VIII Congresso AIRO Giovani

I TRATTAMENTI MULTIMODALI IN ONCOLOGIA

Implicazione cliniche per il radio-oncologo

Il trattamento multimodale per la preservazione d'organo nelle neoplasie del distretto cervico-cefalico

Pierfrancesco Franco, MD
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University of Torino School of Medicine
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Larynx-preservation

- ✓ **Total laryngectomy (TL) provides consistent disease control in LAHNC (laryngeal and hypopharyngeal cancer)**
- ✓ **TL has a negative impact on QoL**
- ✓ **Larynx-preservation strategies developed in the '90s: ICT + definitive RT had similar survival rates than TL**
- ✓ **Subsequent phase III trials investigated this field but:**
  - **Different inclusion criteria**
  - **Different endpoints to assess larynx preservation**
  - **Functional assessment not refined (long-term sequalae on swallowing)**

LARYNX

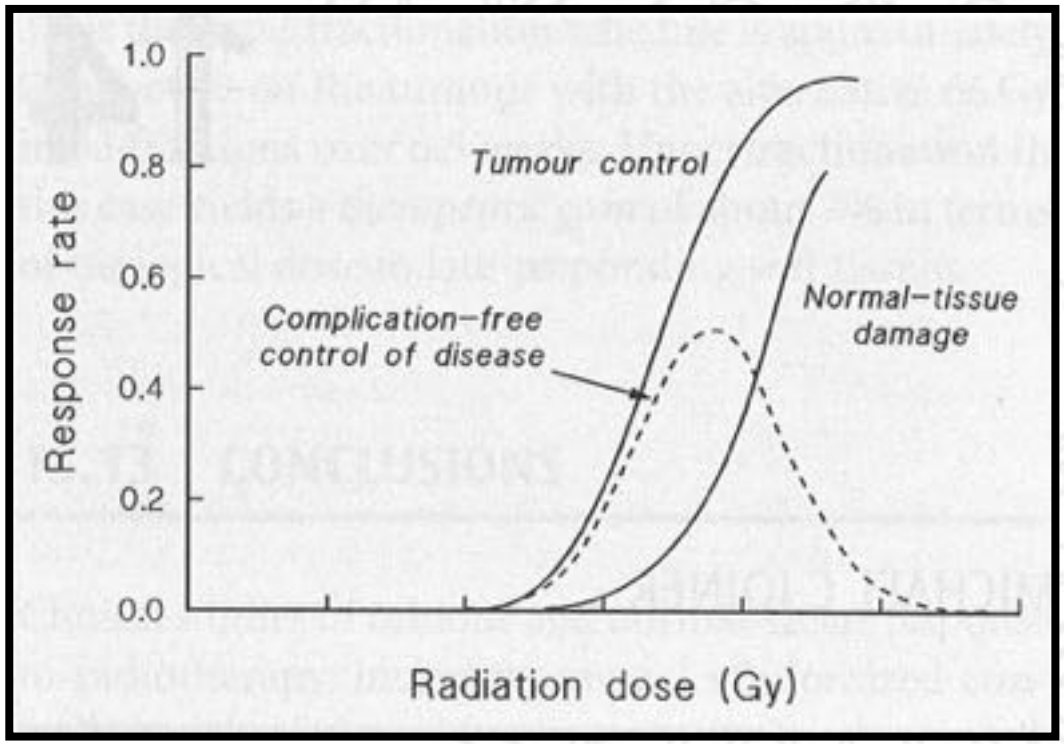
Choice of treatment

Disease control

Treatment morbidity

Uncomplicated local tumour control rate

as a bell-shaped curve



Cogent in head and neck cancer

Holthusen H, Strahlentherapie 1936

LARYNX

Factors influencing treatment choice

Tumor related

- Histology
- Site of origin
- Biological characteristics (grading, HPV-16, nuclear ploidy, EGFR, p53 mutations, neoangiogenesis)
- T-N category
- Distant metastasis

Patient related

- Age
- Gender
- Comorbidity
- Previous treatments
- Compliance
- Professional activity
- Patient's choice

Courtesy P Nicolai - ESTRO Multidisciplinary Teaching Course H&N Cancer – Cordoba 2012

The goal of treatment is to achieve larynx preservation with good functional outcome withour compromising overall survival

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE ARCHIVE

Speech and Survival — Tradeoffs between Quality and Quantity of Life in Laryngeal Cancer

Barbara J. McNeil, M.D., Ph.D., Ralph Weichselbaum, M.D., and Stephen G. Pauker, M.D.

N Engl J Med 1981; 305:982-987 | October 22, 1981 | DOI: 10.1056/NEJM198110223051704

PRIORITIZING TREATMENT OUTCOMES: HEAD AND NECK CANCER PATIENTS VERSUS NONPATIENTS

Marcy A. List, PhD,[1] Judith Lee Rutherford, PhD,[2] John Stracks, BA,[1] Barbara Roa Pauloski, PhD,[3] Jerilyn A. Logemann, PhD,[3] Donna Lundy, MA, CCC,[4] Paula Sullivan, MS, CCC,[4*] William Goodwin, MD,[4] Merrill Kies, MD,[5] Everett E. Vokes, MD[5,6]

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[3] Department of Communication Sciences and Disorders, Northwestern University, Chicago, Illinois
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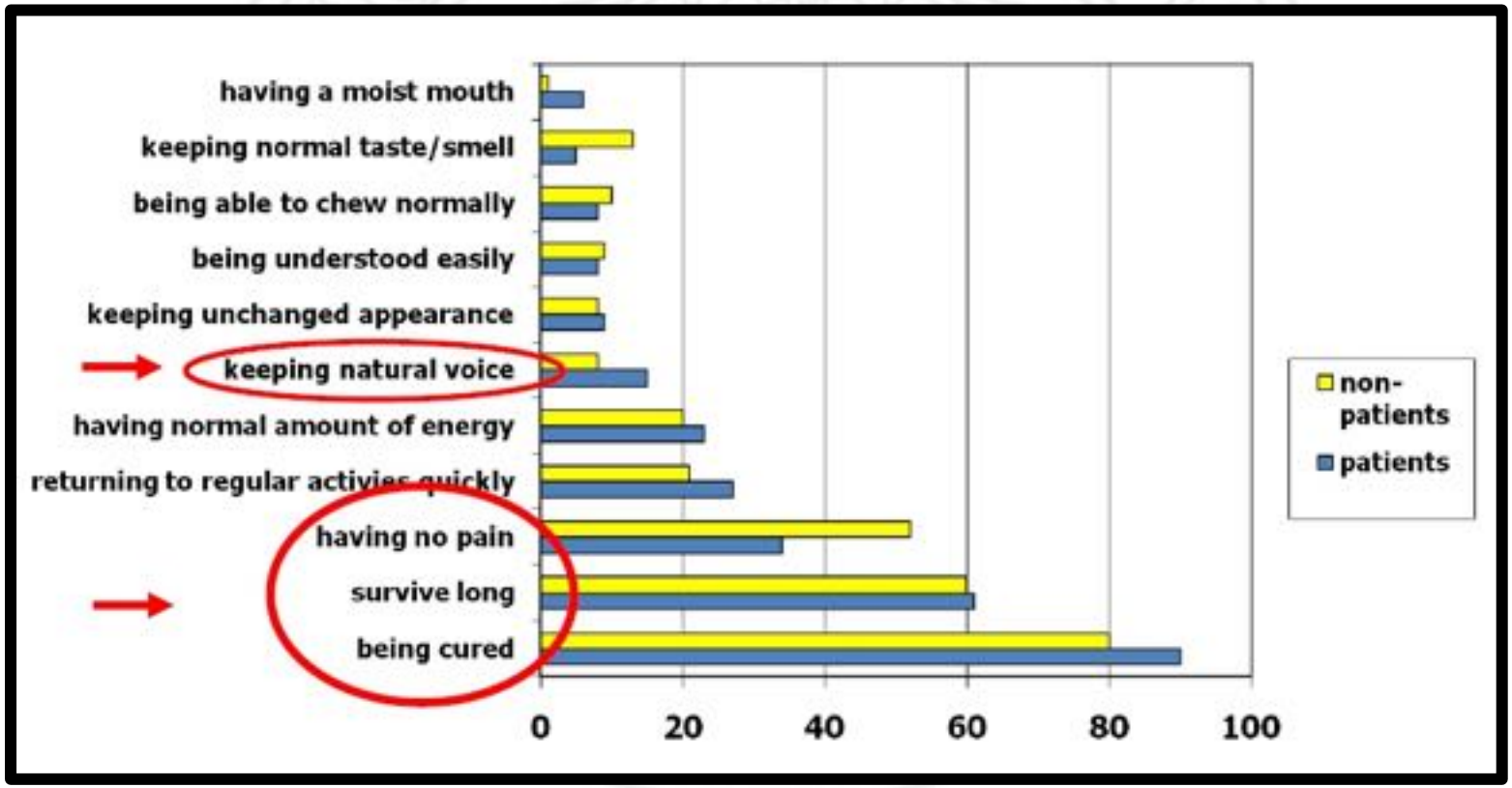
[5] Northwestern University Feinberg School of Medicine and The Robert H Lurie Comprehensive Cancer Center, Chicago, Illinois
[6] Department of Medicine, University of Chicago, Chicago, Illinois

247 H&N cancer pts and 141 non-pts



List et al et al, Head and Neck 2004

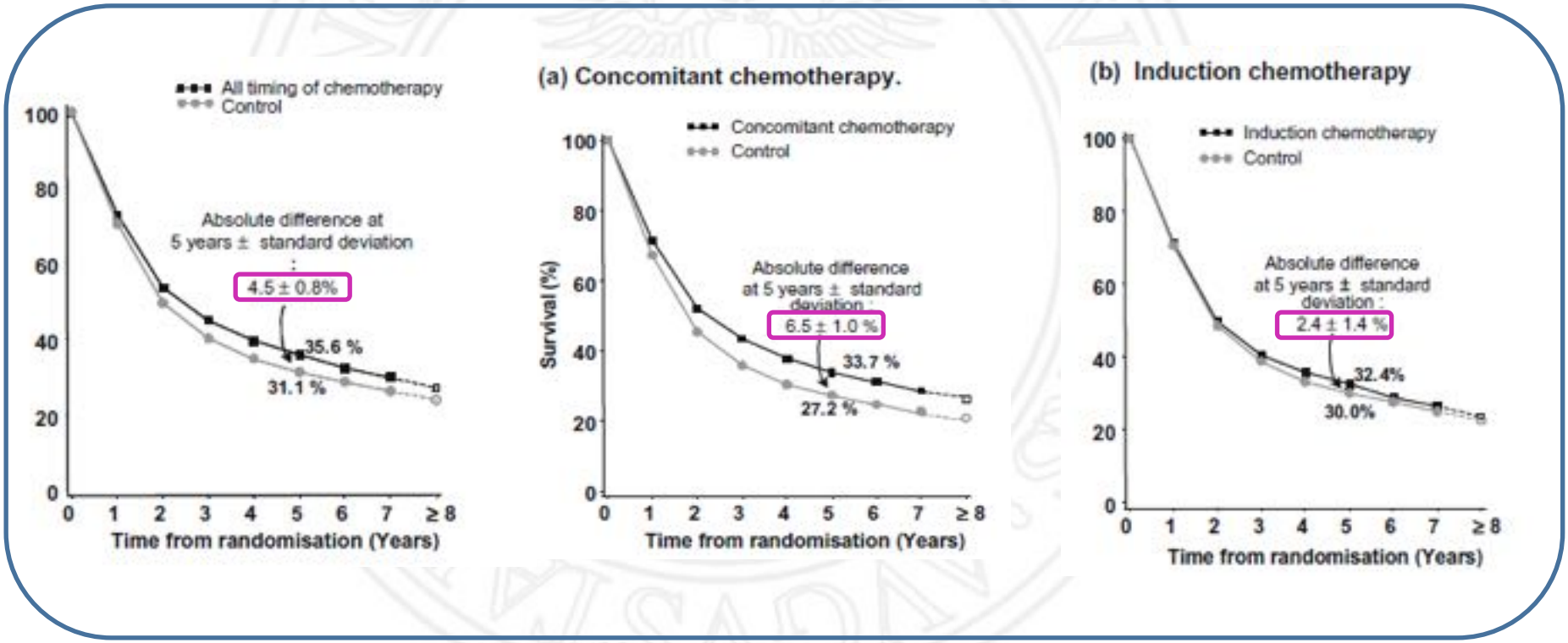
ESMO Clinical Practice Guidelines 2010
Locoregionally advanced disease

	Level of evidence	Grade of recommendation
Surgery → RT or CCRT	I	A
Concomitant CT and RT*	I	A
Cetuximab plus RT	II	B
ICT → RT for organ preservation	II	A
CCRT for organ preservation	II	A

Gregoire V et al; Ann Oncol 2010

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]



Pignon et al, R&O 2009

"Sequential approach" improve outcomes?

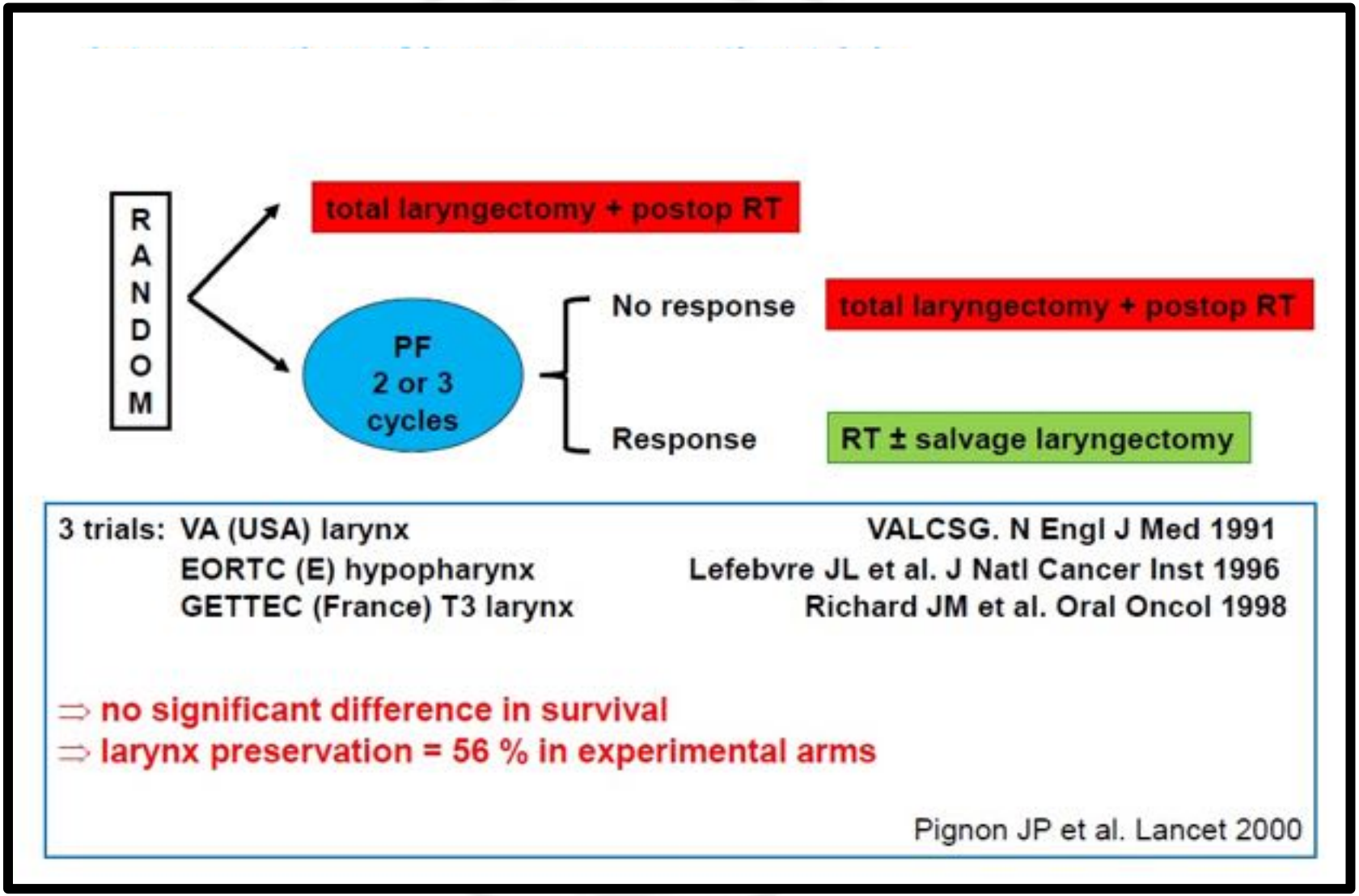
May

ICT before a "lighter" CRT be better or more tolerable?

- **SWOG-0427** (III-IV Oropharynx): 1-3TPF → RT+3P vs RT+3P
- **DeCIDE** (N2-N3): 2TPF → HFRT+PFH vs HFRT+PFH
  - No difference OS
- **Paccagnella** (III-IV): RT+2PF vs 3 TPF → RT+2PF
  - CR rates: 21% vs 51%
  - Median PFS 19.7 vs 30.4; OS 33.3 vs 39.6
- **PARADIGM** (III-IV): 3TPF → RT+CBDCA weekly vs HFRT+2P
  - 3ys- OS: 73% vs 78%
- **INTERCEPTOR** (III-IV): 3TPF → RT + Cetuximab weekly vs RT+3P
- **GORTEC** (III-IV): 3TPF → RT + Cetuximab weekly vs RT+CBDCA-5FU

Benasso et al, Oral Oncol 2013

First generation of larynx-preservation trials



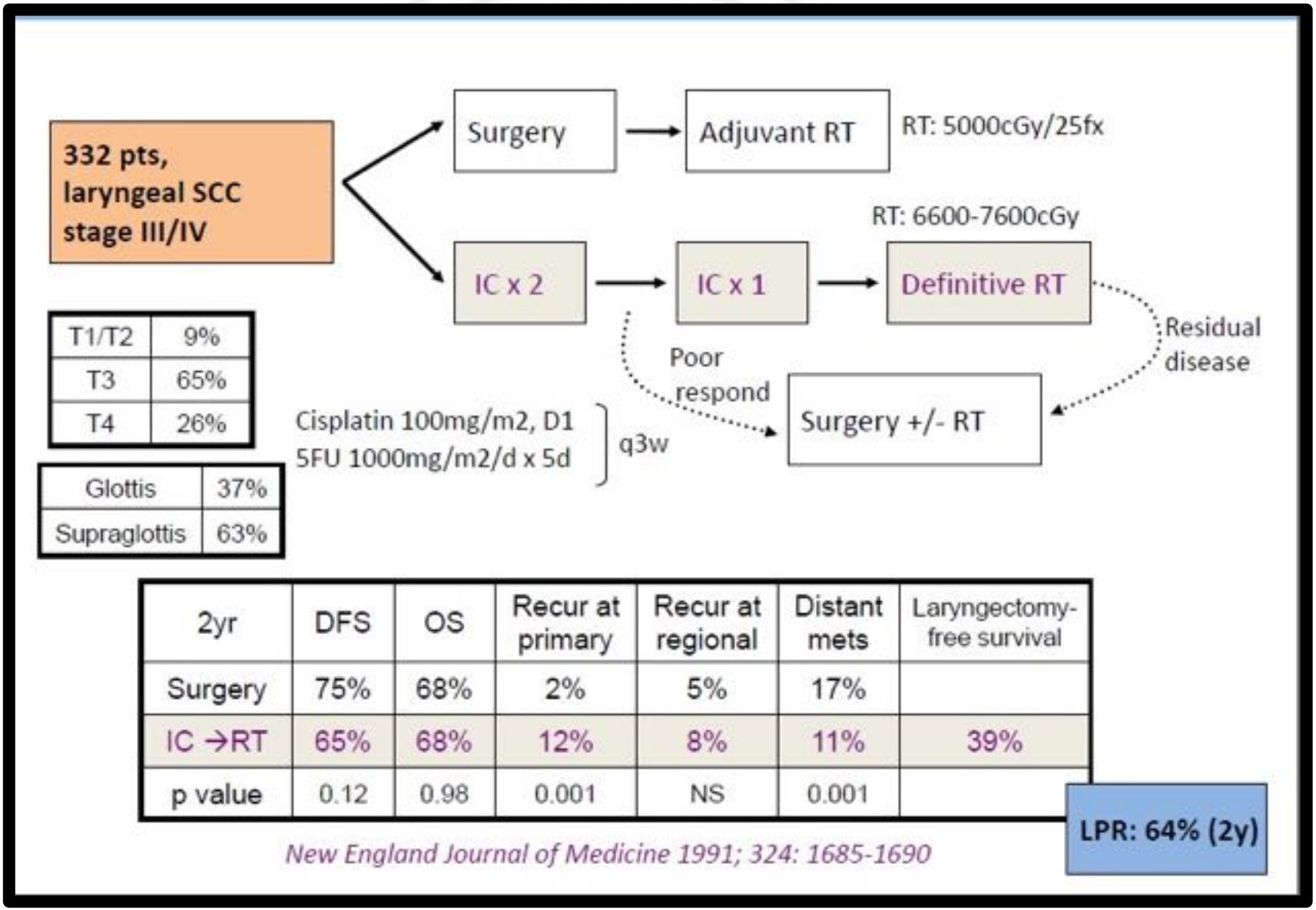
3 trials: VA (USA) larynx — VALCSG. N Engl J Med 1991
EORTC (E) hypopharynx — Lefebvre JL et al. J Natl Cancer Inst 1996
GETTEC (France) T3 larynx — Richard JM et al. Oral Oncol 1998

⇒ no significant difference in survival
⇒ larynx preservation = 56 % in experimental arms

Pignon JP et al. Lancet 2000

Courtesy JL Lefebvre ESTRO Multidisciplinary Teaching Course H&N Cancer – Cordoba 2012

Veterans Affairs Laryngeal Cancer Study Group



T1/T2	9%
T3	65%
T4	26%

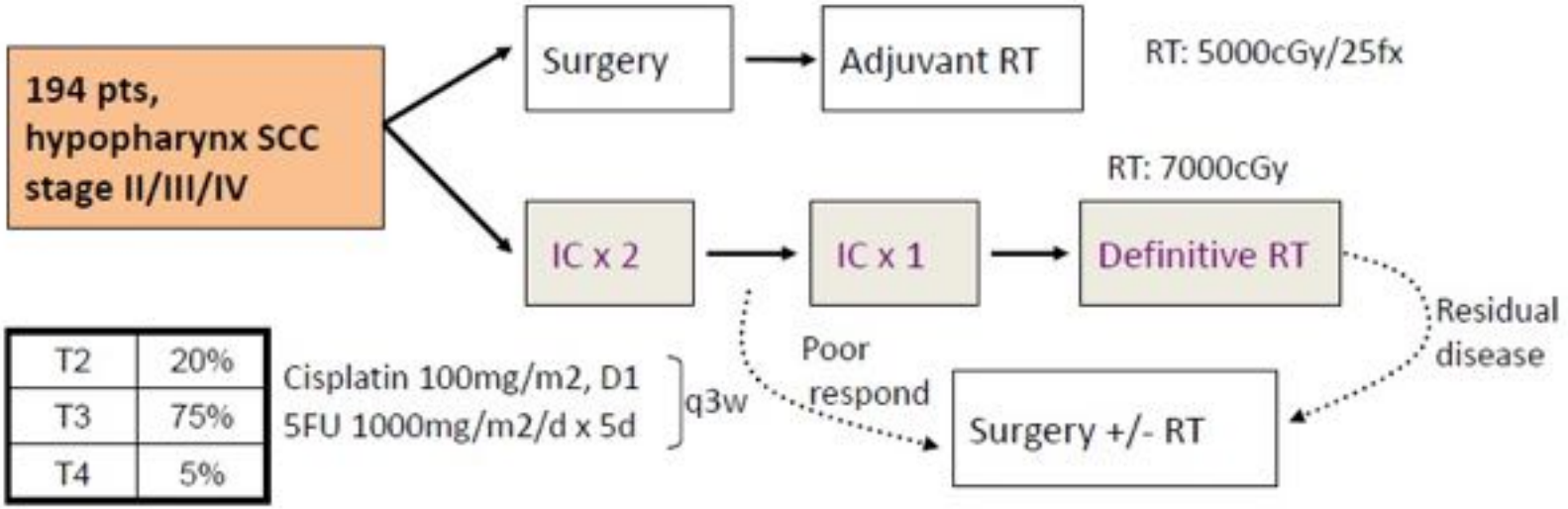
Glottis	37%
Supraglottis	63%

2yr	DFS	OS	Recur at primary	Recur at regional	Distant mets	Laryngectomy-free survival
Surgery	75%	68%	2%	5%	17%	
IC →RT	65%	68%	12%	8%	11%	39%
p value	0.12	0.98	0.001	NS	0.001	

LPR: 64% (2y)

New England Journal of Medicine 1991; 324: 1685-1690

EORTC 24891

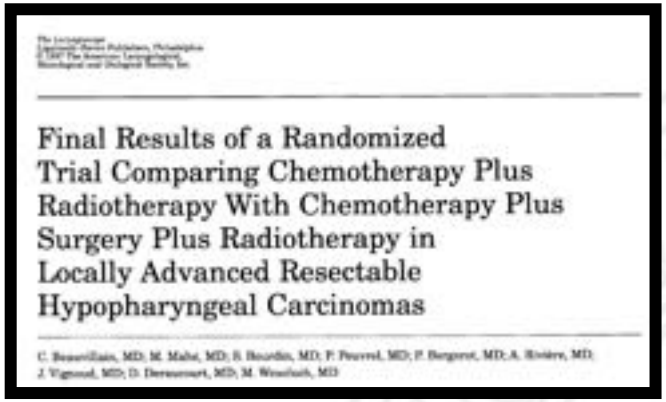


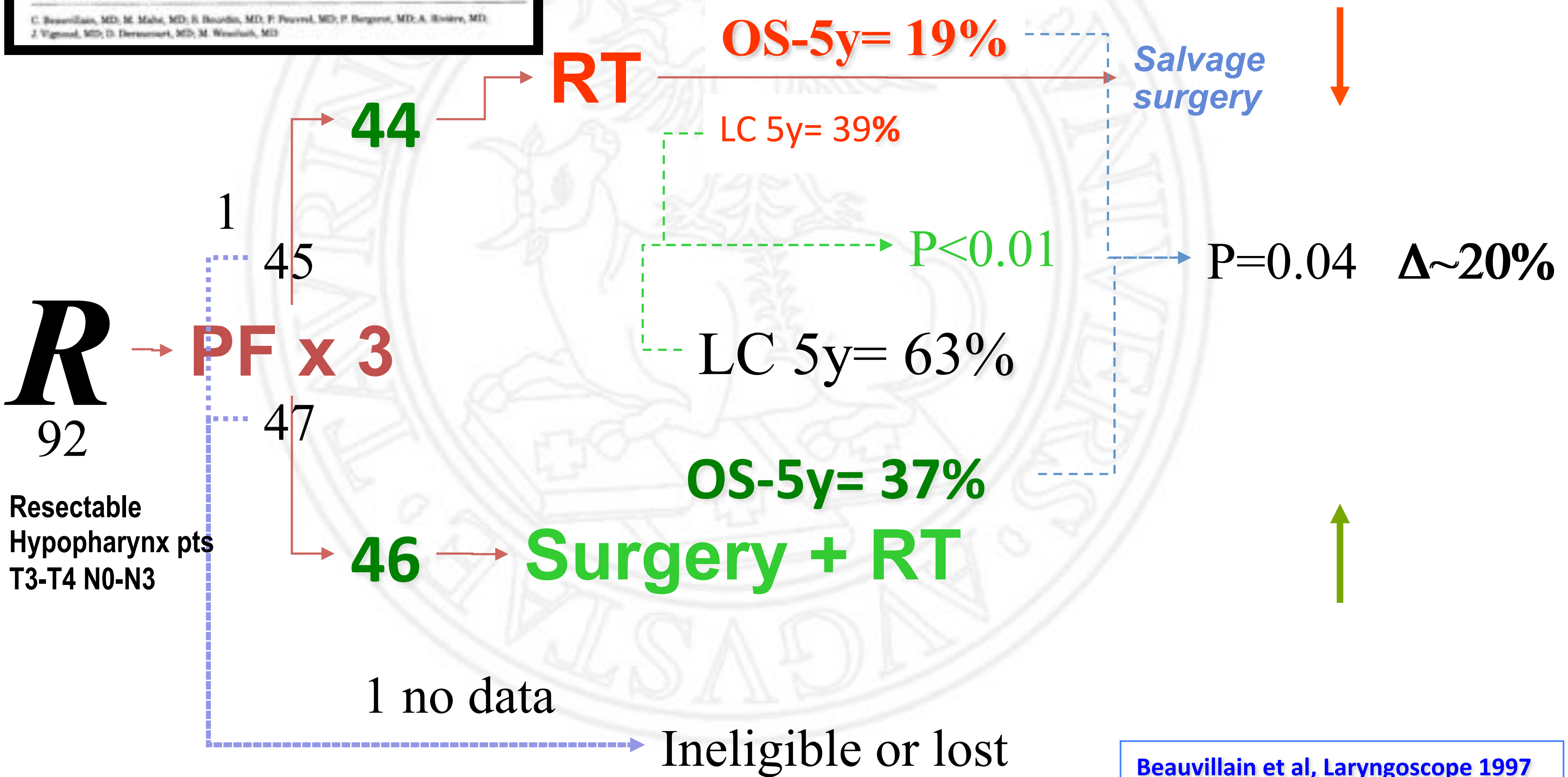
T2	20%
T3	75%
T4	5%

Pyriform sinus	78%
Aryepiglottic fold	22%

5yr	DFS	OS	Recur at local	Recur at regional	Distant mets	Laryngectomy-free survival
Surgery	32%	35%	17%	23%	36%	
IC →RT	25%	30%	12%	19%	25%	42% (2y) 35% (5y)
p value	NS	NS	NS	NS	0.041	

Journal of National Cancer Institute 1996; 8: 890-899


Final Results of a Randomized Trial Comparing Chemotherapy Plus Radiotherapy With Chemotherapy Plus Surgery Plus Radiotherapy in Locally Advanced Resectable Hypopharyngeal Carcinomas

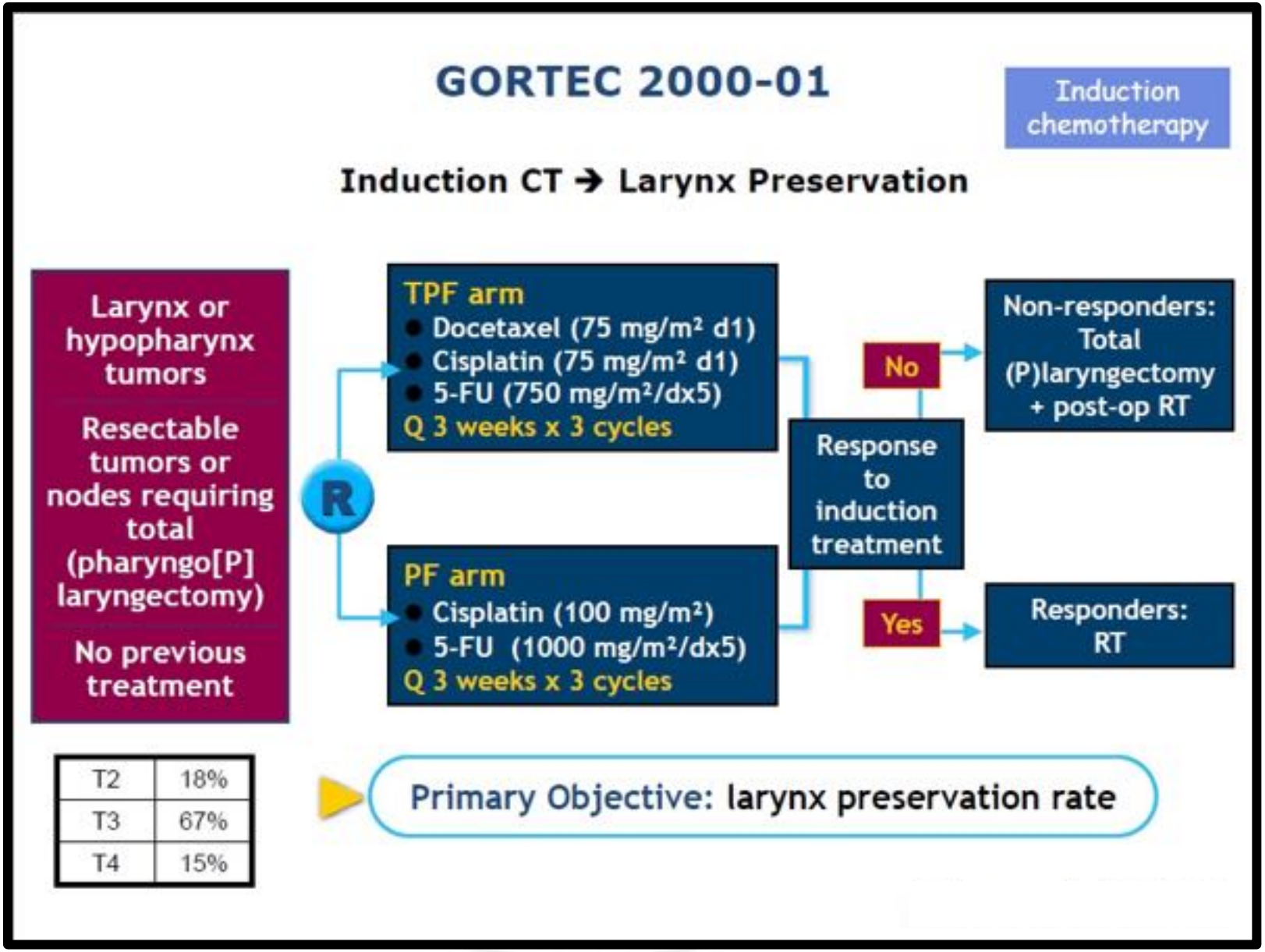


Beauvillain et al, Laryngoscope 1997

ICT as chemo-selection tool

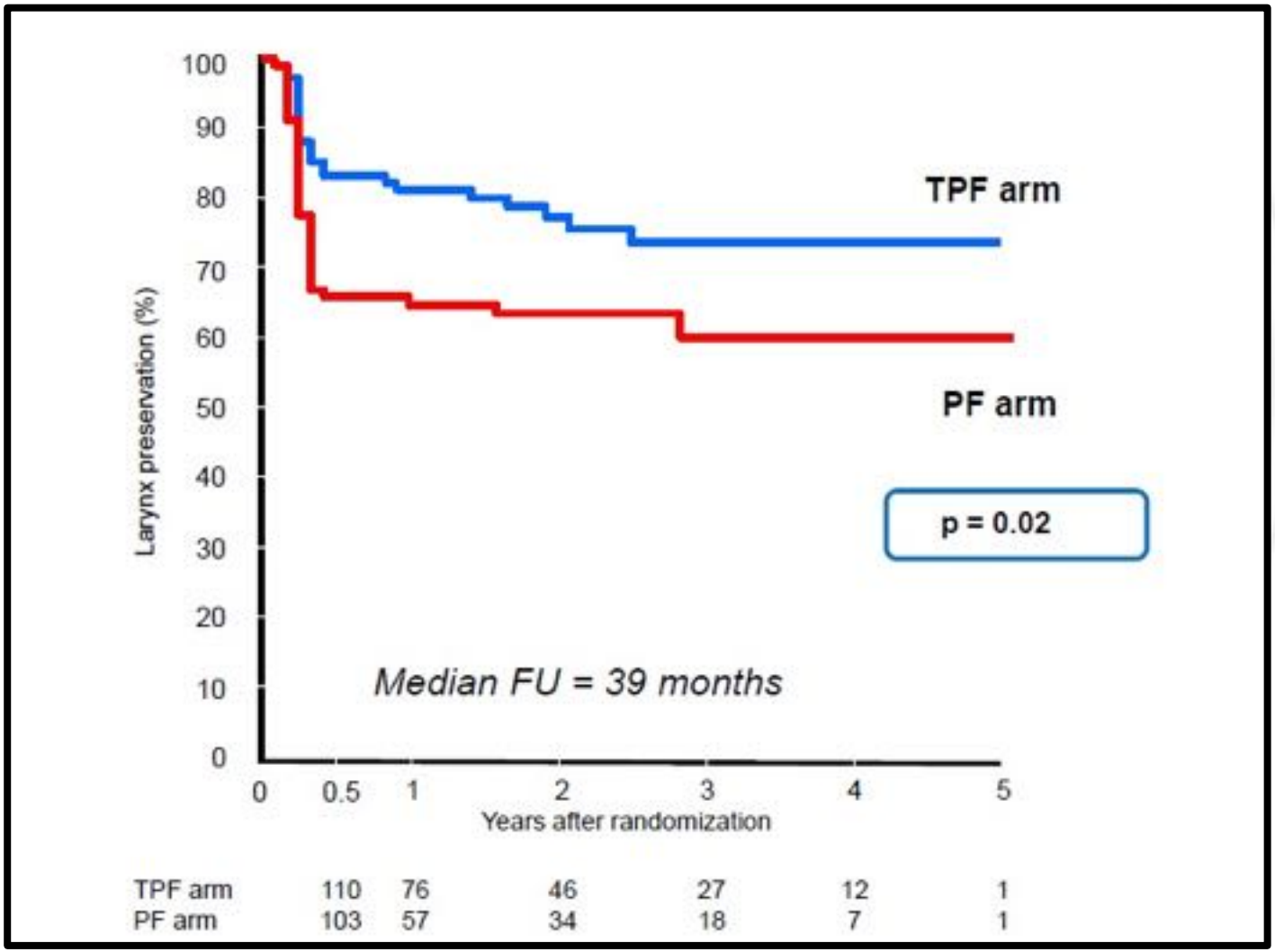
Trial/ site of tumour	N	Therapy aproach	Larynx Preservation	LFS	Survival Difference
VALCSG (larynx)	332	S → RT *vs* PF[1]x3 → RT	64%(2y)	39%(2y)	No difference
EORTC 24891 (hypopharynx)	202	S →RT *vs* PFx3 → RT	40,5% (5y)	42% (2y) 35% (5y)	No difference

PF as ICT + sequential RT may be effective with a high rate of larynx preservation, with no detrimental effect on OS



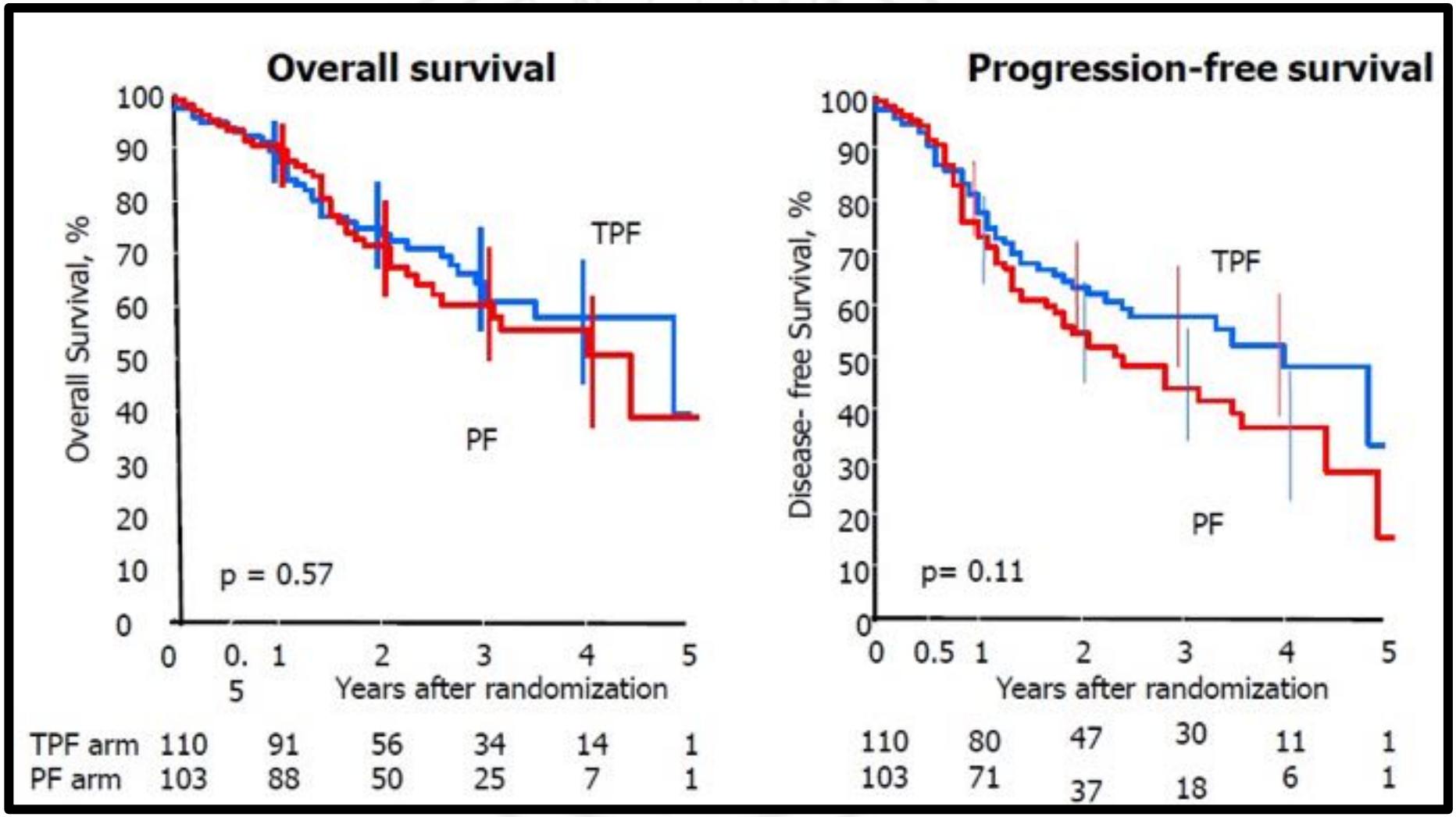
Pointreau et al – JNCI 2009

GORTEC 2000-01 Primary end-point: Larynx preservation



Pointreau et al – JNCI 2009

GORTEC 2000-01 Secondary end-points



Pointreau et al – JNCI 2009

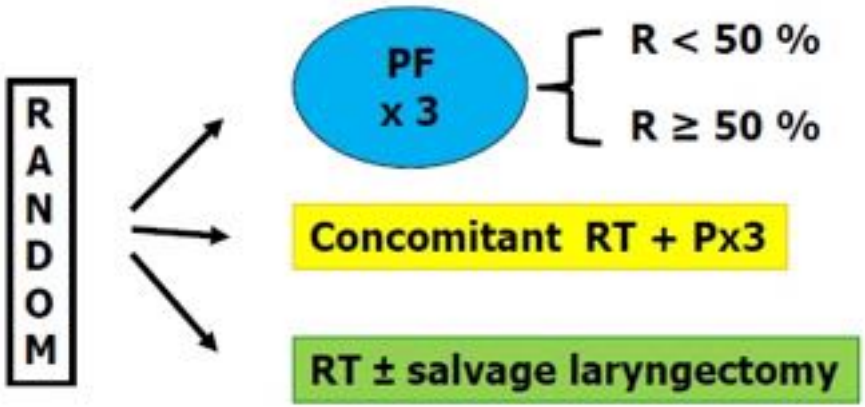
GORTEC 2000-01 Toxicity profile (G3-G4) events

	% of patients		
NCI/CTC Grade 3/4*	TPF	PF	*p*
Mucositis	4.6	7.8	0.49
Neutropenia	55.6	37.3	0.01
Febrile neutropenia	13.9	7.8	0.24
Thrombocytopenia	1.9	7.8	0.09
Deaths	3.6	2.9	0.71

*Among patients treated with RT alone, no differences were observed between the 2 arms in: xerostomia, fibrosis, larynx edema, dysphagia, % of patients with permanent feeding tube.

Pointreau et al – JNCI 2009

2nd generation of larynx preservation trials



T2	12%
T3	78%
T4	10%

Supraglottis	69%
Glottis	31%

1 trial: RTOG 91-11 (USA) larynx

	induction	concomitant	RT
Larynx preservation	72 %	84 %	67 %
Laryngectomy-free survival	43 %	45 %	38 %
Overall survival	55 %	54 %	56 %
Progression-free survival	38 %	36 %	27 %
gr 3-4 mucositis during RT	38 pts	73 pts	41 pts

Forastiere A et al. N Engl J Med 2003

Courtesy JL Lefebvre ESTRO Multidisciplinary Teaching Course H&N Cancer – Cordoba 2012

RTOG 91-11: ASCO 5-year update

	IC(PF)	CRT	XRT	
LFS	44.6%	46.6%	33.9%	*P* < .011
LRC	54.9%*	68.8%*	51%	*P* < .0018
LPR	70,5%	83%	66%	*P*<.0029
DM	14.3%	13.2%	22.3%	
DFS	38.6%*	39%	27.3%*	*P* < .0016
Survival	59.2%	54.6%	53.5%	

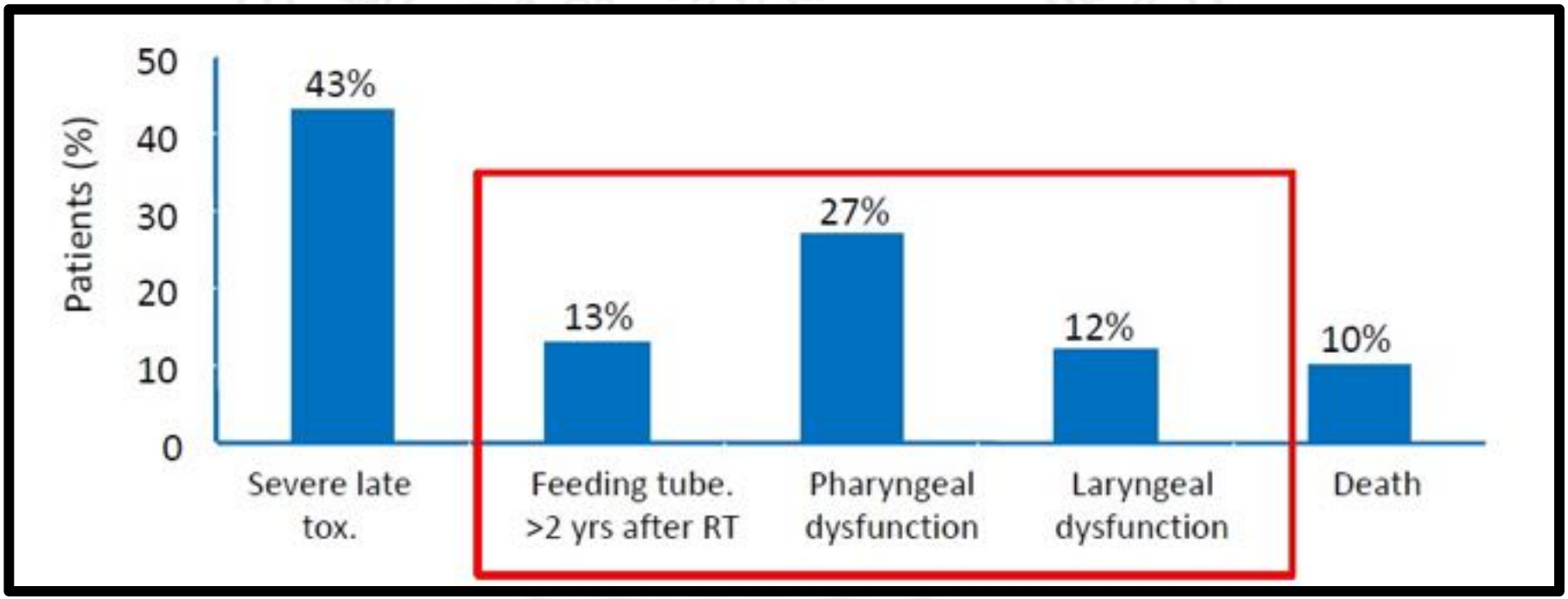
1. PF was equivalent to CRT for LFS
2. CRT had better LRC than PF
3. DFS was identical but overall survival favored PF

Forastiere AA, et al. ASCO 2006. Abstract 5517

Severe late toxicities after RT-CT

180 days after end of treatment

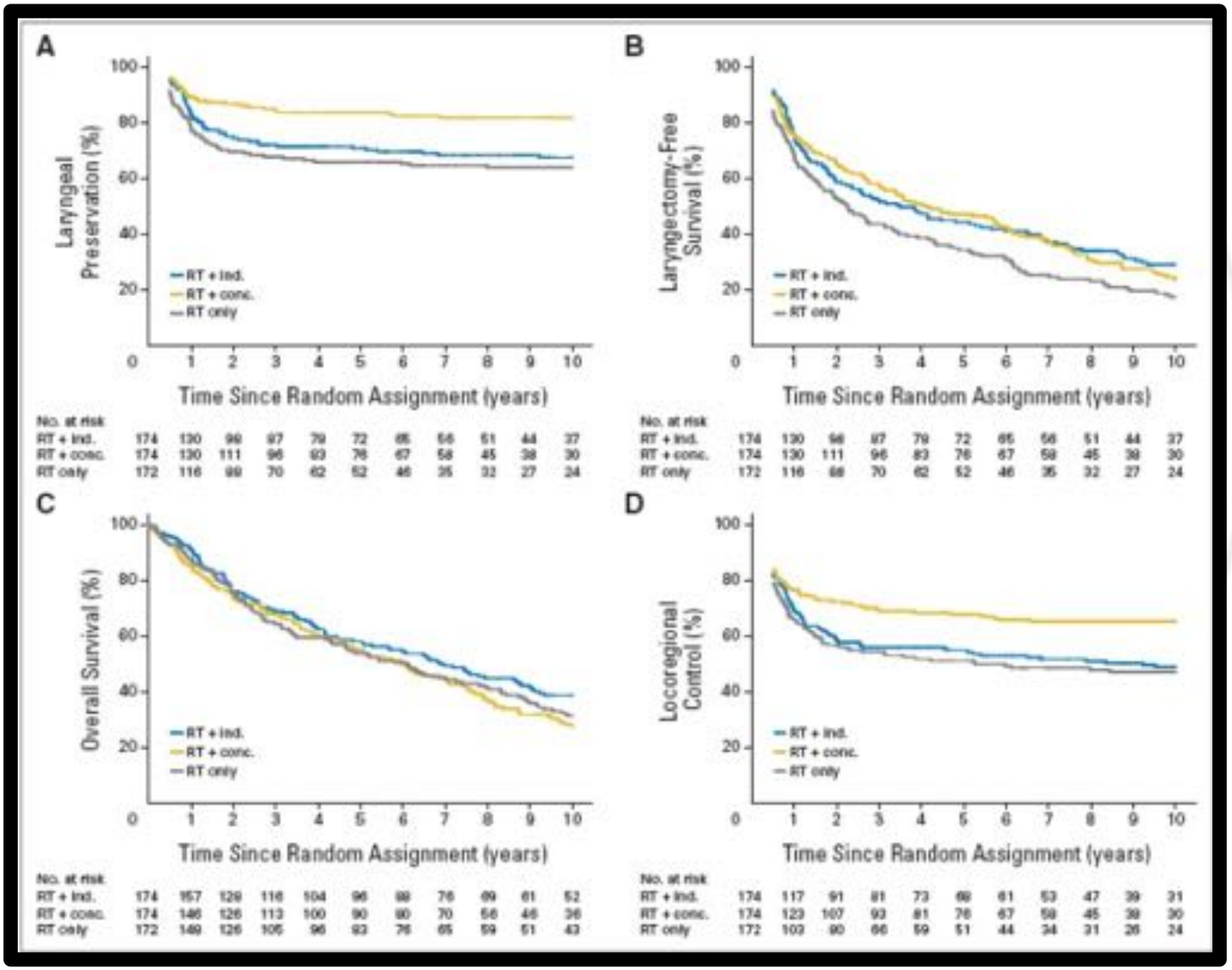
- ❑ **Chronic G3-G4 events (larynx and pharynx)**
- ❑ **NGS > 2 yrs after registration**
- ❑ **Treatment-related death within 3 yrs after treatment**



Data from CT-RT arms of RTOG 91-11, 97-03, 99-14

Machtay et al, JCO 2008

RTOG 91-11: 10-year results



Forastiere A et al, JCO 2013

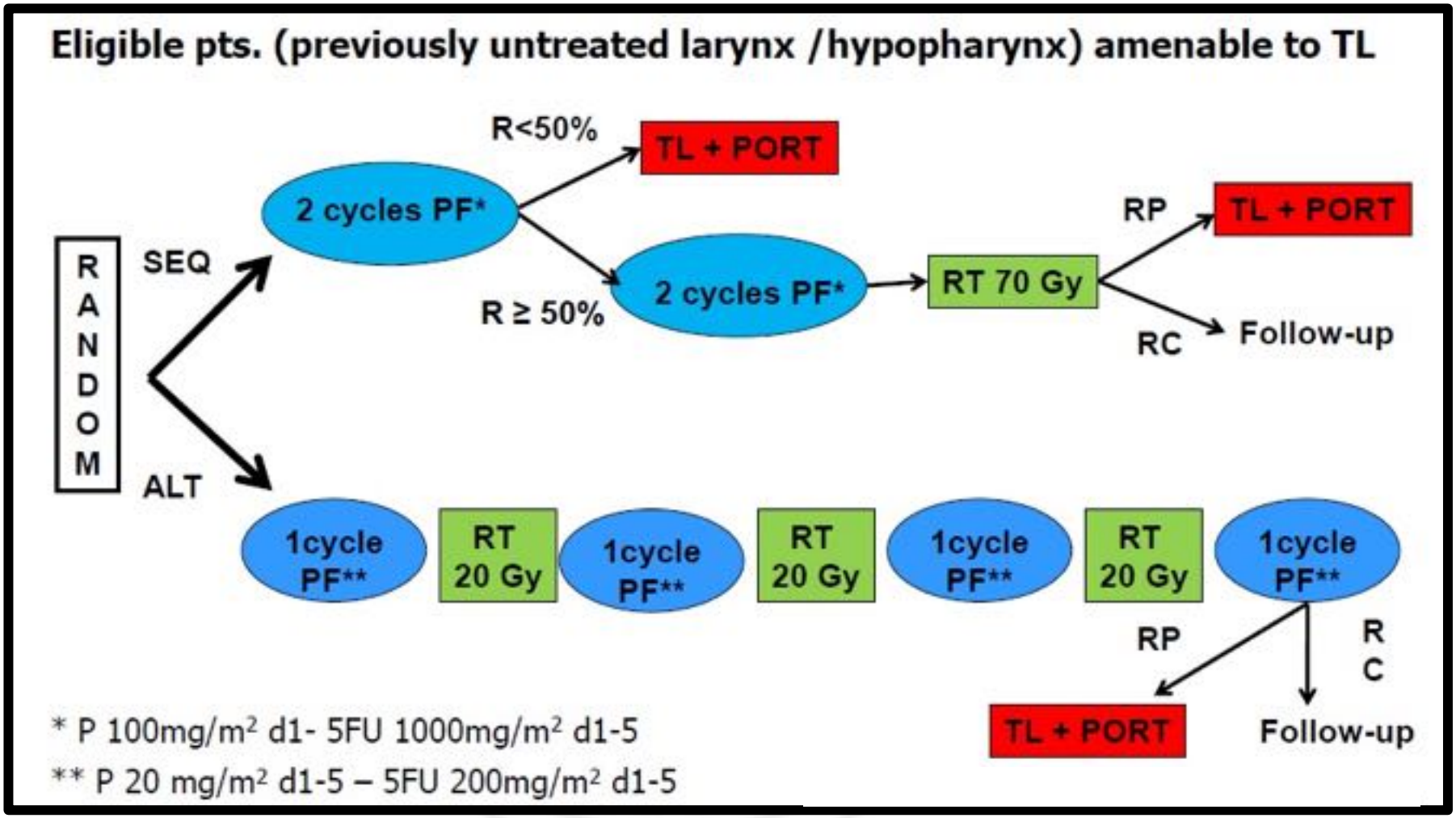
RTOG 91-11: 10-year results

Toxicity:

- The rate of high grade toxic effects was greater in Ch-based regimens 81% (Chi->RT), 82% (Ch-RT) & 61% (XRT)
- The mucosal toxicity of concurrent RT-CDDP was nearly twice as frequent as the mucosal toxicity of the other two treatments during RT
- No differences in late toxicity or speech or swallowing function were demonstrated between treatment groups

Forastiere A et al, JCO 2013

EORTC 24954



Lefebvre JM et al, JNCI 2009

EORTC 24954: 5-year results

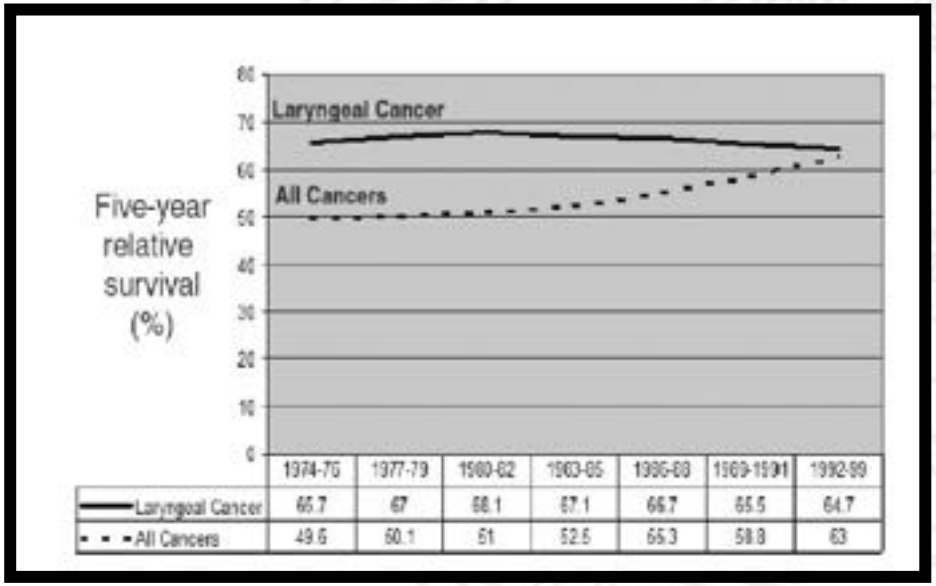
	Sequential (N=224)		Alternating (N=226)		
	Events	% without event	Events	% without event	p-value
Survival with functional larynx	160	30.5	154	36.2	0.15
Larynx preservation	107	53.2	94	59.8	0.10
Progression-free survival	140	41.0	139	41.8	0.75
Overall survival	125	48.5	122	51.9	0.45

Acute toxicity: SEQ > ALT
Late toxicity: SEQ = ALT

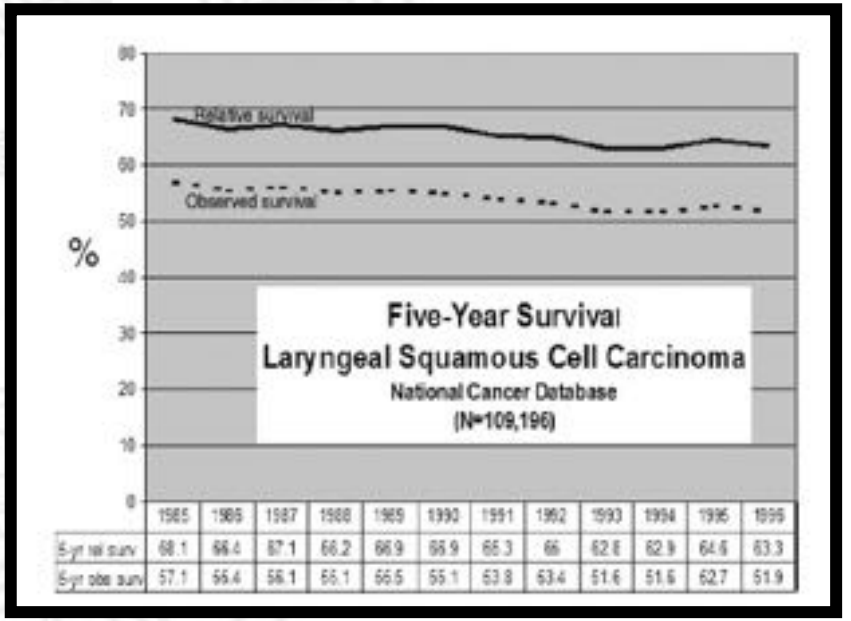
Lefebvre JM et al, JNCI 2009

Laryngeal Cancer in the United States: Changes in Demographics, Patterns of Care, and Survival

Henry T. Hoffman, MD, MS, FACS; Kimberly Porter, MPH; Lucy H. Karnell, PhD; Jay S. Cooper, MD; Randall S. Weber, MD; Corey J. Langer, MD; Kie-Kian Ang, MD, PhD; Greer Gay, PhD; Andrew Stewart, MA; Robert A. Robinson, MD, PhD



SEER Cancer Statistics Review, 1975-2000



NCDB Cancer Statistics Review, 1985-2001

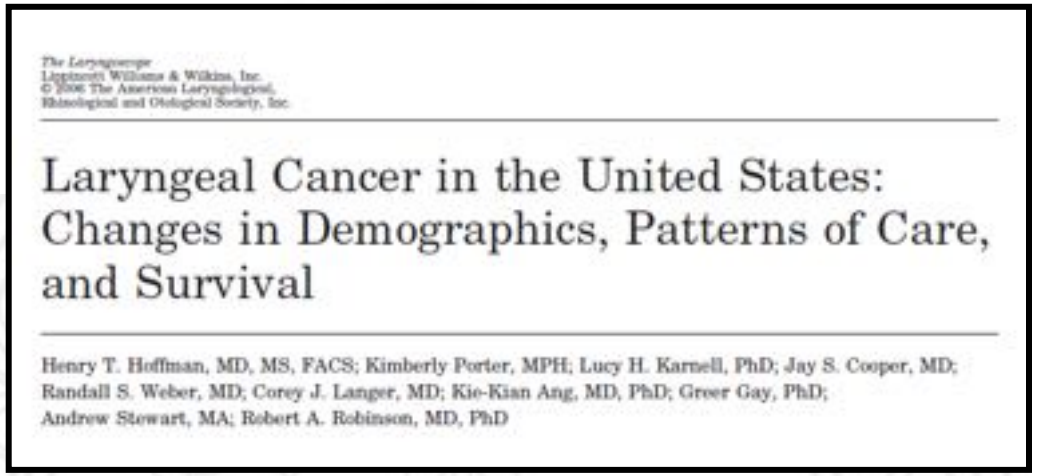
Hoffman HT et al, Laryngoscope 2006

In particular a decreased survival was observed for:

- **Advanced-stage glottic cancer**
- **Early stage supraglottic cancer**
- **Supraglottic cancer with T3N0 stage**

For T3N0M0 laryngeal cancers at all sites: 5-year relative survival better with surgery + RT

Hoffman HT et al, Laryngoscope 2006



The Laryngoscope
Lippincott Williams & Wilkins, Inc.

Laryngeal Cancer in the United States: Changes in Demographics, Patterns of Care, and Survival

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Treatment hypotesis – Change in the initial management by use of less effective treatment has resulted in worse survival through the following:

- ❑ **Expanded use of non-surgical organ-preservation strategies**
- ❑ **Expanded use of endoscopic surgical management**
- ❑ **Less aggressive surgical management of neck nodes**

Hoffman HT et al, Laryngoscope 2006

original article

Cancer mortality in the European Union, 1970–2003, with a joinpoint analysis

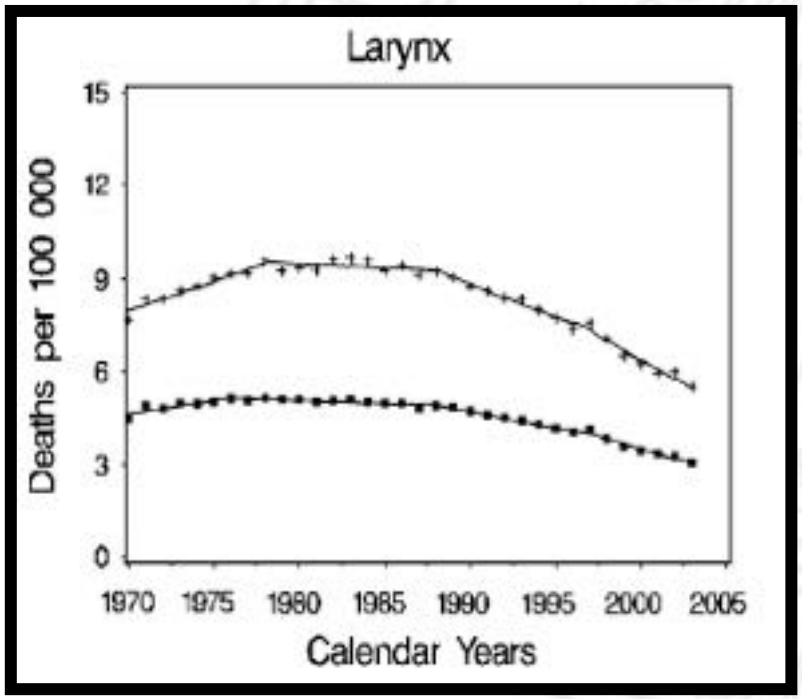
C. Bosetti[1*], P. Bertuccio[1], F. Levi[2], F. Lucchini[2], E. Negri[1] & C. La Vecchia[1,3]

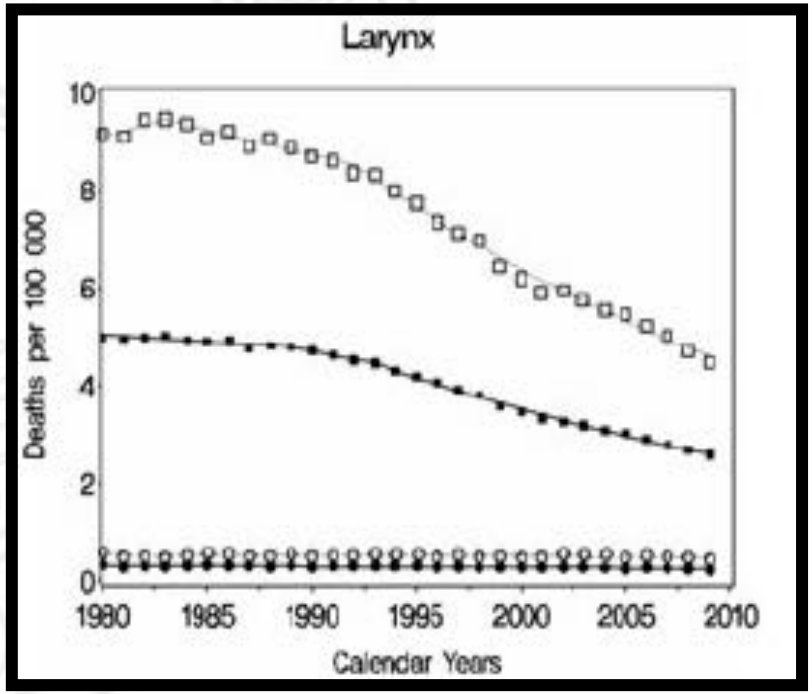
Annals of Oncology

original articles

Cancer mortality in Europe, 2005–2009, and an overview of trends since 1980

C. Bosetti[1*], P. Bertuccio[1,2], M. Malvezzi[1,2], F. Levi[3], L. Chatenoud[1], E. Negri[1] & C. La Vecchia[1,2]





Bosetti C et al, Ann Oncol 2008 and 2013

EDITORIAL

REEXAMINING THE TREATMENT OF ADVANCED LARYNGEAL CANCER

Kerry D. Olsen, MD

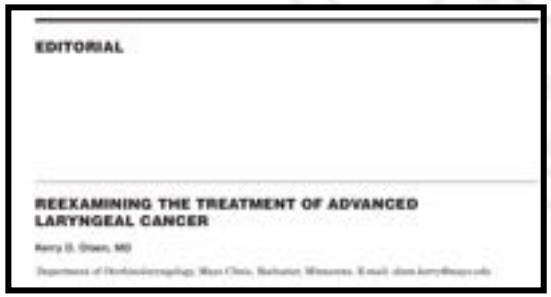
Department of Otorhinolaryngology, Mayo Clinic, Rochester, Minnesota. E-mail: olsen.kerry@mayo.edu

Major effects on management of advanced laryngeal cancers

- ✓ **VALCSG trial: ICT and sequential RT resulted in negligible survival difference over TL + PORT**
- ✓ **RTOG 91-11: concurrent RT-CT was superior to sequential CT and RT and to RT alone for stage III and IV laryngeal cancer (T2-T3 and 'low volume' T4)**

Holsen KD, Head and Neck 2009

- **Selection bias**: most US cancer are advanced glottic cancers; RTOG 91-11 has 68% of supraglottic tumors
- **Mobile vocal cords**: inclusion of pts with 'advanced' laryngeal cancers needing TL; but RTOG 91-11 (42%) and VA (48%) enrolled tumors with mobile cords. No TL needed usually. No real data on fixed cord tumors
- **Unclear definition of 'advanced disease'**: 'low volumeT4' difficult to assess; advanced refers to T stage or overall stage?
- **Health and age of patients**: KPS > 90 (80%); only 70% finished treatment and 5% treatment related death; normally pts: smoking, alcohol, social issues; how results can be applied for > 70 yrs pts?
- **Toxicity and unknown deaths**: G3-G4 toxicity (82% pts); high death rate for unknown causes (aspiration and pneumonia)

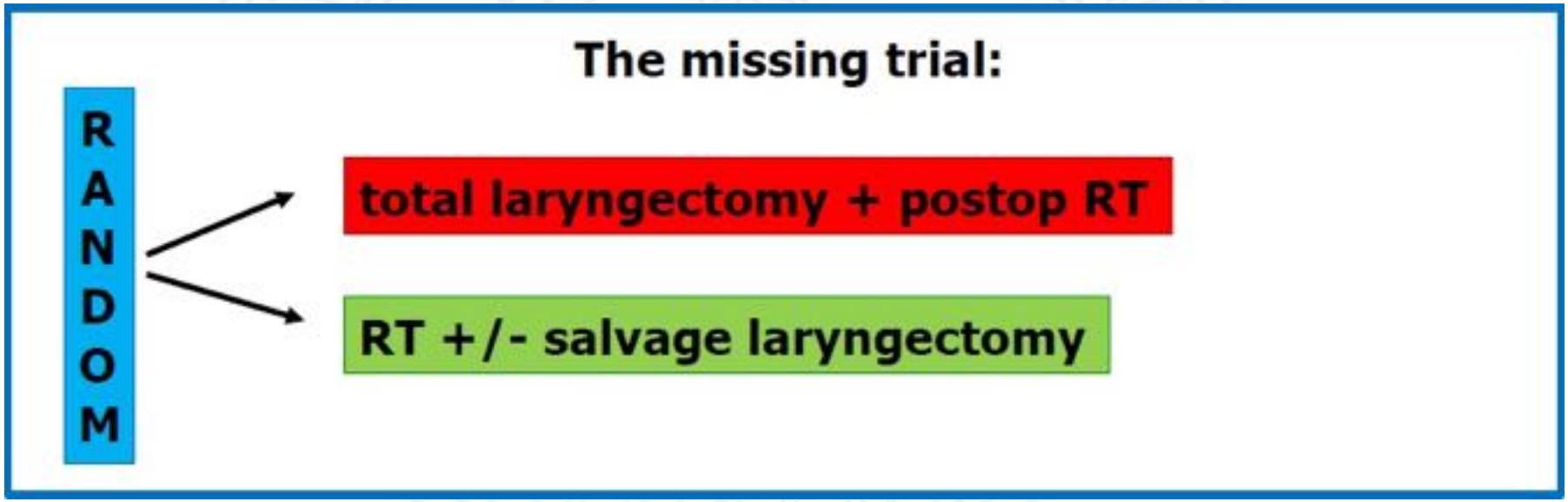

EDITORIAL

REEXAMINING THE TREATMENT OF ADVANCED LARYNGEAL CANCER

Holsen KD, Head and Neck 2009

Surgery and RT approached have been assessed and compared:

- ✓ **On a retrospective frame**
- ✓ **Within different pts/tumors subsets**
- ✓ **During different time periods**



Courtesy JL Lefebvre ESTRO Multidisciplinary Teaching Course H&N Cancer – Cordoba 2012

The Oncologist

Larynx Preservation Clinical Trial Design: Summary of Key Recommendations of a Consensus Panel

K. Kian Ang

Department of Radiation Oncology, University of Texas M. D. Anderson Cancer Center, Houston, Texas, USA

Table 1. Questions about larynx preservation trials addressed by the panel [11]

Patient selection and stratification	Which patients are suitable for larynx preservation trials?
	Once selected, what are the stratification variables of highest importance to obtain the most valuable information from randomized trials?
Assessments	What are the optimal assessments to conduct in patients enrolled in larynx preservation trials to assess the risks and benefits of the study treatment?
Endpoints	What are the optimal endpoints to use in larynx preservation trials?
	How are these endpoints defined?
Tissue banking and biomarker assessment	What are the most promising translational research opportunities that should be explored?
	What clinical trial practices will foster translational research?

Ang KK – The Oncologist 2010

Which patients are suitable for larynx preservation trials?

- Larynx cancer pts (VALCSG)
- Hypopharyngeal cancer pts (EORTC 24891)
- GETTEC + RTOG 91-11 (larynx) and GORTEC 2000-01 + TAX 324 + EORTC 24954-22950 (larynx/ hypopharynx)

Which patients are suitable for larynx preservation trials (T stage)?

Is T4 stage an exclusion criteria?

- Data from VALCSG study had a lower tumor response rate to ICT and had higher salvage laryngectomy rate
- T1-T3 vs T4: OR = 5.6 (95% IC: 1.45-20.8;p=0.0108) for CR
- Among responders to ICT: salvage laryngectomy required in 56% of T 4 pts and 28% of T1-T3 pts (p=0.001)

Clinical practice: T4 disease with massive cartilage involvement or extension in soft tissue through the neck are not considered proper candidates for larynx-preservation

Bradford CR et al – Otolaryngol Head Neck Surg 1999

Which patients are suitable for larynx preservation trials (T and N stage)?

Is T2 disease in pts candidate for partial laryngectomy an appropriate context?

- **Excluded from EORTC 24891, GORTEC 2000-01 and RTOG 91-11**
- **To avoid the need for TL in case of PD after ICT**

Clinical practice: different approaches worldwide but it is generally accepted not to include them

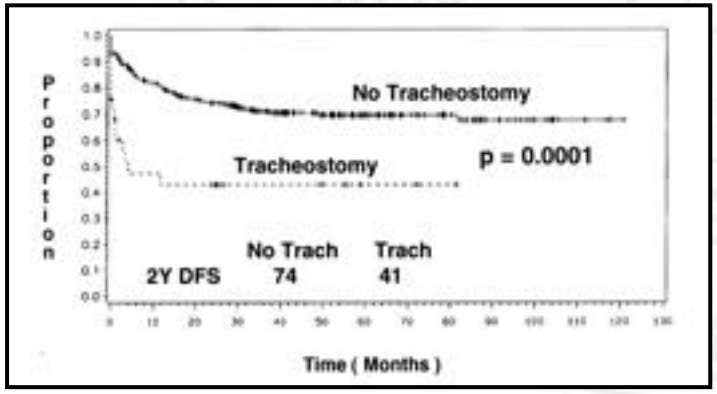
Advanced nodal stage? Not an exclusion criteria

Ang KK – The Oncologist 2010

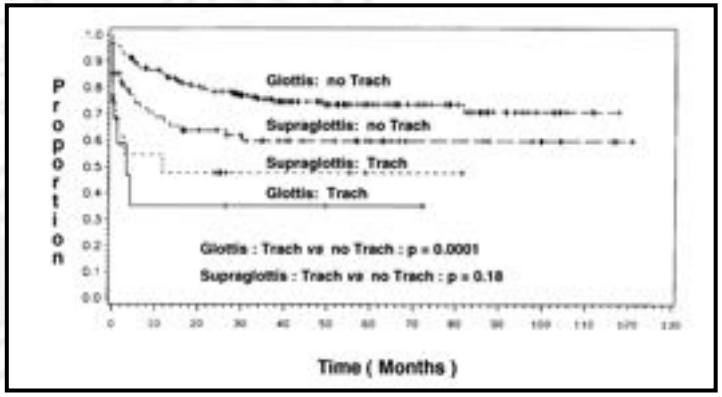
Which patients are suitable for larynx preservation trials (laryngeal function)?

Is laryngeal disfunction in pts candidate for partial laryngectomy an appropriate context?

- **Baseline indicators: tracheotomy , feeding tube and recent history of pneumonia**
- **Pre-treatment tracheotomy: 25% in VALCSG, included in RTOG 91-01 and excluded in EORTC 24654 trial**
- **Influence on outcome: controversial**



MacKenzie et al – IJROBP 1998



Ang KK – The Oncologist 2010

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Cancer Treatment Reviews

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Swallowing dysfunction in head and neck cancer patients treated by radiotherapy: Review and recommendations of the supportive task group of the Italian Association of Radiation Oncology

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Pre-treatment rate: 11-53%

Post-treatment rate: 11-62%

Authors	Year	Pts	Anatomical site	Stage	Aspiration at diagnosis [silent]	After [silent]*
Stenson et al.[45]	2000	79	Oral cavity Oropharynx Larynx Hypopharynx	III–IV	43% (34/78)[b]	
Wu et al.[118]	2000	31	Nasopharynx	Dysphagia		(93.5% (29/31) *[41.9% (13/31)]* *[22% (11/49)]*
Hughes et al.[175]	2000	49	Nasopharynx	Treated pts		
Rosen et al.[174]	2001	27	Oral cavity Oropharynx Larynx Hypopharynx	III–IV	41% (11/27) *[18.5%(5/27)]*	
Eisbruch et al.[24]	2002	22	Not specified	Non resectable	14% (3/22) *[9% (2/22)]*	62% (8/13) *[38% (5/13)]*
Carrara-de Angelis et al.[177]	2003	19	Larynx Hypopharynx	II–IV		26% (5/19) *[26%(5/19)]*
Granet et al.[176]	2003	11	Oropharynx Larynx Hypopharynx	III–IV	18% (2/11)	54% (6/11)
Smith et al.[177]	2004	29	Oropharynx Hypopharynx	III–IV	n.r.	81% (13/16 → 74 Gy) 11% (1/9 → 60 Gy)
Kotz et al.[178]	2004	12	Oral cavity Oropharynx Larynx Unknown	III–IV	0%	41% (5/12)
Nguyen et al.[179]	2006	63	All[§]	II–IV	17% (10/63)[c]	59% (37/63)
Langerman et al.[56]	2007	130	All[§] and unknown	II–IV	53% (33/62) (15% frank[**])	62% (81/130) (23.1% frank aspiration)
van der Molen et al.[2]	2009	55	All[§]	III–IV	18% (10/55) *[13% (7/55)]*	
Dirix et al.[57]	2009	53	All[§]	III–IV	32.1% (17/53)	26.4% (14/53)
Feng et al.[180]	2010	73	Oropharynx	III–IV	11% (8/73)	26% (18/73) *[60% (12/18)]*

Russi EG et al; Cancer Treat Rev 2013

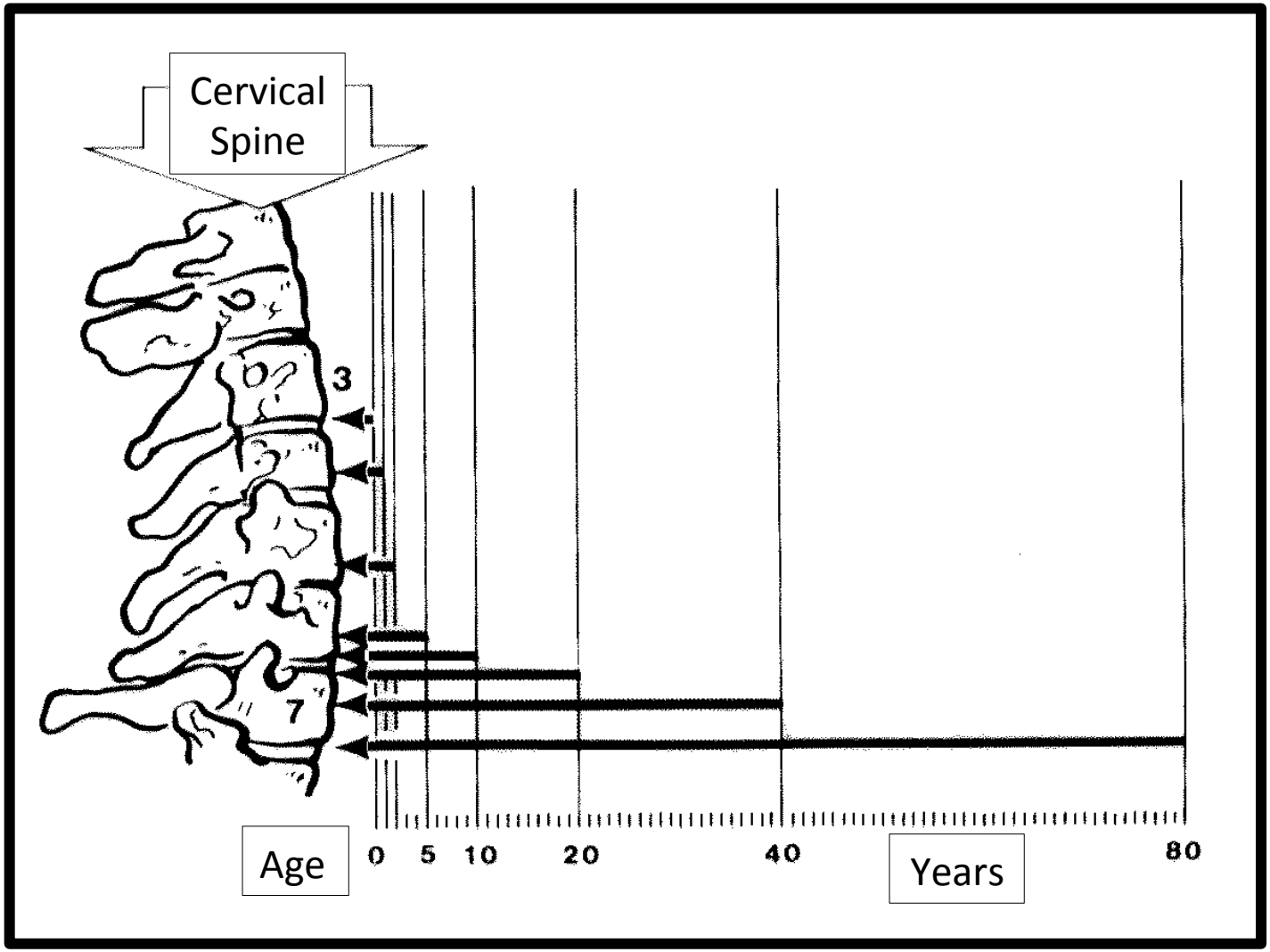
Age

Is age > 70 an exclusion criteria:

- **MACH-CH meta-analysis: pts > 70 yrs did not benefit from addition of CT**
- **Potential worse tolerance to treatment**
- **Less functional larynx**

Ang KK; The Oncologist 2010

Presbiphagia



Baseline assessment

Swallowing function

- Modified barium swallowing
- Penetration aspiration scale
- Oropharyngeal swallow efficiency

Voice quality

- Voice Handicap Index-10 (VHI-10)
- Voice-related QoL

Ang KK; The Oncologist 2010

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Systematic review

A systematic review of current and emerging approaches in the field of larynx preservation

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Endpoints definition

Study	Primary End Point	Secondary End Points
VALCSG [5]	LP	OS Tumor response Patterns of relapse
EORTC 24891 [7]	LP	OS Survival with functional larynx cancer related death PFS
GETTEC [14]	OS PFS	LP
RTOG 91-11 [8]	LP	LFS laryngeal function preservation (speech and swallowing)*
GORTEC [12]	LP	OS DFS, laryngoesophageal dysfunction-free survival *
EORTC 24954 [50]	Survival with functional larynx. Larynx in place, without tumor, tracheotomy or feeding tube	PFS
TREMPLIN [17]	LP	Larynx function preservation, OS feasibility of salvage surgery tolerance to treatment

Denaro et al, R&O 2014

Primary endpoints definition

Larinx in place

Without capturing other data: Tracheotomy? Feeding tube?

LPR (3y) Gortec 2000-01

Larinx in place, and death from local progression

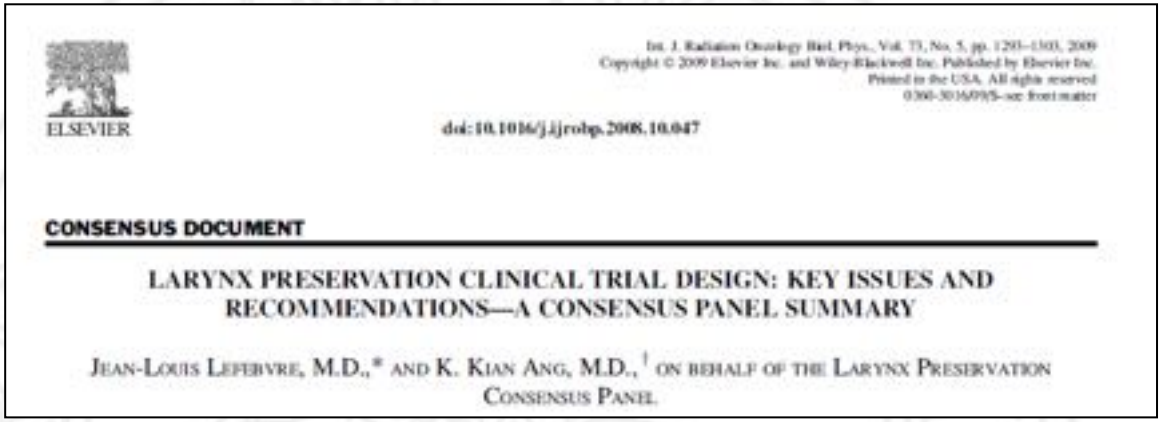
Lefebvre 1996 EORTC 24891

Survival with a functional larynx

Survival is included in the primary endpoint (few studies)

EORTC 24954 (Lefebvre 2009)

Primary endpoint



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0360-3016/09/$–see front matter

doi:10.1016/j.ijrobp.2008.10.047

CONSENSUS DOCUMENT

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

JEAN-LOUIS LEFEBVRE, M.D.,* AND K. KIAN ANG, M.D.,† ON BEHALF OF THE LARYNX PRESERVATION CONSENSUS PANEL

Laryngo-Esophageal Dysfunction (LED)-free survival (includes death, local relapse, total or partial laryngectomy, tracheotomy at 2 years, or feeding tube at 2 years)

Lefebvre JL et al, IJROBP 2009

Improving ICT

TPF is the standard of ICT for larynx preservation but

- no impact on survival (over PF)
- selection of pts (all are not offered RT)
- acute toxicity

How to improve efficacy (survival, response rate):

- more cycles of TPF?
- TPF+Erbitux instead of TPF?

How to decrease toxicity:

- TPErbitux instead of TPF?
- supportive care?

Improving CRT:

RT + 3 cycles of CDDP is the standard of CRT for larynx preservation but

- no impact on survival (over ICT)
- acute toxicity
- late toxicity

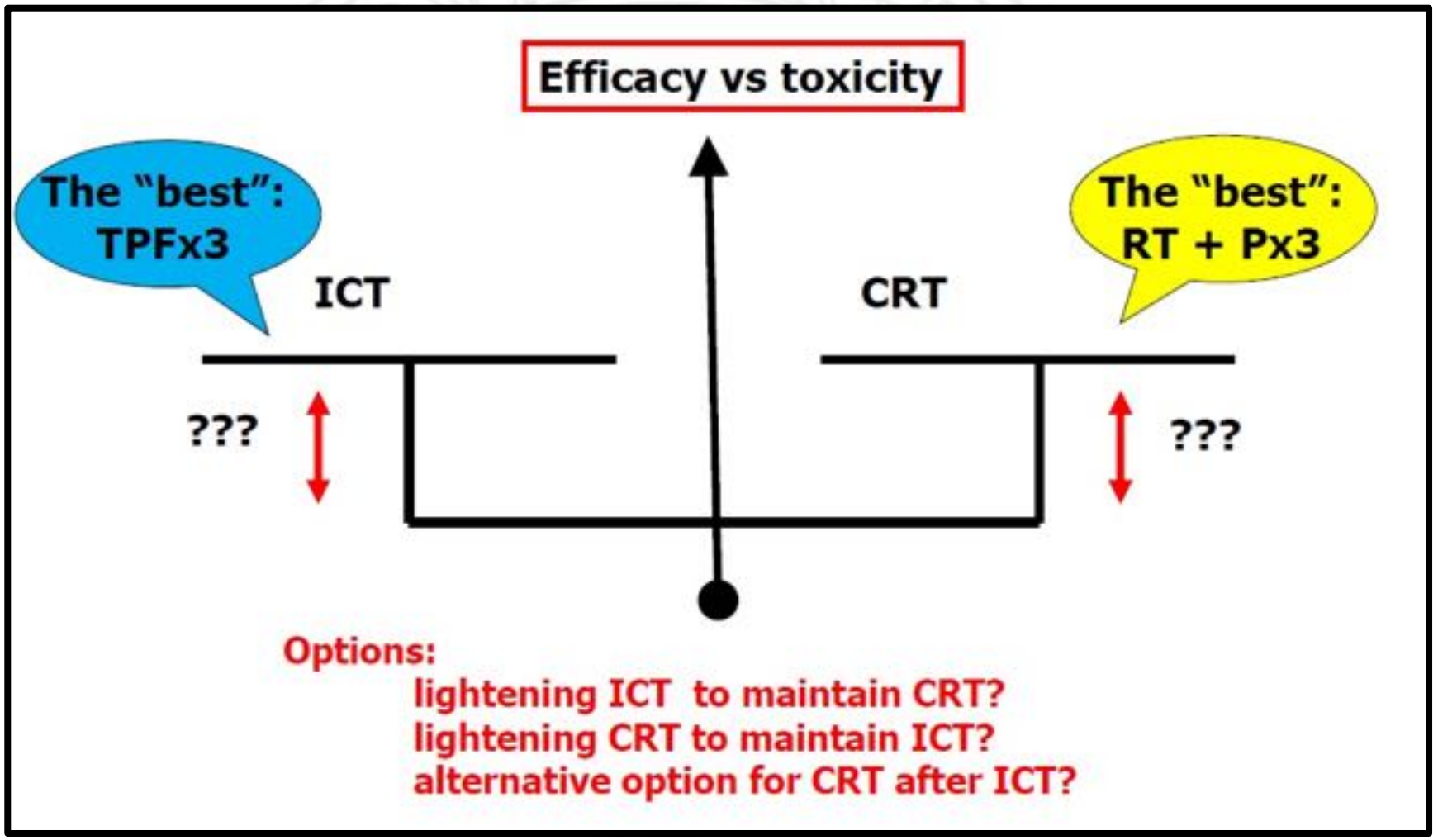
How to improve efficacy (survival, response rate):

- RT + CDDP + Erbitux

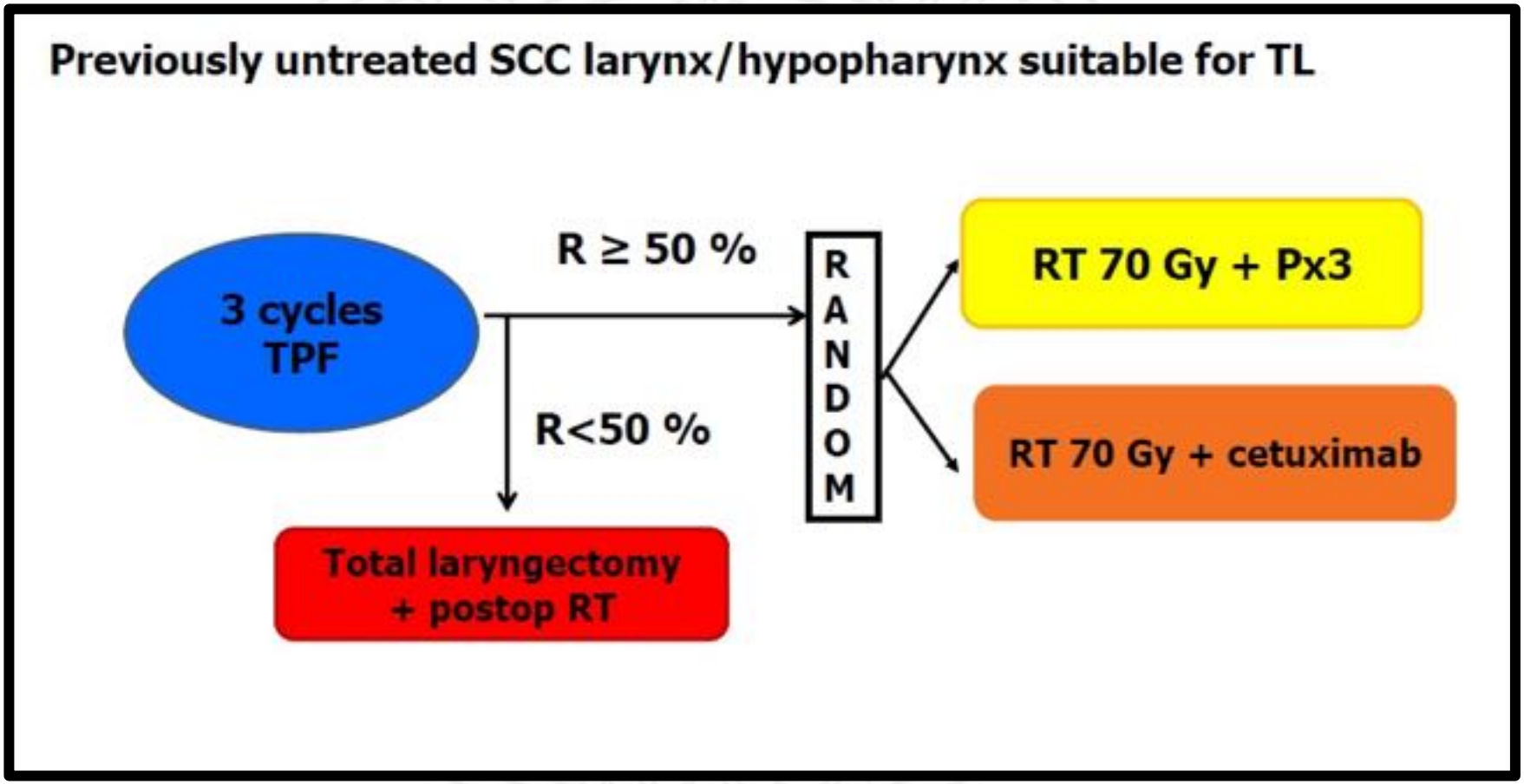
How to decrease toxicity:

- weekly CDDP?
- carboP instead of CDDP?
- Erbitux instead of CDDP?
- alternating CRT with E?
- supportive care?
- new RT techniques

Sequencing ICT and CT-RT: which option?

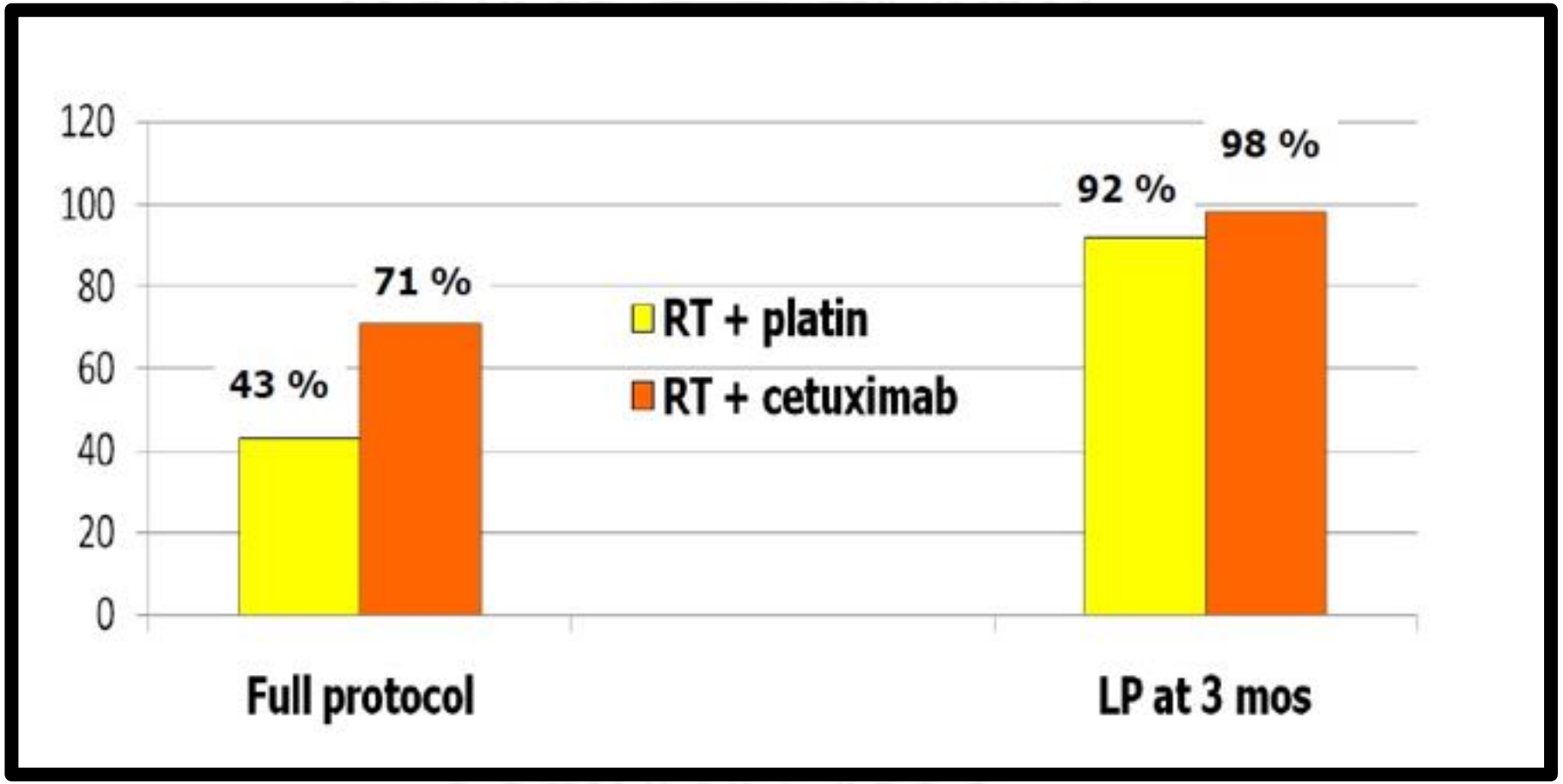


GORTEC-GETTEC randomized phase II trial: TREMPLIN



Lefebvre JL– JCO 2013

GORTEC-GETTEC randomized phase II trial: TREMPLIN



Lefebvre JL– JCO 2013

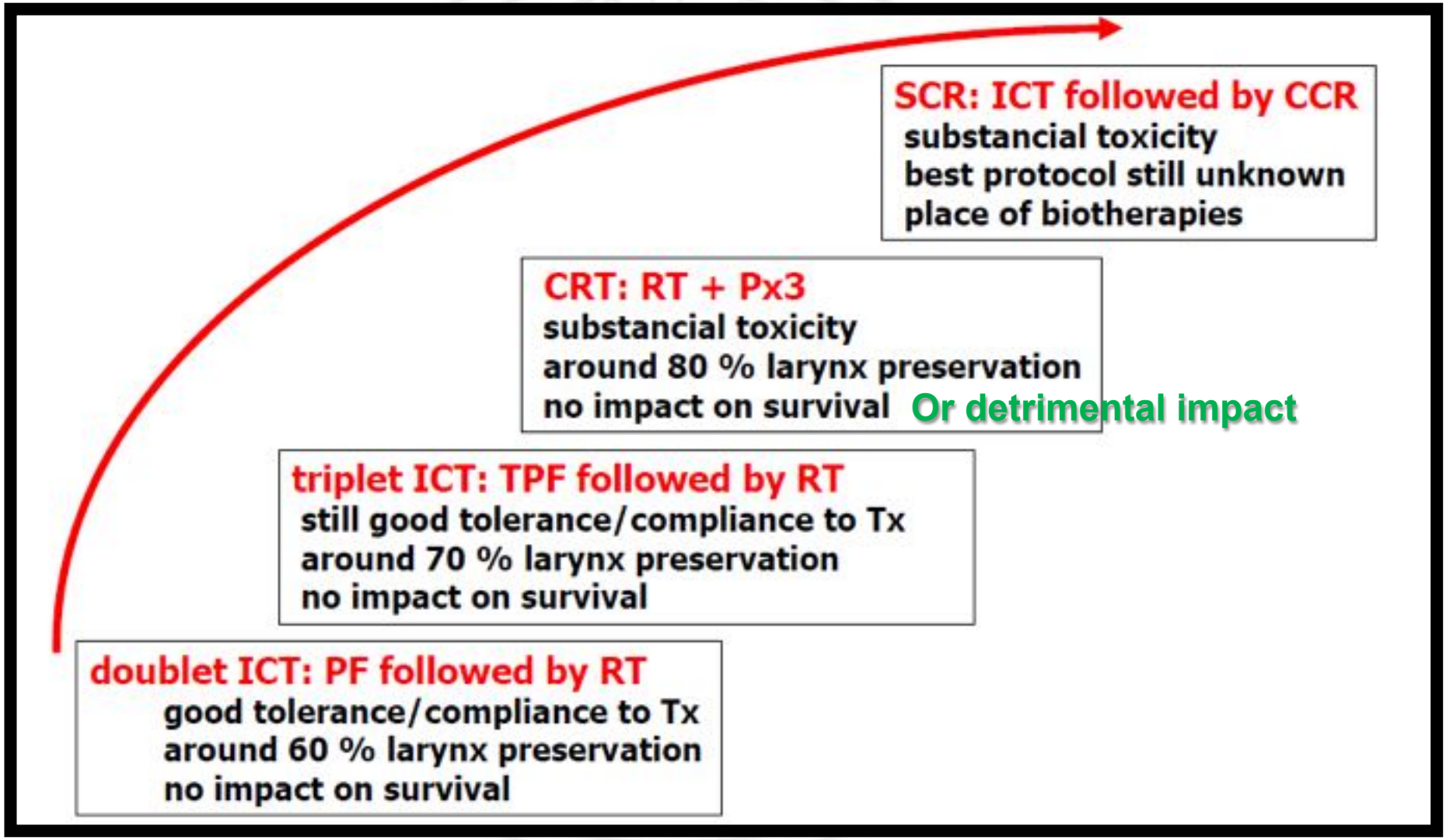
GORTEC-GETTEC randomized phase II trial: TREMPLIN

1) Primary endpoint at 3 months after treatment
   - larynx preservation → no significant difference

2) Secondary endpoints at 18 months after treatment:
   - Larynx function preservation → no significant difference
   - Overall survival → no significant difference
   - Acute toxicity compromising the treatment and late toxicity
     → more common in the cisplatin arm
   - Local control and salvage surgery
     → trend for fewer local failures in the cisplatin arm
     → successful salvage only in the cetuximab arm
     → no significant difference for ultimate local control

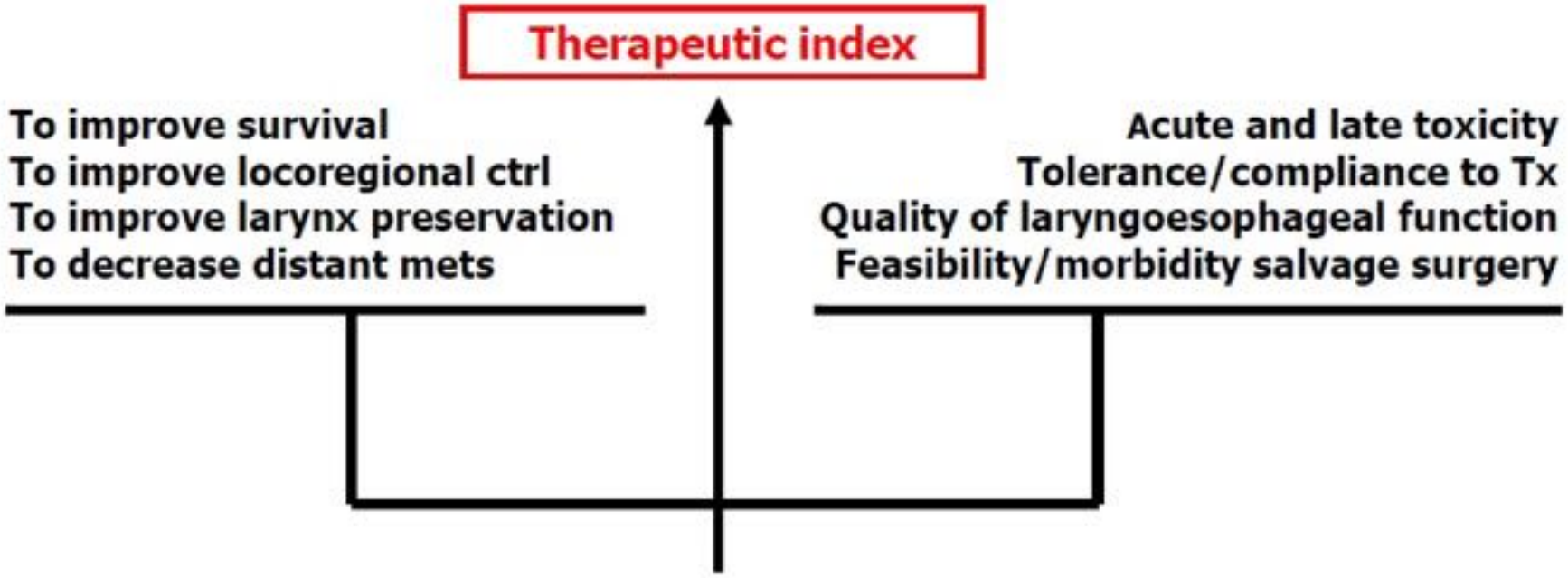
Lefebvre JL– JCO 2013

Larynx preservation trend



Courtesy JL Lefebvre ESTRO Multidisciplinary Teaching Course H&N Cancer – Cordoba 2012

- Survival remains rather disappointing:
  5-yr OS = 45-55 % according to primary site
- Larynx preservation up to 80 %, but larynx function not always clearly reported



Courtesy JL Lefebvre ESTRO Multidisciplinary Teaching Course H&N Cancer – Cordoba 2012

LAHNC: larynx and hypopharynx

Due to the complexity and the multiplicity of clinical situations in the daily practice, asserting that there is only one golden standard of treatment for advanced larynx/hypopharynx SCC is meaningless.
There is a panel of therapeutic options:

- **surgery ± PORT or POCRT**
- **CRT**
- **ICT* followed by RT**

- **RT ± altered fractionation**
- **RT + biotherapy****

- **clinical trials (sequential approaches)**

* TPF > PF ** Cetuximab

Multidisciplinary Team Approach

Pierfrancesco Franco

Grazie dell' attenzione

Mario Schifano – Indicazione - 1963