



La chemioterapia neoadiuvante nei tumori della testa e del collo: novità e attuali indicazioni

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Induction Chemotherapy Rationale for LA-H&N tumours

Organ preservation

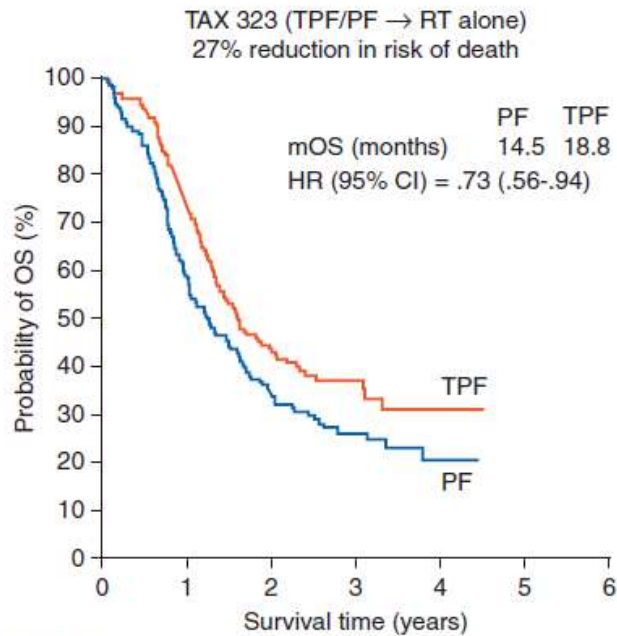
Decrease tumor Volume

Response is predictive of subsequent response to RT

Eliminate clinically occult micrometastatic disease

Response is transient and should be followed by definitive treatment

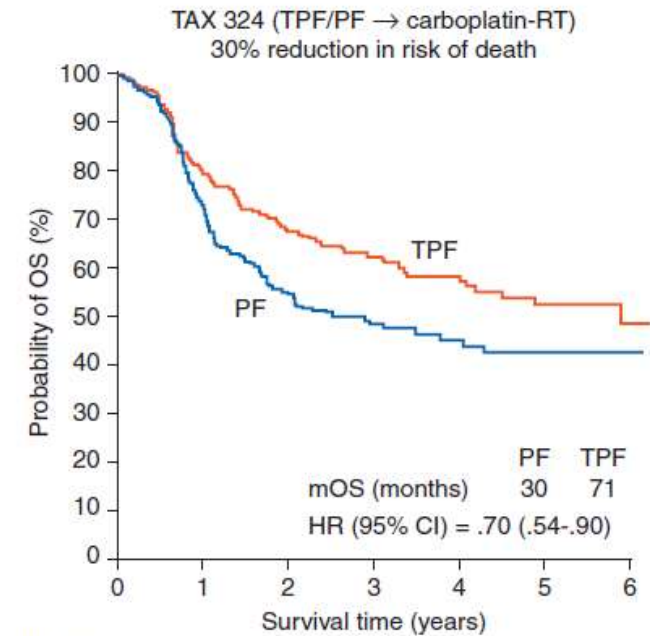
An easy question: which is the best IC regimen?



No. at risk

TPF	177	127	57	21	1
PF	181	97	49	20	4

Vermoken et al, NEJM 2007
Unresectable disease



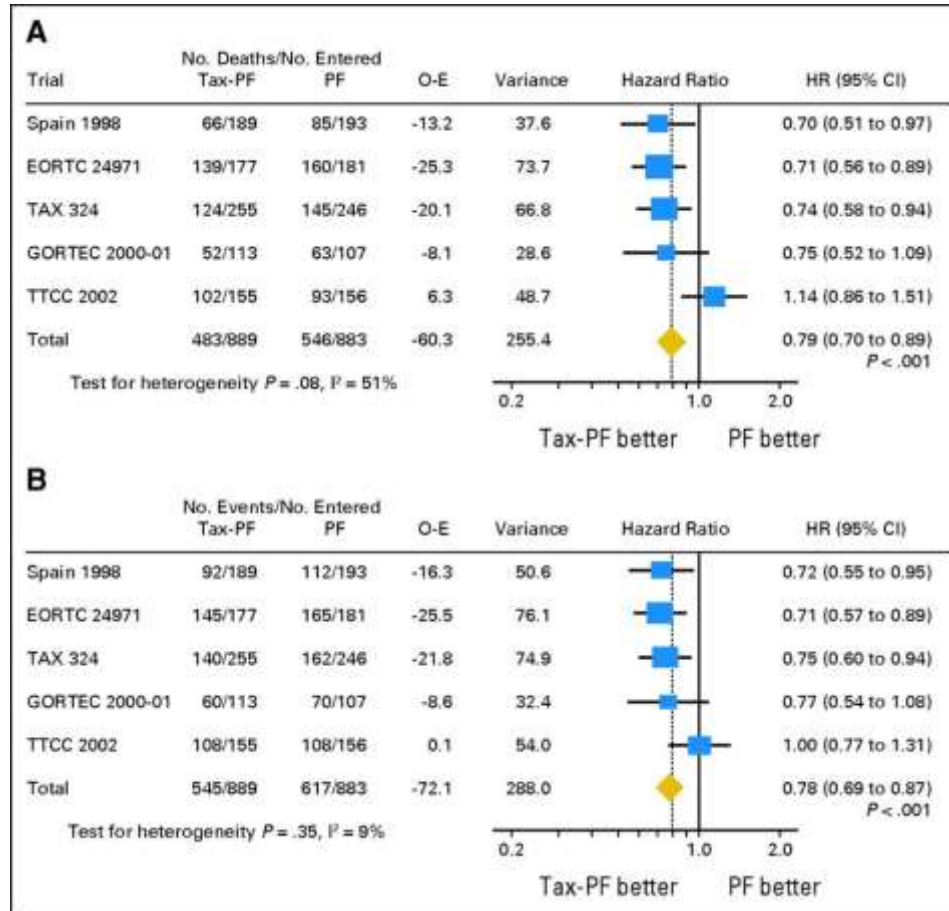
No. at risk

TPF	255	196	163	105	52	37	11
PF	246	169	130	85	36	28	7

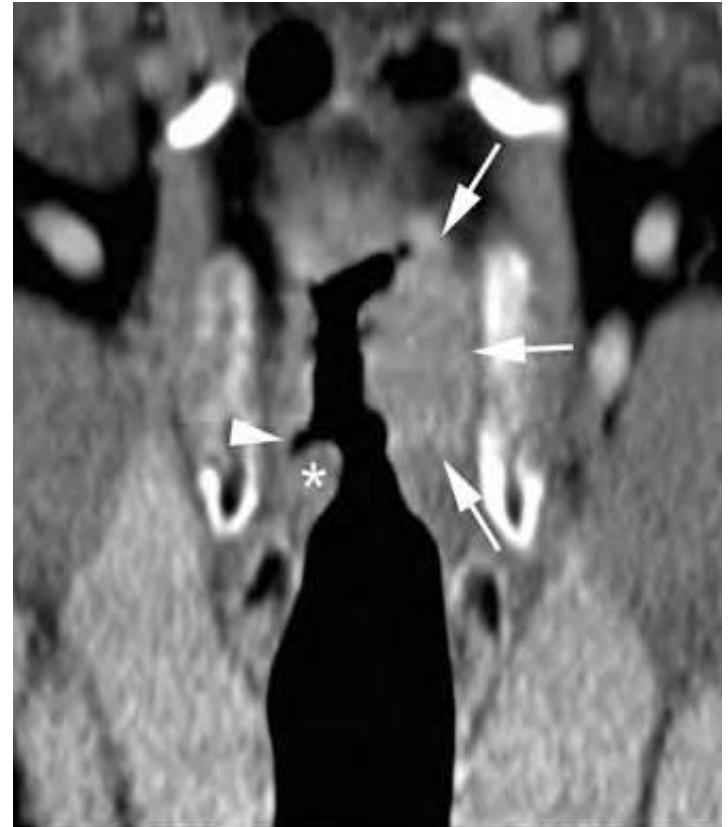
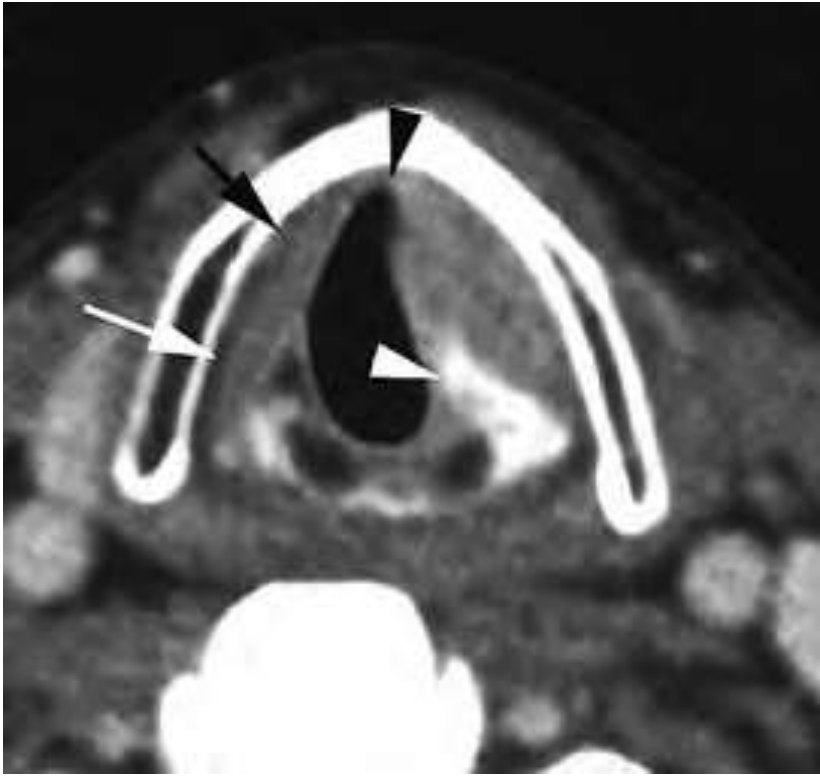
Posner et al, NEJM 2007
Resectable/unresectable disease

Impact of Taxane on Platinum doublet as IC

OS



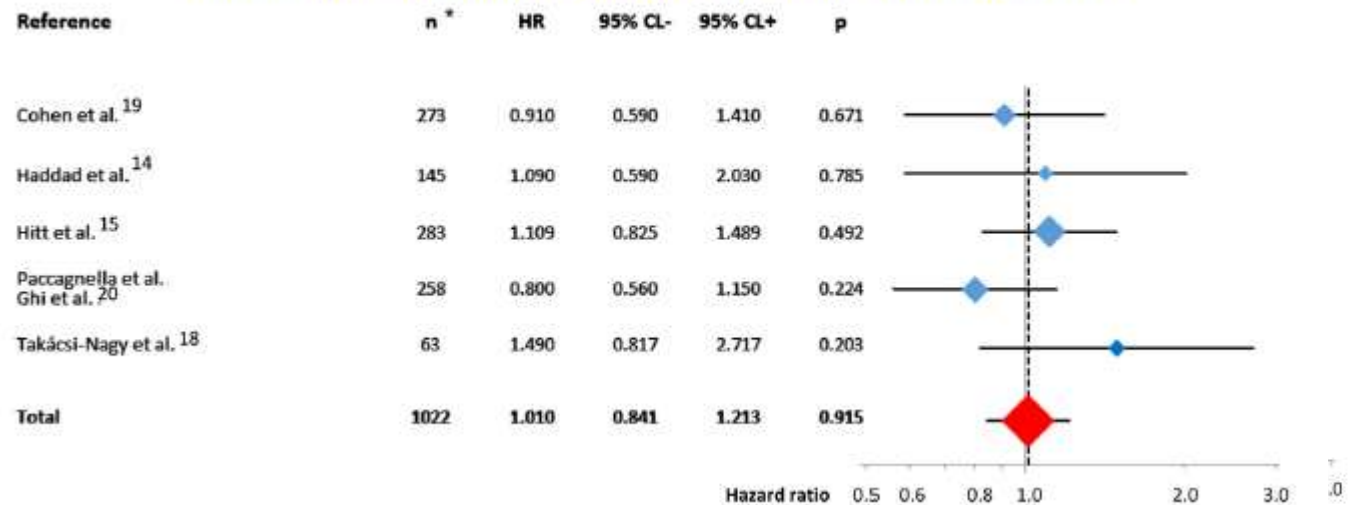
PFS



LOCALLY ADVANCED SCCHN

Adding IC to CRT: a clear benefit?

Meta-analysis of randomized controlled trials: Overall Survival

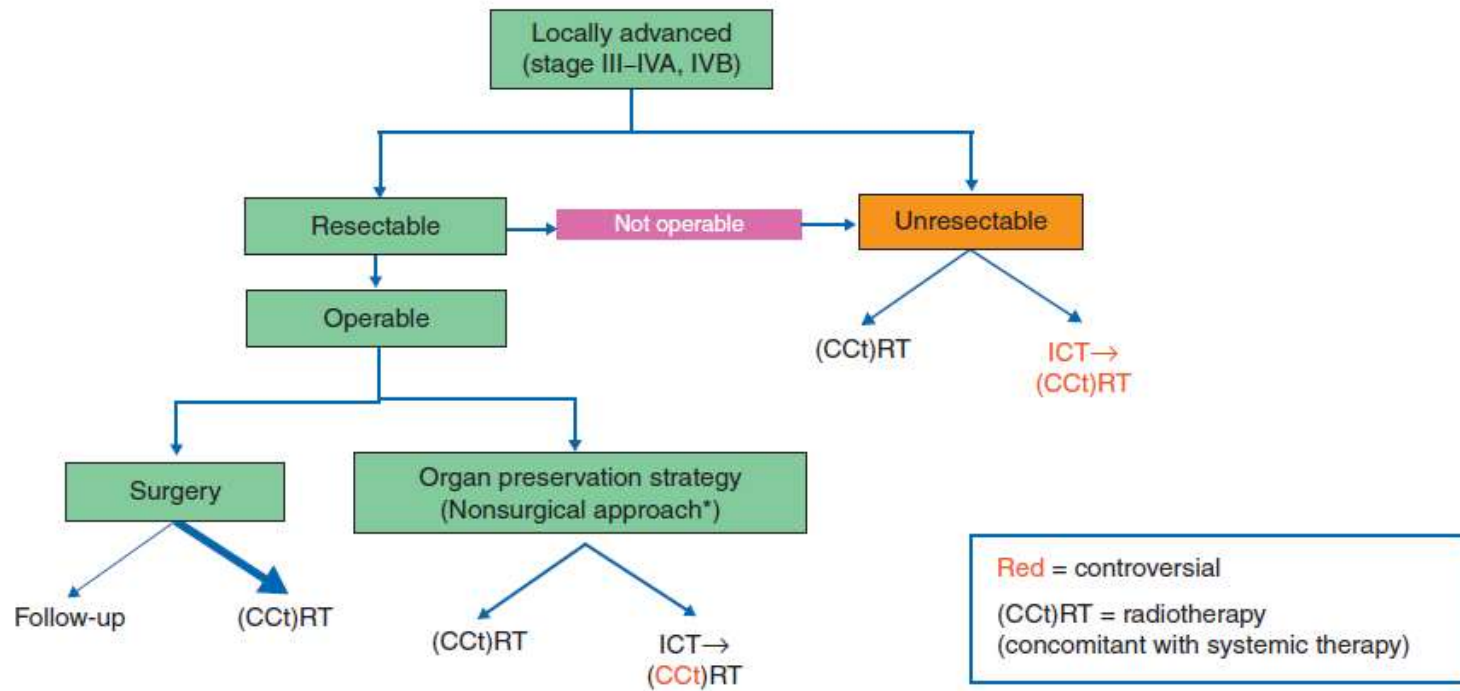


No significant improvement of OS (Hazard Ratio: 1.010, 95% CL 0.84–1.21, p = 0.92)

..nor in a statistically significant benefit of PFS (Hazard Ratio: 0.91, 95% CL 0.75–1.1, p = 0.32).

NB: Results from Ghi study were still preliminary!

Current standard-of-care paradigm in LA SCCHN



IC is only an accepted standard approach for larynx preservation in locoregionally advanced larynx and hypopharynx cancer

IC for laryngeal preservation

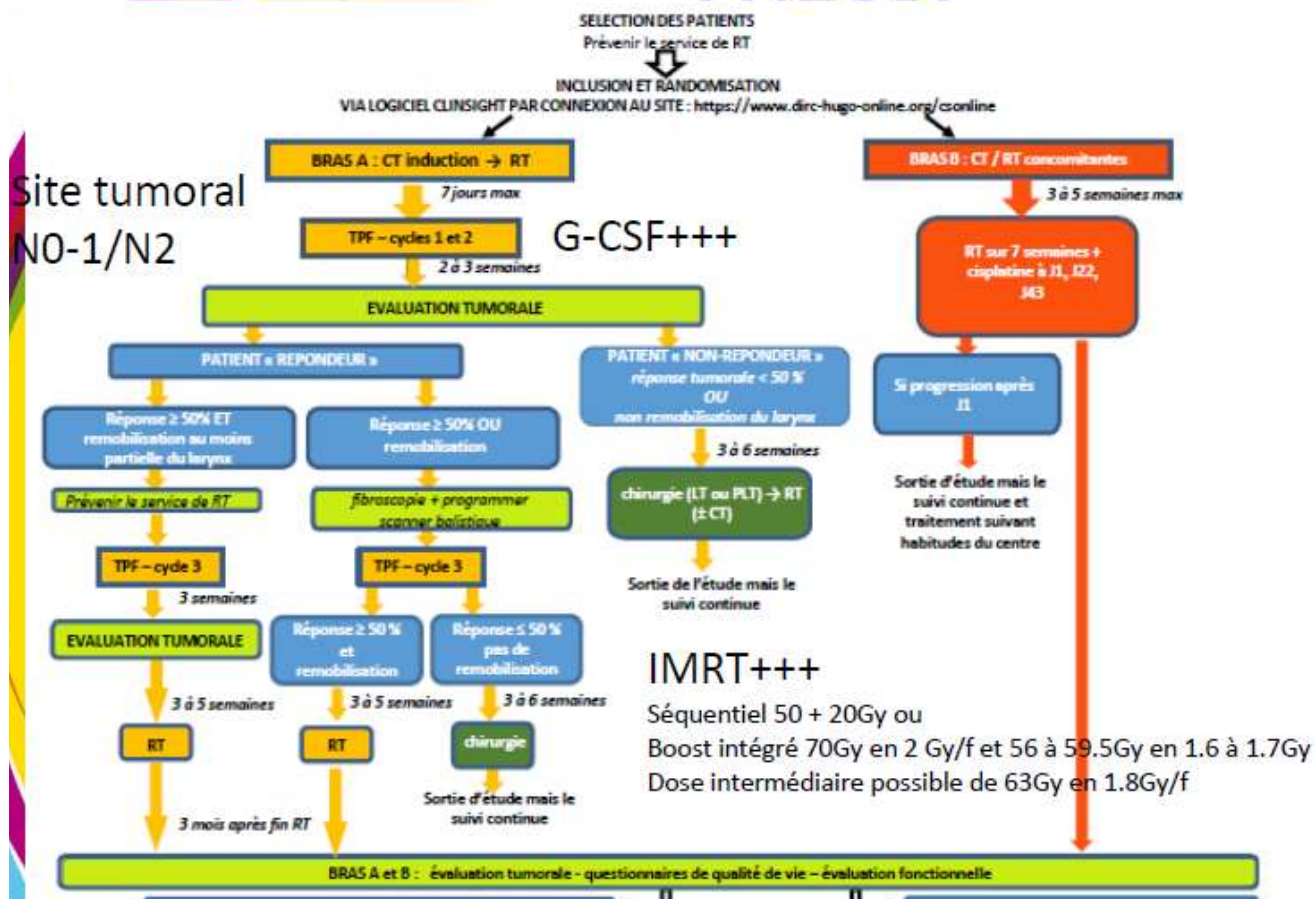
Study	N	Treatment	Primary End point (Larynx Preservation)	OS
VA Study Group	332	<ul style="list-style-type: none"> • Surgery → RT • Cis + 5FU X 3 → RT ± Surgery 	64% at 2 yrs	68% 68% P= NS
EORTC 24891	202	<ul style="list-style-type: none"> • Surgery → RT • Cisplatin + 5-FU x 2-3 cycles → RT or Surgery → RT 	35% at 5 yrs	35% 30% P=NS
RTOG 91-11	525	<ul style="list-style-type: none"> • RT alone (70 Gy) • Cis + 5-FU 1000/m² X 2 CR/PR → Cis/5FU X 1 → RT NR → Surgery → RT • Cis X 3 + RT 	70% (65.7%) 75% (70.5%) 88% (83.6%)	56% (53.5%) 55% (59.2%) 54% (54.6%)

VA laryngeal Ca Study. NEJM 1991;324:1685-1690

Lefebvre JL et al. JNCI 1996;88:890-899; Lefebvre. Ann of Oncology 2012;23:2708

Forastiere AA et al. JCO 2013;31: 845

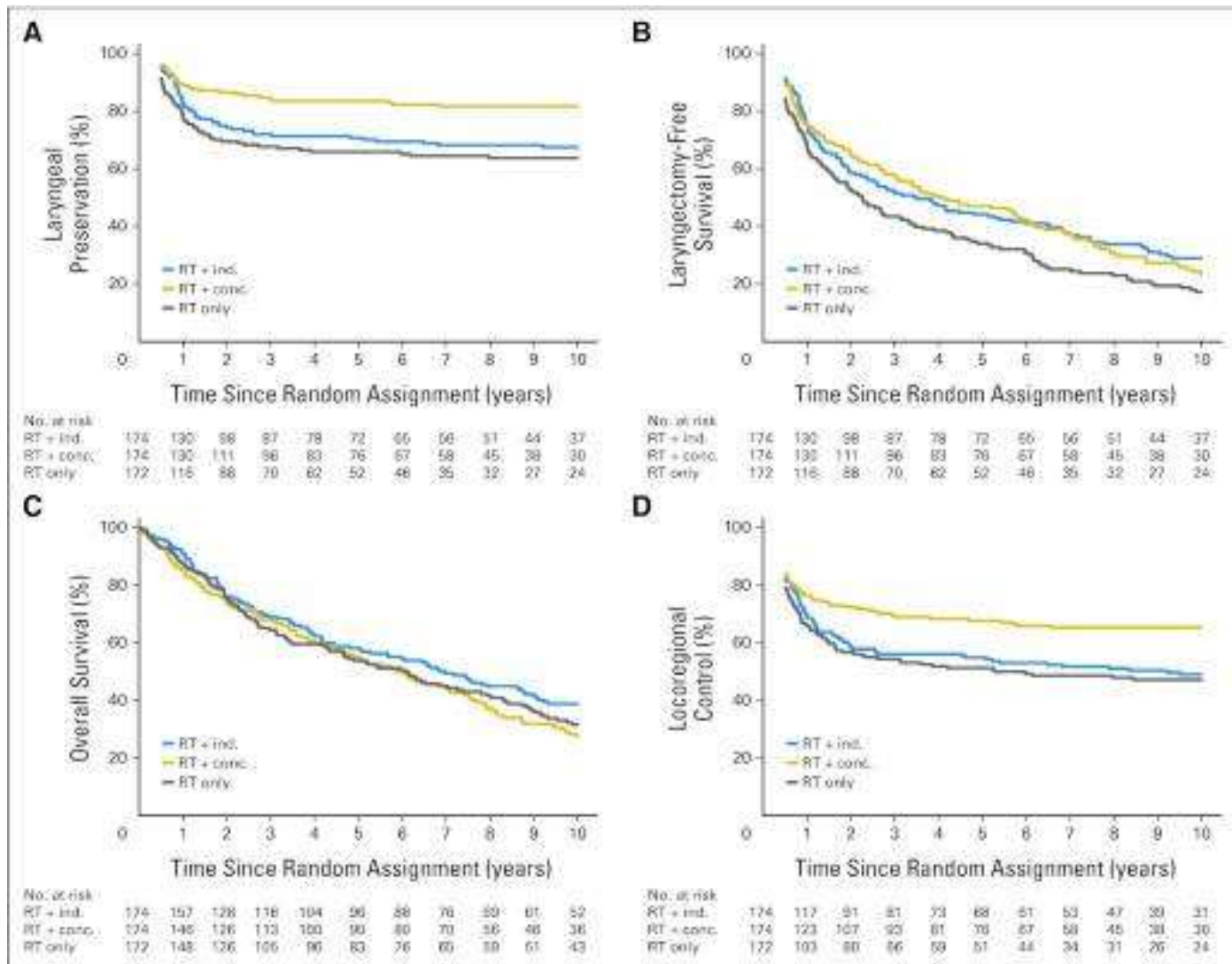
SALTORL TRIAL: the definitive answer regarding laryngeal preservation



Estimated primary completion date: 2019

First results: 2021...

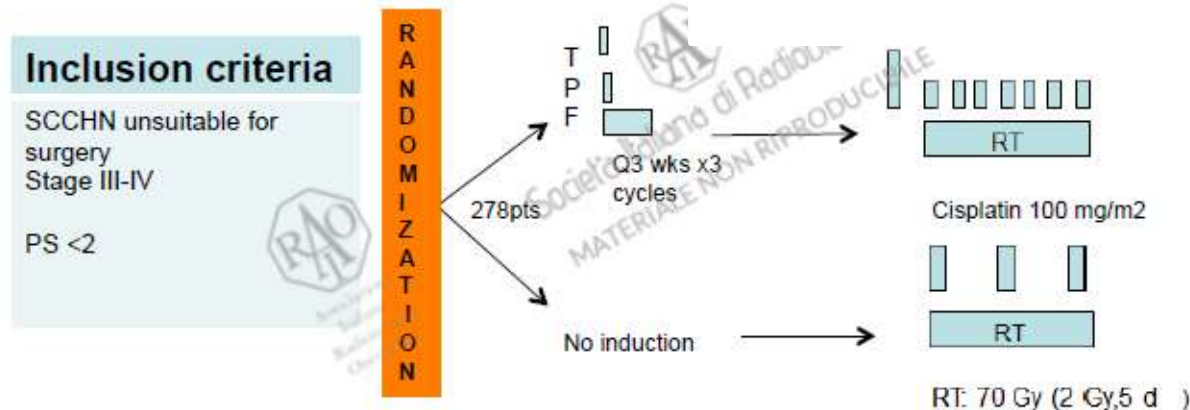
RTOG 91-11: 10 years update



INTERCEPTOR: Italian study

INTERCEPTOR: CRT vs TPF → Cetuximab + RT in unresectable locally advanced SCCHN

Open-label, randomized, multi-center Phase III trial
Lead investigator: M. Merlano
Gruppo Oncologico del Nord-Ovest



Primary endpoint: OS (5yr)
Secondary endpoint include: PFS, LRC, RR, safety (all 5yr)

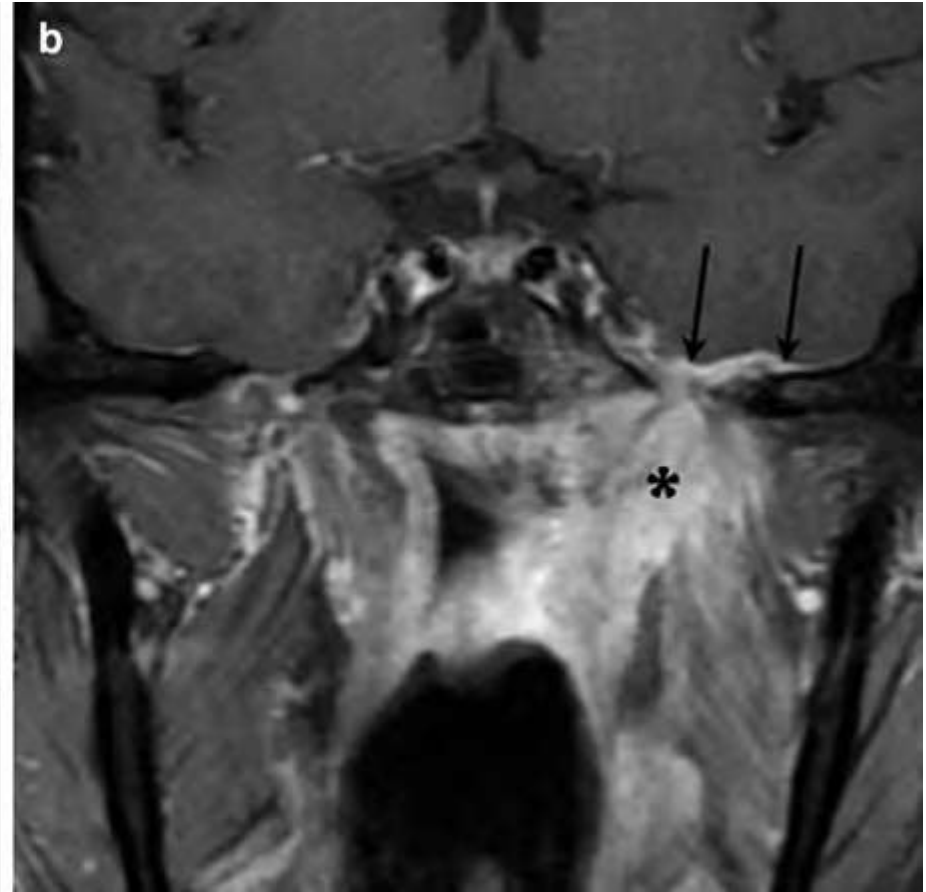
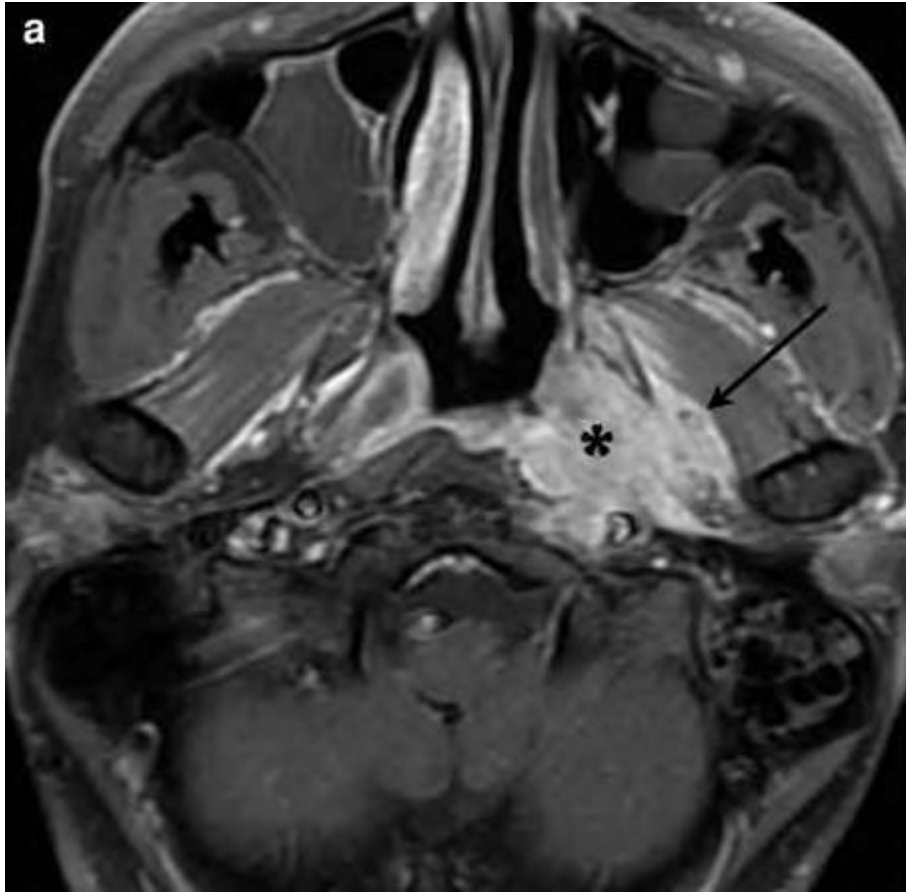
ClinicalTrials.gov Identifier:
NCT00999700

TPF=docetaxel 75mg/m² D1+cisplatin 75mg/m² D1 + 5-FU 750mg/m² D1-4

Recruitment terminated (December 2016)

Toxicity data presented at last ICHNO Meeting

Final results expected very soon to be published



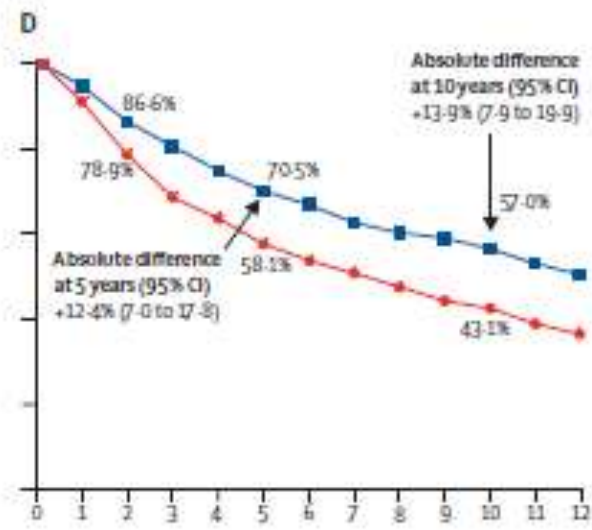
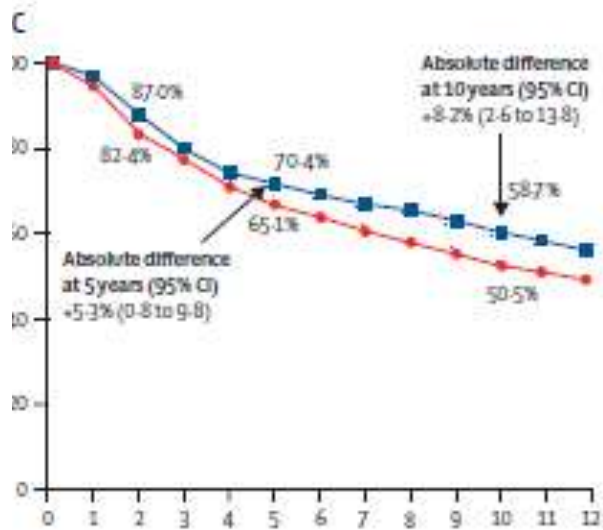
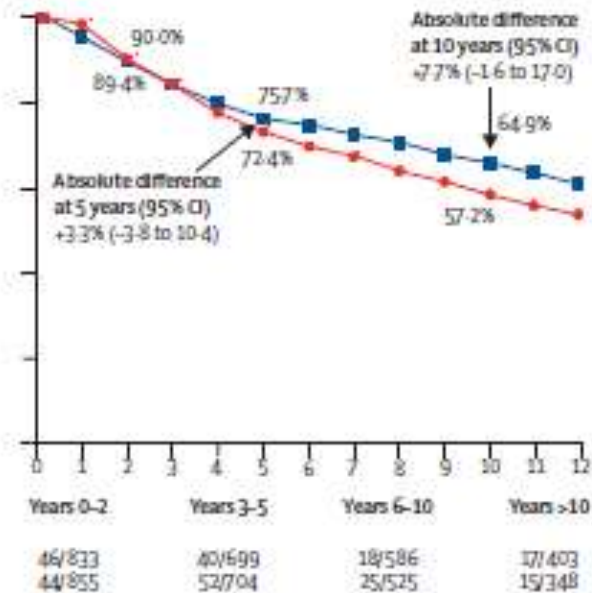
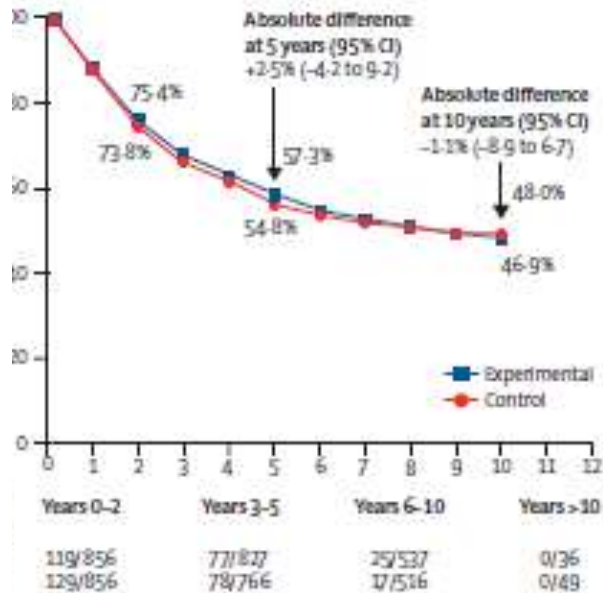
LOCALLY ADVANCED NASOPHARYNGEAL CARCINOMA

Main Rationale for IC in LA-NPC

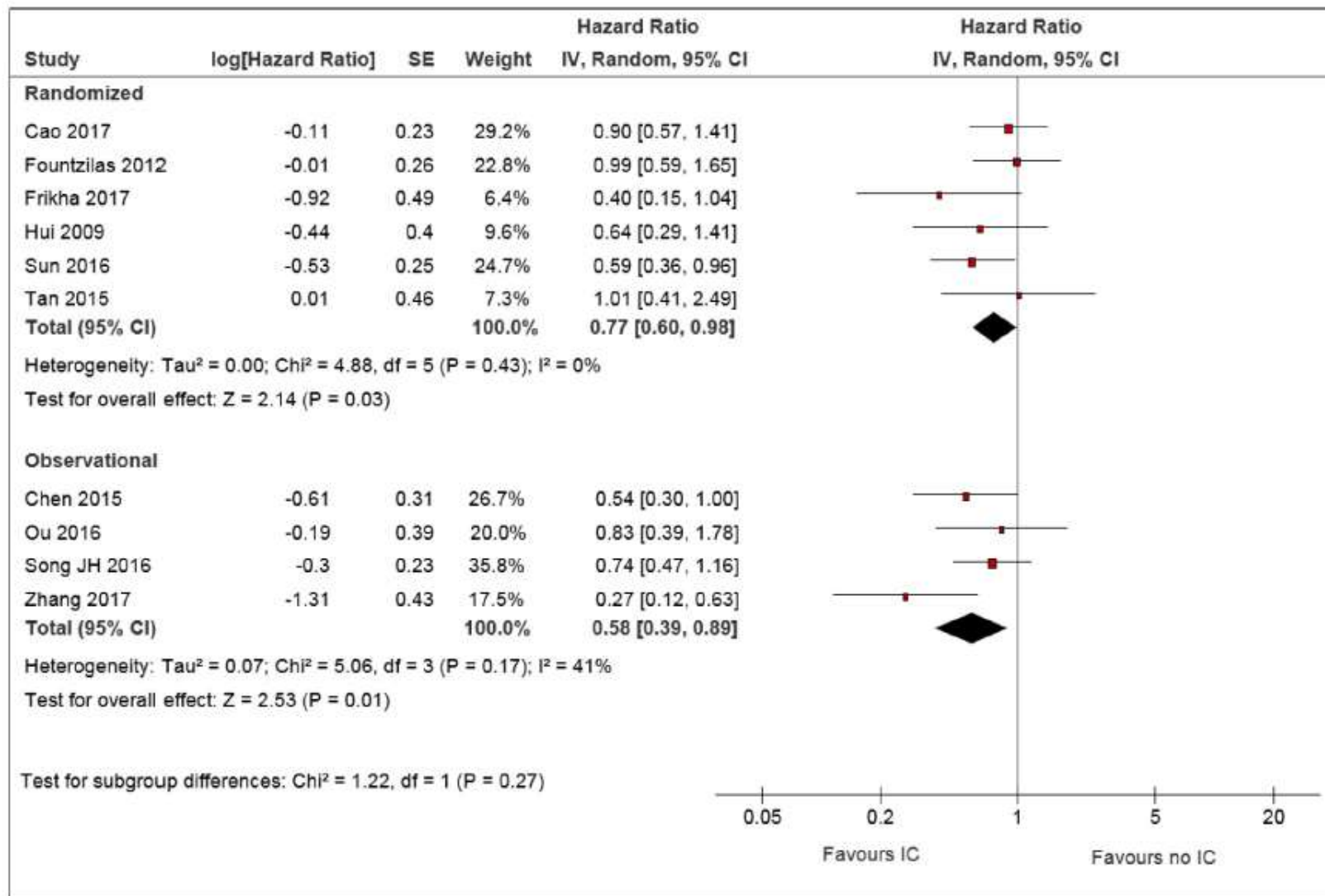
The disease shrinkage and the subsequently RT volumes reduction can allow more effective and less toxic RT

Multiple-agents up-front chemotherapy can influence distant metastases and overall survival.

Impact of IC in LA-NPC (1)

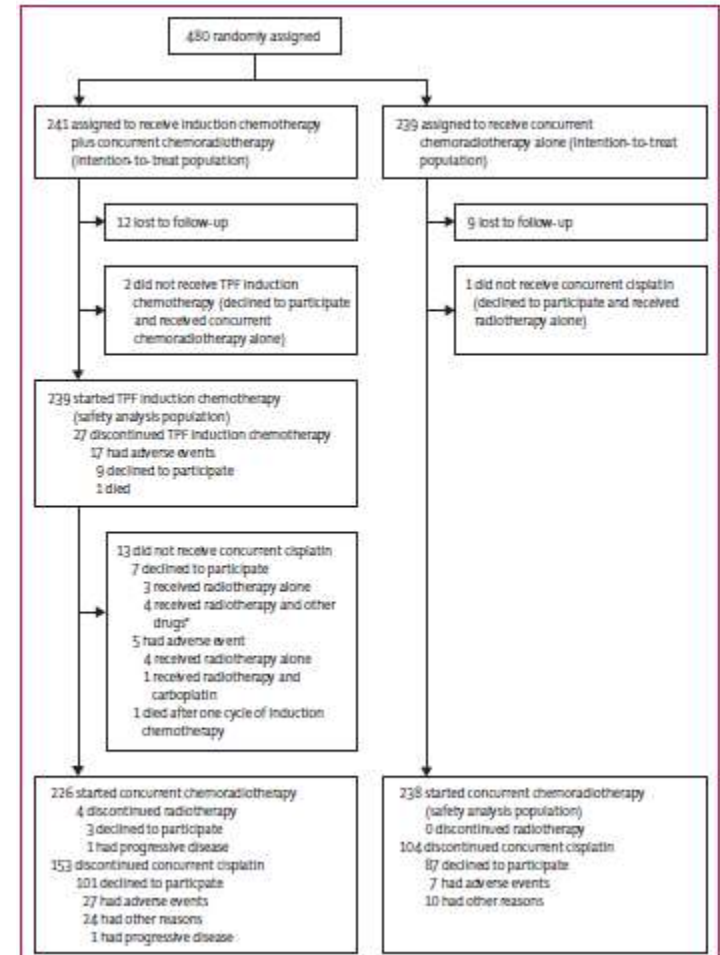


Impact of IC in LA-NPC (2)

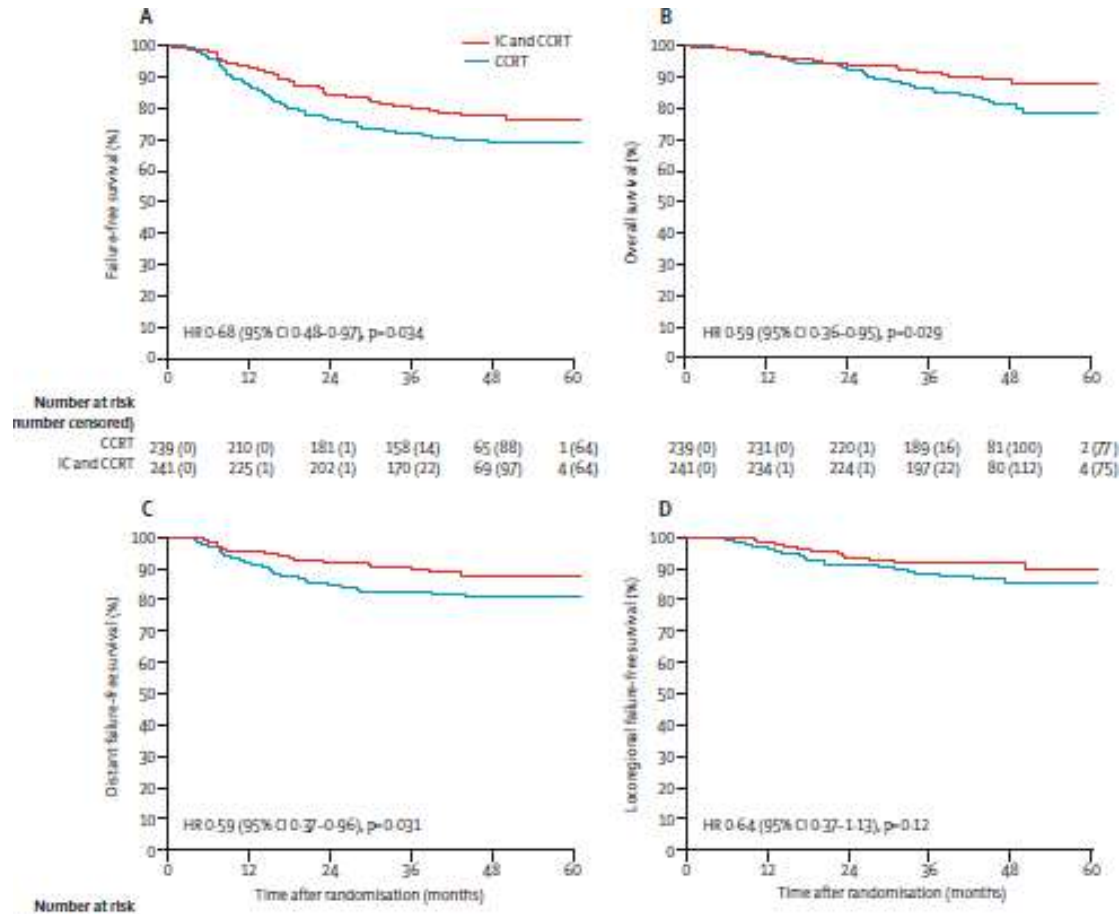


Modern trial assessing IC in LA-NPC

- Phase 3 RCT
- 480 patients
- LA-NPC
- TPF-> CCRT vs CCRT
- **IMRT mandatory**



Outcomes of IC in LA-NPC receiving IMRT



Conclusions

TPF is the IC regimen of choice

Larynx preservation is currently the only widely accepted setting for patients with resectable LA SCCHN in which IC has consensus value.

In LA-NPC CCRT is the treatment of choice; IC may be considered in selected cases (T4? N3 bulky?) after multidisciplinary discussion