

*Sequencing Chemo with Radiation therapy
Locally Advanced Head and Neck Cancer*

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H&N Ca - Disease Burden

- ▶ 15-20% of all cancers in India, 8% worldwide
- ▶ 60% presents with locally advanced disease
- ▶ Average 3yr survival – 30%-50%

HNSCC - Goals of Rx

- Survival - Cure
- Preserving Organ & Function
- Minimizing the morbidity

Quantity and Quality of life!

LAHNSCC - How best we can achieve?

- Surgery vs Radiotherapy
- Radiotherapy vs RT + Chemo
- What drugs? Two vs Three drugs
- Neoadj Chemo vs Concurrent
- Conclusions



Surgery vs Radiotherapy

Can we preserve the Organ & Function ?
Without compromising the survival?

Locally advanced Laryngeal & Hypo-pharyngeal ca

Dept of Veterans Affairs Laryngeal Study

NEJM '91

VA study: 332 pts

- **Experimental arm** Larynx Preservation
 - 2 cycles of chemo (Cisplatin and 5 FU)
 - PR or CR had 3rd cycle of chemo followed by XRT
 - Non-responders - TL+PORT
- **Control arm** Total Laryngectomy
 - TL + PORT

Dept of Veterans Affairs Laryngeal Study Group, *NEJM* '91

VA study

Stage III/IV

Glottic/supraglottic larynx

N=332

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Experimental arm

3 cycles PF
in responders RT

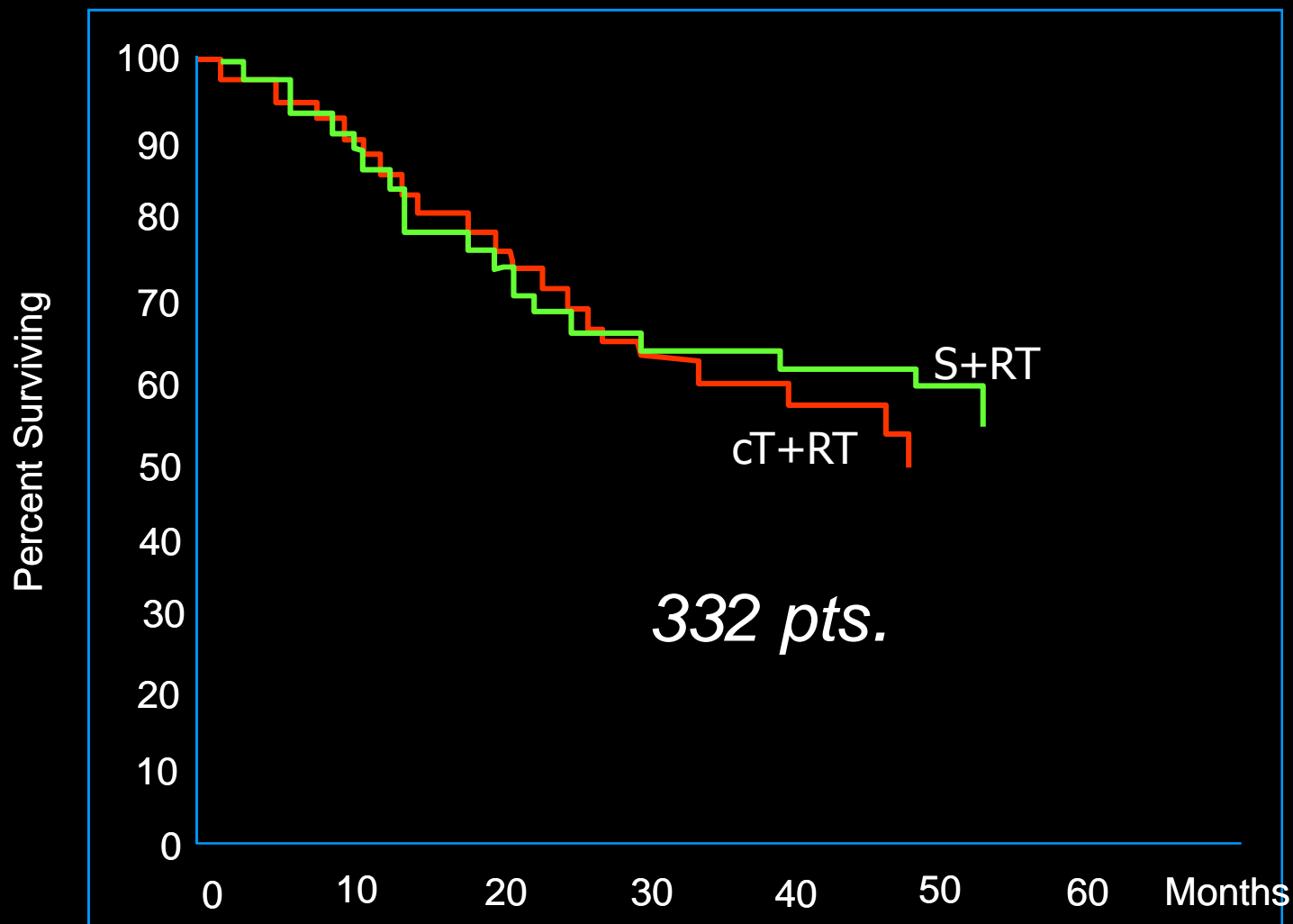


Control arm

Non Responders
TL + RT

✓ *Neo adj Chemo --→ RT alone*

Veterans Affairs Laryngeal Cancer Study Grp



OS at 2 yrs - 68 % both groups

Surgery vs Radiotherapy

VA study: results

- 2 & 10yr f.u. show no significant diff in survival
- Overall laryngeal preservation rate =64%

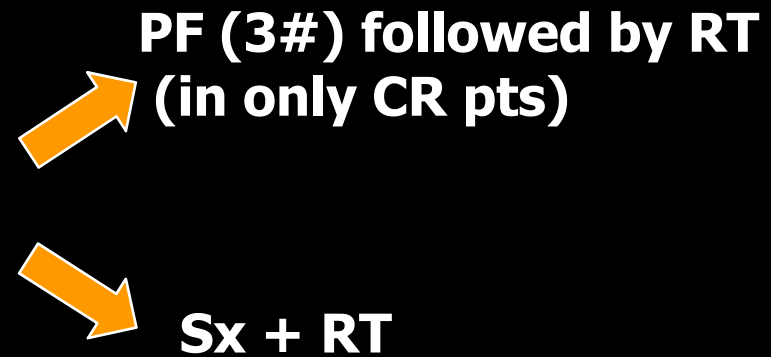
NEJM '91

Larynx Preservation in Pyriform Sinus Ca EORTC Phase III Trial

JNCI '96

Hypopharynx 78%
Larynx 22%
T2(19%), T3(75%), T4(6%)
N= 202

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- OS : chemo (57%) > surgery (43%) at 3 yr, equal at 5 yrs
- No difference in Loco-regional failure
- Increase in distant mets in surgery (36%) Chemo (25%)

Surgery vs Radiotherapy

VA and EORTC studies

- Overall survival is similar
- Organ preservation is feasible
- Better QOL with CT +RT
- Exact role of CT not certain!

Neo adj CT => RT alone is equally good to Surg!

Terrell JE, Arch Otolaryngol Head Neck Surg '98

➤ RT alone or RT + CT ?

Defining the role of chemo..

- Does it make a diff?
- Neo adjuvant? or
- Concurrent?

Defining the role of Chemotherapy...

- RTOG 91-11

Determine role of induction vs concurrent chemo vs radiation alone in

Laryngeal preservation for pts with Stage 3 & 4, SCC of Larynx

RTOG 91-11

Larynx: stage III-IV

Karnofsky \geq 60
Glottic or supra-glottic SCC
No metastasis
No synchronous T
No previous RT

Randomization

RT
(n=170)

70 Gy
2 Gy/F
7 weeks

Ind. CT =>RT or S
(n=171)

CDDP 100mg/m²d1
5FU 1g/m²,d1-5
X 2-3
 \geq PR: 70 Gy
< PR: surgery

Conc CT+RT
(n=169)


70 Gy, 2Gy/F, 7 w
CDDP 100 mg/m²,
D 1, 22, 43

Forastiere, NEJM 2003, JCO 2006

RTOG 91-11 study: results

- OS did not differ @ 3 & 5 year
 - 76% at 2 years overall
- Local-regional control
 - **Conc Chemo / RT > induction chemo or XRT**
- Laryngeal preservation at 3.8 yrs median f/u
 - **84% conc CT/RT > 72%induc > 67% XRT**

✓ **Concurrent Chemoradiotherapy**



➤ **Role of Chemotherapy**
Neo-adj vs Concurrent ?

Chemotherapy added to locoregional treatment for head and neck squamous-cell carcinoma: three meta-analyses of updated individual data

Pignon group for MACH-NC collaborative Grp

Lancet 2000

*J P Pignon, J Bourhis, C Domenge, L Designé, on behalf of the MACH-NC Collaborative Group**

- No. of patients analyzed =10,741
- 63 Randomised trials 1965-1993

Trial Category	No. of Trials	No. Patients	Absolute Benefit at 5 years	p value
All trials	65	10850	+4	<0.0001
Adjuvant	8	1854	+1	0.74
Induction	31	5269	+2	0.10
Concomitant	26	3727	+8	<0.0001

Pignon et al Lancet 2000

Conclusions

- ICT inferior to Conc CTRT in terms of Organ preservation, Loco-regional control
- No survival benefit with NACT
- **Cisplatin + 5-FU** most effective combination

Data for conc CT+RT more robust & consistent



New Neo adjuvant trials.....

Addition of Doce/pacl?

- TAX323,
- TAX 324,
- Hitt 2005,
- Paccognella 2006,
- Hitt 2009....

ORIGINAL ARTICLE

Cisplatin, Fluorouracil, and Docetaxel in Unresectable Head and Neck Cancer

Jan B. Vermorken, M.D., Ph.D., Eva Remenar, M.D., Carla van Herpen, M.D., Ph.D.,
Thierry Gorlia, M.Sc., Ricard Mesia, M.D., Marian Degardin, M.D.,
John S. Stewart, M.D., Svetislav Jelic, M.D., Jan Betka, M.D.,
Joachim H. Preiss, M.D., Ph.D., Danielle van den Weyngaert, M.D.,
Ahmad Awada, M.D., Ph.D., Didier Cupissol, M.D., Heinz R. Kienzer, M.D.,
Augustin Rey, M.D., Isabelle Desauvais, M.Sc., Jacques Bernier, M.D., Ph.D.,
and Jean-Louis Lefebvre, M.D., for the EORTC 24971/TAX 323 Study Group*

Vermorken et al, EORTC 24971, TAX 323 study

Unresectable SCC - Head and Neck Ca
(excluding NP, nasal and paranasal cavities)

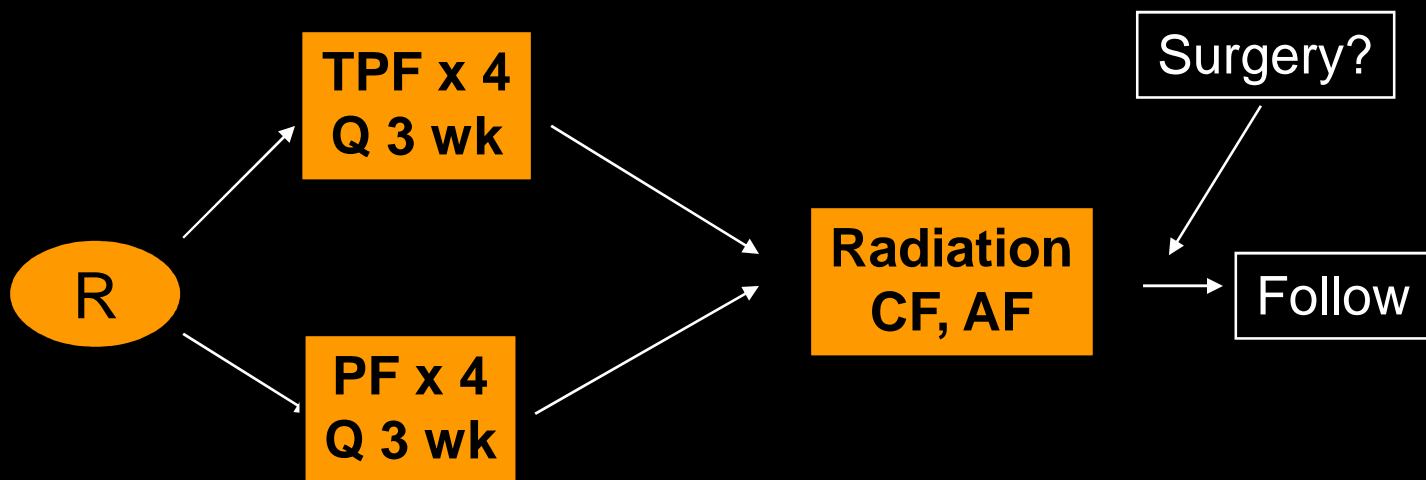
Stage III or IV, Mo
Age 18 to 70
Median f/u 32.5 mths

Vermorken et al, EORTC 24971, TAX 323

Study Design

*Unresectable
SCCHN*

Stratification:
Institution
Primary Site



TPF – 181 pts, PF – 177 pts

Response assessment at end of cycles 2&4

Chemotherapy Regimens

Standard arm (PF)

- Cisplatin 100 mg/m^2 , day 1
- 5-FU $1000 \text{ mg/m}^2/\text{day}$, day 1 to 5

Experimental arm (TPF)

- Docetaxel 75 mg/m^2 , day 1
- Cisplatin 75 mg/m^2 , day 1
- 5-FU $750 \text{ mg/m}^2/\text{day}$, day 1 to 5

End point	TPF (mths)	PF (mths)	P value
Median PFS	11	8.2	0.007
Median OS	18.8	14.5	0.02

Median fu 38 months

Drop outs!....

	TPF	PF
Protocol completed	75.7%	65.7%
Chemo discontinued	38 pts (21%)	60 pts (34%)

.....Significant!

Vermorken et al, EORTC 24971, TAX 323

- CR significant in TPF arm
- Overall RR significant in TPF arm in induction & RT phase
- 28% reduction in rate of progression or death

Toxicity

- Alopecia, infections more in TPF arm
- Severe leucopenia more in TPF
- Vomiting, stomatitis, diarrhea, hearing loss more in PF arm
- Anemia, thrombocytopenia more in PF?

ORIGINAL ARTICLE

TAX 324

Cisplatin and Fluorouracil Alone or with Docetaxel in Head and Neck Cancer

Marshall R. Posner, M.D., Diane M. Hershock, M.D., Ph.D., Cesar R. Blajman, M.D.,
Elizabeth Mickiewicz, M.D., Eric Winkvist, M.D., Vera Gorbounova, M.D.,
Sergei Tjulandin, M.D., Dong M. Shin, M.D., Kevin Cullen, M.D.,
Thomas J. Ervin, M.D., Barbara A. Murphy, M.D., Luis E. Raez, M.D.,
Roger B. Cohen, M.D., Monica Spaulding, M.D., Roy B. Tishler, M.D., Ph.D.,
Berta Roth, M.D., Rosana del Carmen Viroglio, M.D.,
Varagur Venkatesan, M.B., B.S., Ilya Romanov, M.D., Ph.D., Sanjiv Agarwala, M.D.,
K. William Harter, M.D., Matthew Dugan, D.O., Anthony Cmelak, M.D.,
Arnold M. Markoe, M.D., Sc.D., Paul W. Read, M.D., Ph.D., Lynn Steinbrenner, M.D.,
A. Dimitrios Colevas, M.D., Charles M. Norris, Jr., M.D.,
and Robert I. Haddad, M.D., for the TAX 324 Study Group*

TAX 324: study design

Locally advanced
SCCHN:
organ preservation,
resectable with
low curability,
unresectable

R

3 x TPF q3w

T	Taxotere	75 mg/m ²	D1
P	Cisplatin	100 mg/m ²	D1
F	5-FU	1000 mg/m ²	D1-5

3 x PF q3w

P	Cisplatin	100 mg/m ²	D1
F	5-FU	1000 mg/m ²	D1-5

Carboplatinum
AUC 1.5 weekly



Daily
radiotherapy



TAX 324	TPF	PF
Median OS	71mths	30mths
3yr OS	62%	48% (p=.002)
Median PFS	36 mths	13 mths
LRF	30%	38% (p=.04)
Dist mets	5%	9%
Grade3/4 neutropenia	83%	56%
Grade3/4 thrombocytopenia	4%	17%
Rx delays	29%	65% (p=.001)

Sequential therapy for the locally advanced larynx and hypopharynx cancer subgroup in TAX 324: survival, surgery, and organ preservation

M. R. Posner^{1*}, C. M. Norris², L. J. Wirth¹, D. M. Shin³, K. J. Cullen⁴, E. W. Winquist⁵, C. R. Blajman⁶, E. A. Mickiewicz⁷, G. P. Frenette⁸, L. F. Plinar⁹, R. B. Cohen¹⁰, L. M. Steinbrenner¹¹, J. M. Fraue¹², V. A. Gorbunova¹³, S. A. Tjulandin¹⁴, L. E. Raez¹⁵, D. R. Adkins¹⁶, R. B. Tishler¹⁷, M. R. Roessner¹⁸ & R. I. Haddad¹ for the TAX 324 Study Group

TAX 324

TPF

PF

Median OS

59 mths

24 mths

Median PFS

21 mths

11 mths

Drop outs!

Patients	TPF	PF
Chemo discontinuation	68 pts (27%)	79 pts (32%)

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**

Questions:

Is survival benefit sustained at longer follow-up?

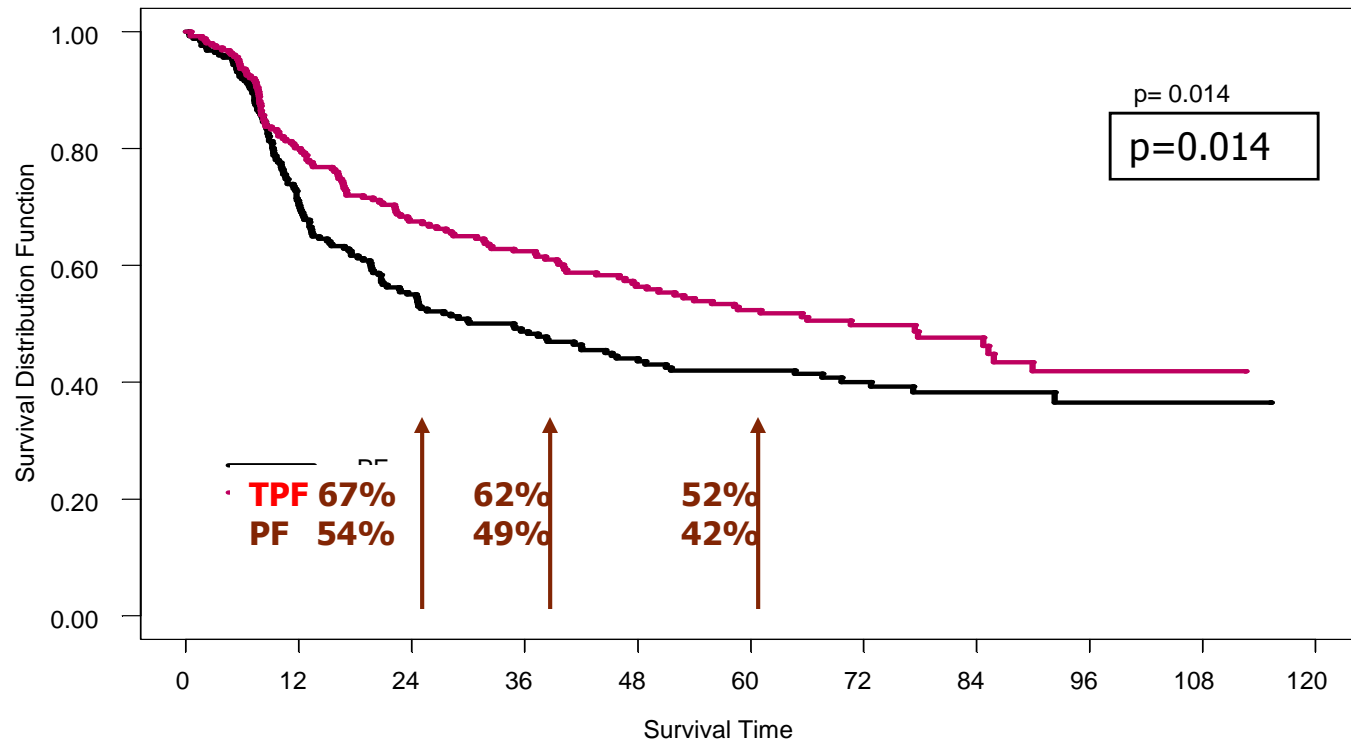
Any sub-sites that benefit particularly - or not?

Tracheotomy and gastric feeding tube at longer follow-up?

Feb 2011, Lancet Oncology

TAX 324 5-year follow-up: Overall Survival

Feb 2011, Lancet Oncology



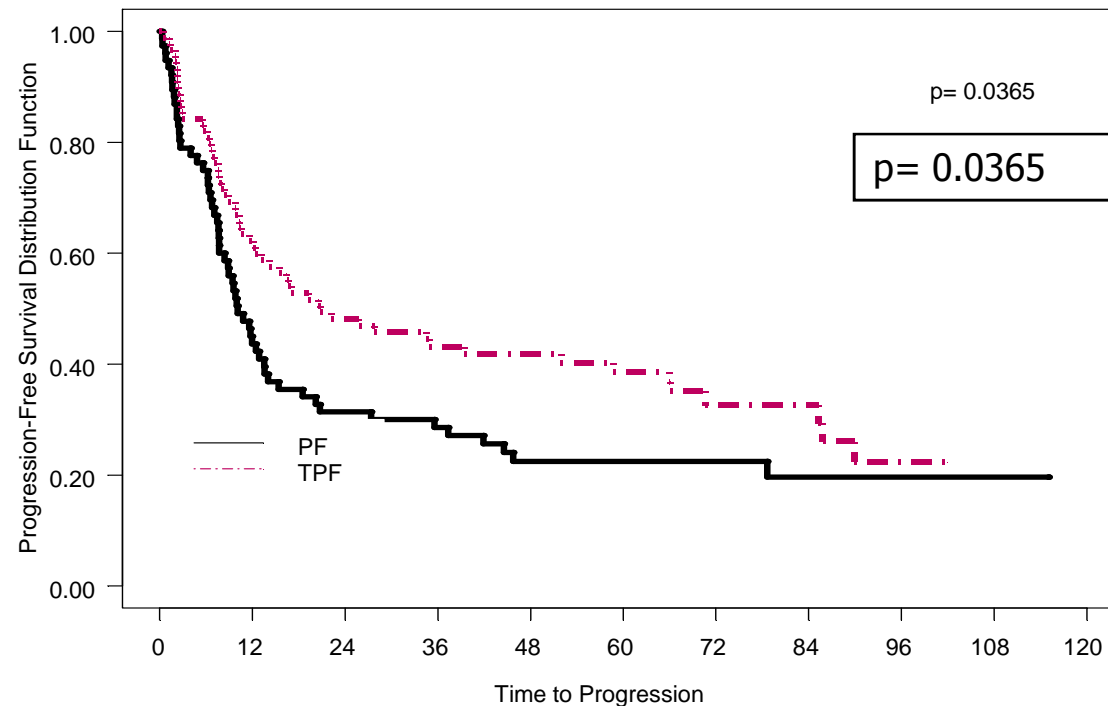
Number of patients at risk
PF :
TPF :

246	173	134	112	88	76	52	28	17	4
255	200	166	141	116	96	64	36	20	6

Sustained survival advantage at 5 years for TPF versus PF
Median OS - 71 vs 35 months (HR 0.74, p=0.0129)

TAX324 5-year follow-up: PFS

Larynx and Hypopharynx



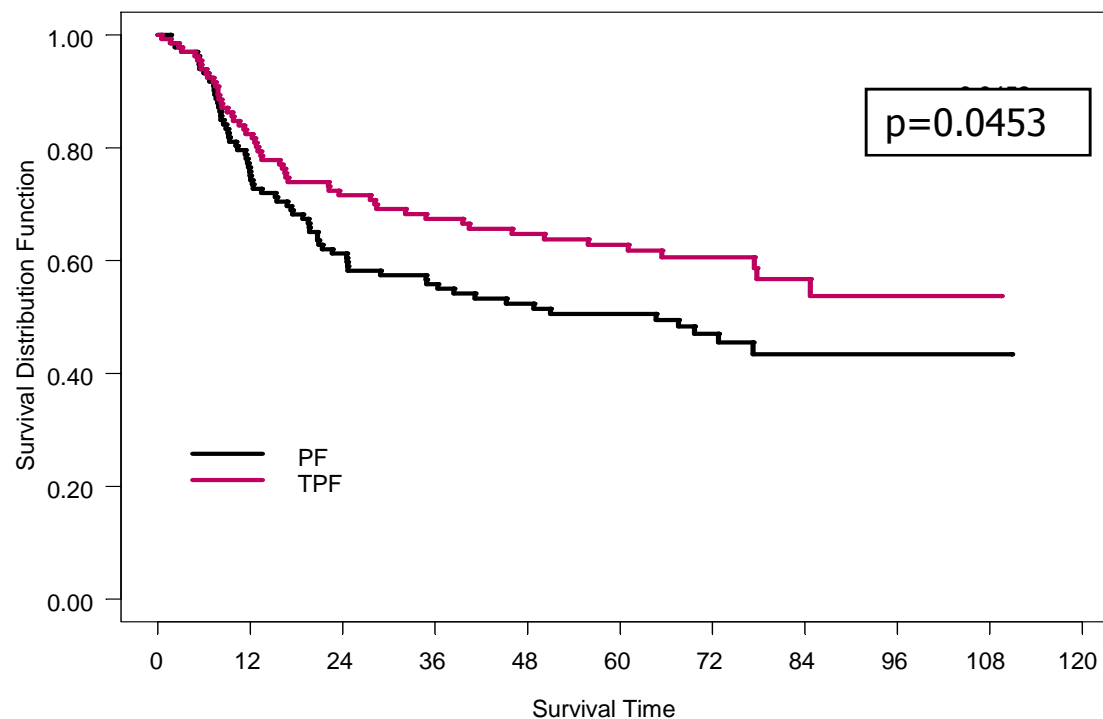
Number of patients at risk
 PF :
 TPF :

	0	12	24	36	48	60	72	84	96	108	120
PF :	76	33	24	21	15	14	10	7	5	2	
TPF :	90	54	41	34	28	24	14	11	4		

Sustained improvement in patients with laryngeal and hypopharyngeal primary tumors with a 50% reduction of the risk of progression or death compared with PF (20.86 months, CI 12.42-58.65 versus 10.09 months, CI 7.72-13.60).

Feb 2011, Lancet Oncology

TAX324 5-year follow-up: OS Oropharynx



Number of patients at risk
PF :
TPF :

132	100	81	70	59	50	32	15	9	2
132	108	92	78	70	63	43	21	13	5

Improvement in OS for pts on TPF with Oroph tumors at 5 years ($p=0.045$)

TAX324 5-year follow-up: Overall Survival

	TPF (255)	PF (NR246)	Hazard Ratio	P Value
Overall Survival (Mo) at 3y	71	30	.70 (.54-.90)	.006
at 5y	71	35	.74 (.58-.94)	.014
Oropharynx at 3y	NR	NR	.70 (.47-1.03)	.07
at 5y	NR	65	.69 (.58-.94)	.045
Hypopharynx at 3y	32	20	.67 (.37- 1.20)	.18
at 5y	32	20	.74 (.42-1.3)	.29
Larynx at 3y	59	25	.58 (.32- 1.04)	.07
at 5y	58	25	.72 (.41-1.24)	.29
Oral Cavity at 3y	37	14	.87 (.47-1.6)	.66
at 5y	37	14	.89 (.5-1.59)	.70

TAX324 5-year follow-up:

No significant difference in long-term toxicities

Toxicity	TPF N (%)	PF N (%)	Fisher's exact test, two sided
Enteral feeding tube	3/91 (3%) n/a 40*	8/63 (13%) n/a 30 *	P=0.14
Tracheostomy	6/86 (7%) n/a 39 *	8/63 (12%) n/a 30 *	P=0.60

No statistically significant difference in tracheostomy and enteral feeding tube dependence.

* no information could be obtained

Tax 323, 324 results....

- TPF is superior to PF as induction in LAHNC
- TPF improve survival, loco-regional control
- TPF induction reduces risk of death by 30%
- No additional toxicity with Docetaxel to PF

Pitfalls...

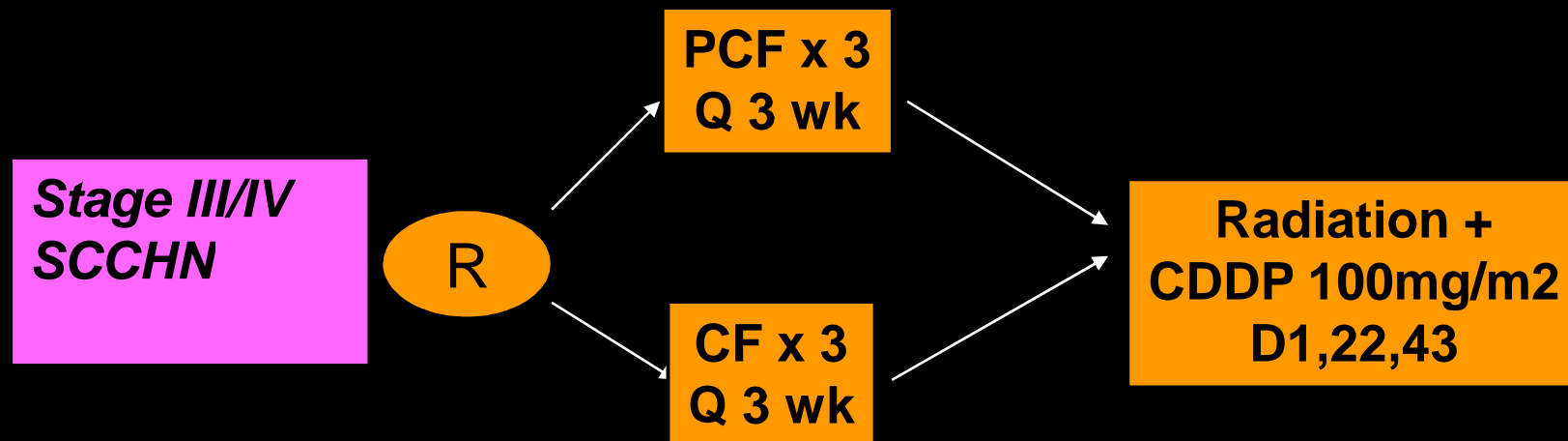
- Three drugs (TPF) vs two drugs (PF)
- Not compared with chemo-radiation
- Weekly carboplatin is not the standard (TAX 324)
- Significant drop outs and treatment delays

Hitt trial 2005

Phase III Study Comparing Cisplatin Plus Fluorouracil to Paclitaxel, Cisplatin, and Fluorouracil Induction Chemotherapy Followed by Chemoradiotherapy in Locally Advanced Head and Neck Cancer

Ricardo Hitt, Antonio López-Pousa, Javier Martínez-Trufero, Vicente Escrig, Joan Carles, Alfredo Rizo, Dolores Isla, M. Eugenia Vega, Juan L. Martí, Francisco Lobo, Pedro Pastor, Vicente Valentí, Joaquín Belón, Miguel A. Sánchez, Carlos Chaib, Cinta Pallarés, Antonio Antón, Andrés Cervantes, Luis Paz-Ares, and Hernán Cortés-Funes

Hitt et al Ph III, JCO 2005



PCF – 189 pts, CF – 193 pts
Median f/u 23.2 mths

No direct Comparison to CTRT

Hitt et al 2005, JCO 2005

End point	PCF	CF
Median OS	43 mths	37 mths (p=.03)
2yr OS	66.5%	53.6%
Median TTF	20 mths	12 mths (p=0.003)
TTF	57%	66%

TPF is superior to PF

Randomized Trial of Induction Chemotherapy With Cisplatin and 5-Fluorouracil With or Without Docetaxel for Larynx Preservation

Yoann Pointreau, Pascal Garaud, Sophie Chapet, Christian Sire, Claude Tuchsais, Jacques Tortochaux, Sandrine Faivre, Stephane Guerrif, Marc Alfonsi, Gilles Calais

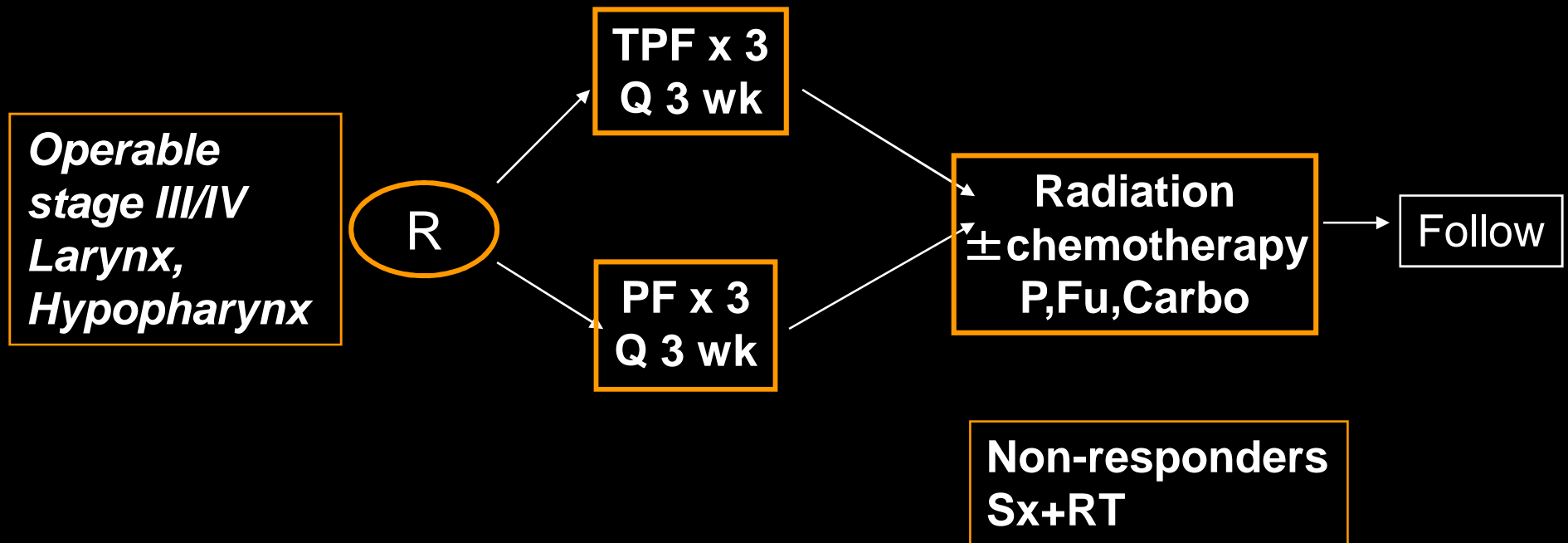
213 patients randomized

Median follow-up 36months

Primary end point-Larynx preservation rate

Randomized Trial of Induction Chemotherapy With Cisplatin and 5-Fluorouracil With or Without Docetaxel for Larynx Preservation

Yoann Pointreau, Pascal Garaud, Sophie Chapet, Christian Sire, Claude Tuchais, Jacques Tortochaux, Sandrine Faivre, Stephane Guerrif, Marc Alfonsi, Gilles Calais



Larynx preservation is better with TPF

	TPF Arm	PF Arm
Rx as per Protocol	90%	80%
ORR	80%	59%, p=0.002
3yr Lnx Preservation	70%	57%, p=0.03
DFS	58%	44%, p=ns
OS	60%	60%

Better larynx preservation rate with TPF as compared to PF
Better tolerance with TPF
No improvement in OS

Calais G et al



*Tax 323, 324,
Hitt et al, Calais G et al...*

- TPF is superior to PF as induction
- Better Larynx preservation is possible
- No direct comparison to CT+RT



➤ Neo Adj vs Conc CT

Phase II RCT Paccagnella A et al, *Proc ASCO 2006*

Conc CRT vs TPF => Conc CRT in LAHNC

Locally advanced
SCCHN:
unresectable
Stage III/IVa



3 x TPF q3w

T	Taxotere	75 mg/m ²	D1
P	Cisplatin	80 mg/m ²	D1
F	5-FU	800 mg/m ²	D1-4

→ Same CRT

2 x PF wk 1&6

P	Cisplatin	20 mg/m ²	D1-4
F	5-FU	800 mg/m ²	D1-4

→ Daily radiotherapy

Paccagnella A et al, Phase II RCT

Proc ASCO 2006

Conc CRT vs TPF => Conc CRT in LAHNC

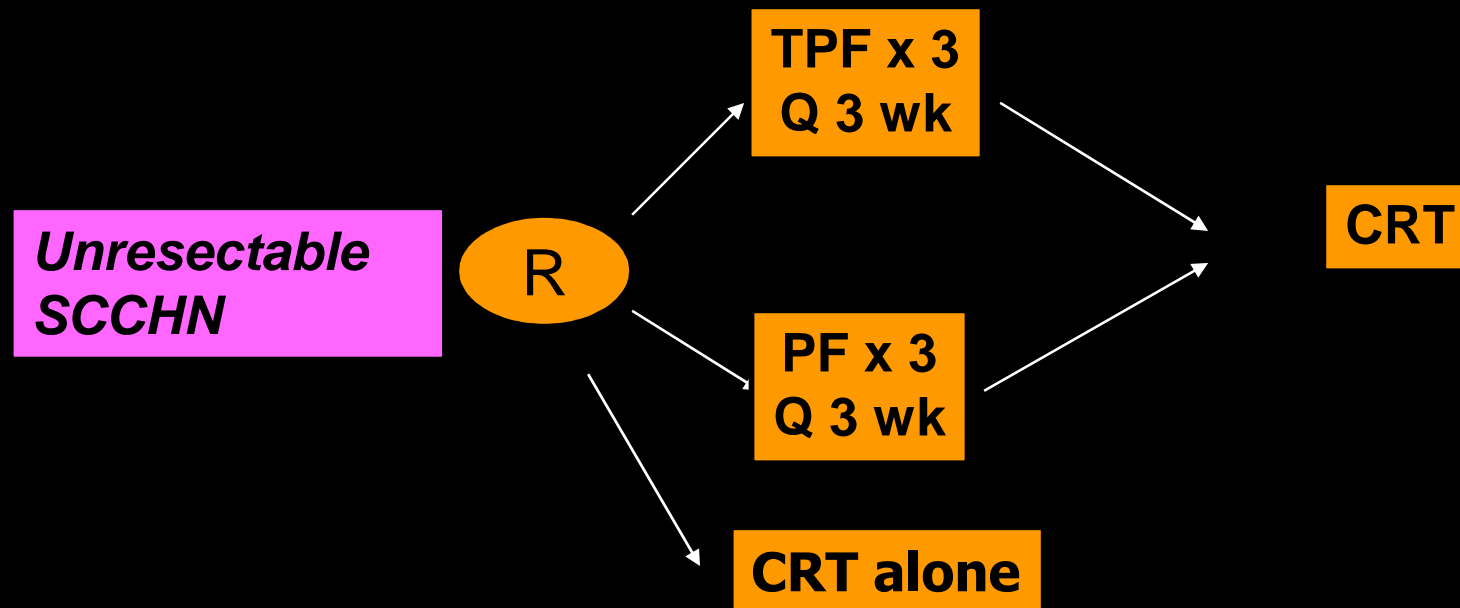
- N=96
- Radiological CR at the end of CRT
 - 20% vs 64% in sequential arm
- Comparable toxicity
 - Weight loss, mucositis, skin reactions, dysphagia

*Phase II and small no. of patients (96)
=> Ph III study ongoing*

Hitt R, Proc ASCO 2009

Final Results of Phase III Trial

Induction Chemo TPF vs PF followed by CRT vs CRT



TPF – 155 pts, PF – 156 pts, CRT alone - 128

Induction Chemo TPF vs PF followed by CRT vs CRT

Final Results of Phase III Trial

Hitt R, Proc ASCO 2009

	IC/CRT	CRT
Median TTF	12.5 mths	4.9mths
LRC	61%	44%
Gr ³ / ₄ AEs	83%	69%
Neutropenia	10%	1%

Long follow up needed



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 Group¹

^a Department of Biostatistics and Epidemiology, Institut Gustave-Roussy, Villejuif, France

^b Department of Radiotherapy, Institut Gustave-Roussy, Villejuif, France

MACH-NC an update of 93 Randomized Trials

(MACH-NC 2000 10,741 pts, 64 trials)

Inclusion of trials 1994-2000, 17,346 pts!

24 new RCTs for concurrent chemo-rad (5744 pts)

Pignon et al 2009 Rad & Onc

Pignon grp MACH-NC update 2009

Concurrent CT-RT

- OS benefit of 6.5% at 5 yrs ($p < 0.0001$)
- EFS benefit of 6.2% at 5 yrs ($p < 0.0001$)
- No diff in mono vs poly chemotherapy
- Significantly higher with Cisplatin than others
- Decreased effect of chemo with age
($p = 0.003$)

NACT

- OS benefit 2.4% at 5 yrs

Induction vs Concurrent

MACH-NC, Pignon et al 2009 Rad & Onc

Concurrent CT RT

- Better Survival 6.5% vs 2.4%
- Significant better OS, EFS, LRC
- Similar benefits in distant failure



On going trials....

Induction vs CT RT..

Recent Trials

Docetaxel Based Chemo Plus or Minus Induction Chemo to Decrease Events in H N Ca [DeCIDE]

N2, N3 HNC

Arm A – Induction +CRT

Arm B – CRT alone

Induction – 2cycles TPF q 21days

CRT – five -14 day cycles of T, F & HU with
twice daily radiation (days 1-5)

***Docetaxel Based Chemotherapy Plus or Minus Induction
Chemotherapy to Decrease Events in Head and Neck
Cancer [DeCIDE]***

ASCO 2012 (Oral Abst.Session)

**Phase III, open label
N2, N3 HNC
KPS > 70%
N = 280 pts (b/w 2004-09)
55% oropharynx
2yrs min. f/u**

Arm A – CRT alone

**5days D (25mg/m²), F(600mg/m²), H(500mg BID)
RT 150cGy BID followed by 9days break**

Arm B – IC + CRT

Induction – 2cycles TPF (D1-D5) q 21days

Results:

- 87% pts in Arm B received CRT after IC
- <75% in both arms received target 5-Fu dose
- Grade $\frac{3}{4}$ leucopenia significantly higher in IC arm

3yr outcome

	IC (%)	CRT (%)	P value
OS	75	73	0.70
RFS	67	59	0.18
Cumulative DF Incidence	10	19	0.02
Cumulative LRF Incidence	9	12	0.55

Conclusions:

- **Higher survival rates in both arms**
- **Reduced distant failure rates didn't translate into better OS??**

Pitfalls

- **No HPV prognostication**
- **Poor accrual (planned for 400pts)**
- **Control arm did well**
- **Limited follow-up**



*Combination Chemo & Radiotherapy in stage III/IV
Head and Neck Ca*
PARADIGM TRIAL

Arm A

3 cycles of TPF q 21days

If pCR at primary, cCR at node => RT+ wkly carbo

Else : weekly T + RT

Arm B

RT + CDDP week 1 & 4

Combination Chemotherapy and Radiotherapy *Stage III/IV Head & Neck Cancer* (PARADIGM TRIAL)

LAHNC

145 pts enrolled (300 planned)

Accrual closed in 2008

Median f/u 49mths

Arm A (n=70)

- IC - 3 cycles of TPF q 21days
- If pCR at primary, cCR at node
 - RT (once daily)+ weekly carboplatin
- Else
 - wkly T + RT (Accelerated Boost)

Arm B (n=75)

Accelerated Boost RT + CDDP week 1 & 4

Results:

	Arm A	Arm B	
3yr OS	73%	78%,	p=0.7
3yr PFS	67%	73%,	p=0.5

Conclusions:

No survival difference

***Paccagnella A et al. Proc ASCO 2011
Phase III RCT***

Study Design

420 patients
LAHNC
Oral cavity, oropharynx, hypopharynx
Unresectable, non-metastatic stage III/IV

Arm A



A1
CRT alone

A2
Cetuximab/RT

Arm B
3cycles TPF



B1
CRT

B2
Cetuximab/RT

Summary

Neo-adj. vs Conc Chemo

Randomized Clinical Trials

On going trials- induc?

DeCIDE Trial / PARADIGM Trial
Paccagnella et al RCT

Conc CTRT is superior

MACH-NC Update, **Radiother Oncol '09**

TPF > PF

TAX 324 update 2011, Lancet Oncology
TAX 323, 324 **NEJM, Annals of Oncolgy**
Hitt et al, **JCO '05** / GORTEC 2000-01, **JCO '06**

CTRT>Ind>RT

RTOG 91-11, Forastiere A, **NEJM '03**

CTRT>Ind>RT

MACH-NC, Pignon J, **Lancet '00**

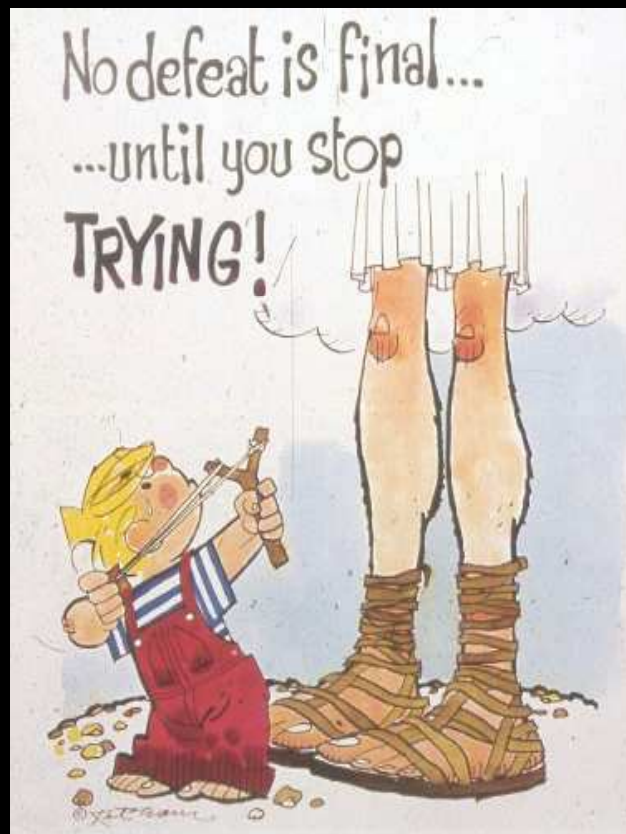
C->RT=Sur

VA Study, **NEJM '91** / Lefebvre (EORTC Study), **JNCI '96**

Summary

- ✓ Conc Chemo RT is still standard of care
- ✓ Induction CT followed by CRT:
 - ✓ Promising, under active investg
- ✓ Multidisciplinary approach considering
Age, PS, tolerability, QOL
- ✓ LRC, OS end points

Neo adjuvant chemo...



■ Positives

- Taxanes
- Helps us to select pts
- Larynx preservation
- Made easy RT / Surg
- Reduce mets

■ Issues

- Tolerance (May be T + P only)
- Discontinuation of Rx
- Prolonged Rx time



Selection of patients...

*Single-cycle induction chemotherapy
selects pts with advanced laryngeal ca for
combined chemoRT: a new treatment paradigm.*

*Urba S, Wolf G, Eisbruch A, et al.
University of Michigan, J Clin Oncol 2006;24:593–598.*

Probably...

Induction	Concurrent
High Vol disease	Low Vol disease
T 3, T4	T2 N0
N 2B, C,	T3 N0
N 3	T1,2 N1

When decision of surgery or radiotherapy is difficult

LAHNC... *Take Home!*

- Conc CT+RT is standard
- Induction CT is promising
 - Large vol disease
 - Young, Good PS
 - Hypo pharynx, Oropharynx
 - Larynx preservation

Thank you



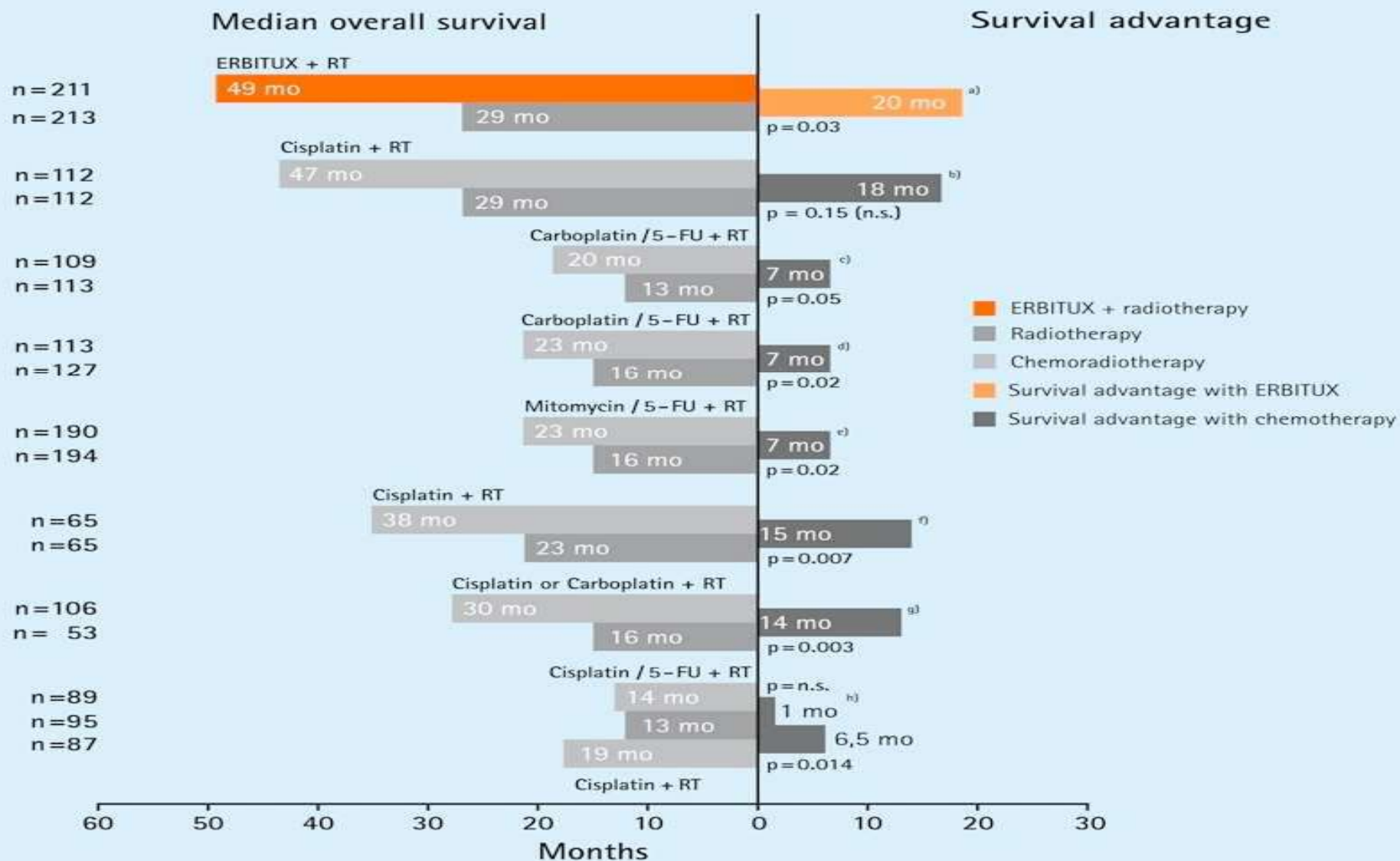
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CRT vs. RT: Median Survival



^{a)} Bonner et al., NEJM 2006; ^{b)} Huguenin et al., JCO 2004 ^{c)} Denis et al., JCO 2004 ^{d)} Semrau et al., Int J Rad Onc 2006; ^{e)} Budach et al., JCO 2005; ^{f)} Jeremic et al., JCO 2000 ^{g)} Jeremic et al., JCO 2004 ^{h)} Adelstein et al., JCO 2003