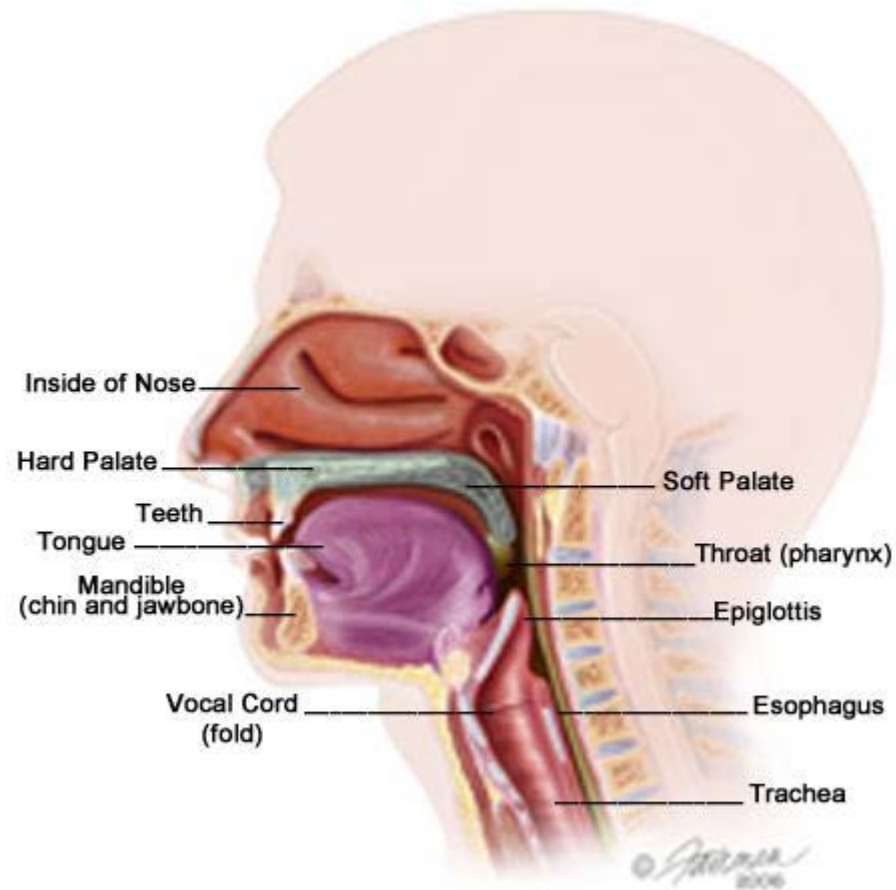


Organ preservation: Role of induction chemotherapy

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HeSHNO 21 OCT 2016

Head and neck squamous cell carcinoma (HNSCC)



Meta-Analysis of chemotherapy in HNC (MACH-NC)


- ▶ 63 randomized trials (1965-1993)
- ▶ N=10,717 pts with SCC of the oropharynx, oral cavity, larynx or hypopharynx
- ▶ Comparison of locoregional treatment with and without chemotherapy
- ▶ Median follow-up: 6 years
- ▶ Overall benefit of chemotherapy: 4% at 5 years (32% vs 36%)

	Trials	N	RR	P value	Absolute benefit (5 years), %
Adjuvant	8	1854	0.98	NS	1
Induction	31	5245	0.95	NS	2
Concomitant	26	3727	0.81	<0.0001	8

Update of MACH-NC

- ▶ 24 added trials—87 studies, 16,485 patients
- ▶ MACH-HN I: 8% absolute benefit Concurrent-no significant effect of IC
- ▶ No significant difference ($p = 0.19$) was seen between mono-chemotherapy (HR 0.84) and poly-chemotherapy (HR 0.78)
- ▶ Mono-chemotherapy group:
 - ▶ the effect of chemotherapy was significantly higher ($p = 0.006$) with PLATIN than with other types of mono-chemotherapies

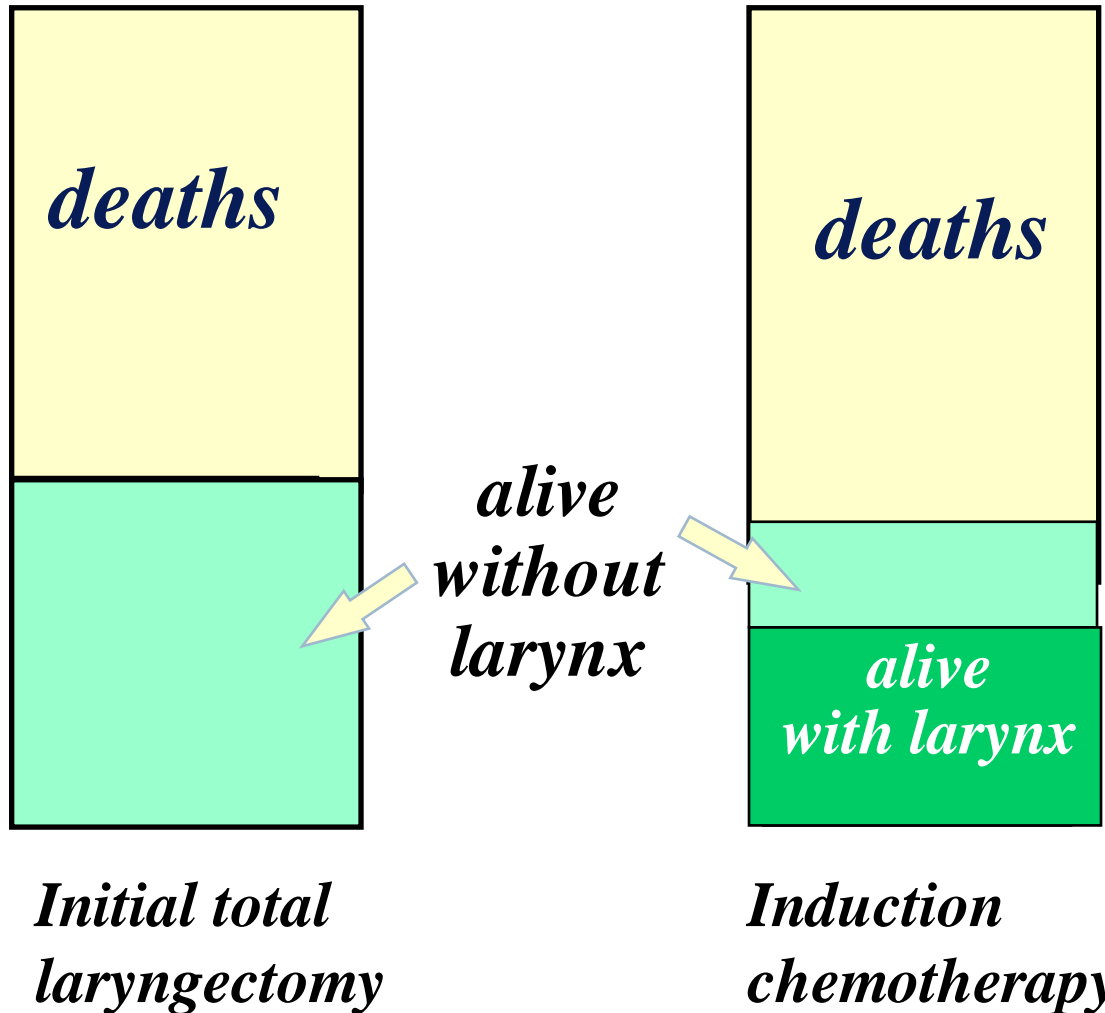
**Platin + radiotherapy
is the standard
for locally advanced HNSCC**



MACH-NC: neo-adjuvant chemo and local control for laryngeal tumors

	Induction CT+ RT if good response (n=305)	Total laryngectomy (n=297)
Recurrence	42%	34%
Local	25%	12%
Metastatic	14 %	19%
Both	3%	3%
Second primary	9%	12%
Death/other cause	19%	16%
Alive w/o disease	30%	38%

*Larynx preservation trials at 5 years :
survival differences = **NS***



**Induction PF followed by RT
was a viable alternative to up-front total
laryngectomy
in good responders**



The ways to optimise the chemo-selection approach

- ▶ Better patients selection (comorbidities, exclude T4 with cartilage invasion ...)
- ▶ Optimise the induction regimen
- ▶ Optimise radiotherapy
- ▶ Combine RT with the best drug(s)



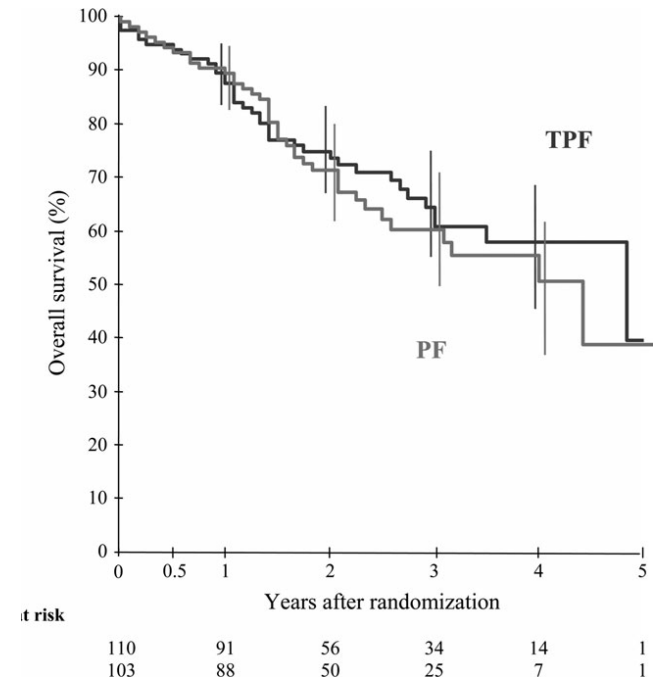
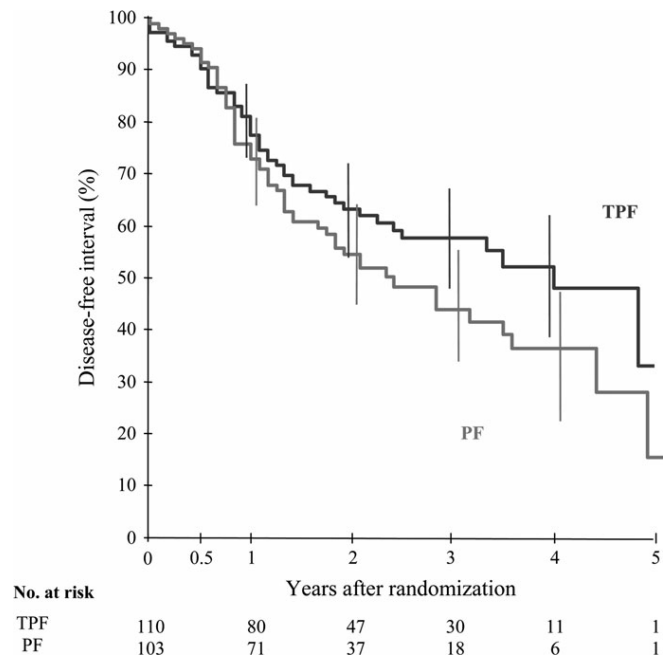
Optimise the induction regimen: Randomized trials of induction PF+/- taxane

	Eligibility	N	T+PF CR+PR (%)	PF CR+PR (%)	TPF/PF PFS mos	TPF/PF OS mos	P value (HR)
Hitt JCO 2005	Stage III-IV	382	80%	68%	20 vs 12	43 vs 37	0.03 (0.67)
TAX 323 NEJM 2007	Unresectable	358	68%	54%	11 vs 8	18.6 vs 14.2	0.005 (0.71)
TAX 324 NEJM 2007	III-IV	538	72%	64%	2y PFS 53% vs 42%	70 vs 30	0.006 (0.7)

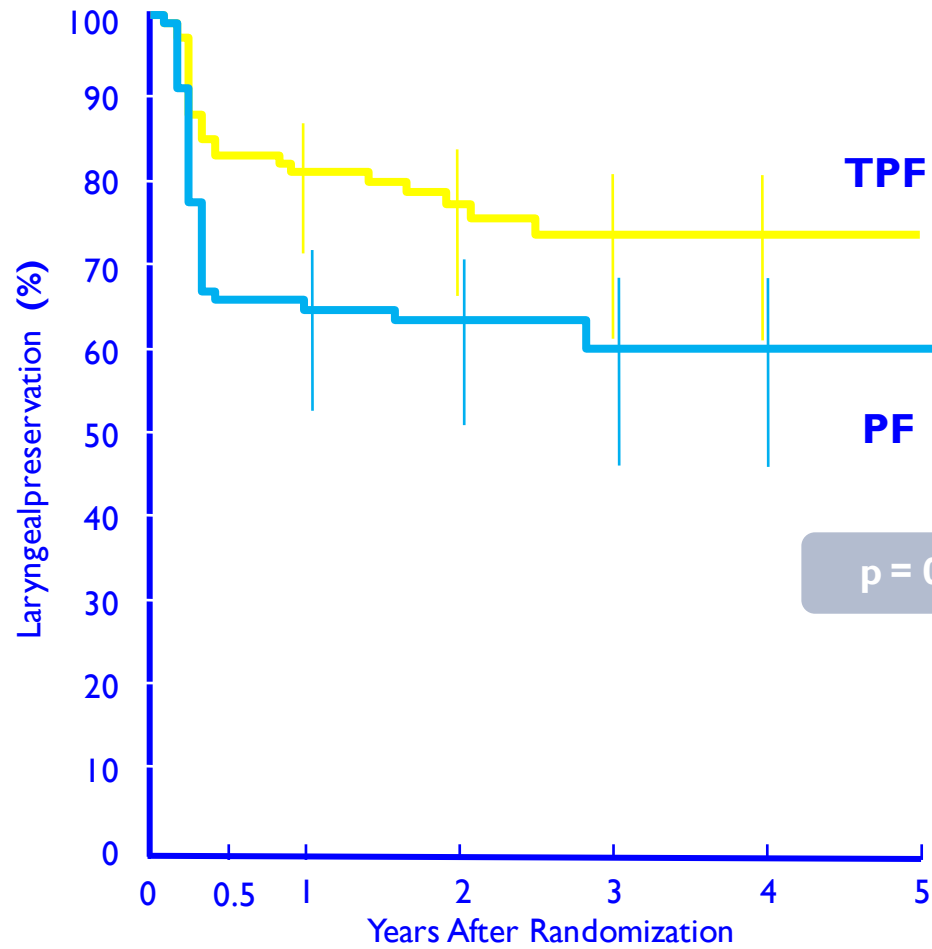


TPF vs PF for larynx preservation

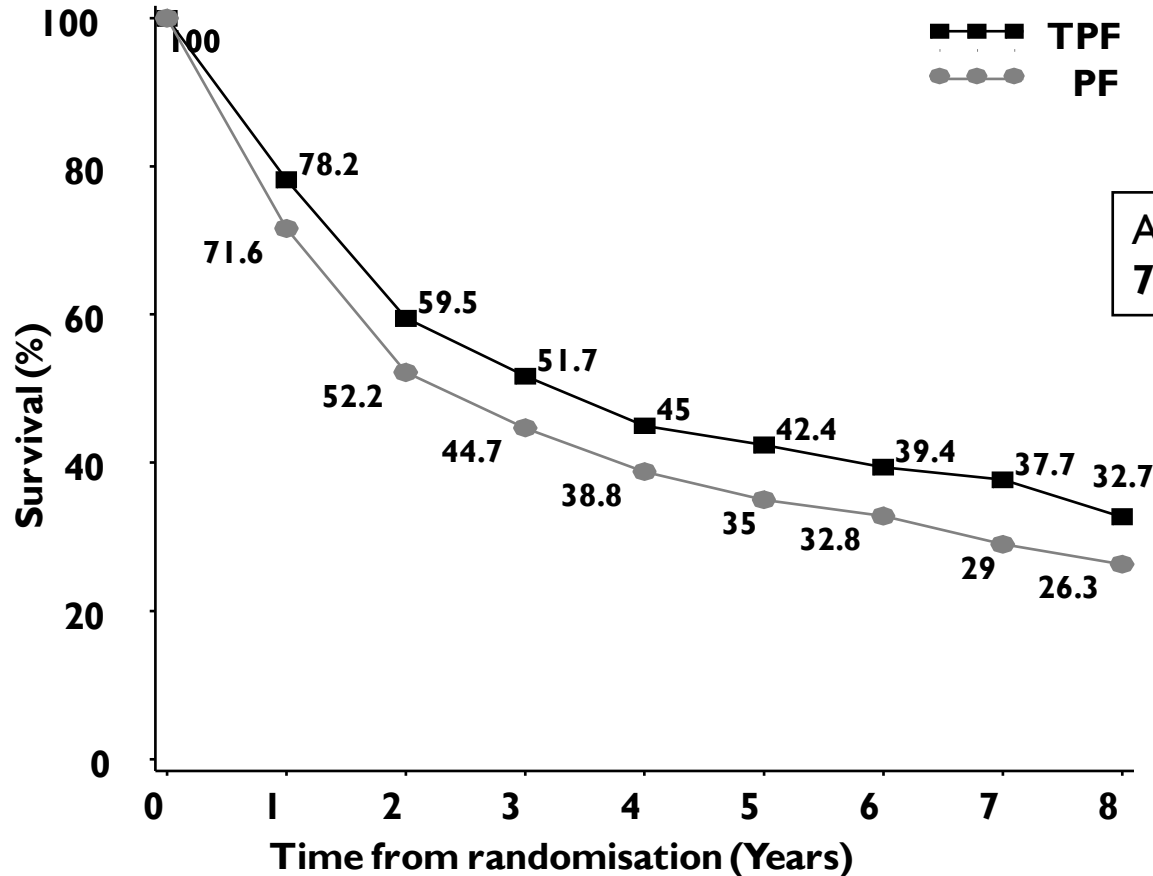
- ▶ GORTEC
- ▶ Larynx/hypopharynx
- ▶ Stage II to IV
- ▶ N=213



TPF vs PF: laryngeal preservation




Updated meta-analysis : 6 randomised trials taxan-PF vs PF



TPF improves OS

-
- ▶ TPF is the recommended regimen for induction chemotherapy of locally advanced HNSCC, especially for laryngeal preservation
-
- 

Does induction TPF followed by RT+/-CT do better than upfront RTCT?



Randomized trials of sequential therapy: definitive chemo RT +/- induction

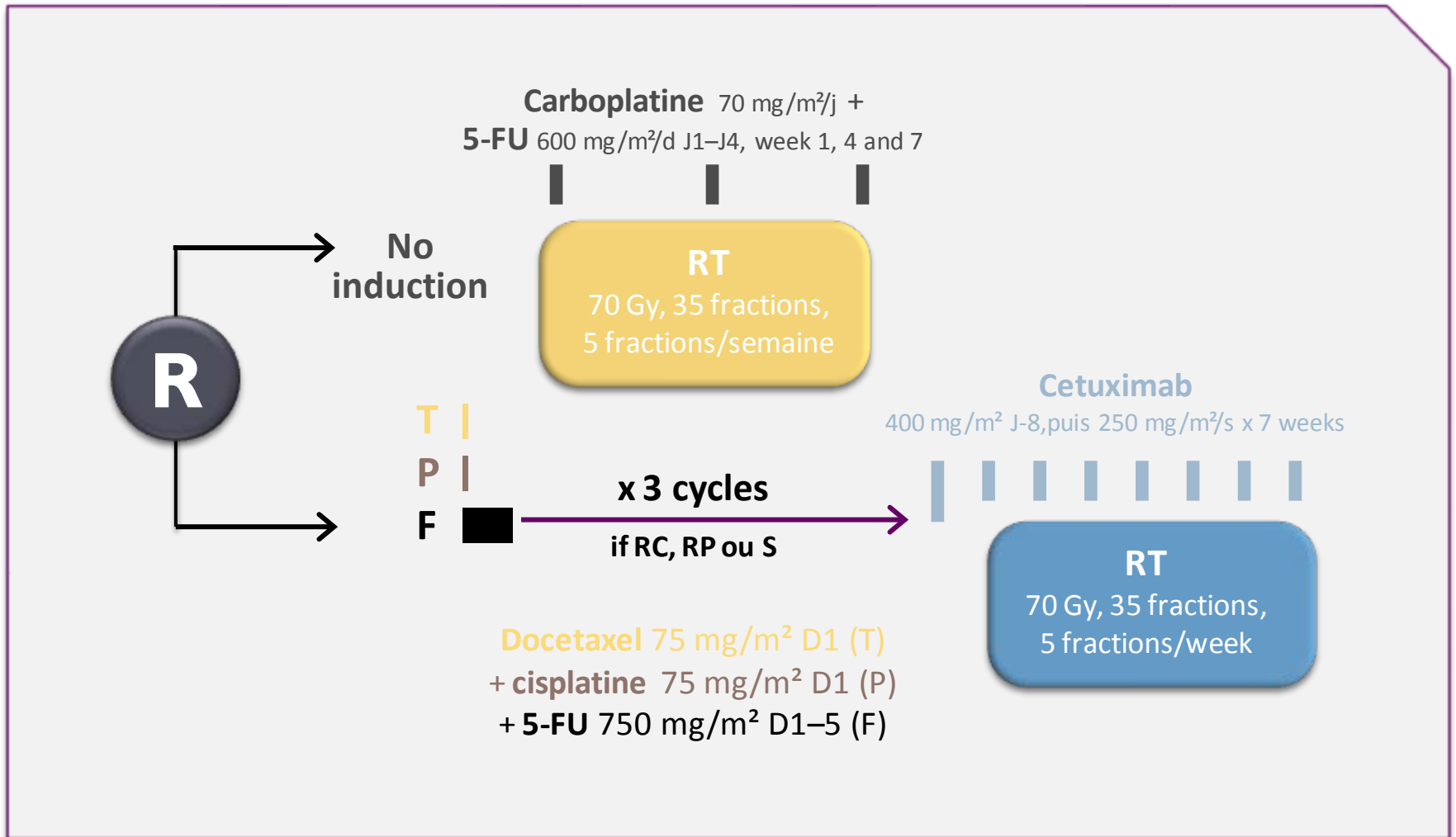
Trial	Eligibility	Target N	Actually enrolled	Control	Experimental arm	OS
DeCIDE	N2-3	400	285	DHFX	TPFx2 DHFX	NS
Paradigm	Stage III-IV	300	145	Cisplatin CB-RT	TPFx3 Carbo-RT or D-CB-RT	NS
SWOG	Oropharynx	400		Cisplatin RT	TPFx1-3 Surgery or cisplatin-RT	
Hitt	Stage III-IV	439	439	Cisplatinx3- RT	PF or TPF CRT	NS
Ghi	Unresectable	361	361	Cisplatinx2- RT Or cetux- RT	TPFx3 Cisplatin*2 or cetux	P=0,02

CB, concomitant boost; DHFX, docetaxel, fluorouracil, and hydroxyurea



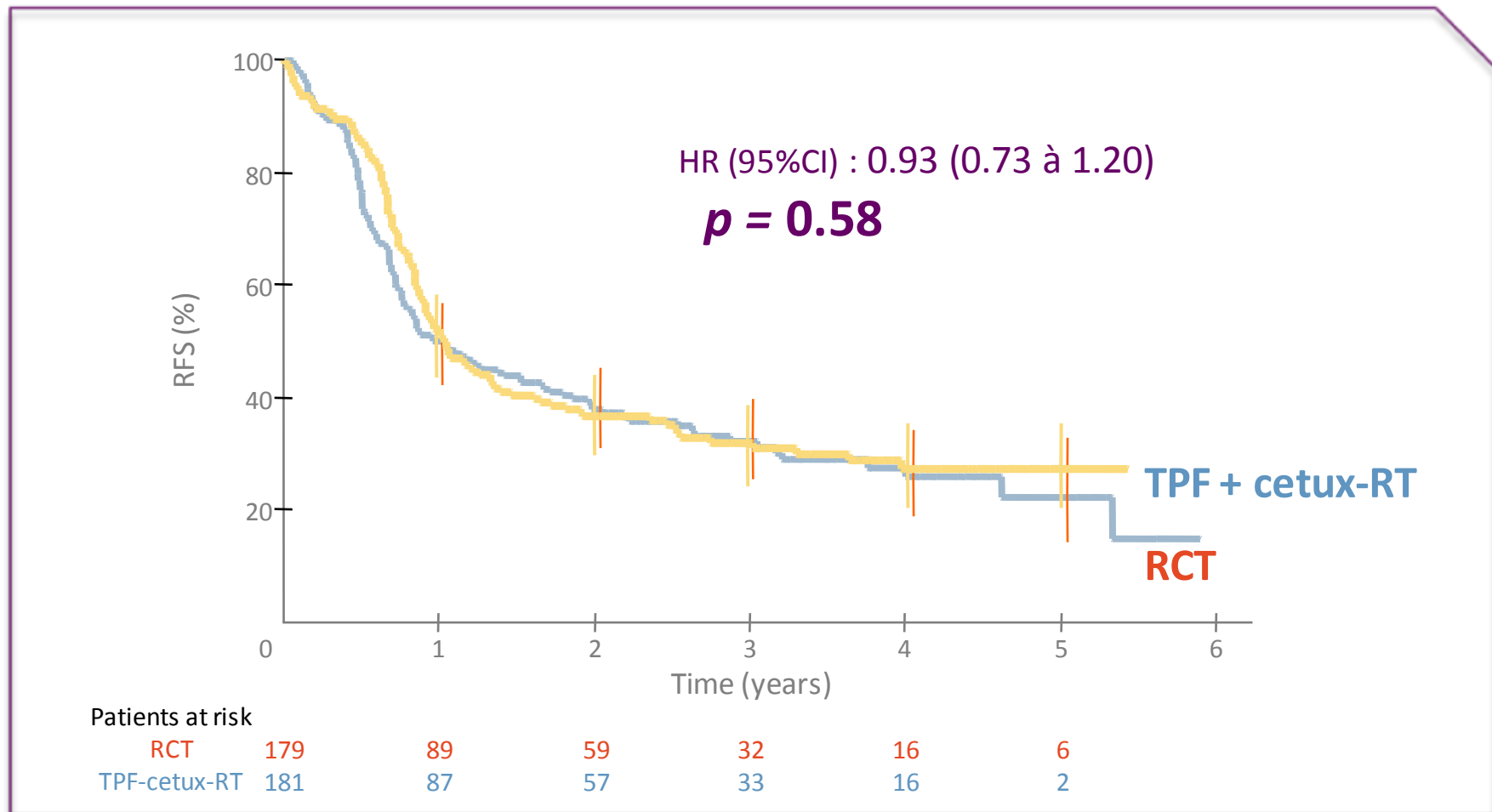
GORTEC 2007-02

phase III randomised trial



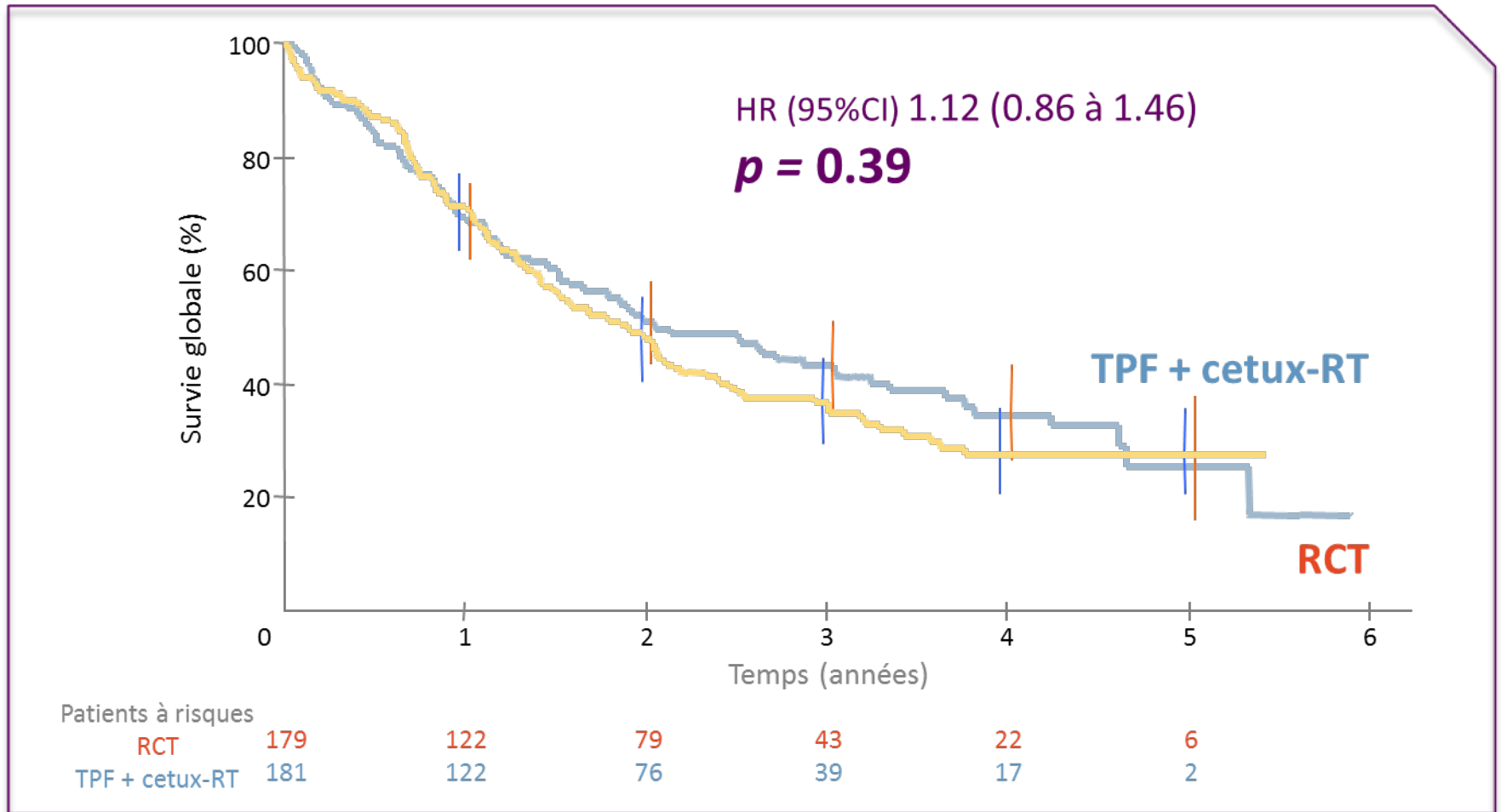
GORTEC 2007-02

Recurrence free survival (RFS)



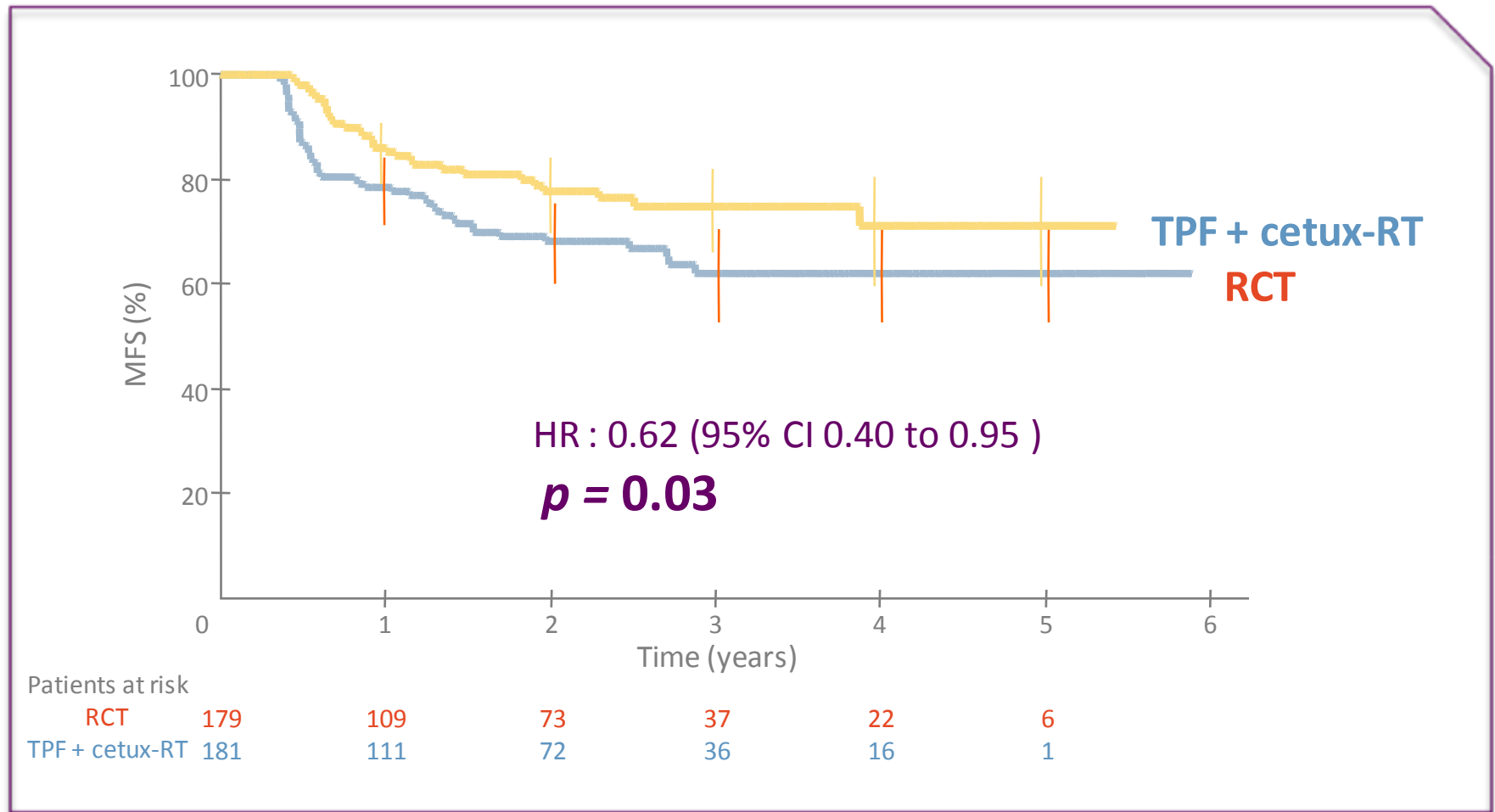
GORTEC 2007-02

Overall survival (OS)



GORTEC 2007-02

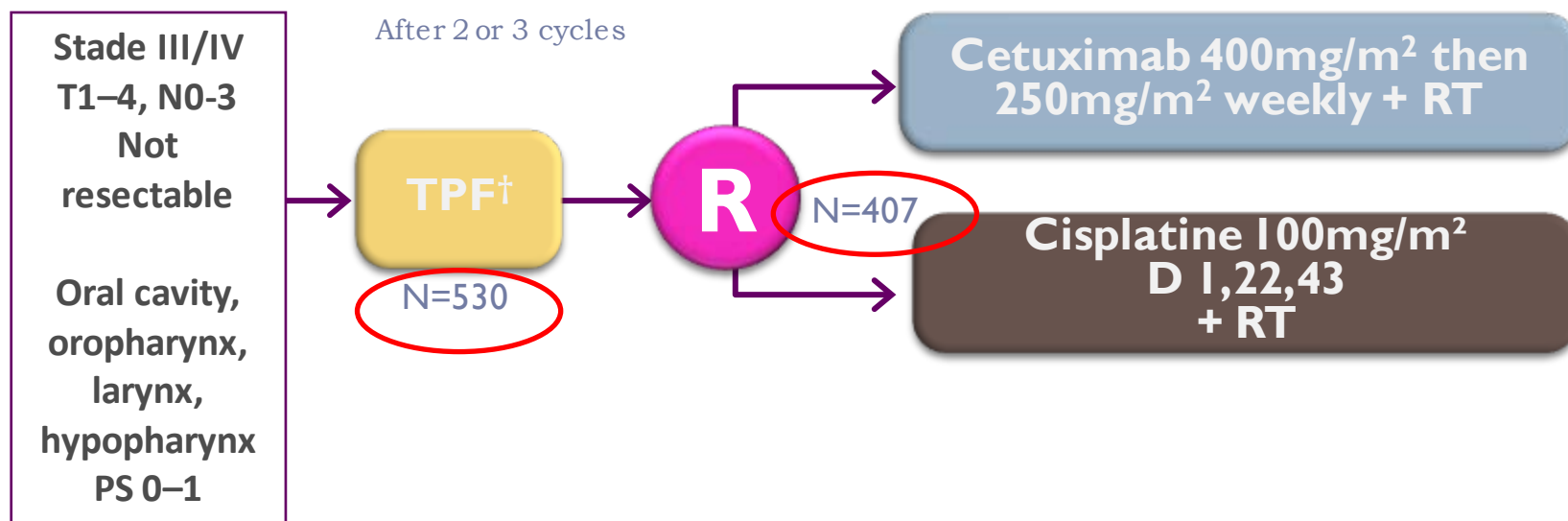
Metastasis free survival (MFS)



GORTEC 2007-02

- ▶ **No benefit of induction followed by Cetux-RT**
 - ▶ In terms of RFS, OS, local control
- ▶ **Significant decrease of distance metastasis associated with induction**
- ▶ **Standard treatment remains RCT**
- ▶ **Induction is an option that provides equivalent results when compared with RCT**

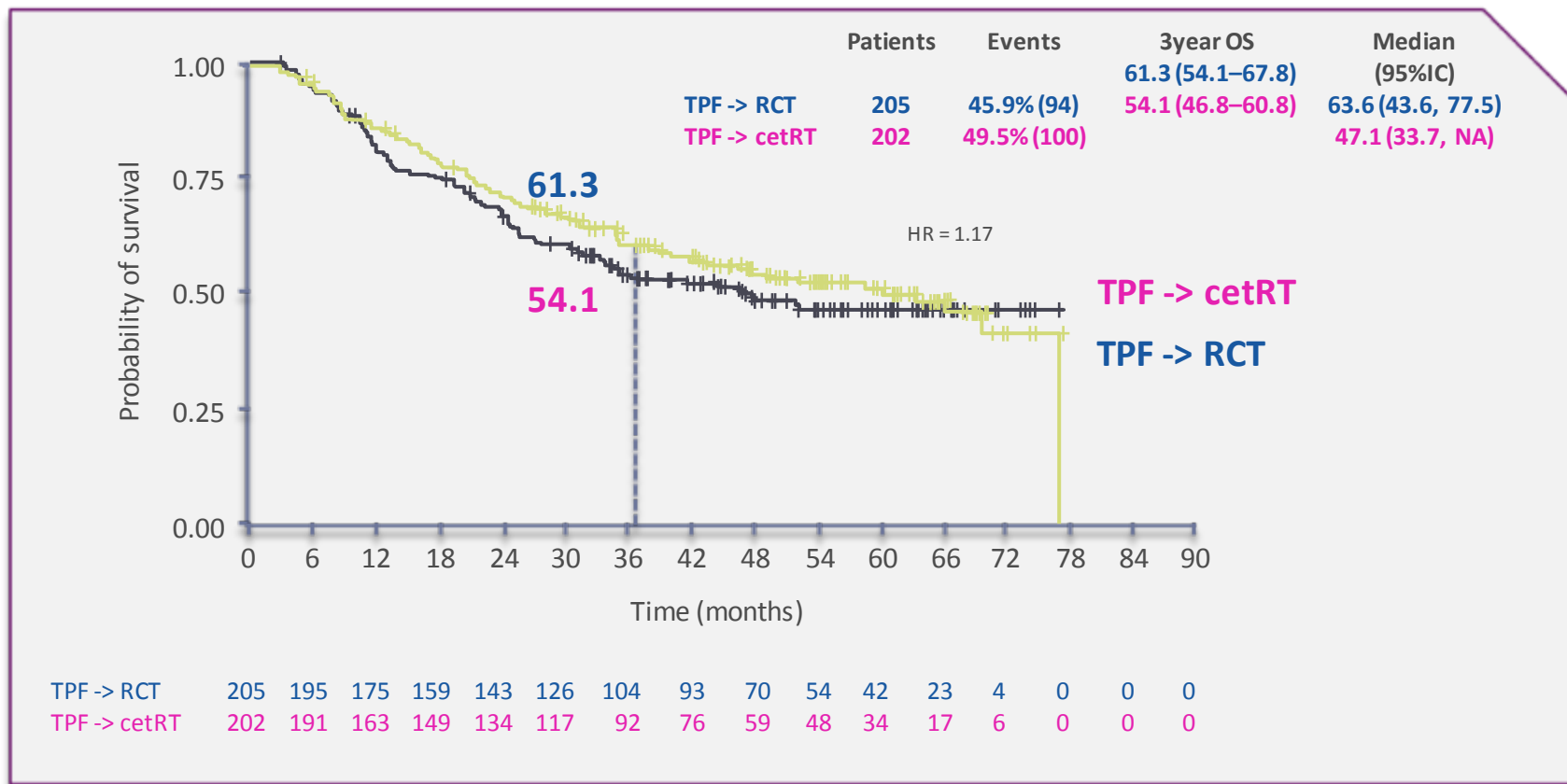
What is the best concomitant chemo after induction phase III randomised trial



Primary endpoint:

→ Non-inferiority of cetuximab-RT vs CRT in terms of OS

OS



- PFS: NS
- Local control: NS

GORTEC 2007-02

- ▶ **It seems that RT+ cetux or RT+cisplatin provide equivalent results after TPF induction**
- ▶ **In both arms, the 3 year local control rate is excellent (>50%)**
- ▶ **42% of patients did not receive the 3 cycles of high dose cisplatin with RT**

Conclusion

- ▶ **Induction TPF**

- ▶ **is not a Standard of Care** in LA HNSCC
- ▶ is an important option for **Larynx preservation**
- ▶ reference treatment, but has to be carefully handle if co-morbidities



Thanks



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