Unità di Radioterapia
Dip. di Specialità Medico Chirurgiche,
Scienze Radiologiche e Sanità Pubblica
Università degli Studi di Brescia

U.O. Radioterapia
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Head and Neck Cancer: multi-modal therapeutic integration

P. Ponticelli, L. Lastrucci, R. De Majo, A. Rampini

U.O.C. Radioterapia

Ospedale S. Donato ASL 8 - AREZZO

Summary

- Biological considerations
- Clinical results of chemo-radiation in locally advanced H&N cancer
- Radiotherapy associated with cetuximab
- Role of neoadjuvant chemotherapy
- Possible integration between chemotherapy and cetuximab associated with radiotherapy
- Clinical results of chemo-radiation in larynx preservation programs

Rationale of radiation and chemotherapy association in head and neck cancer

- **Temporal modulation** enhances tumor response to fractionated RT through the 4 R's of radiotherapy: repair, repopulation, reoxygenation, and redistribution
- **Biological cooperation** using different mechanism of cell killing
- **Cytotoxic enhancement** by modulating the induction or processing of intracellular demage

Bernier J, 2009

HPV-associated head and neck cancer

	HPV-positive tumours	HPV-negative tumours
Anatomical site	Tonsil and base of tongue	All sites
Histology	Non-keratinised	Keratinised
Age	Younger cohorts	Older cohorts
Sex ratio	3:1 men	3:1 men
Stage	Tx, T1–2	Variable
Risk factors	Sexual behaviour	Alcohol and tobacco
Incidence	Increasing	Decreasing
Survival	Improved	Unchanging

***Table 2*: Differences between HPV-positive and HPV-negative head and neck squamous-cell carcinomas**

Marur S et al, 2010

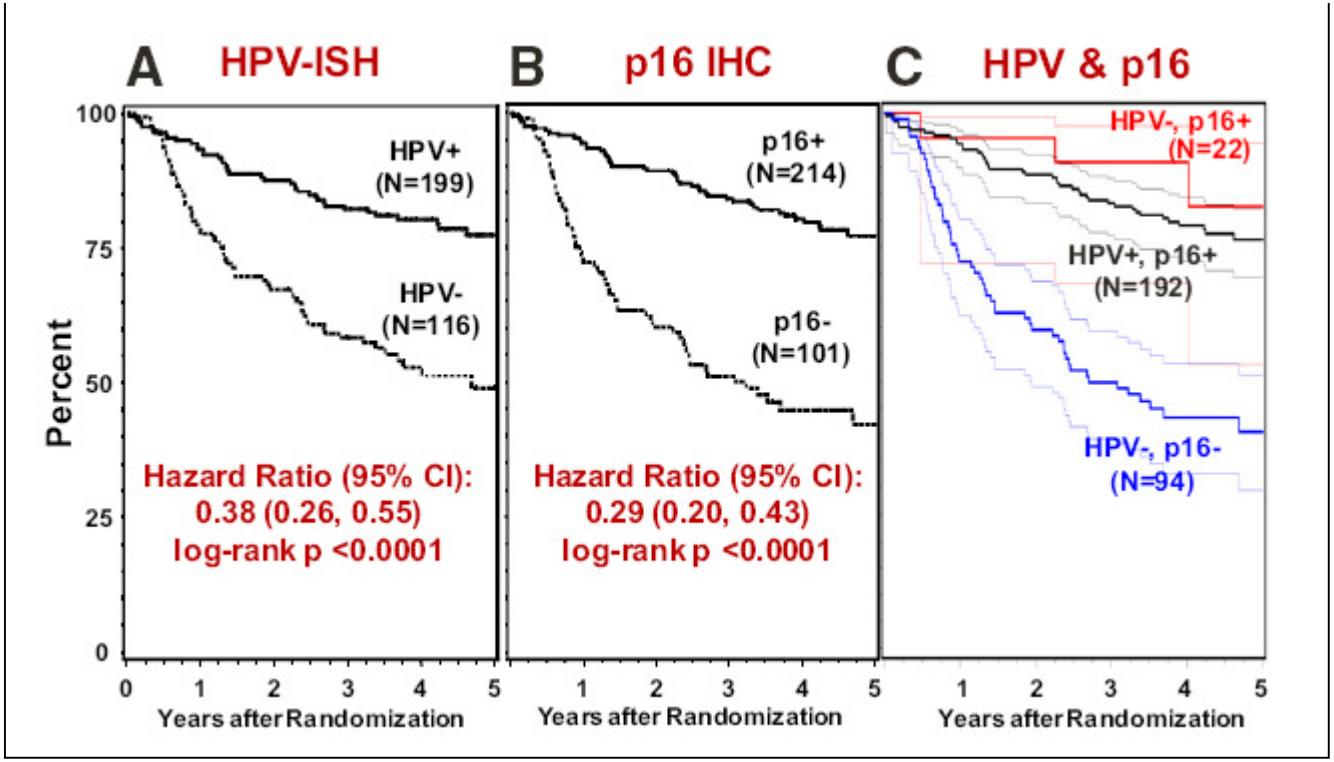
ELSEVIER

Seminars in
RADIATION
ONCOLOGY

Human Papillomavirus as a Marker of the Natural History and Response to Therapy of Head and Neck Squamous Cell Carcinoma

Kie Kian Ang, MD, PhD,* and Erich M. Sturgis, MD†,‡

2012



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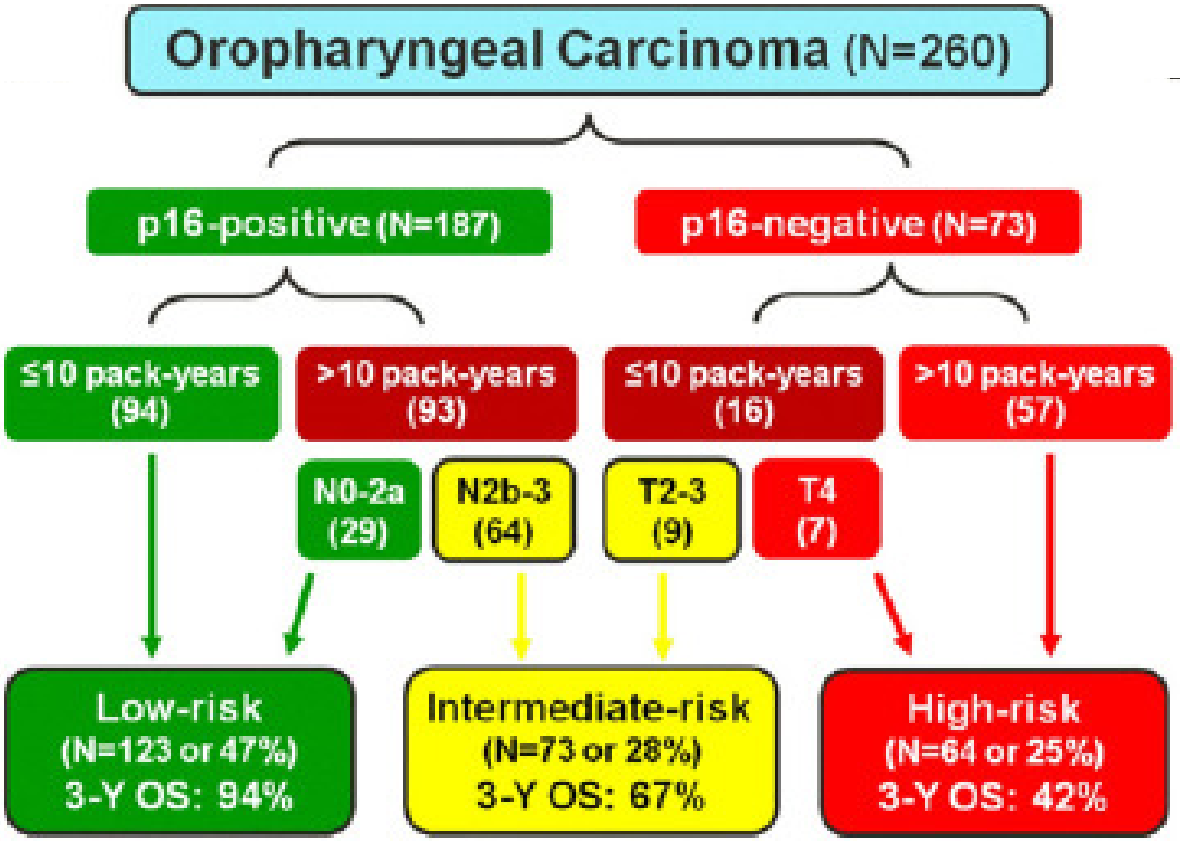


Clinical results of chemo-radiation in locally advanced head and neck cancer

Inclusion of the randomised trials performed between 1994 and 2000

Radiotherapy and Oncology 92 (2009) 4–14

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

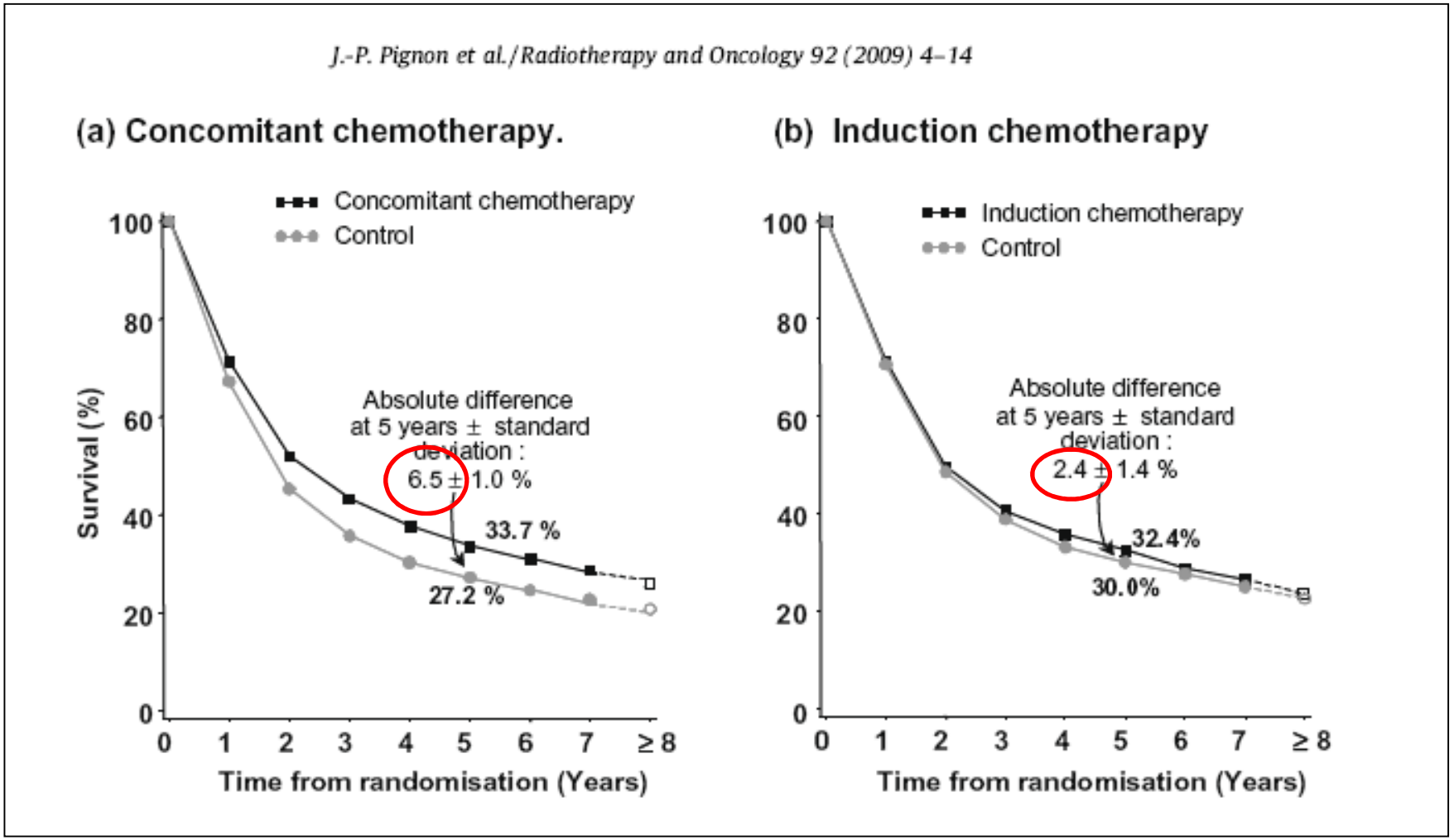
Meta analysis

Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 93 randomised trials and 17,346 patients

Jean-Pierre Pignon [a,*], Aurélie le Maître [a], Emilie Maillard [a], Jean Bourhis [b], on behalf of the MACH-NC Collaborative Group [1]

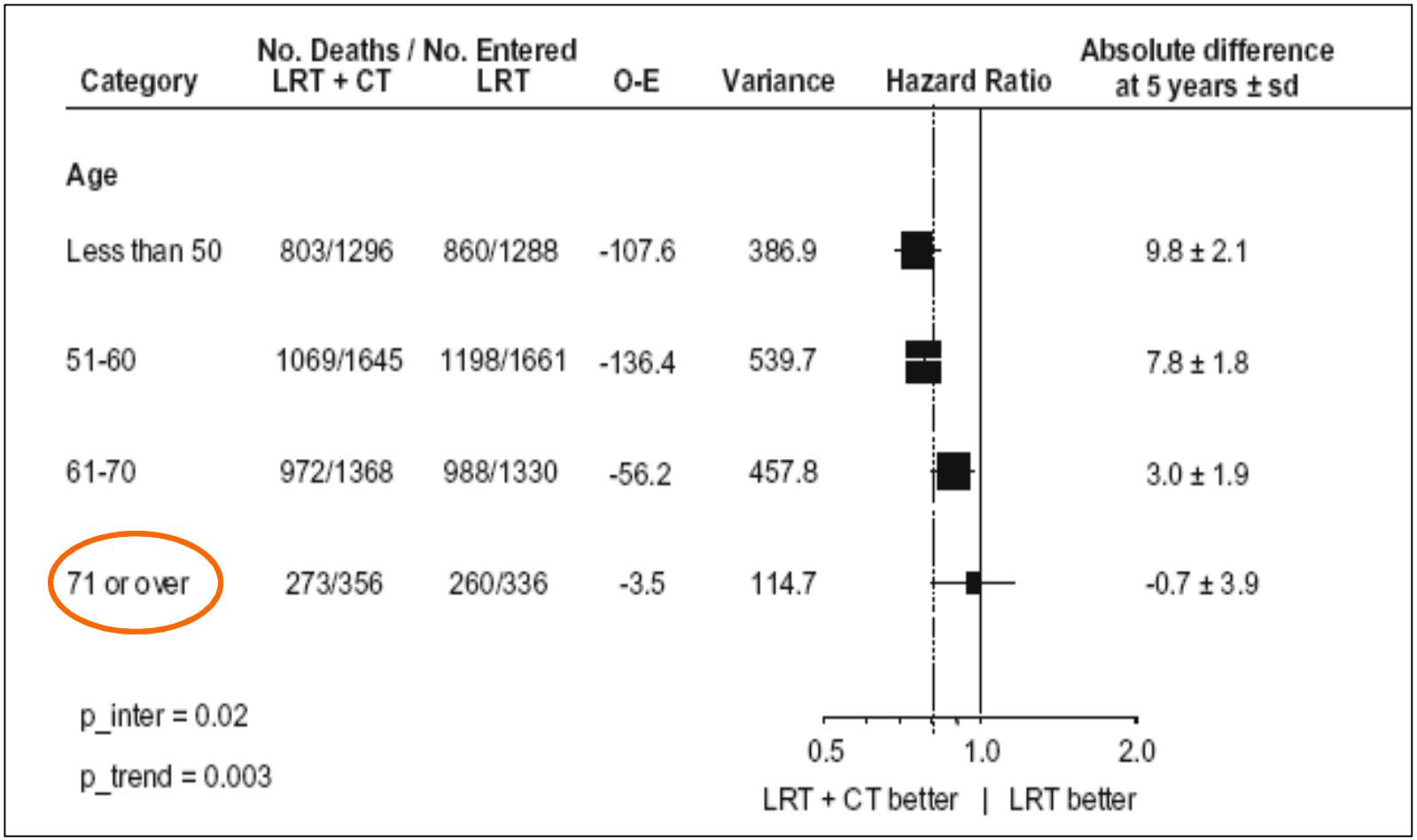
[a] *Department of Biostatistics and Epidemiology, Institut Gustave-Roussy, Villejuif, France*
[b] *Department of Radiotherapy, Institut Gustave-Roussy, Villejuif, France*

Platinum based chemotherapy



Pignon JP et al, 2009

Hazard ratio of death by age



Pignon JP et al, 2009

Altered fractionation RT and chemotherapy

RTOG 0129 phase III trial:accelerated (AFX) vs standard RT (SFX) in combination with cisplatin 100 mg/mq for 2-3 cycles

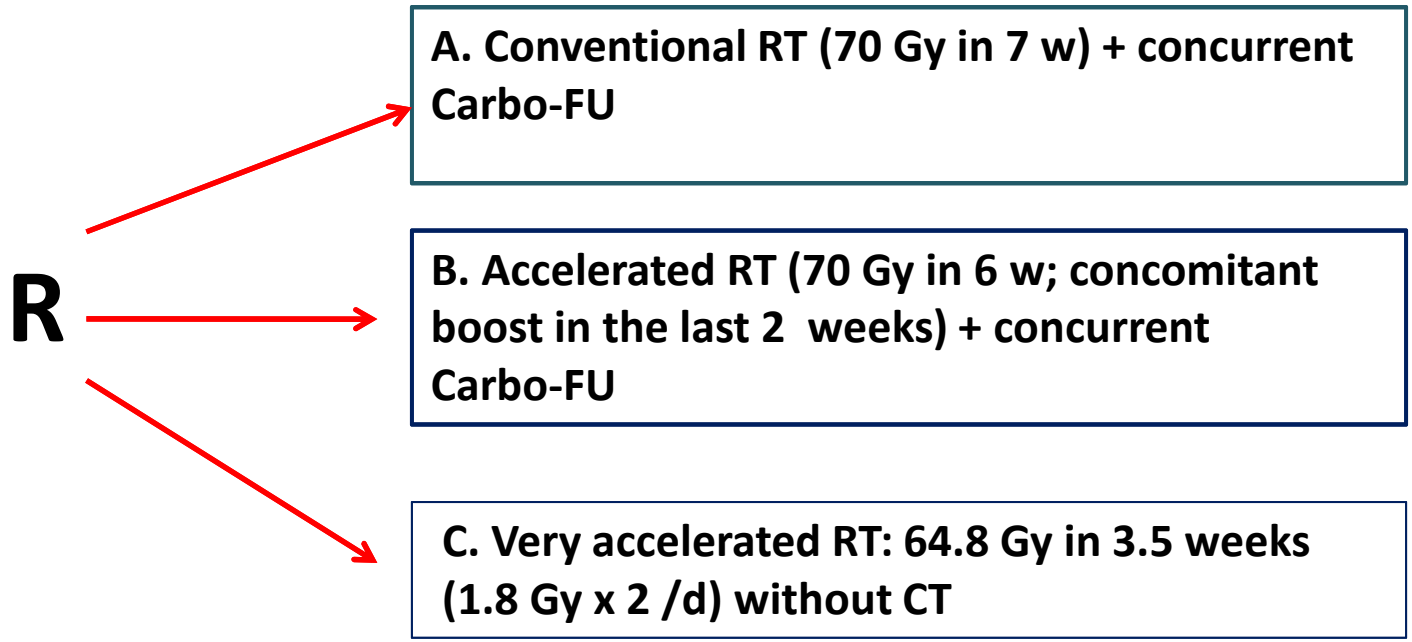
Ang K et al, ASCO, 2010

Prescribed radiation (RT) were 72 Gy/42 F/6 W and 70 Gy/35 F/7 W for AFX-C and SFX, and cisplatin doses were 100 mg/m2 q3W for 2 and 3 cycles, respectively

	AFX	SFX	Sign
OS	59%	56%	0.18
DFS	45%	44%	0.42
LRF	31%	28%	0.76
DM	18%	22%	0,06
G3-4 acute mucositis	33%	40%	
Worst G3-4 late toxicity	26%	21%	
Feeding tube pretreatment	22%	25%	
Feeding tube at therapy end	67%	69%	
Feeding tube at 1 year	28%	29%	

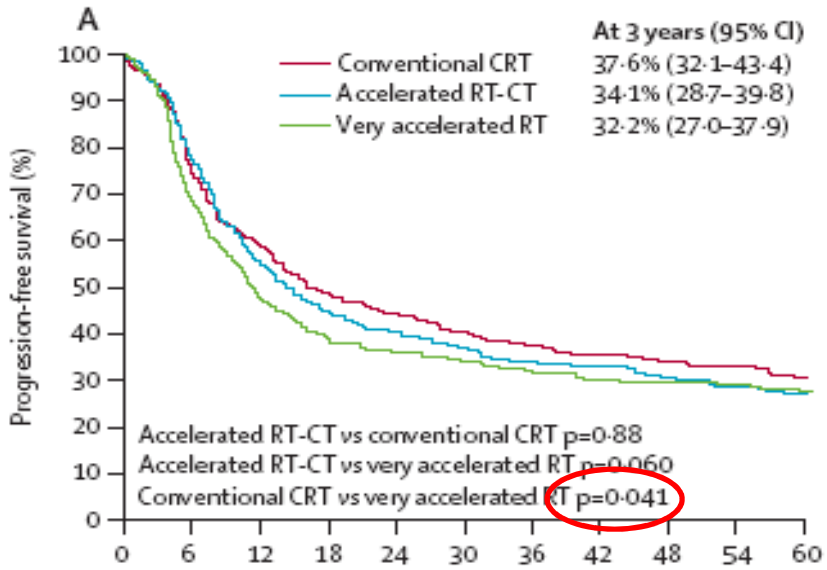
Concomitant chemoradiotherapy versus acceleration of radiotherapy with or without concomitant chemotherapy in locally advanced head and neck carcinoma (GORTEC 99-02): an open-label phase 3 randomised trial

Jean Bourhis, Christian Sire, Pierre Graff, Vincent Grégoire, Philippe Maingon, Gilles Calais, Bernard Gery, Laurent Martin, Marc Alfonsi, Patrick Desprez, Thierry Pignon, Etienne Bardet, Michel Rives, Lionel Geoffrois, Nicolas Daly-Schveitzer, Sok Sen, Claude Tuchais, Olivier Dupuis, Stéphane Guerif, Michel Lapeyre, Véronique Favrel, Marc Hamoir, Antoine Lusinchi, Stéphane Temam, Antonella Pinna, Yun Gan Tao, Pierre Blanchard, Anne Aupérin



Lancet Oncol 2012; 13: 145–53

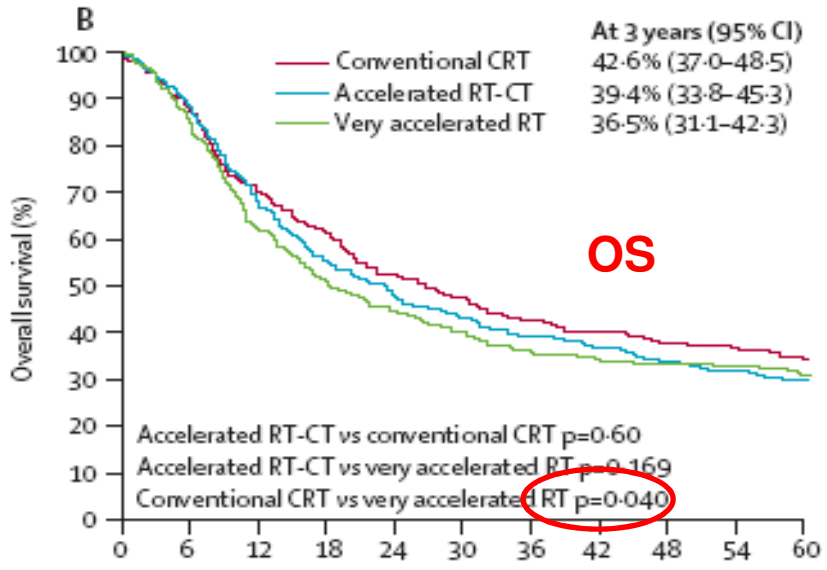
PFS



Number at risk

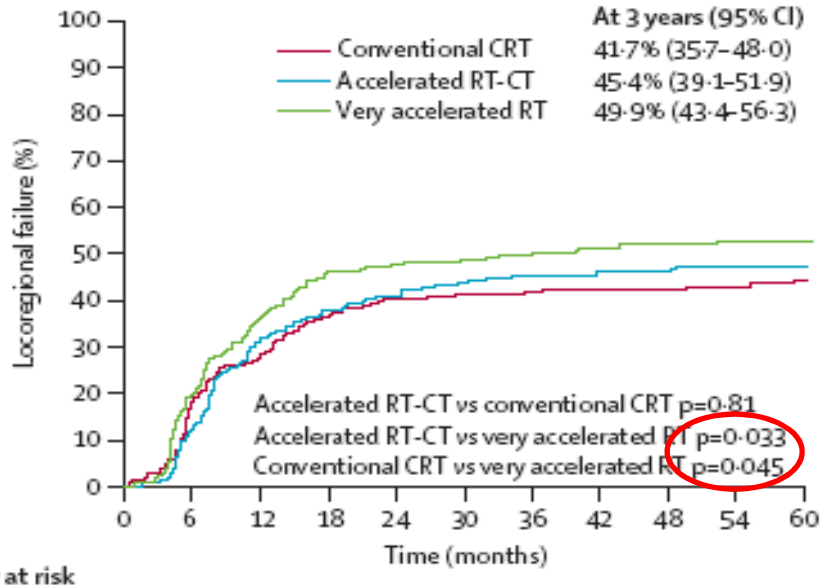
Conventional CRT	279	208	165	136	124	113	104	92	81	77	59
Accelerated RT-CT	280	215	155	124	112	103	93	84	77	69	52
Very accelerated RT-CT	281	195	133	109	101	96	90	83	75	68	58

OS



	279	244	196	171	146	133	118	104	90	86	66
	280	245	189	153	131	120	108	94	83	75	55
	281	239	174	143	124	112	102	94	84	75	64

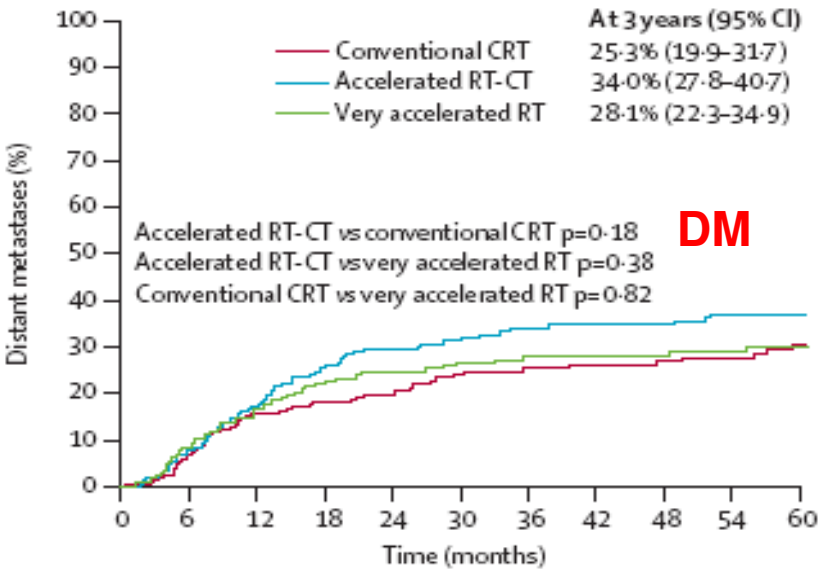
LRF



Number at risk

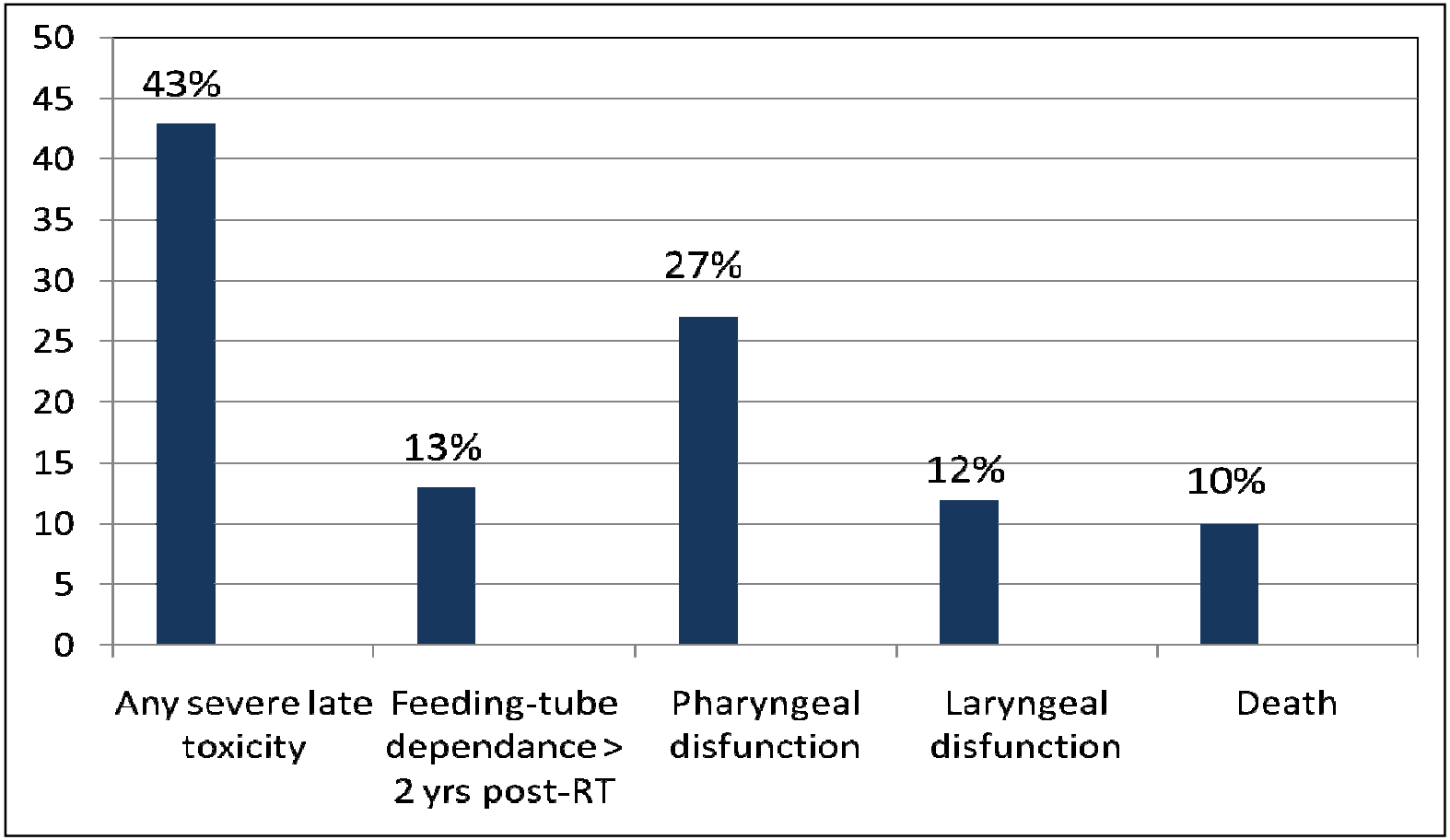
Conventional CRT	278	212	174	142	127	118	108	95	83	79	61
Accelerated RT-CT	279	222	162	131	120	109	98	87	79	72	53
Very accelerated RT-CT	280	205	140	112	103	99	93	85	76	69	59

DM



	277	229	181	159	137	123	111	98	87	83	63
	279	229	172	142	121	113	100	88	81	72	54
	280	223	159	131	115	107	98	92	83	74	63

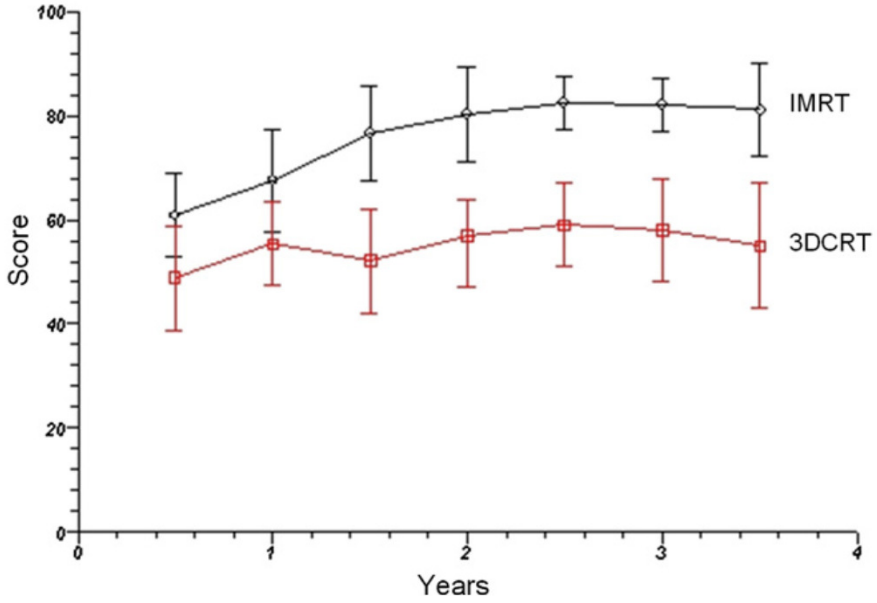
Analysis of 230 patients receving CRT in 3 studies (RTOG 91-11, 97-03,99-14)



Macthay M et al, 2008

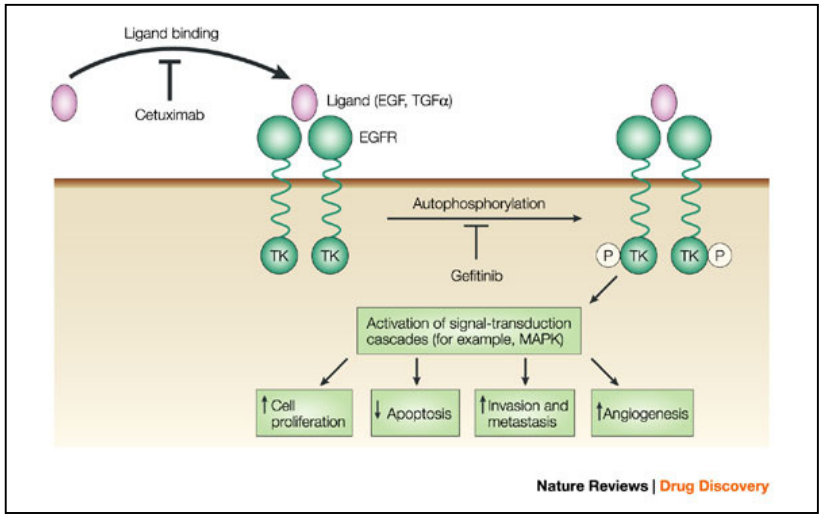
Intensity-Modulated Radiotherapy is Associated With Improved Global Quality of Life Among Long-term Survivors of Head-and-Neck Cancer

Allen M. Chen, M.D.,* D. Gregory Farwell, M.D.,† Quang Luu, M.D.,†
Esther G. Vazquez, R.N.,* Derick H. Lau, M.D., Ph.D.,‡ and James A. Purdy, Ph.D.*



IJROBP, 2012

Targeted therapy and radiotherapy



EGFR (epidermal growth factor receptor) is overexpressed in 90-100% of the HNSCC cases and is considered an unfavourable prognostic marker. EGFR costitutive activation is linked with HNSCC pathogenesis.

Cetuximab is a monoclonal anti-EGFR antibody blocking the activation of the receptor and signal transduction.

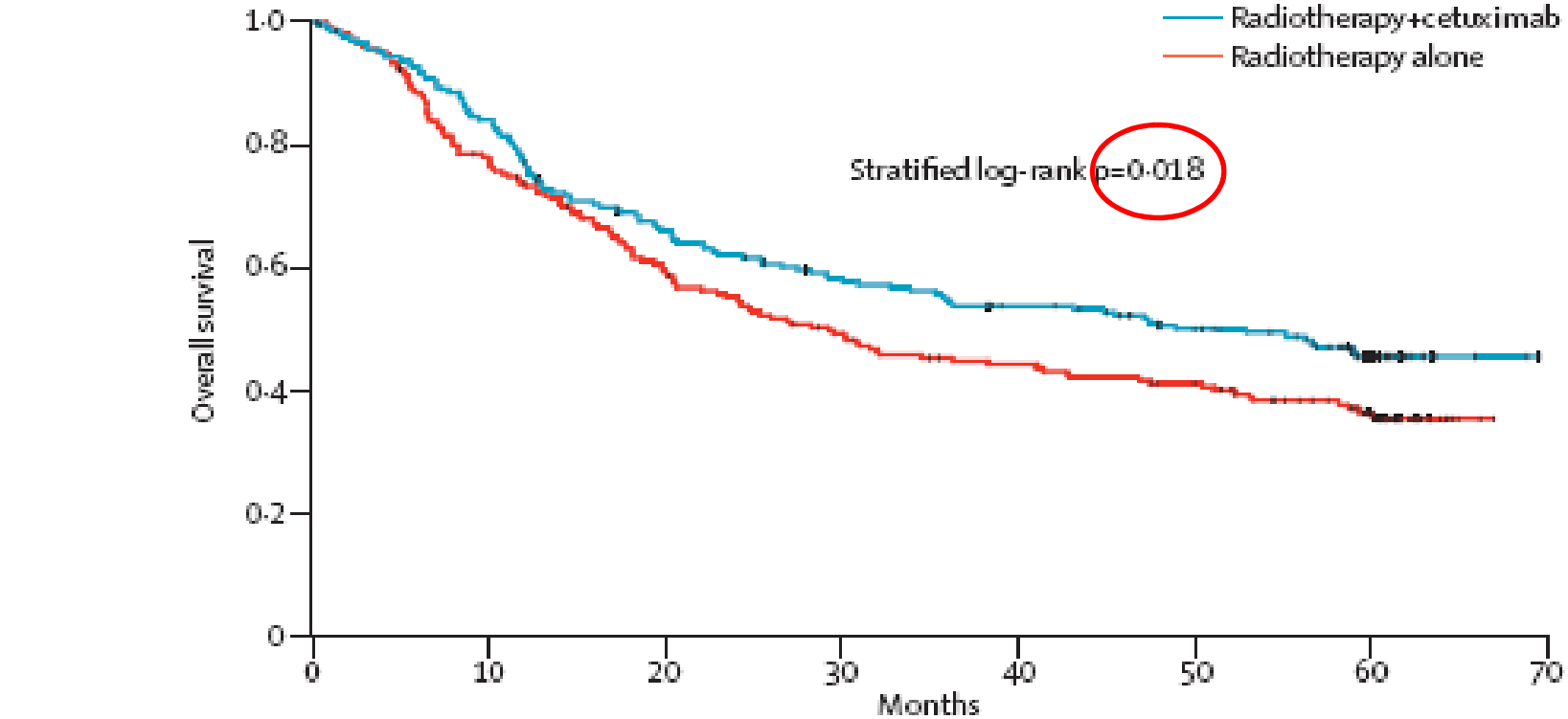


Figure 2: Overall survival by treatment: 5-year update (median follow-up 60 months)

Bonner JA et al, 2010

Table 4. Adverse Events.*

Adverse Event	Radiotherapy Alone (N=212)		Radiotherapy plus Cetuximab (N=208)		P Value†	
	All Grades	Grades 3–5	All Grades	Grades 3–5	All Grades	Grades 3–5
	percent of patients					
Mucositis	94	52	93	56	0.84	0.44
Acneiform rash	10	1	87	17	<0.001	<0.001
Radiation dermatitis	90	18	86	23	0.24	0.27
Weight loss	72	7	84	11	0.005	0.12
Xerostomia	71	3	72	5	0.83	0.32
Dysphagia	63	30	65	26	0.68	0.45
Asthenia	49	5	56	4	0.17	0.64
Nausea	37	2	49	2	0.02	1.00
Constipation	30	5	35	5	0.35	1.00
Taste perversion	28	0	29	0	0.83	—
Vomiting	23	4	29	2	0.18	0.42
Pain	28	7	28	6	1.00	0.84
Anorexia	23	2	27	2	0.26	1.00
Fever	13	1	26	1	0.001	1.00
Pharyngitis	19	4	26	3	0.10	0.80
Dehydration	19	8	25	6	0.16	0.57
Oral candidiasis	22	0	20	0	0.63	—
Coughing	19	0	20	<1	1.00	0.50
Voice alteration	22	0	19	2	0.47	0.06
Diarrhea	13	1	19	2	0.11	0.50
Headache	8	<1	19	<1	0.001	1.00
Pruritus	4	0	16	0	<0.001	—
Infusion reaction	2	0	15	3	<0.001	0.01
Insomnia	14	0	15	0	0.89	—
Dyspepsia	9	1	14	0	0.13	0.50
Increased sputum	15	1	13	<1	0.78	0.62
Infection	9	1	13	1	0.28	1.00
Anxiety	9	1	11	<1	0.75	1.00
Chills	5	0	11	0	0.03	—
Anemia	13	6	3	1	<0.001	0.006

RT+cisplatin *vs* RT+cetuximab

Until now no one phase III trial was published

Retrospective analysis showed inconsistent results

Cetuximab Plus Radiotherapy Versus Cisplatin Plus Radiotherapy in Locally Advanced Head and Neck Cancer (CTXMAB+RT)

ClinicalTrials.gov Identifier:
NCT01216020

Phase 2

R

Arm A: Radical radiotherapy (doses and volumes) concomitant with chemotherapy with Cisplatin (40 mg/mq/week)

Arm B: Radical radiotherapy (doses and volumes) concomitant with therapy with the monoclonal antibody Cetuximab (400 mg/m2 ["loading dose"] and subsequently 250 mg /m2/week)

PRIMARY OBJECTIVES:
Evaluation and comparison of the compliance of the two treatments;
SECONDARY OBJECTIVES:
Evaluation and comparison of the grade and incidence of acute toxicity; Evaluation and comparison of local control; Evaluation and comparison of event free survival (both local control and distant metastases); Evaluation and comparison of cause specific and overall survival.

Cetuximab Plus Radiotherapy Versus Cisplatin Plus Radiotherapy in Locally Advanced Head and Neck Cancer (CTXMAB+RT)

Estimated Enrollment: 140
Study Start Date: October 2010
Estimated Study Completion Date: October 2016

Partecipating Centers

- **Brescia**
- **Siena**
- **Genova**
- **Firenze**
- **Arezzo**
- **Prato**
- **Pistoia**

Enrolled until now = 57 pts

September, 2013

RADIATION THERAPY ONCOLOGY GROUP

RTOG 1016

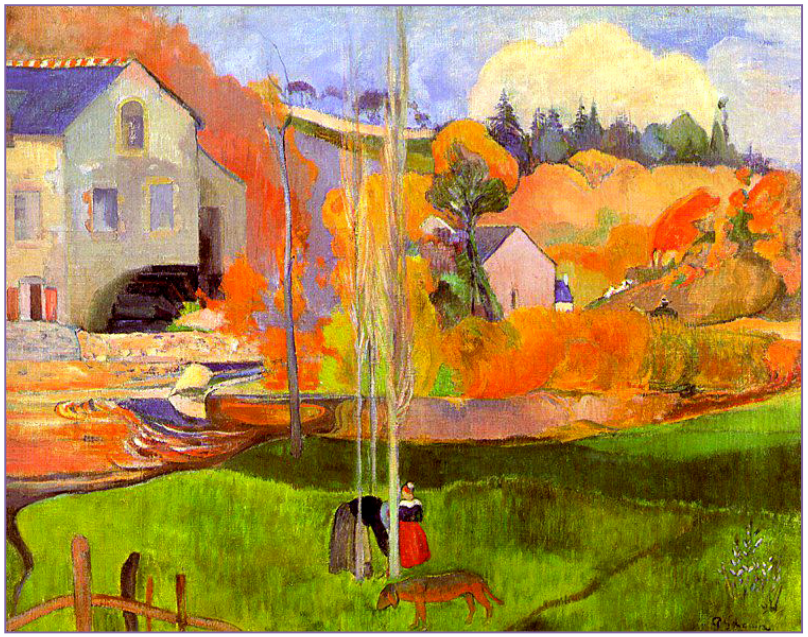
PHASE III TRIAL OF RADIOTHERAPY PLUS CETUXIMAB VERSUS CHEMORADIOTHERAPY IN HPV-ASSOCIATED OROPHARYNX CANCER

Study Team (6/28/12)

SCHEMA

			T Stage		
R		**S**	1. T1-2	**R**	
E		**T**	2. T3-4	**A**	**Arm 1 (Control)**:
G	**Mandatory p16**	**R**	**N Stage**	**N**	Accelerated IMRT, 70 Gy for 6 weeks
I	**analysis**	**A**	1. N0-2a	**D**	+ high dose DDP (100 mg/m^2) Days 1 and 22
S		**T**	2. N2b-3	**O**	(Total: 200 mg/m^2)
T		**I**	**Zubrod**	**M**	
E		**F**	**Performance Status**	**I**	**Arm 2**: Accelerated IMRT, 70 Gy for 6 weeks
R		**Y**	1. 0	**Z**	+ 8 doses of cetuximab (400 mg/m^2) loading dose
			2. 1	**E**	pre-IMRT, 250 mg/m^2 weekly during IMRT,
			Smoking History		and for 1 week after IMRT)
			1. ≤ 10 pack-years		
			2. > 10 pack-years		

Induction chemotherapy (IC) with TPF followed by radiotherapy (+/- concomitant CT)



Docetaxel/Cisplatin/5-FU vs Cisplatin/5-FU Sequential Therapy in Advanced SCCHN: Randomized Phase III trials

TRIAL	INCLUSION CRITERIA	N° CYCLES OF ICT	RADIOTHERAPY
EORTC 24971/TAX 323*	Unresectable stage III-IV	4	RT alone (CFRT or AFRT)
TAX 324**	Resectable or unresectable stage III-IV	3	CFRT + Carboplatin AUC 1.5 weekly

** Vermorken JB et al, 2007; ** Posner MR et al, 2007 ,*

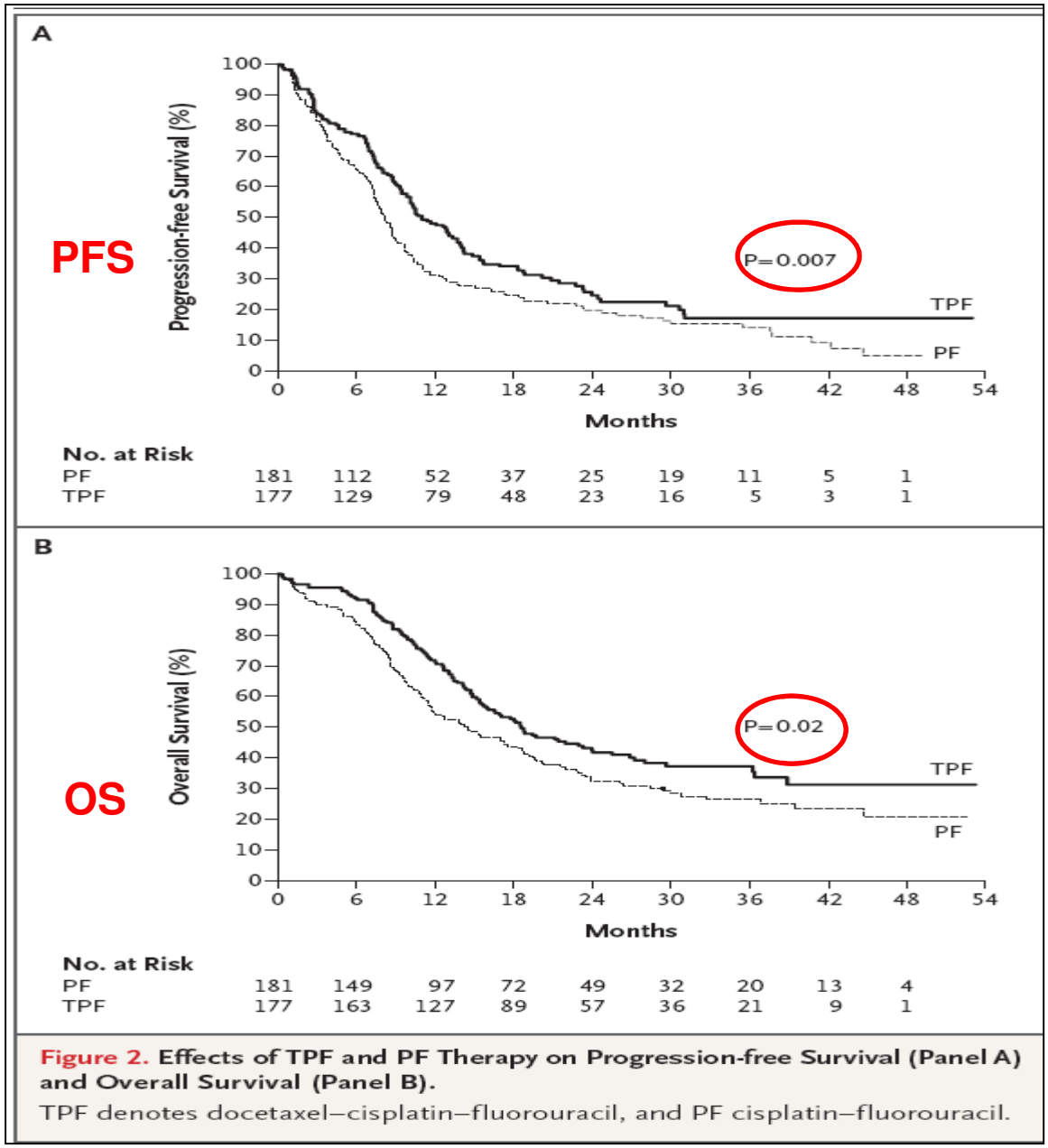
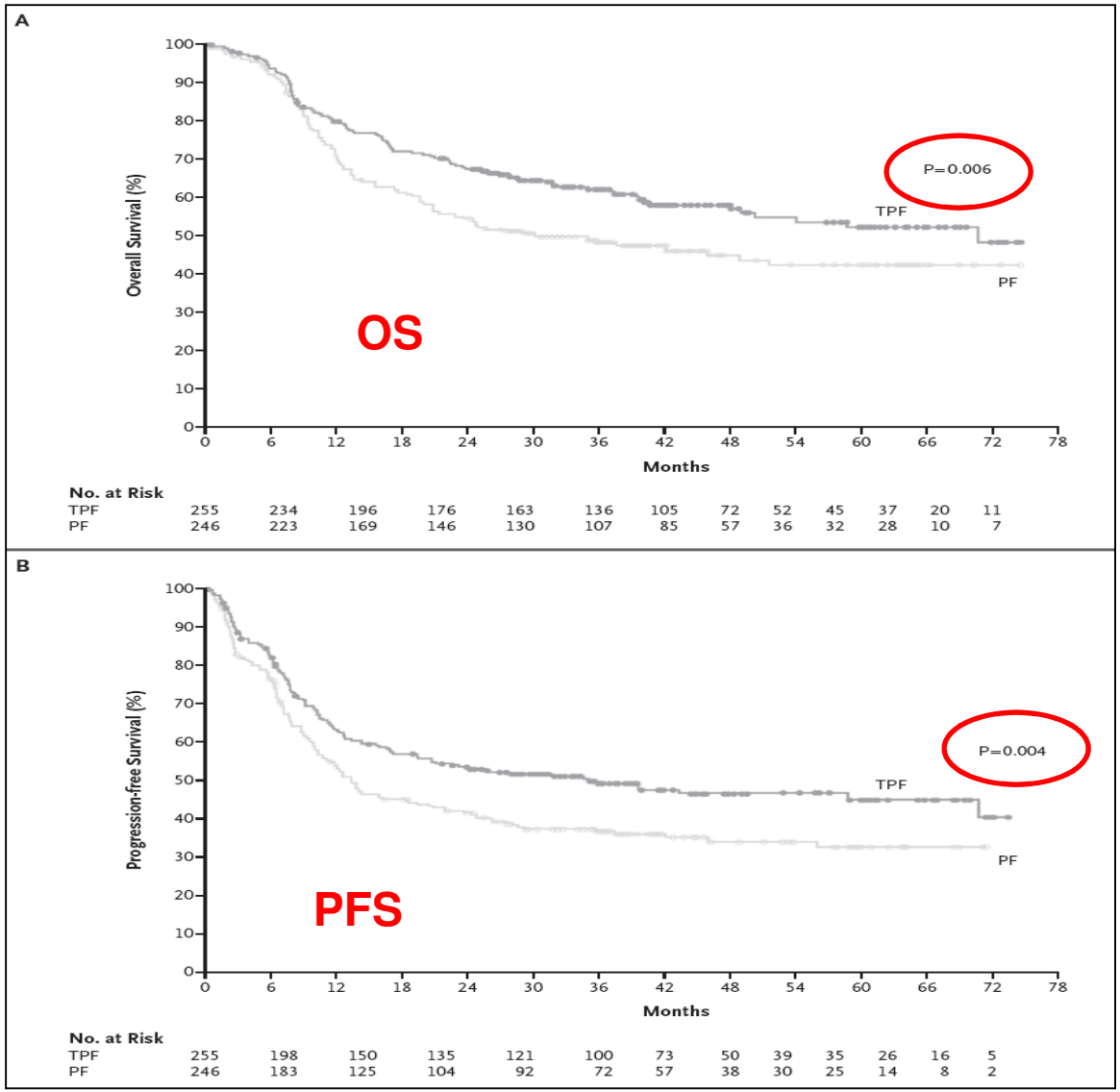


Figure 2. Effects of TPF and PF Therapy on Progression-free Survival (Panel A) and Overall Survival (Panel B).

TPF denotes docetaxel–cisplatin–fluorouracil, and PF cisplatin–fluorouracil.

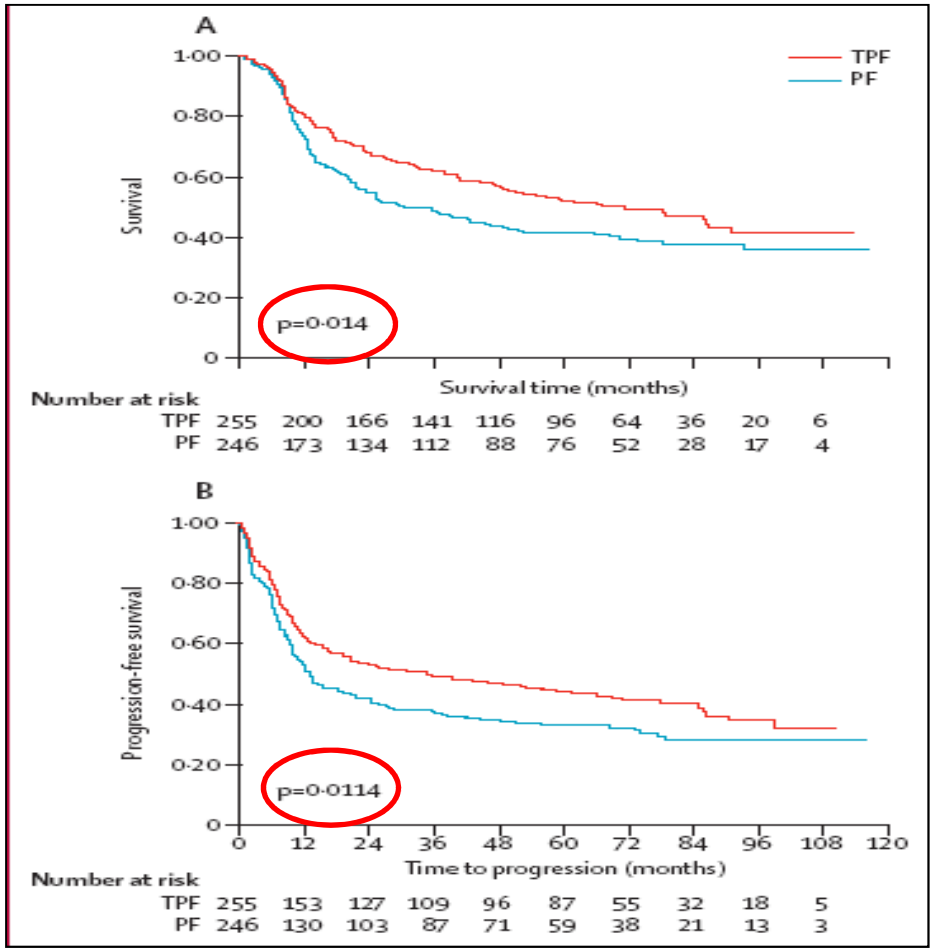
Vermorken JB et al, NEJM, 2007
ASCO 2011



Posner MR et al., NEJM, 2007

Induction chemotherapy with cisplatin and fluorouracil alone or in combination with docetaxel in locally advanced squamous-cell cancer of the head and neck: long-term results of the TAX 324 randomised phase 3 trial

*Jochen H Lorch, Olga Goloubeva, Robert I Haddad, Kevin Cullen, Nicholas Sarlis, Roy Tishler, Ming Tan, John Fasciano, Daniel E Sammartino, Marshall R Posner, for the TAX 324 Study Group**



Ext OS at 5 y 52% *vs* 42%

Lancet Oncol 2011; 12: 153-59

Radiotherapy and Oncology 106 (2013) 112–117

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Functional imaging

Changes in functional imaging parameters following induction chemotherapy have important implications for individualised patient-based treatment regimens for advanced head and neck cancer

Ceri Powell [a], Maria Schmidt [a], Marco Borri [a], Dow-Mu Koh [a], Mike Partridge [a], Angela Riddell [a], Gary Cook [d], Shreerang A. Bhide [a,c], Christopher M. Nutting [b], Kevin J. Harrington [b,c], Katie L. Newbold [a,*]

[a] *The Royal Marsden NHS Trust, Surrey;* [b] *The Royal Marsden NHS Trust, London;* [c] *The Institute of Cancer Research, London; and* [d] *Guys and St Thomas' NHS Trust, London, United Kingdom*

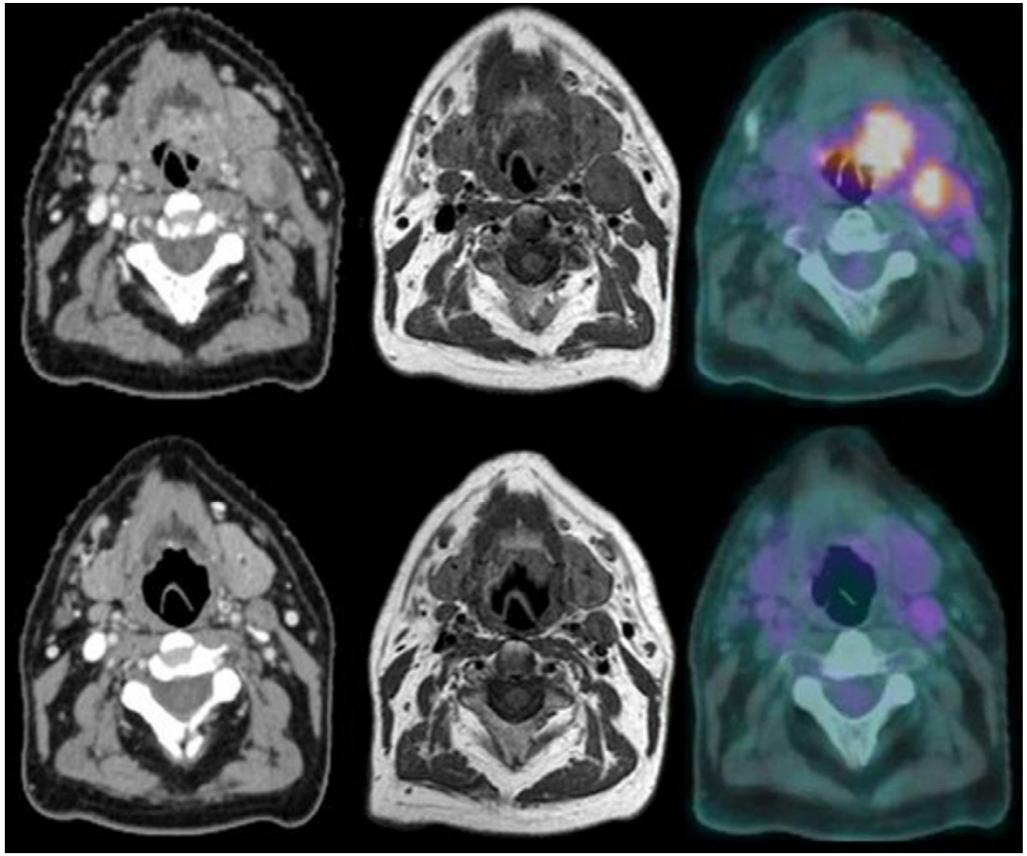


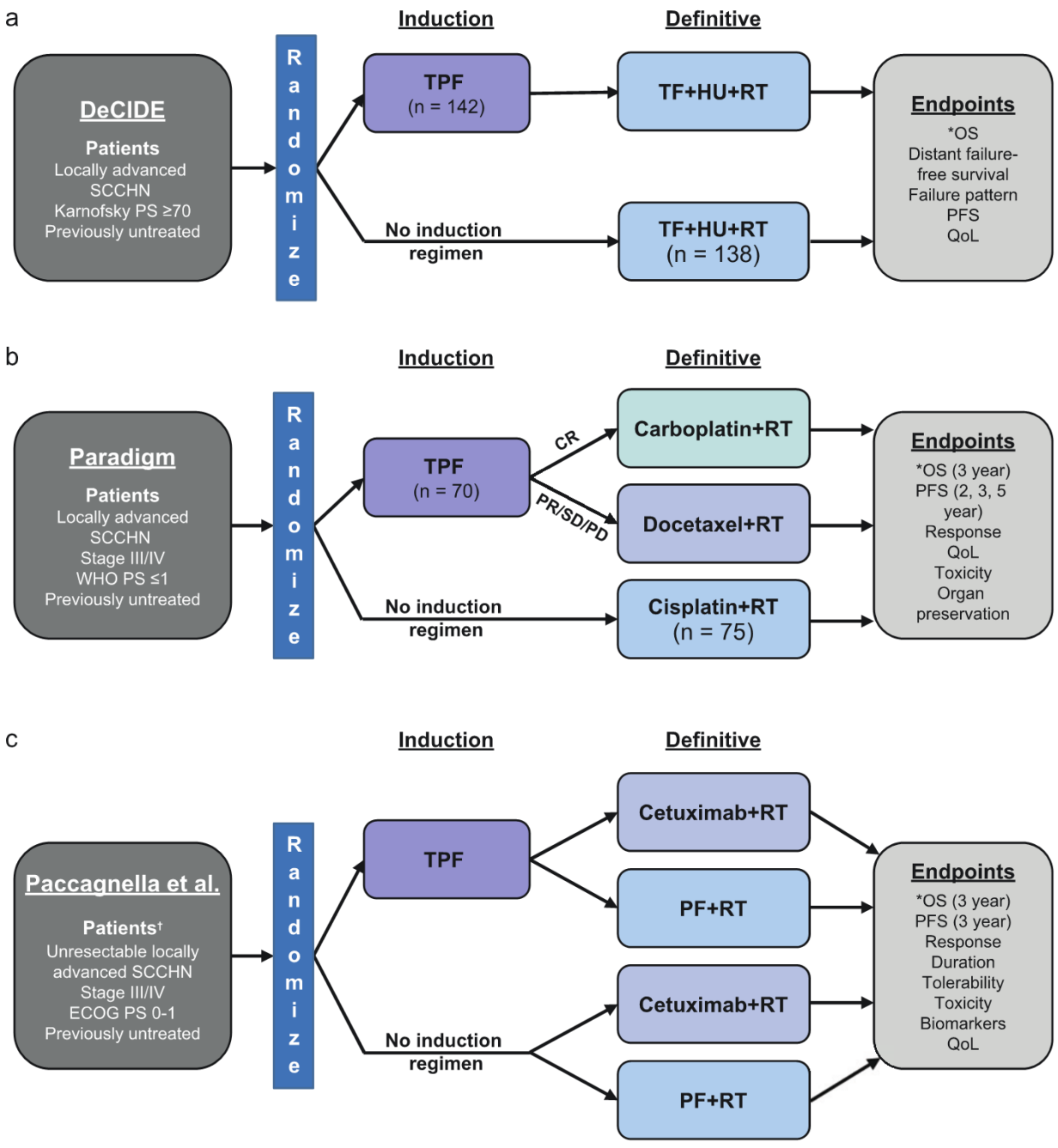
Table 1. Recommendations and guidelines for RT planning when using IC

1.	Evaluation by all managing physicians, especially radiation oncologist, before delivery of any IC is crucial for proper coordination of care and optimal RT planning.
2.	Nutritional evaluation before beginning therapy, as well as ongoing nutritional support during treatment and recovery, is essential. The use of feeding tube support should be individualized; no specific feeding tube policy was recommended by Panel.
3.	All dentulous patients should be evaluated by dentist before beginning cancer therapy to avoid delaying any component of therapy.
4.	High-quality preinduction RT planning contrast-enhanced CT scan of head and neck should be obtained to generate reference anatomy for postinduction RT planning.
5.	Although PET/CT in RT planning is being rapidly adopted, its precise role in target delineation is still in development; no clear guidance on PET/CT in RT planning can be given at this time.
6.	RT should begin within 3–4 weeks from last dose of IC.
7.	If patient underwent RT simulation before IC, in most cases, a new immobilization device should be created that approximates the anatomic position of pre-IC device as closely as possible.
8.	Preinduction primary site and nodal GTVs should be used for RT planning. Post-IC targets should correspond as closely as possible to originally diseased tissue in all dimensions. All structures involved by tumor before IC should be included, even if not grossly involved after IC.
9.	Fusion of preinduction CT simulation image with postinduction CT simulation image could be helpful.
10.	Radiation doses should not be modified according to response to IC, even if complete response achieved.

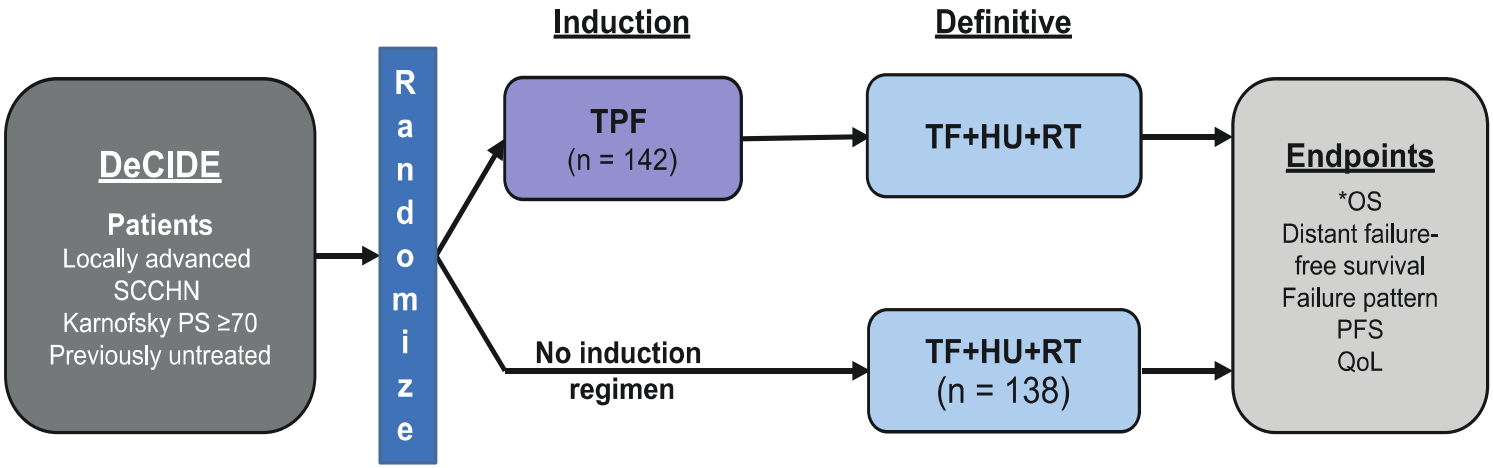
Abbreviations: RT = radiotherapy; IC = induction chemotherapy; PET = positron emission tomography; CT = computed tomography; GTV = gross tumor volume.

Salama JK et al, 2009

IC with TPF followed by RT/CRT *vs* RT/CRT only

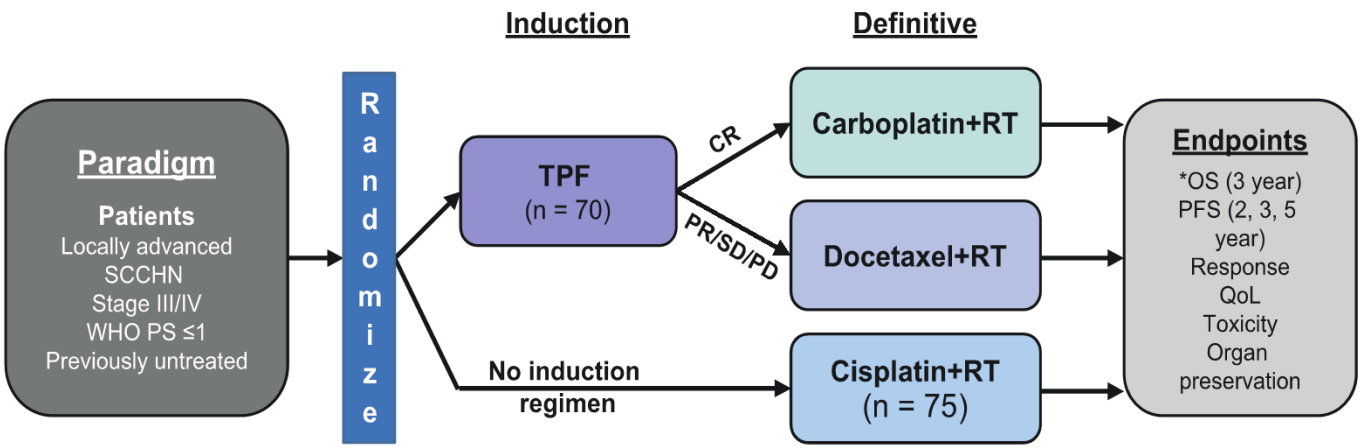


Argiris, 2013


Induction
Definitive
DeCIDE
Patients
Locally advanced
SCCHN
Karnofsky PS ≥70
Previously untreated
Randomize
TPF
(n = 142)
TF+HU+RT
No induction
regimen
TF+HU+RT
(n = 138)
Endpoints
*OS
Distant failure-
free survival
Failure pattern
PFS
QoL

Endpoint	IC arm (%)	CRT arm (%)	P value
OS	75	73	0.7
DFS	69	64	0.39
RFS	67	59	0.18
DF	10	19	0.025
LRF	9	12	0.55

Cohen EEW et al., ASCO 2012


Induction
Definitive
Paradigm
Patients
Locally advanced
SCCHN
Stage III/IV
WHO PS ≤1
Previously untreated
Randomize
TPF
(n = 70)
CR
PR/SD/PD
No induction regimen
Carboplatin+RT
Docetaxel+RT
Cisplatin+RT
(n = 75)
Endpoints
*OS (3 year)
PFS (2, 3, 5 year)
Response
QoL
Toxicity
Organ preservation

The PARADIGM trial: A phase III study comparing sequential therapy (ST) to concurrent chemoradiotherapy (CRT) in locally advanced head and neck cancer (LANHC).

Arm A (70 pts): IC (TPFx3) followed by CRT

Arm B (75pts): RT + Cisplatin x2

	A	B	P
3y OS	73%	78%	0.77
3y PFS	67%	73%	0.55

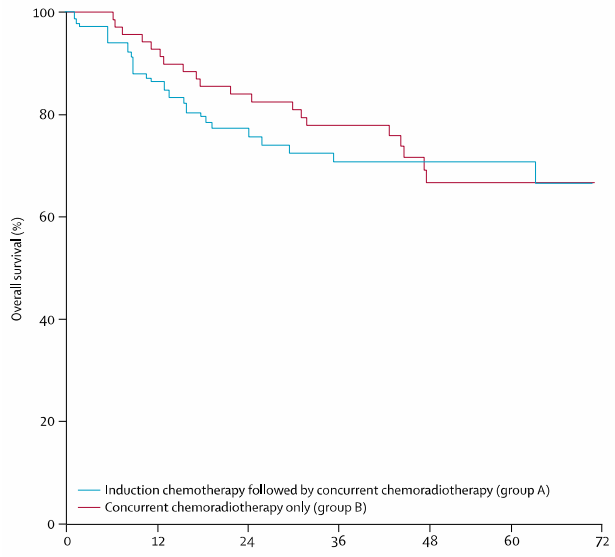
Similar toxicity profiles. Febrile neutropenia more frequent in arm A

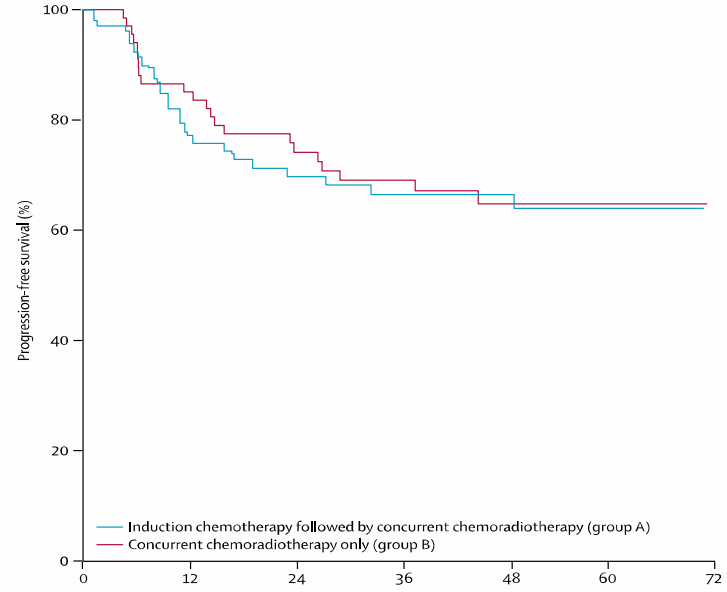
Haddad RI et al., ASCO 2012

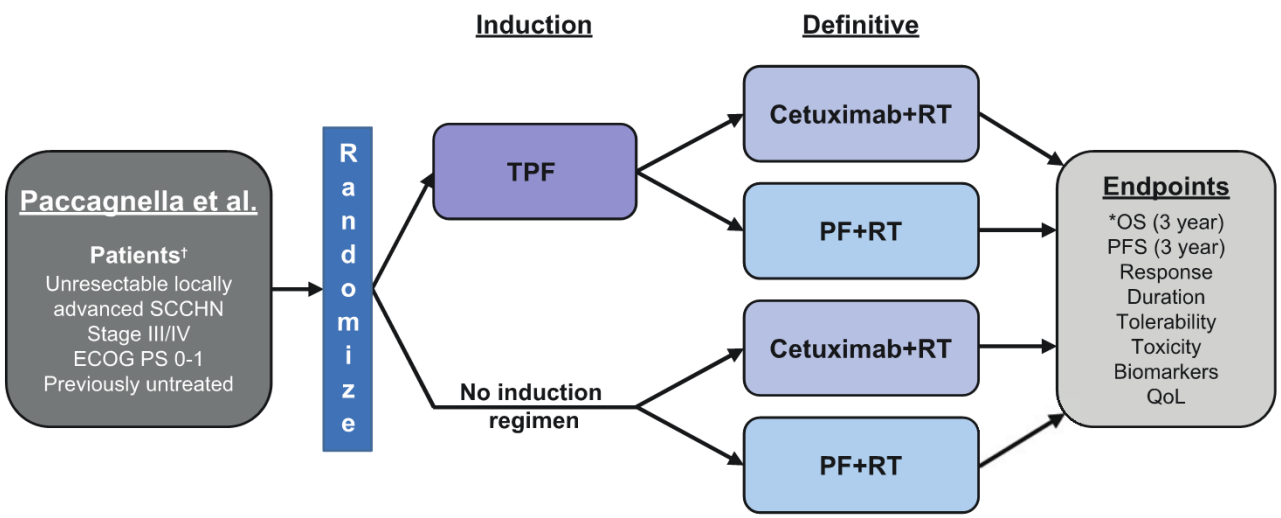
Induction chemotherapy followed by concurrent chemoradiotherapy (sequential chemoradiotherapy) versus concurrent chemoradiotherapy alone in locally advanced head and neck cancer (PARADIGM): a randomised phase 3 trial

Robert Haddad, Anne O'Neill, Guilherme Rabinowits, Roy Tishler, Fadlo Khuri, Douglas Adkins, Joseph Clark, Nicholas Sarlis, Jochen Lorch, Jonathan J Beitler, Sewanti Limaye, Sarah Riley, Marshall Posner

Lancet Oncol **2013; 14: 257–64**



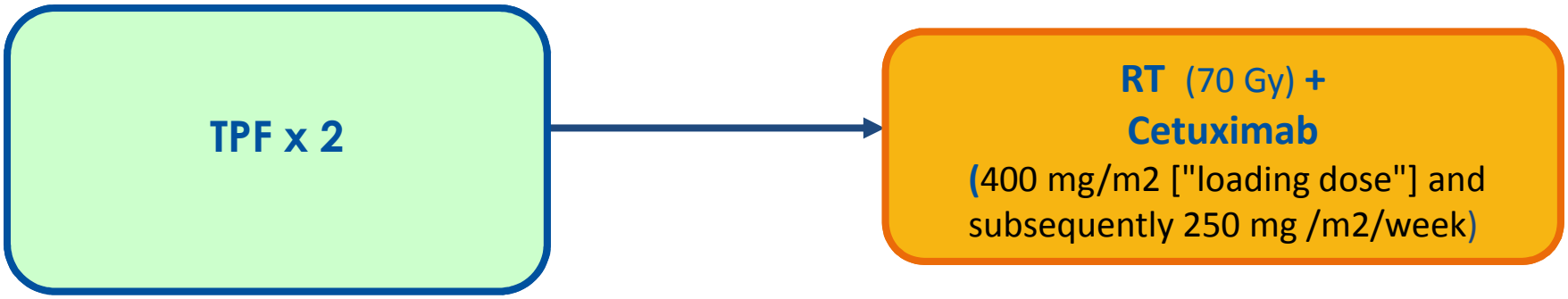



Induction
Definitive
Paccagnella et al.
Patients†
Unresectable locally advanced SCCHN
Stage III/IV
ECOG PS 0-1
Previously untreated
Randomize
TPF
No induction regimen
Cetuximab+RT
PF+RT
Cetuximab+RT
PF+RT
Endpoints
*OS (3 year)
PFS (3 year)
Response
Duration
Tolerability
Toxicity
Biomarkers
QoL

How do we integrate targeted therapies into chemoradiotherapy programs?

Efficacy and feasibility of induction chemotherapy and radiotherapy plus cetuximab in head and neck cancer.

Rampino M, Bacigalupo A, Russi E, Schena M, Lastrucci L, Iotti C, Reali A, Musu A, Balcet V, Piva C, Bustreo S, Munoz F, Ragona R, Corvò R, Ricardi U



Primary endpoint

- ORR at the end of treatment

RESULTS:

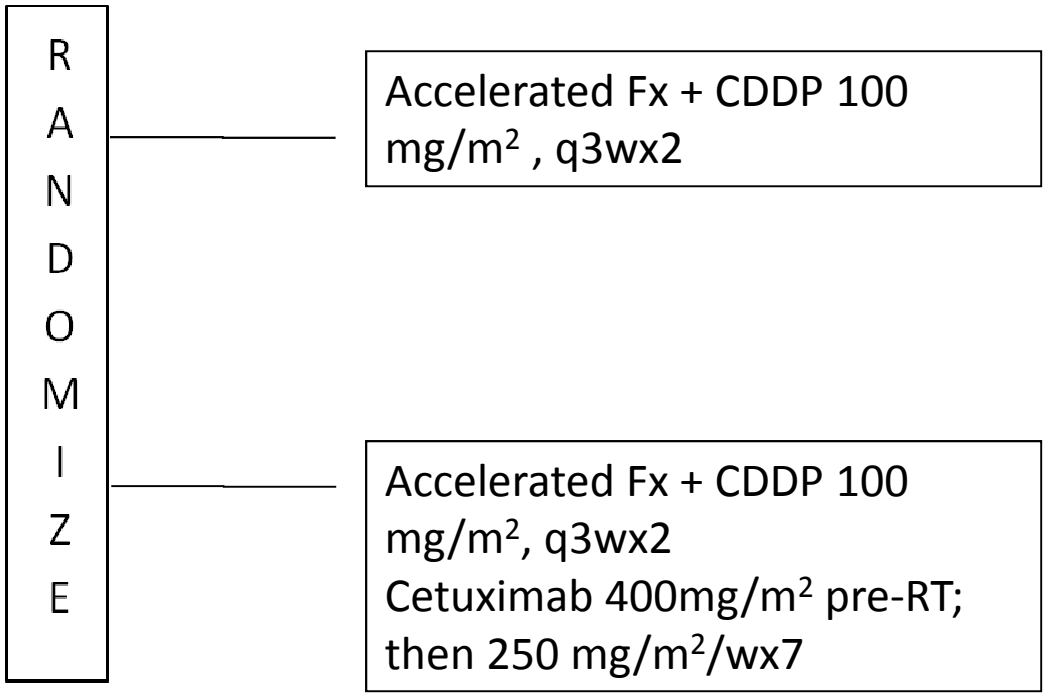
Eighty-one percent of patients had stage IV disease and 42% had hypopharyngeal and oral cavity primaries. The **overall response rate was 81.8%,** with **60.6% complete response** and 33.3% partial response. Severe toxicities were febrile neutropenia (6%) during induction chemotherapy and dermatitis (48%), mucositis (33%) and dysphagia (12%) during the concurrent phase.

Rampino et al, Anticancer Res 2012

RTOG phase III 0522 trial

Stage III-IV SCC of:
- Oropharynx
- Hypopharynx
- Larynx

Statify:
- Larynx vs others
- N0-N1, 2a,2b vs N2c-3
- 3-D vs IMRT
- Pre-Rx PET (yes vs no)



From 2005 to 2009 enrolled 940 patients.
Of 895 evaluable patients, 447 were randomized in arm A (Cetuximab), and 448 in arm B (Cisplatin)
Median follow up = 2.4 years

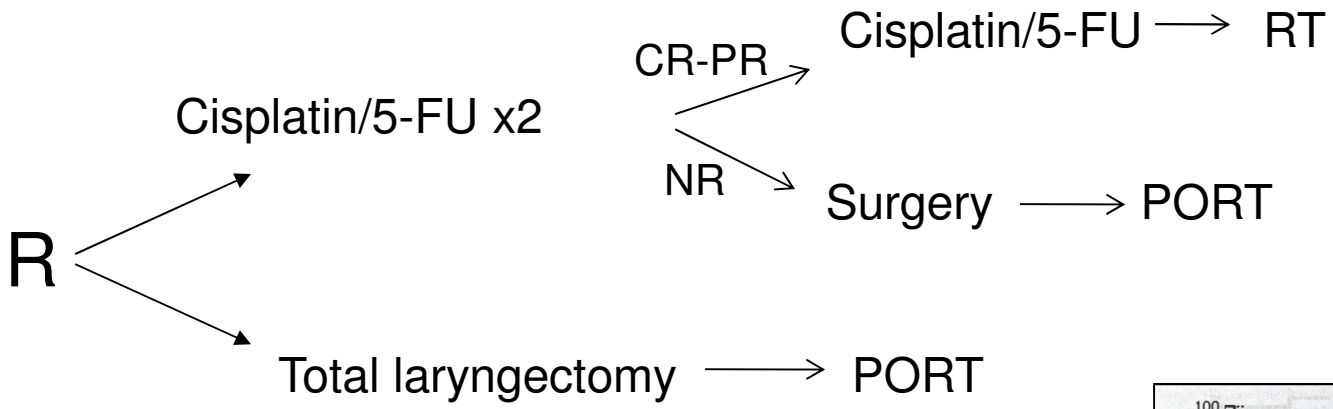
	A	B	Sign
PFS	63%	64%	P=0.66
OS	83%	80%	P=0.17
Death within 30 days	2%	1.8%	P=0.81
g.3-5 adverse effects	92%	90%	P=0.30
g.3-4 mucositis	45%	35%	P=0.003
g.3.4 skin reaction	40%	17%	P<0.0001
g.3-4 dysphagia	63%	66%	P=0.27

Ang K et al, 2011

Larynx preservation

VA Laryngeal Cancer Study Group (NEJM,1991)

- 132 patients with stage III-IV laryngeal cancer



Response to induction CT= 85% (31% CR)

Estimated 2-year larynx preservation rate = 66%

No significant difference in OS after 10 years

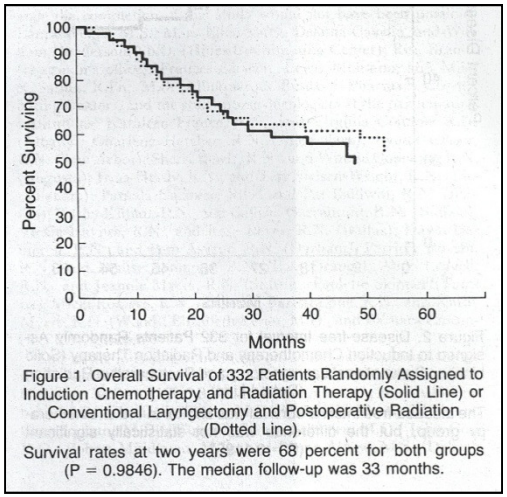
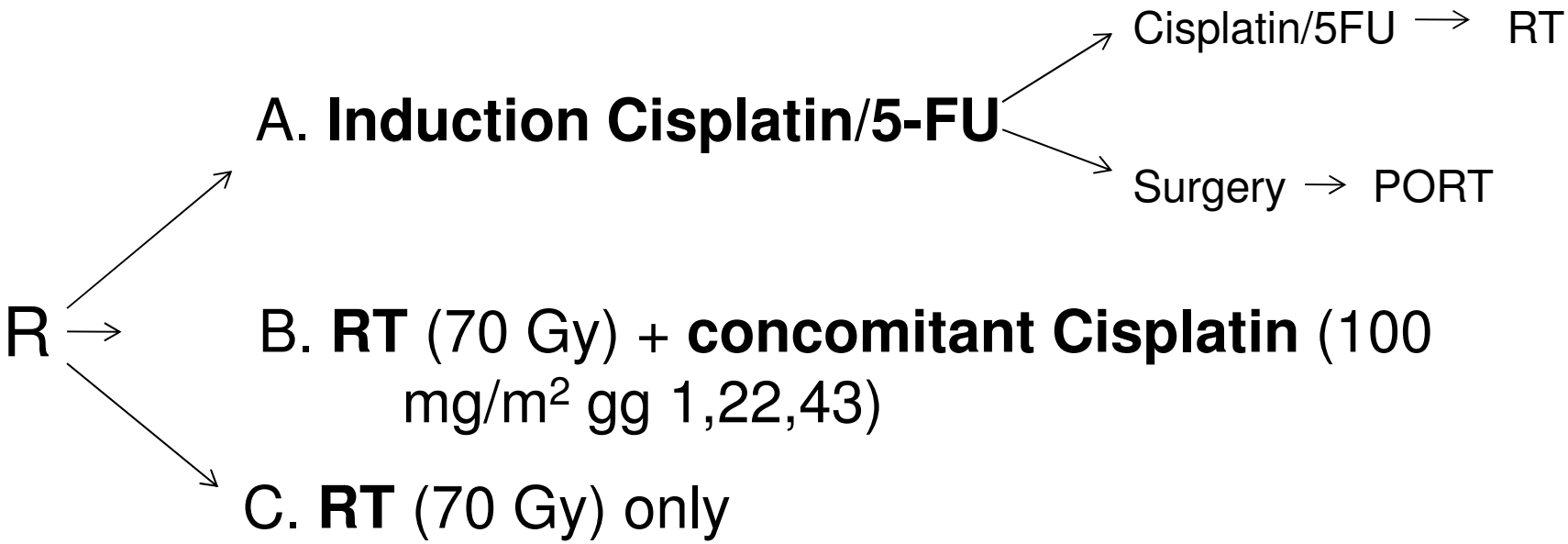


Figure 1. Overall Survival of 332 Patients Randomly Assigned to Induction Chemotherapy and Radiation Therapy (Solid Line) or Conventional Laryngectomy and Postoperative Radiation (Dotted Line).
Survival rates at two years were 68 percent for both groups (P = 0.9846). The median follow-up was 33 months.

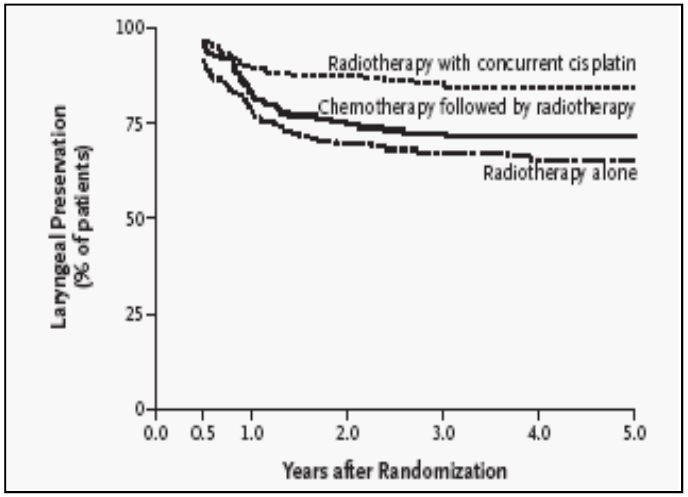
Significant more local failure but decreased distant failure in CT arm

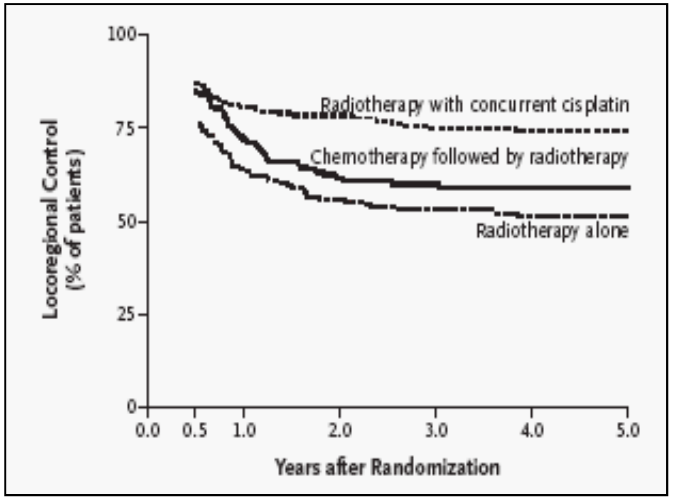
INT 91-11 trial to preserve the larynx
(Forastiere AA et al, NEJM, 2003)



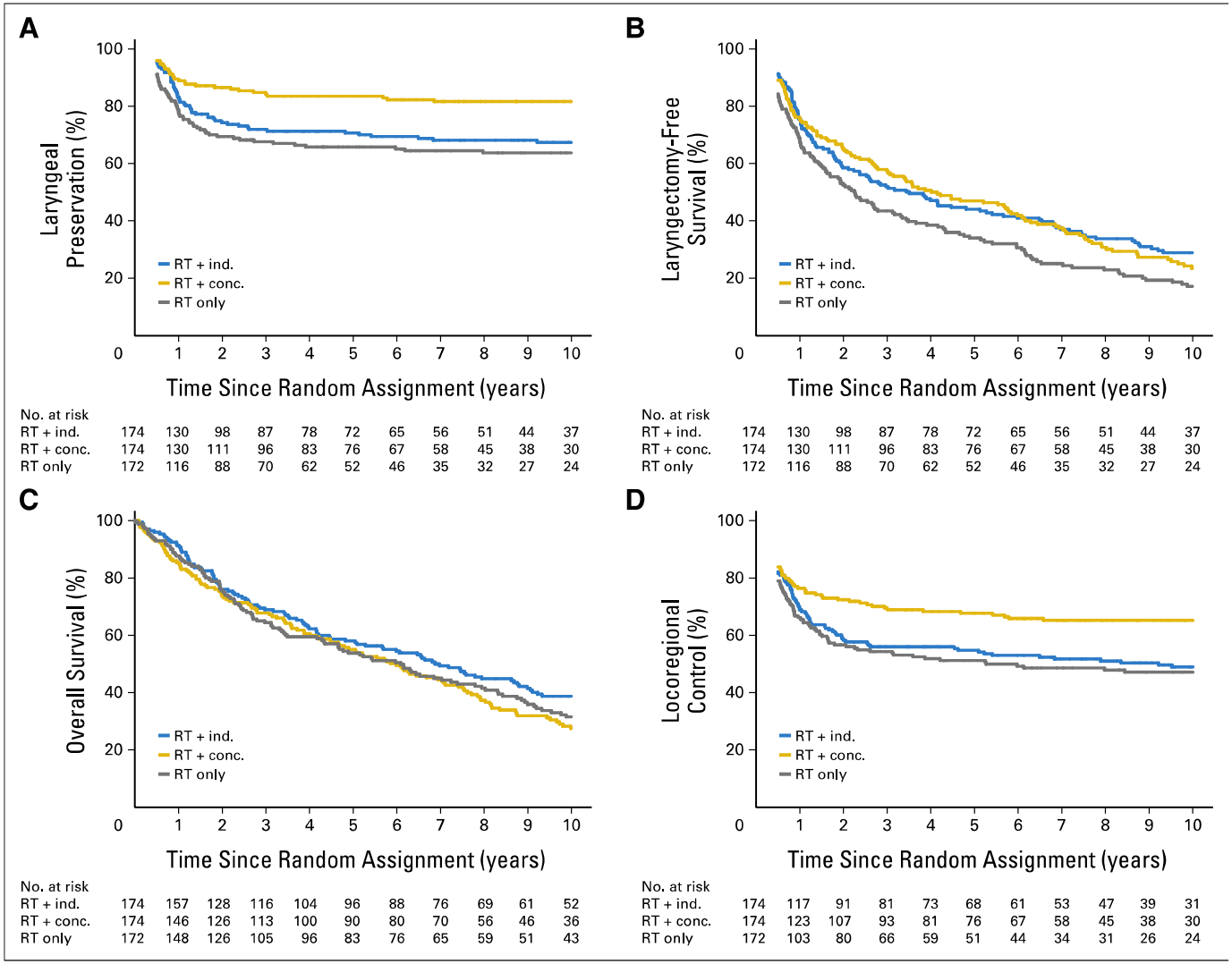
547 patients with locally advanced laryngeal cancer
T3 =78%, N0-1= 70%
Planned neck dissection for N2N3 stage

5 years	A (ind CT)	B (conc)	C (RT alone)
LPR	75%	88%	70%
LRC	61%	78%	56%
High Grade Tox	81%	82%	61%





Long term results of RTOG 91-11



Forastiere AA et al, 2013

Induction chemotherapy followed by either chemoradiotherapy or bioradiotherapy for larynx preservation: the TREMPLIN randomized phase II study.

Lefebvre JR et al, JCO, 2013

Stage III-IV larynx/hypopharynx SCC received 3 cycles of TPF

Poor responders (<50%) → salvage surgery

Responders (>=50%) → **R**

- Arm A : RT (70Gy) + conc. cisplatin 100 mg/mq 1,22,43
- Arm B: RT (70 Gy) + conc. Cetuximab 400 mg/mq loading dose and 250 mg/mq per week

Primary end point: larynx preservation (LP) at 3 months
Secondary end points: larynx function preservation (LFP) and overall survival (OS) at 18 months

1

Induction chemotherapy followed by either chemoradiotherapy or bioradiotherapy for larynx preservation: the TREMPLIN randomized phase II study.

	LP at 3 mo	LFP at 18 mo	OS at 18 mo
Arm A	95%	87%	92%
Arm B	93%	82%	89%

Treatment compliance was higher in arm B

Lefebvre JL et al, 2013

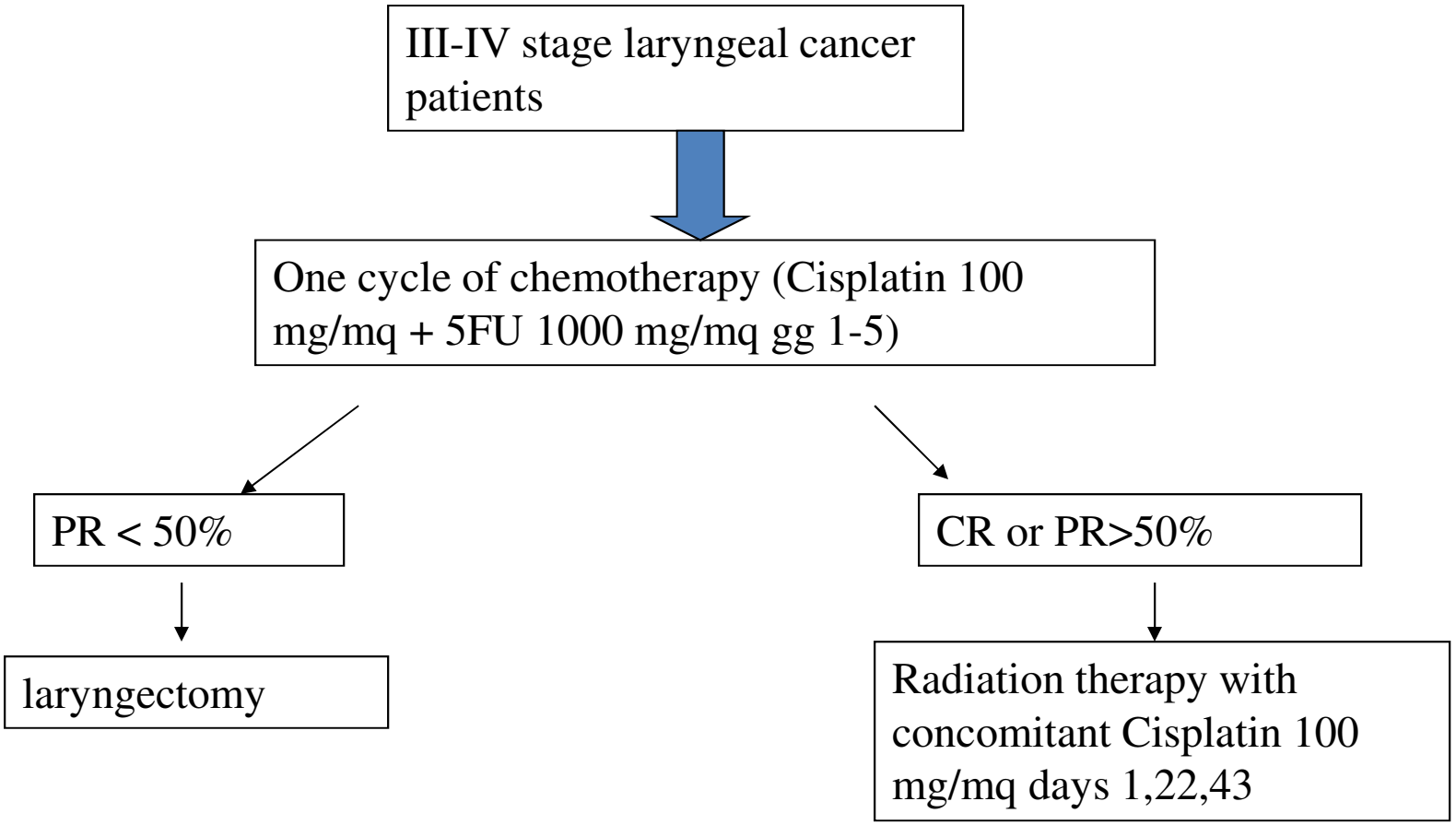
Diapositiva 49

1 ISA CINI; 28/09/13

VOLUME 24 · NUMBER 4 · FEBRUARY 1 2006
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

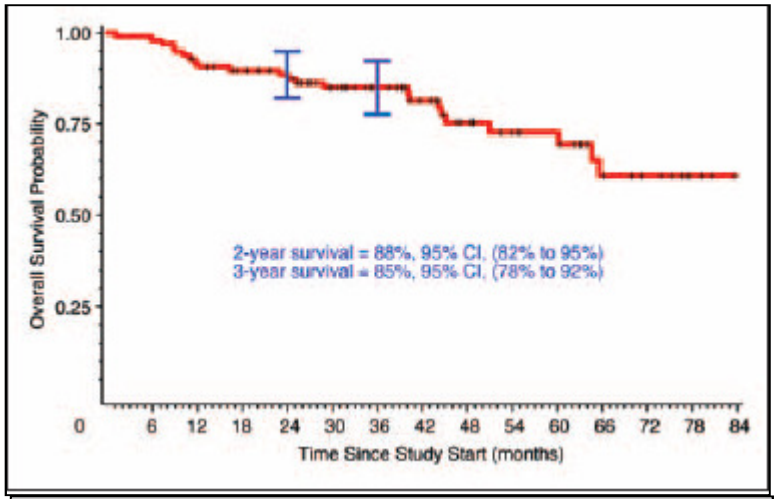
Single-Cycle Induction Chemotherapy Selects Patients With Advanced Laryngeal Cancer for Combined Chemoradiation: A New Treatment Paradigm

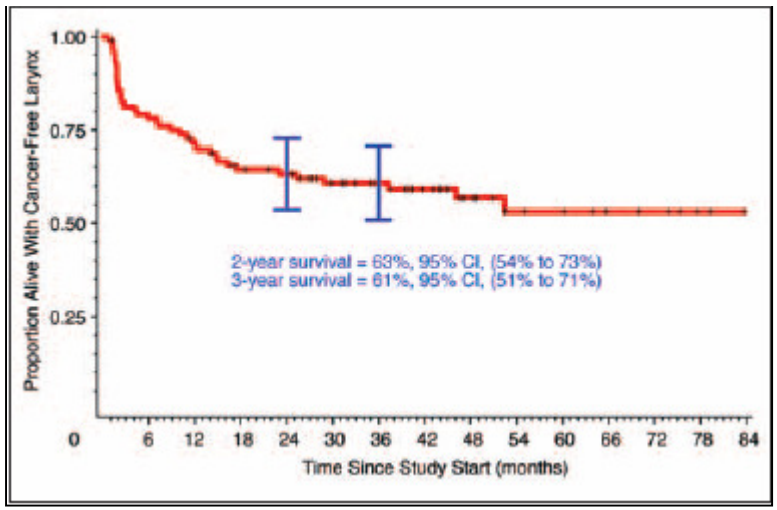
Susan Urba, Gregory Wolf, Avraham Eisbruch, Francis Worden, Julia Lee, Carol Bradford, Theodoros Teknos, Douglas Chepeha, Mark Prince, Norman Hogikyan, and Jeremy Taylor

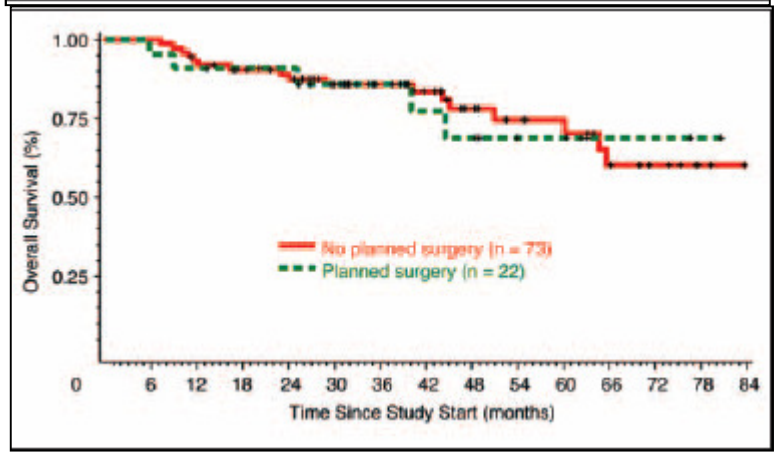


University of Michigan Study - Results

Of 97 eligible patients, 73 (75%) achieved more than 50% response and received chemoradiotherapy. A total of 29 patients (30%) had salvage surgery; 19 patients (20%) had early salvage surgery after the single cycle of induction chemotherapy, three patients (3%) had late salvage surgery after chemoradiotherapy, six patients (6%) eventually had salvage surgery for recurrence, and one patient had laryngectomy for chondroradionecrosis. The median follow-up time was 41.9 months. The overall survival rate at 3 years is 85%. The cause-specific survival rate was 87%. Larynx preservation was achieved in 69 patients (70%).







(Urba S et al, *JCO*, 2006)

LARYNX PRESERVATION CLINICAL TRIAL DESIGN: KEY ISSUES AND RECOMMENDATIONS - A CONSENSUS PANEL SUMMARY

Lefebvre JL, Ang KK on behalf of the Larynx Preservation Consensus Panel

IJROBP, 2009

Main reccomendations

- **The trial population should include patients with T2 or T3 laryngeal or hypopharyngeal carcinoma not considered for partial laryngectomy and exclude those with laryngo-esophageal dysfunction or age over 70 years.**
- **The panel favored a new composite endpoint:**

"laryngo-esophageal dysfunction-free survival"

- **Desired secondary endpoints are: OS, PFS, LRC, time to tracheotomy, time to laryngectomy, time to discontinuation of feeding tube, QoL**
- **Correlative biomarker studies for near-term trials should include: EGFR, ERCC-1, etc**

Lefebvre JL, Ang KK on behalf of the Larynx Preservation Consensus Panel, 2009

Locally advanced H&N Cancer- Conclusions 1

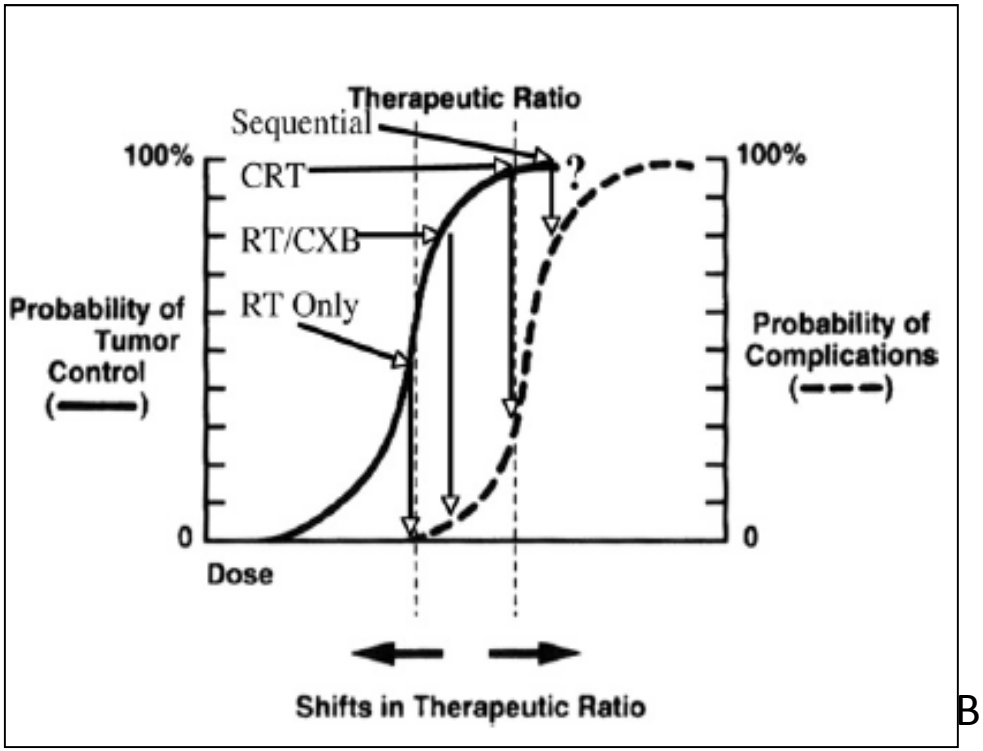
- Concomitant cisplatin-based chemotherapy improves the probability of survival in comparison with radiotherapy alone with a significant increase in severe late toxicity. AFRT does'nt improve the clinical results in comparison with SFRT in chemoradiation (CTRT) setting
- Radiotherapy and cetuximab increases the probability of survival in comparison with radiotherapy alone. Phase II and phase III clinical trials comparing CTRT and RT+ Cetuximab are now ongoing
- IC with TPF increases OS in comparison with IC with PF

Locally advanced H&N Cancer- Conclusions 2

- No one clinical phase III trial until now showed the superiority of IC followed by CTRT, in comparison with CTRT alone
- RTOG 0522 trial failed to show better results adding cetuximab to the standard ciplatin based CTRT
- In larynx preservation trials, RT associated with CT (IC and/or concomitant) obtained the same OS than laryngectomy, with an high proportion of laryngectomy free survival, but with significant toxicity. The primary endpoint of these trials must be not only the laryngectomy free survival but the “laryngo-esophageal dysphunction-free survival”

Locally advanced H&N Cancer- Conclusions 3

- Our porpose must be to optimize the multi-modal therapeutic integration by improving the RT technique (e.g. IMRT) and by reducing the toxicity of the drugs (targeted therapy and/or chemotherapy)



Brizel & Vokes, 2009

Thank you for your Attention!!