

Grandangolo in Radioterapia - 2013

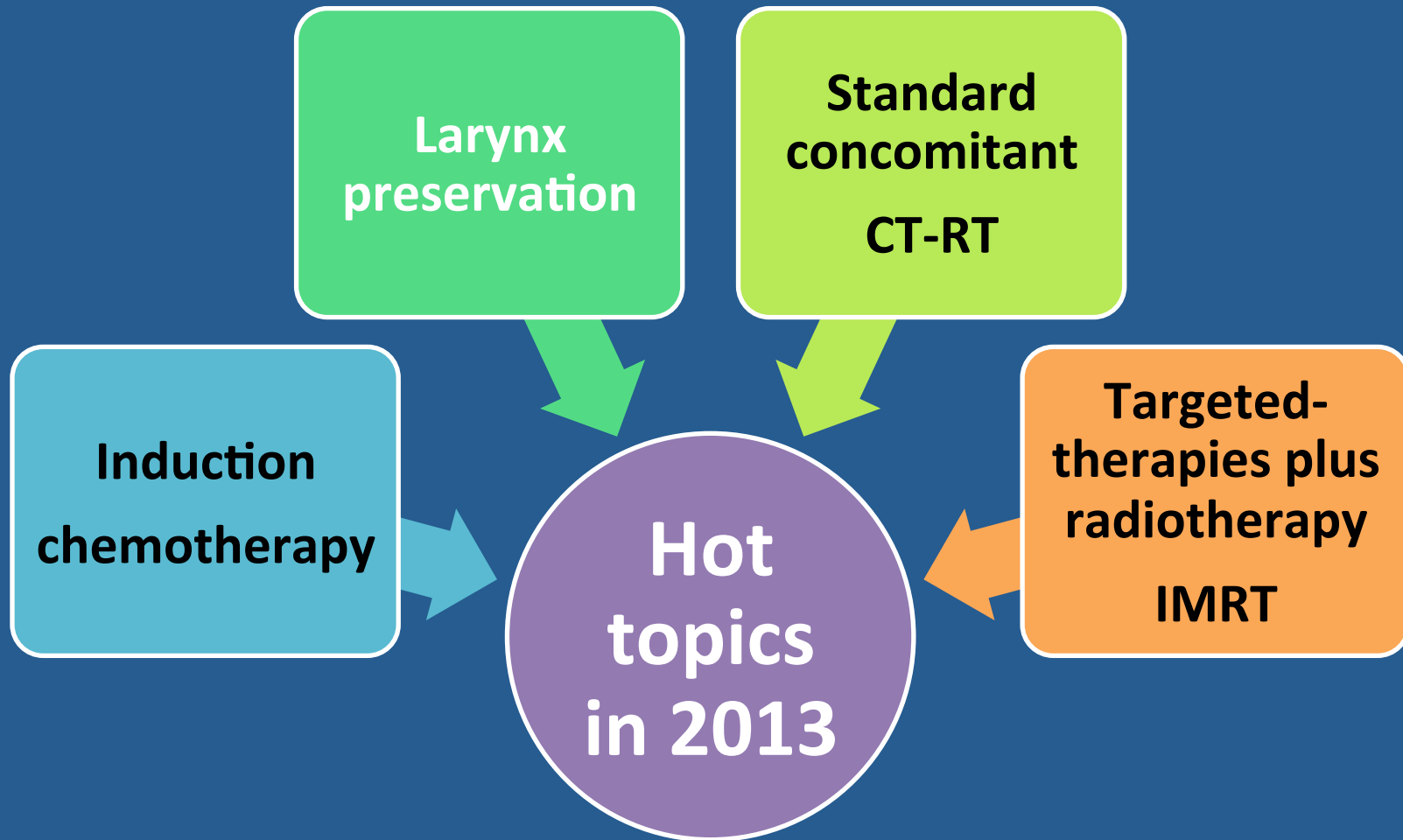
Tumori Testa Collo

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AIRO Giardini Naxos 2013

Updates in Head & Neck Tumors



SCC-H&N

*«The more strategies change
the more outcomes
stay the same»*

Induction chemotherapy (1)

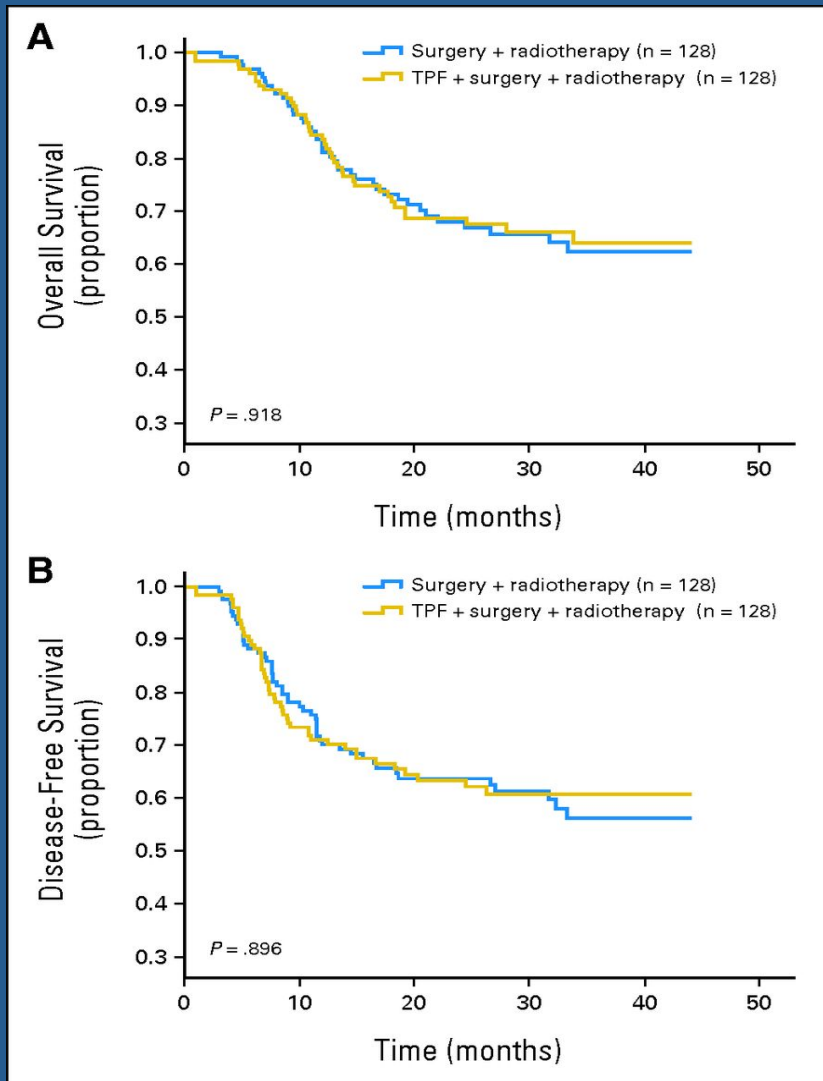
J Clin Oncol 2013, Feb 20; 31(6):744-51

*Randomized phase III trial of **induction chemotherapy** with docetaxel, cisplatin, and fluorouracil followed by surgery versus **up-front surgery** in locally advanced resectable oral squamous cell carcinoma*

Zhong LP et al,

University School of Medicine, Shanghai, China

(A) Overall and (B) disease-free survival in the control and experimental arms.



- 256 pts III-IVa OC-SCC
 - This study failed to show that TPF-induction improves OS compared to upfront-surgery plus RT
- Benefit for cN2?

Zhong L et al. JCO 2013;31:744-751

Induction Chemotherapy (2)

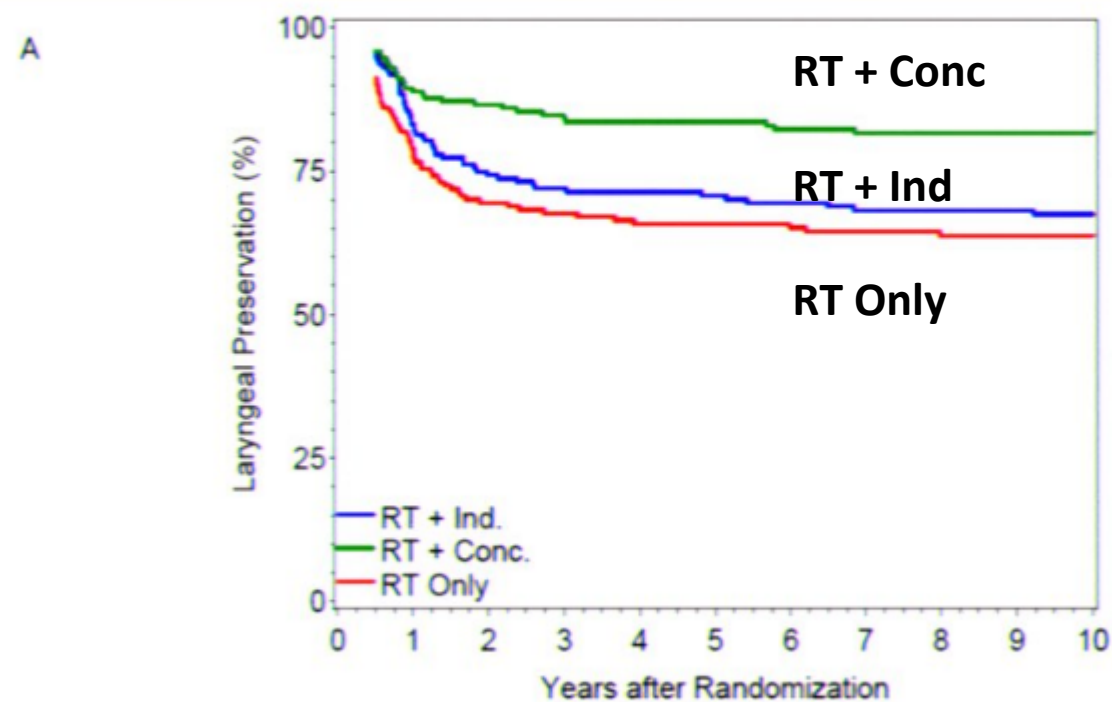
Long Term Results of RTOG R91-11: a comparison of three non surgical treatment strategies to preserve the larynx in pts with Locally Advanced Larynx Cancer

Forastiere A. et al

J Clin Oncol 2013, 31, 7: 845-852

R91-11: Larynx Preservation

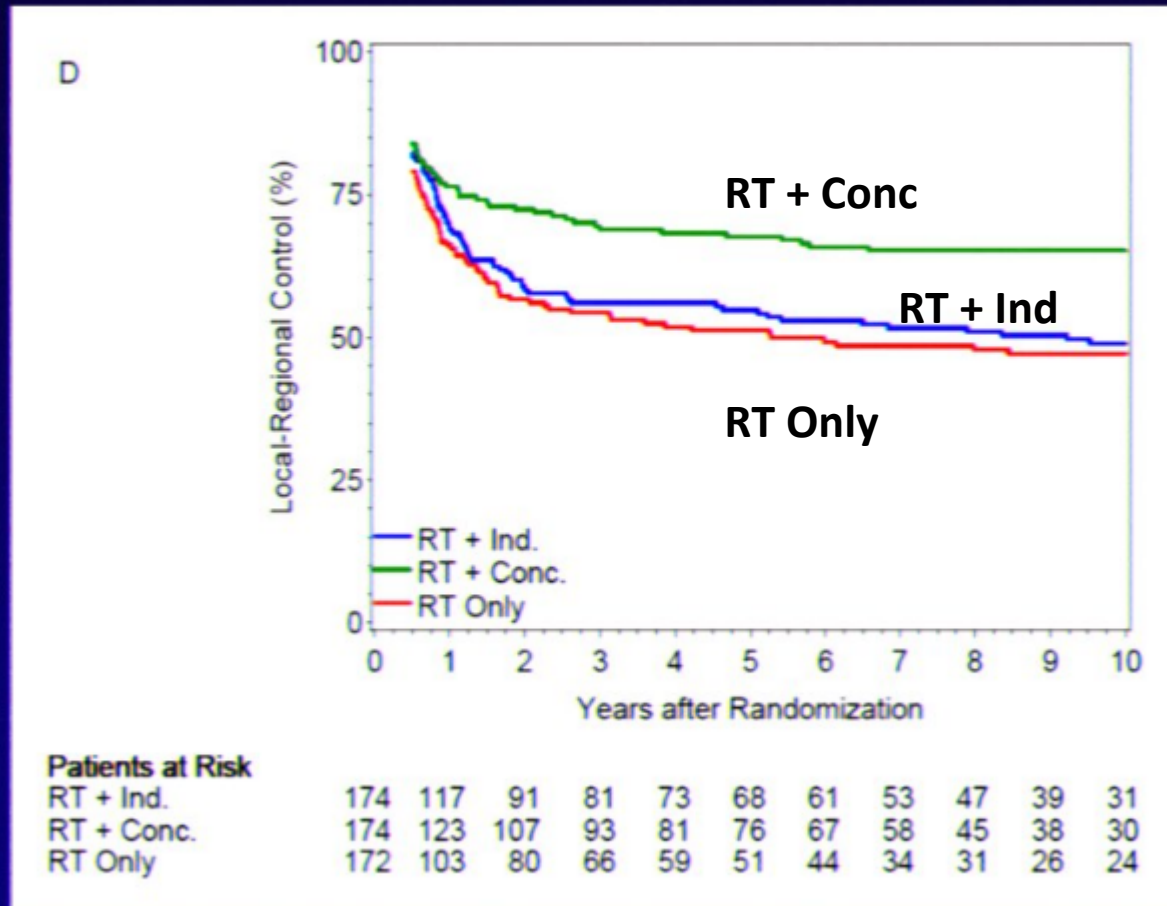
Total laryngectomies – 148: Induction – 55, Concomitant – 32,
RT alone - 61



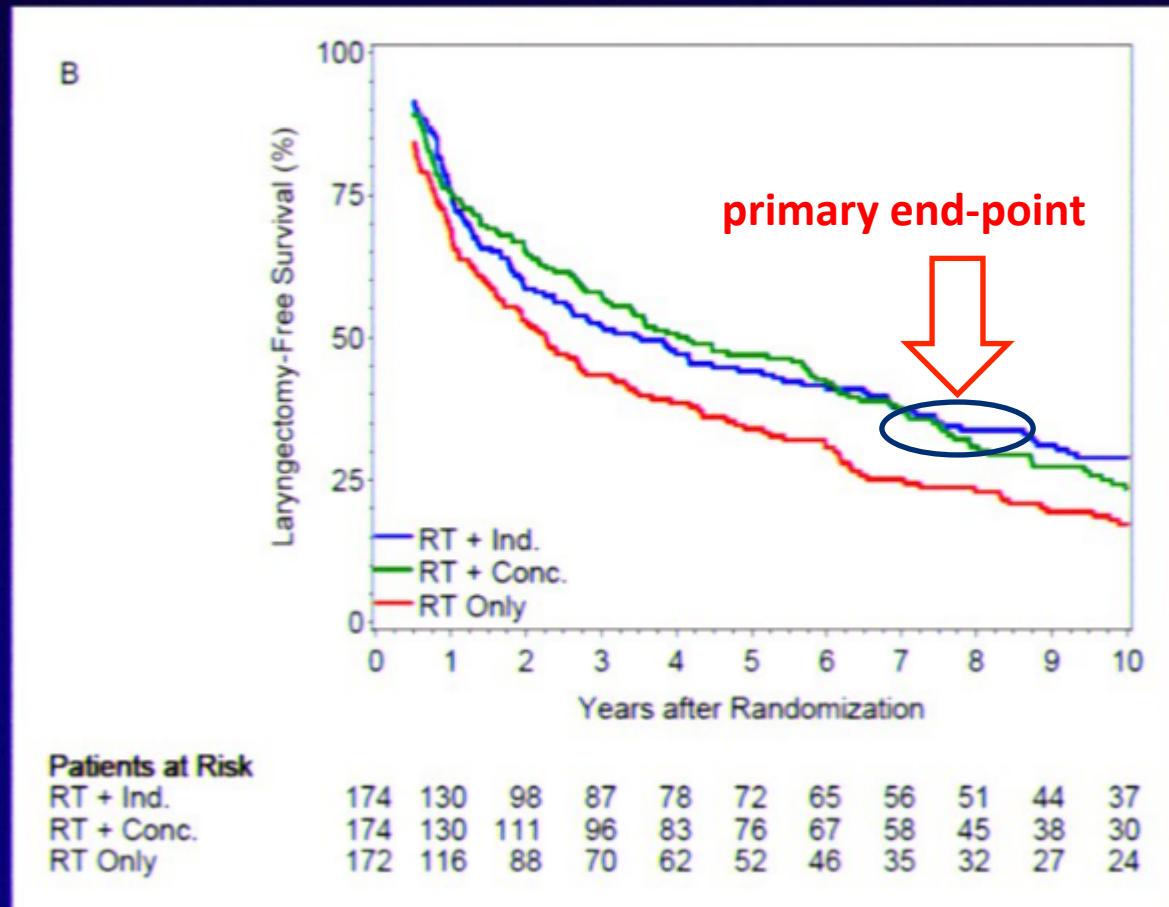
Patients at Risk

RT + Ind.	174	130	98	87	78	72	65	56	51	44	37
RT + Conc.	174	130	111	96	83	76	67	58	45	38	30
RT Only	172	116	88	70	62	52	46	35	32	27	24

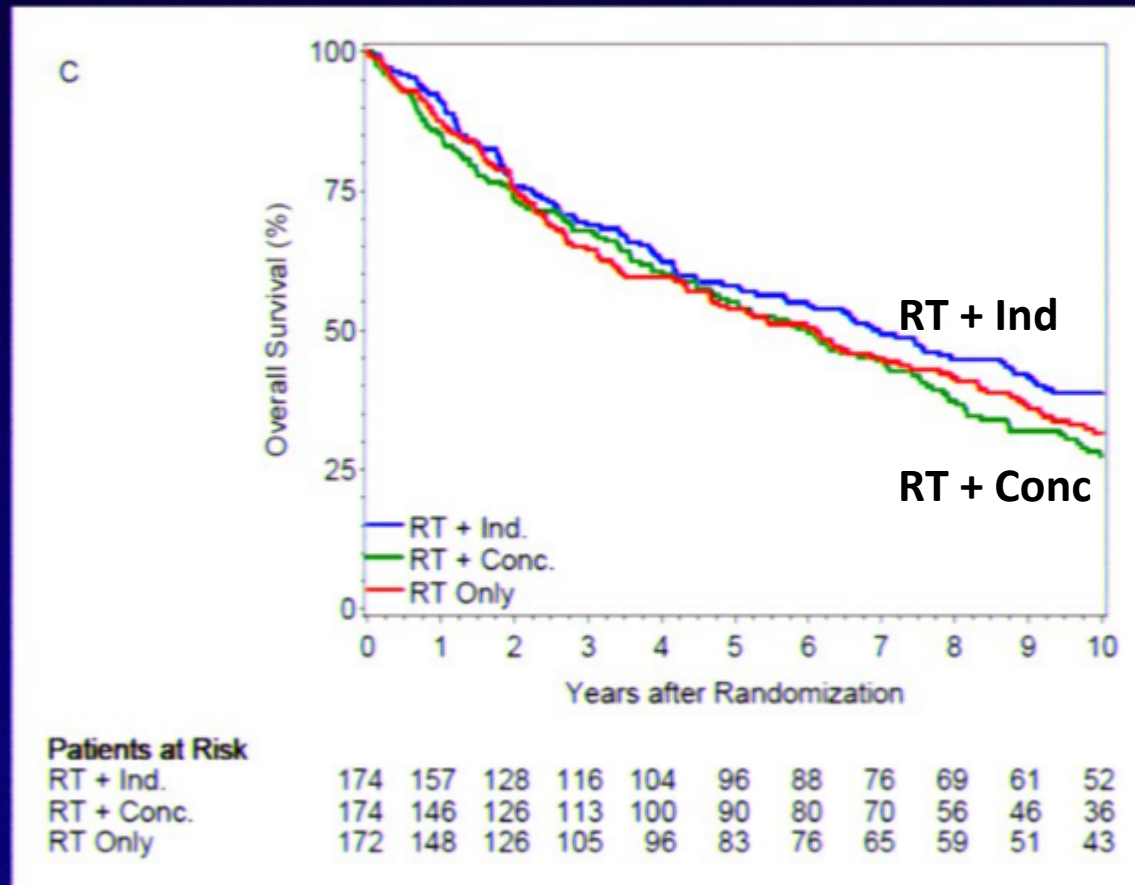
R91-11: Local-regional



R91-11: Laryngectomy-free Survival



R91-11: Overall Survival



Induction chemotherapy for SCC–HN cancer: a neverending story?

M.Benasso - Oral Oncology 2013 – Review

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

Haddad R et al. Lancet Oncol 2013 Mar; 14(3): 257-64

TPF x 3 → SFRT/carbo x 2 vs Acc RT/P x 2

145 pts
randomized

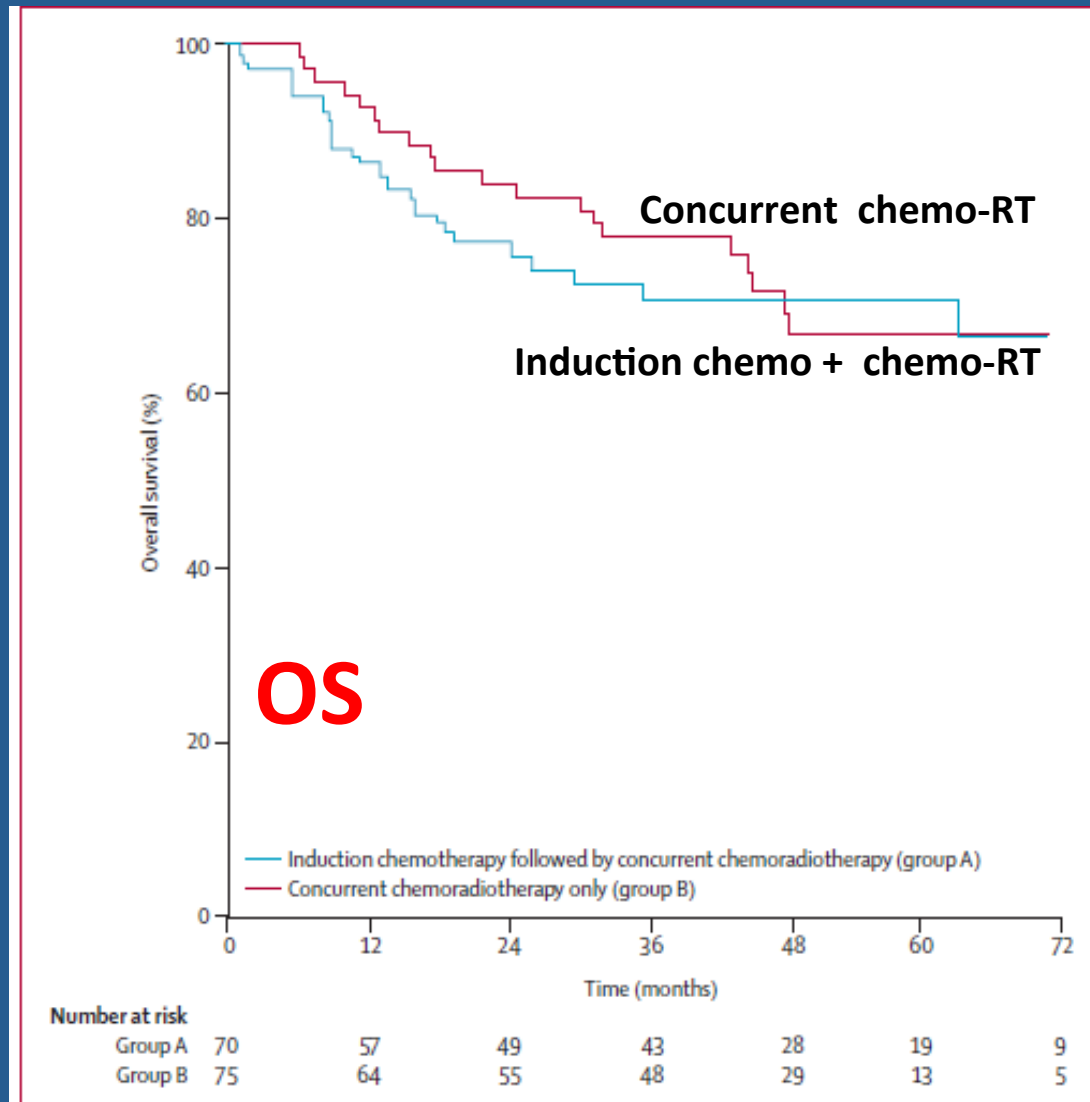


Figure 2: Kaplan-Meier estimates of overall survival

Lancet Oncol 2013 Mar; 14(3): 257-64

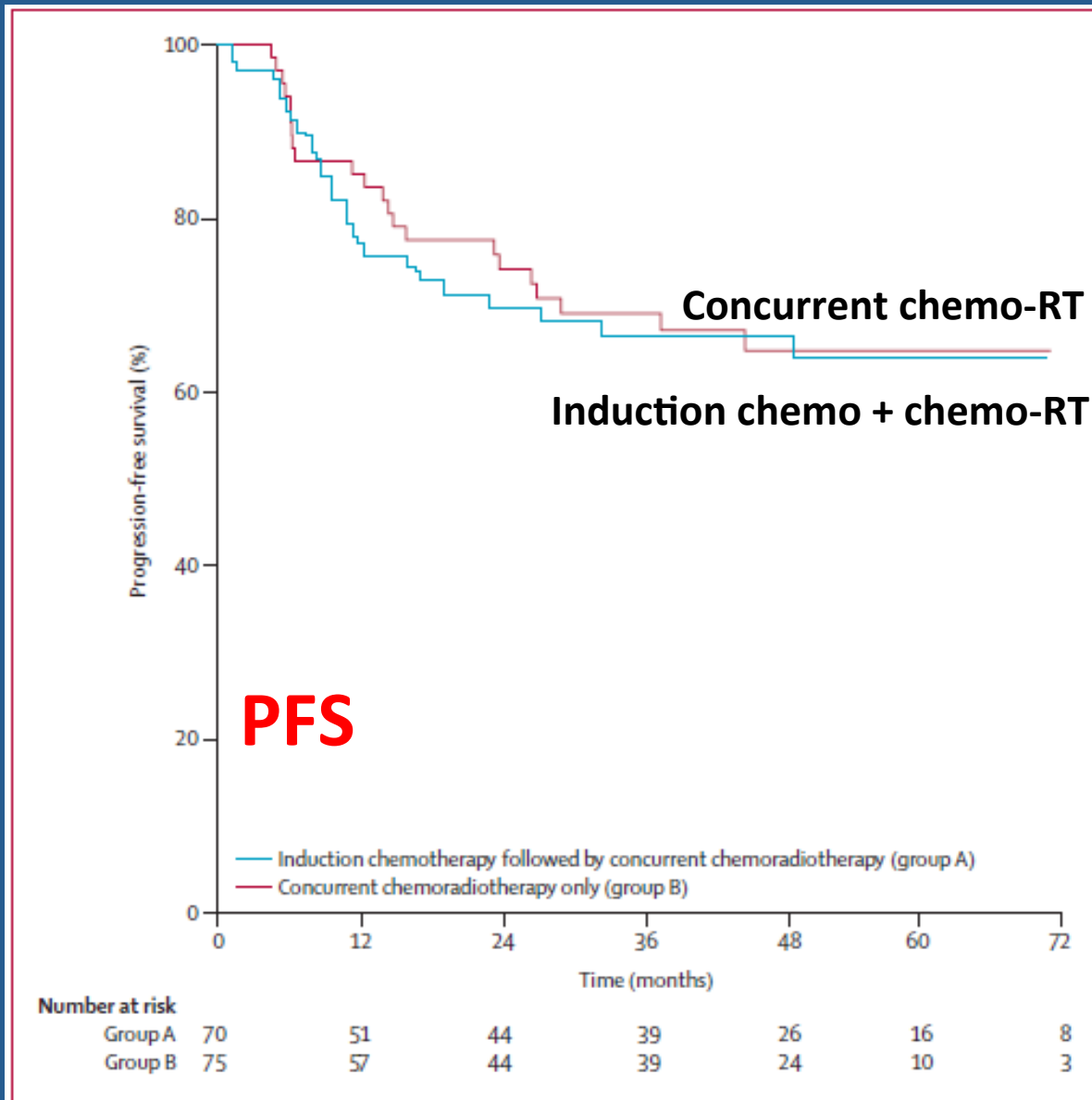


Figure 3: Kaplan-Meier estimates of progression-free survival

How to intensify radiotherapy?

**Cetuximab-Radiotherapy
is better than
Cisplatin-Radiotherapy?**

→ Ghi MG et al, ASCO/ASTRO 2013

→ Lefebvre J et al, JCO 31, 7:853-859

ASCO / ASTRO 2013

A phase II-III study comparing concomitant chemoradiotherapy (CRT) versus cetuximab/RT (CET/RT) with or without Induction docetaxel/cisplatin/5-fluorouracil (TPF) in locally advanced head and neck squamous cell carcinoma (LASCCHN):
Efficacy results (NCT01086826).

Ghi M.G., Paccagnella A., Orecchia R. et al
428 pts randomized

TPF x 3 → SFRT/PF x2 or cetuximab vs SFRT/PF x 2 or cetuximab

Ghi et al, ASCO JCO, Vol 30, No 15_suppl (May 20 Supplement), 2012: 5513

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*Conclusions: no advantage for CET
+RT over cCHT+RT was observed
regarding G3-4 in-field toxicities
and feasibility*

Conclusions: no significant differences in response rate, progression free survival and OS between CRT and CET/RT.

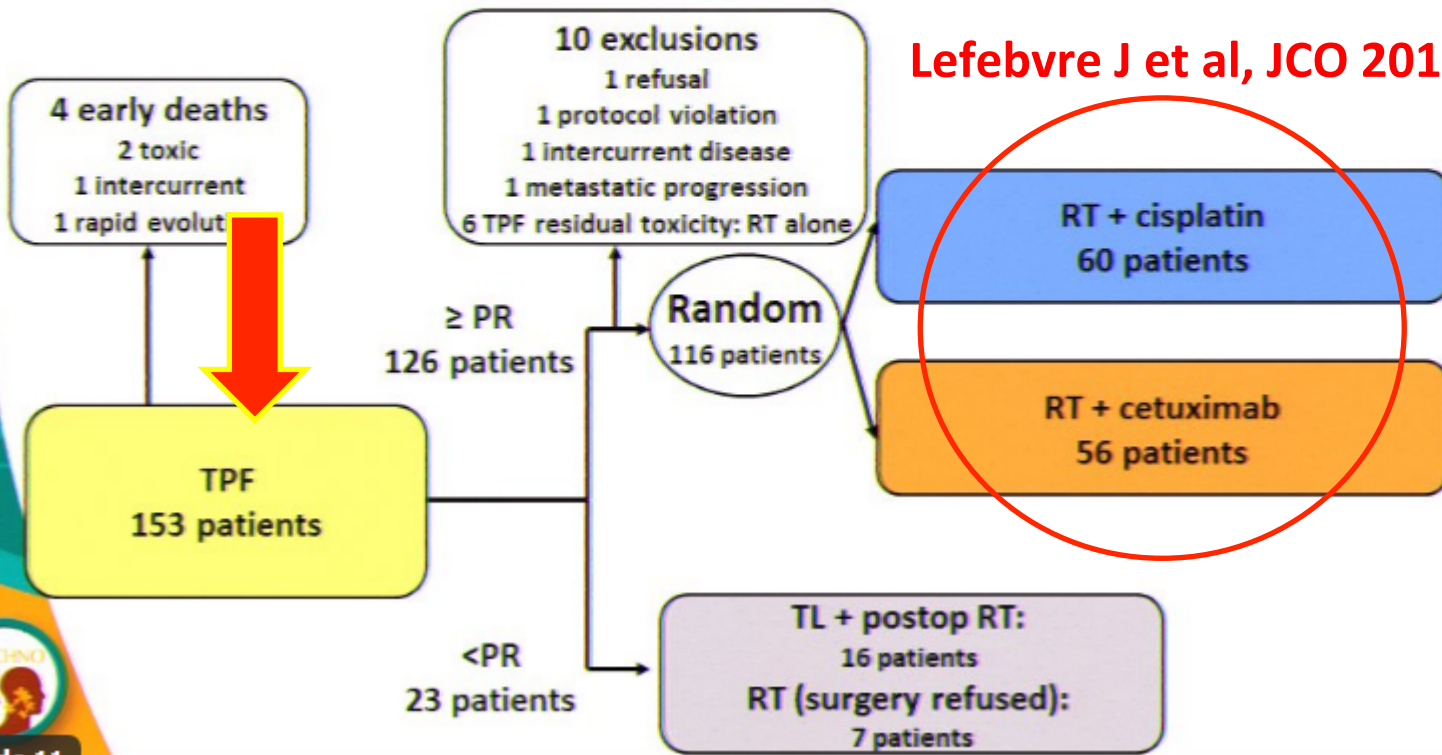
Pts are still being followed-up to assess OS of induction vs. no induction arms.

ASTRO 2013	CRT	CET/RT	HR (95% CI)
Complete response	36%	39%	-
Partial response	47%	49%	-
Complete + partial response	83%	88%	
Stable disease	9%	6%	-
Progressive disease	8%	6%	-
Median PFS (ITT analysis) – months	21.6	20.7	1.05 (0.80-1.39)
Median OS (ITT analysis)-months	44.7	44.7	0.86 (0.62-1.19)

Induction Chemotherapy Followed by Either Chemoradiotherapy or Brachytherapy for Larynx Preservation: The TREMPLIN Randomized Phase II Study

In Press

TREMPLIN - RESULTS



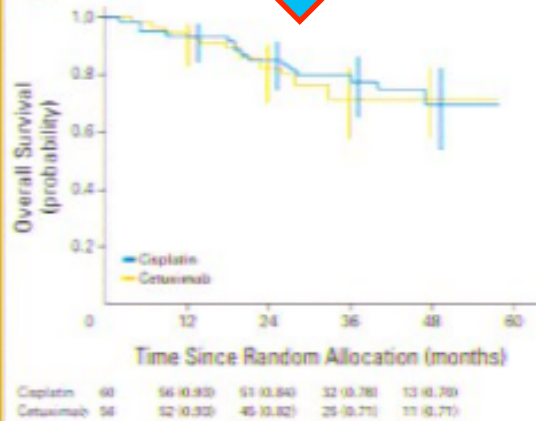
Lefebvre J et al, JCO 2013



Induction Chemotherapy Followed by Either Chemoradiotherapy or Bioradiotherapy for Larynx Preservation: The TREMPLIN Randomized Phase II Study

In Press

TREMPLIN - RESULTS



Good compliance to TPF regimen (74% underwent 3 cycles at the planned doses)
 Good compliance to RT (mean dose 69 and 69.5 Gy)

Better compliance to CTX -radiotherapy

At 18 months:

- No significant difference in LFP (87% CDDP, 82 CTX)
- No significant difference in OS (87% CDDP, 89% CTX)
- Fewer local treatment failures in CDDP arm

- Salvage surgery was feasible in CTX arm

What is the better timing of cisplatin with radiotherapy in concurrent schedules? → weekly or every 3 weeks?

Radiotherapy (RT) potentiation with weekly (q1w) or standard every 3 weeks (q3w) cisplatin chemotherapy (CT) for locally advanced head and neck squamous cell carcinoma (HNSCC)

Yann Molin et al

University of Lyon, Centre Léon Bérard, Lyon, France

J Clin Oncol 31, 2013 (suppl; abstr 6056)

226 pts included and investigated

Overall Survival : trend in favour of **q3w CT**:
2-years OS of 83% vs 74% p=0.089

No difference in cancer outcomes

Toxicity: q3w CT worse than q1w:

Weight loss (p=0.012), renal failure (p=0.022), CT plan completion (p<0.001)

Grade 3/4 toxicities, such as mucositis (p<0.001) and dermatitis (p=0.012)

Parenteral nutrition (p=0.008), analgesics (p<0.001), secondary hospitalization (p<0.001), and had long-term toxicities (p=0.014)

New targeted therapies (1)

Cisplatin and fluorouracil with or without panitumumab in patients with recurrent or metastatic squamous-cell carcinoma of the head and neck (SPECTRUM): an open-label phase 3 randomised trial

Jan B Vermorken et al, on behalf of the SPECTRUM investigators

The Lancet Oncology 2013, 14, 697-710

The Lancet Oncology
Vermonken J et al

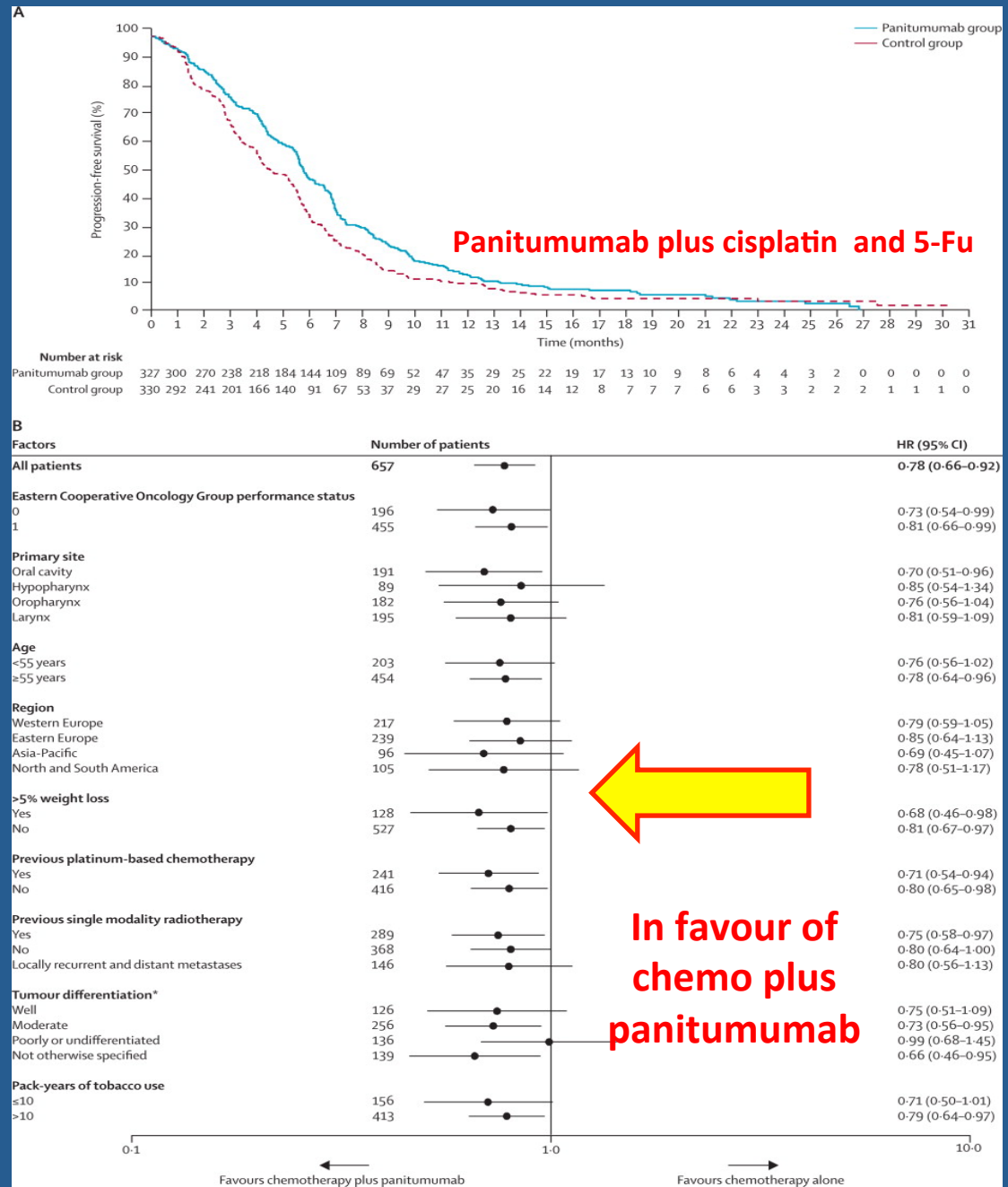
675 pts – 26 countries- 26 centers
Improvement of OS in HPV neg



PFS 5.8 months vs
4.5 months
p= .01

Acceptable toxicity

Recurrent HPV + SCCs
have
longer overall survival
irrespective of therapy
approaches



New targeted therapies plus radiotherapy (2)

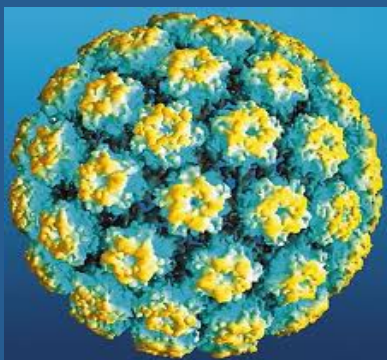
- ECCO –ESTRO-ESMO 2013
- **Zalutumumab** plus radiotherapy (plus nimorazole) vs radiotherapy (plus nimorazole)
- Phase III DAHANCA-9 trial
- Eriksen J et al
- 619 pts LA-SCCHN
- No differences in LRC (78%), OS and DSS



→ **Failure to demonstrate benefit from this EGFR inhibitor**

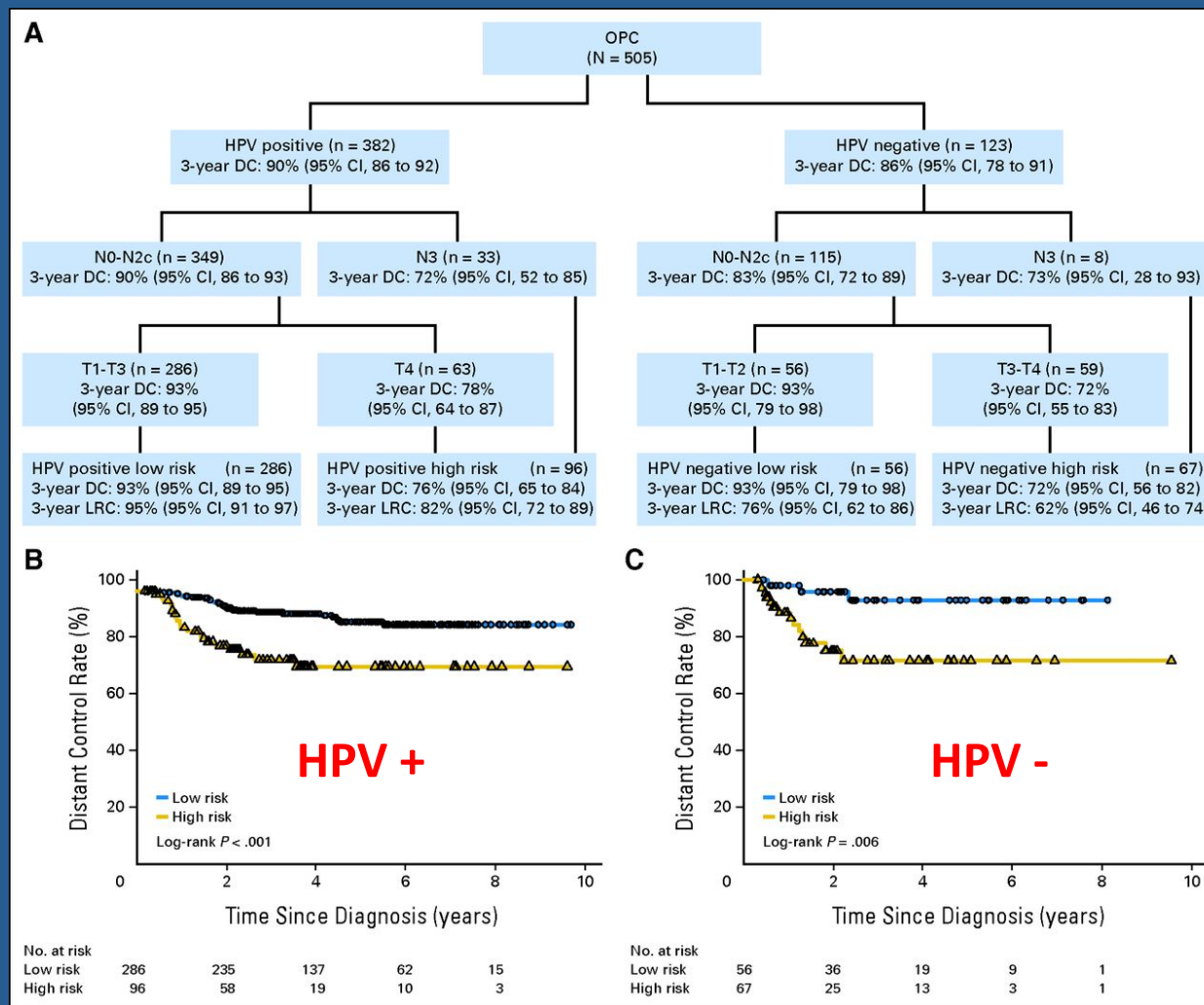
Deintensification Candidate subgroups in Human Papillomavirus–related Oropharyngeal Cancer according to minimal risk of Distant Metastasis

O'Sullivan B et al, JCO 31: 543-550, 2013



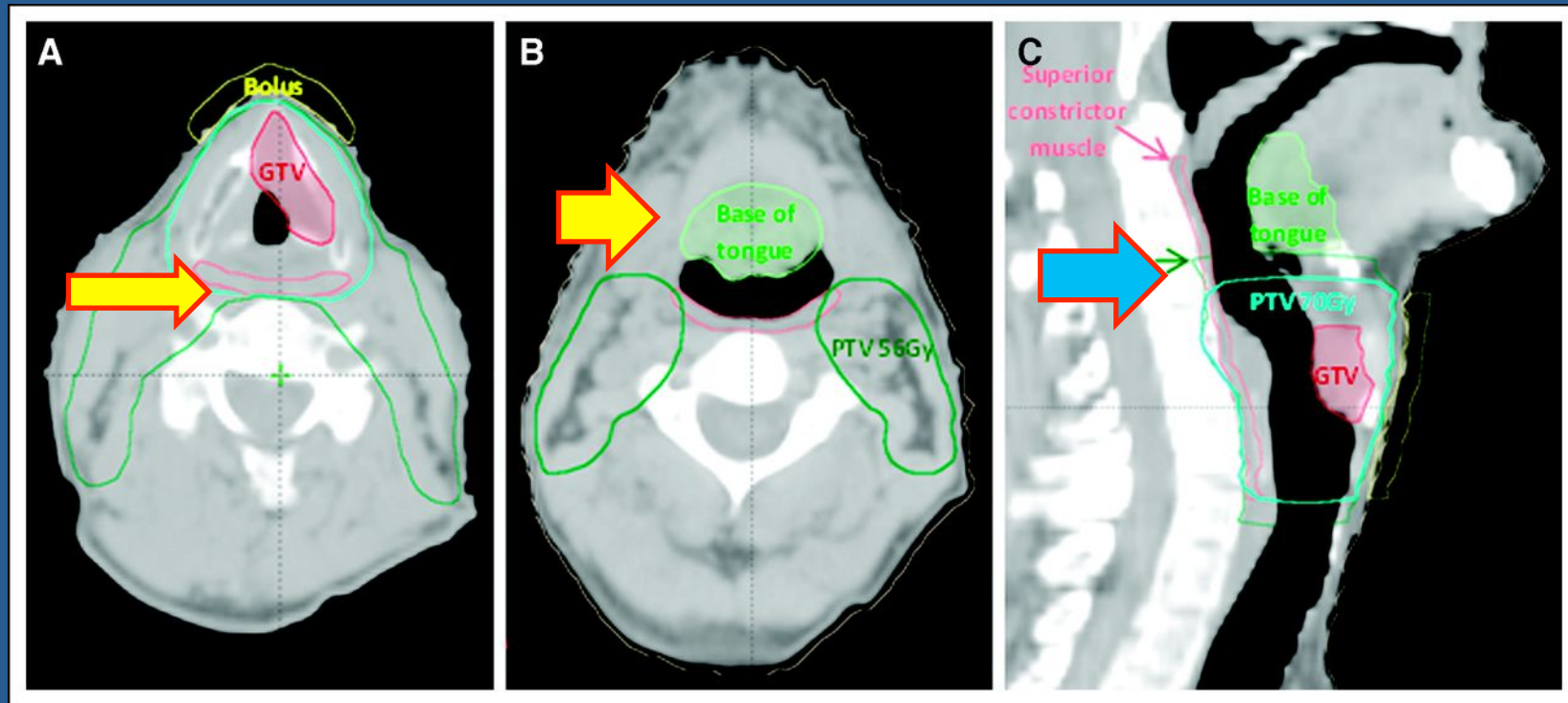
899 patients

HPV positive SCCs
have
higher loco-regional
control than
HPV negative SCCs



Stratify for TNM and Smoke package/year

How to reduce the risk of radiation dysphagia by sparing the base of the tongue and superior constrictors muscles



Corry J et al. JCO 2013;31:840-844

JOURNAL OF CLINICAL ONCOLOGY

EBM 2013 – Tumori Testa Collo conclusioni (1):preservazione laringea

La chemioterapia di induzione (TPF) può ottenere sopravvivenze globali e libere da laringectomia simili a radiochemioterapia concomitante (ma maggiore è il rischio di recidiva locale)

Radiotherapy and Oncology 2013 (in press) :

***A Systematic review of current and
emerging approaches in the field of***

Larynx Preservation

N.Denaro, E.Russi, J.Lefebvre, M.Merlano

EBM 2013 – Tumori Testa Collo conclusioni (2): trattamento standard?

- *La radiochemioterapia concomitante rimane il trattamento standard nella pratica clinica*
- Dopo chemioterapia di induzione i risultati sono simili con cetuximab-RT o cisplatino-RT

EBM 2013 – Tumori Testa Collo conclusioni (3): nuove evidenze

- Nuovi inibitori dell'EGFR:
 - no beneficio clinico se associati a radioterapia
 - minimo beneficio se associati a chemioterapia nella malattia recidivata
- La IMRT migliora l'indice terapeutico
 - ma ...troppi sono gli studi "*in silico*".

Grazie, Buon Congresso AIRO!

