65
	RT/5-FU RT/5-FU	5-FU/FA	1011	] 14 *p* = 0.0001	] 52.8	8.7 7.6 *p* = 0.002	] 56	] 66
Gerard FFCD '06	RT RT/5-FU	5-FU/FA 5-FU/FA	733	3.6 11.4 *p* = 0.0001	52 53	16.5 8.1 *p* = 0.003	56 59	66 67
Bujko Polish '07	RT (5 × 5 Gy) RT/5-FU		312	0.7 15.2 *p* = 0.0001	61 58	9 14	58° 55°	67° 66°

Benefit on resectability and LC
No impact on Survival

Patients With Curative Resection of cT3-4 Rectal Cancer After Preoperative Radiotherapy or Radiochemotherapy: Does Anybody Benefit From Adjuvant Fluorouracil-Based Chemotherapy? A Trial [illegible] Research and Treatment [illegible]

Laurence Collette, Jean-Francois Bosset, Mar[illegible]
Ljiljana Radosevic-Jelic, Marianne Piérart, a[illegible]



Patients with pathological downstaging benefit most from Adjuvant CT

Rectum Topics 2008

Resectable disease

Unresectable disease

All pts with <u>unresectable</u> disease should receive preoperative CMT (50-54 Gy + FU-CT) to enhance resectability

Glimelius et al. Acta Oncol 2003

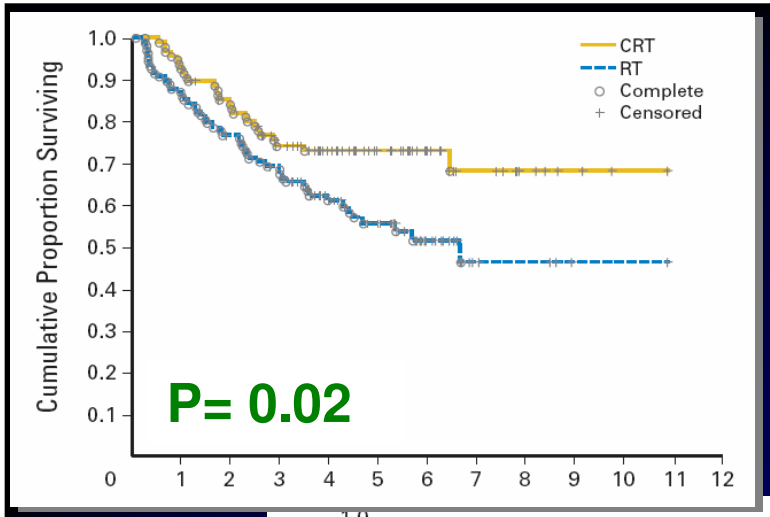
Randomized Phase III Study Comparing Preoperative Radiotherapy With Chemoradiotherapy in Nonresectable Rectal Cancer

Morten Brændengen, Kjell M. Tveit, Åke Berglund, Elke Birkemeyer, Gunilla Frykholm, Lars Påhlman, Johan N. Wiig, Per Byström, Krzysztof Bujko, and Bengt Glimelius

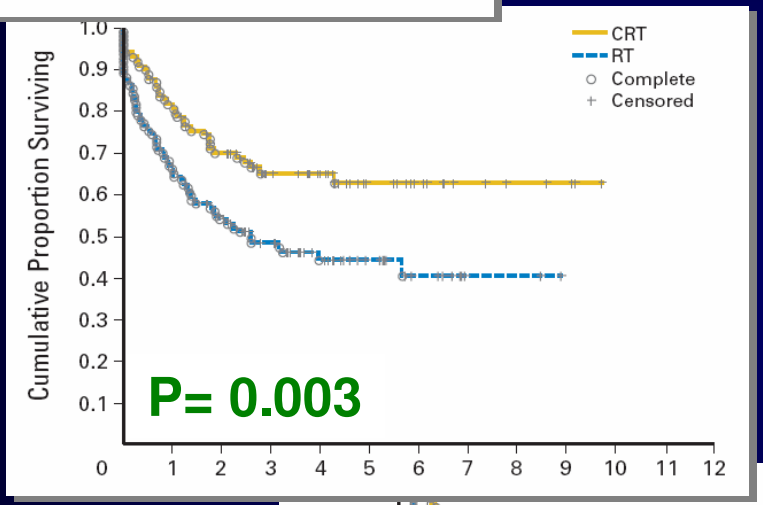
Random → **50 Gy** → **Surgery** → ***+/- FU (stage III)***

Random → **FU + 50 Gy** →

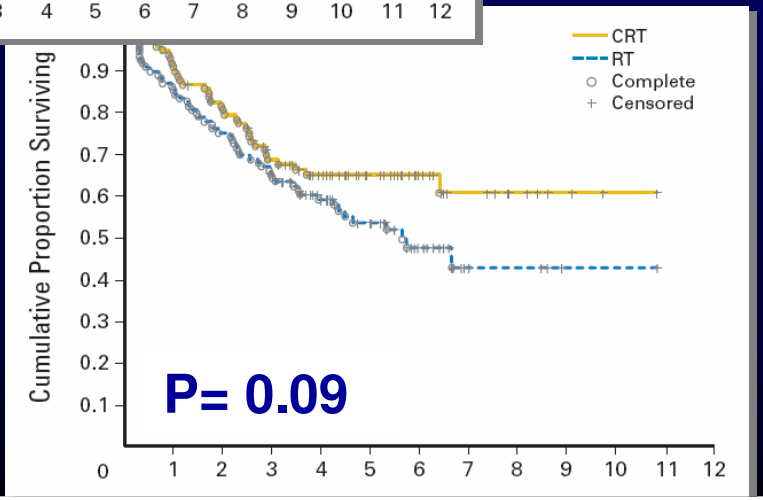
(207 pts.)



Local control

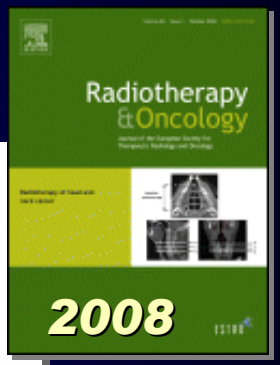


Time to Failure



Overall survival

... what about short-course schedule?



Editorial

The 5 × 5 Gy with delayed surgery in non-resectable rectal cancer: A new treatment option

Krzysztof Bujko*, Milena Kolodziejczyk

Department of Radiotherapy, Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland

Although, the evidence is insufficient to recommend the short-course radiation and delayed surgery for all patients with non-resectable cancer, for those unfit for chemotherapy or requiring chemotherapy dose intensification due to synchronous distant metastases, this management is a new valuable option.

Lunedì 17 Novembre 2008

9.00-10.40
Sala Rossa

• SESSIONE 14

SIMPOSIO AIRO-AIOM

La chemio-radioterapia nel carcinoma del retto: opinioni a confronto

MODERATORI: ***F. Boccardo*** *(Genova)*, ***F. Valvo*** *(Milano)*

Il parere del chirurgo
L. Gennari *(Milano)*

Il parere del radioterapista
V. Valentini *(Roma)*

Il parere dell'oncologo medico
C. Pinto *(Bologna)*

Discussione

Grazie per l'attenzione!

XVIII Congresso Nazionale

15-18 novembre 2008