Induction Chemotherapy for HNSCC

Induction Chemotherapy for Head and Neck SCC

Case presentation

61M, previously healthy. Heavy smoker, quit a couple of months ago.

5 weeks of progressive facial pain.

Seen by local doctors, given antibiotics for a presumed sinus infection.

Purulent drainage.

Dentures stopped fitting.

Face started to go numb.

Admitted, biopsied.

Nasopharyngeal SCC, nonkeratinizing, discharged home.

Case presentation

Exam

Swollen left eye

Numb left cheek and lips

Labs

mild anemia, mild leukocytosis, BMP and LFTs fine, really nothing interesting

Imaging

Similar case on Radiopaedia:

https://radiopaedia.org/cases/59258/studies/66600?lang=us

Questions

What is induction? (What is the difference between induction and neoadjuvant therapy?)

When is induction a good idea?

When is it a bad idea?

Why are the surgeons always asking us to induce?

What regimens are available/have been studied?

How do I select a regimen for a given patient and situation?

induction chemotherapy (ICT) through the ages

1960s

MTX

1970s

MTX vs cisplatin (response rate 14-41%)

cisplatin+bleomycin

cisplatin+bleomycin+[MTX vs vinca]
- cisplatin+bleomycin+vincristine response rate 80%, CR 29%

cisplatin+5-FU (PF)

ICT through the ages

1980s

5x RCT w MTX - 4/5 -ve, 1/5 +ve only for stage II oral cavity disease (and used intra-arterial MTX)

many other RCTs, no benefit (outside of limited stage oral cavity disease)

1990s

Concurrent Cisplatin-based chemoRadioTherapy (CCRT)

Table 11.2 Summary of the meta-analysis of the MACH-NC collaborative Group [27, 28]

Trial category	No. of trials	No. of patients	Absolute benefit at 5 years	Risk reduction	P value
All trials	65	10,850	4%	10%	<0.0001
Adjuvant	8	1854	1%	2%	0.74
Induction	31	5269	2%	5%	0.10

ICT through the ages

2000s

PF vs TPF

European study (TAX323) had RT afterward,
American Study (TAX324) had CCRT afterward.

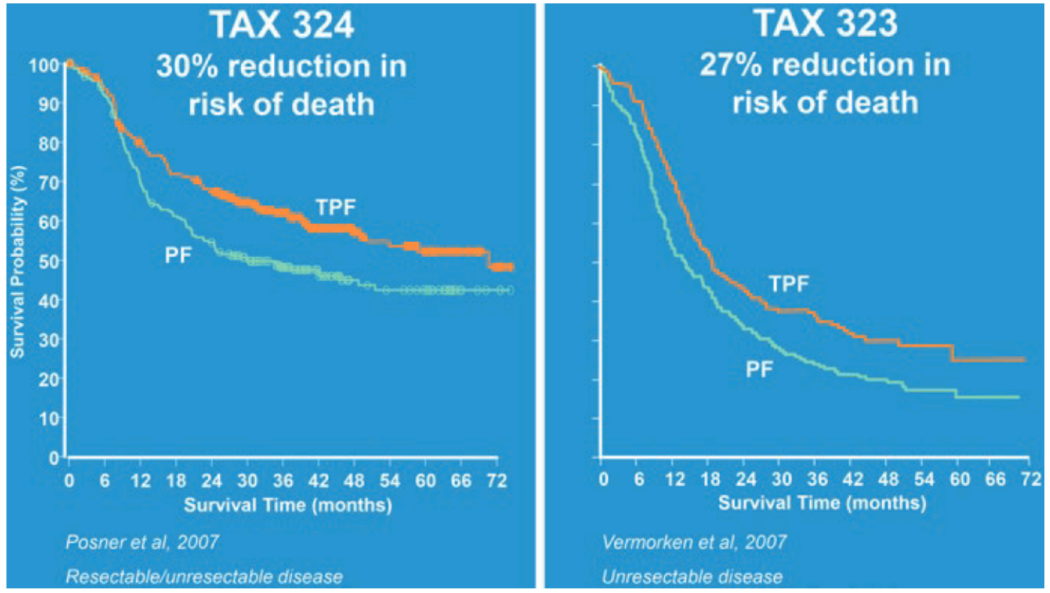

Fig. 11.2 Landmark trials of TPF versus PF in locoregionally advanced HNSCC

ICT through the ages

2000s

ICT + CCRT vs CCRT alone

OS doesn't increase, toxicity does

Table 11.6 Randomized trials of induction chemotherapy followed by concurrent chemoradiotherapy versus concurrent chemoradiotherapy alone in patients with locoregionally advanced HNSCC

Investigators/Trial	Population	Regimens	Survival↑	Tox↑
Hitt et al/TTCC [53]	439 pts, stage III/IV	TPF (or PF)x3→CCRT(P)	No	Yes
	Prim. endpoint: PFS	CCRT (cisplatin)		
Haddad et al/ PARADIGM [54]	145 pts, N2 and N3	TPFx3→CCRT (C or Doce)	No	Yes
	Prim. endpoint: OS	CCRT (cisplatin)		
Cohen et al/DeCIDE [55]	285 pts, N2 and N3	TPFx2→CCRT (THF)	No	Yes
	Prim. endpoint: OS	CCRT (THF)		
Ghi et al./GSTTC [56]	421 pts, stage III/IV	CCRT(PF) w/wo prior TPF	Yes[a]	Yes[b]
	Prim. endpoint: OS	BRT(cet.) w/wo prior TPF		
Geoffrois et al./GORTC 2007-02 [57]	370 pts, N2b/c, N3	TPFx3→BRT (cetuximab)	No	Yes
	Prim. endpoint: 2-yPFS	CCRT (carbo/5-FU)		

nuanced (locoregional vs distant recurrence)

ICT through the ages

2010s

Rise of the mods:

- modified TPF (dose reduced)
- weekly carbo-taxol followed by CCRT
- TPEx (cisplatin, docetaxel, cetuximab)

Our patient:

- docetaxel 75, cisplatin 75, q3wk x3 and reimage

ICT today

NPC
- gem+cis ICT f/b CCRT: +OS benefit if EBV+ (NEJM 2019, JCO 2022)

larynx preservation
- CCRT not clearly better than ICT in pts who qualify for total laryngectomy but not partial - SALTORL trial is comparing ICT and CCRT head-to-head

treatment intensification
- TPF+CCRT in the fittest patients?

converting borderline resectable to resectable
- ~30% conversion rate

oligometastatic disease

ICT for NPC

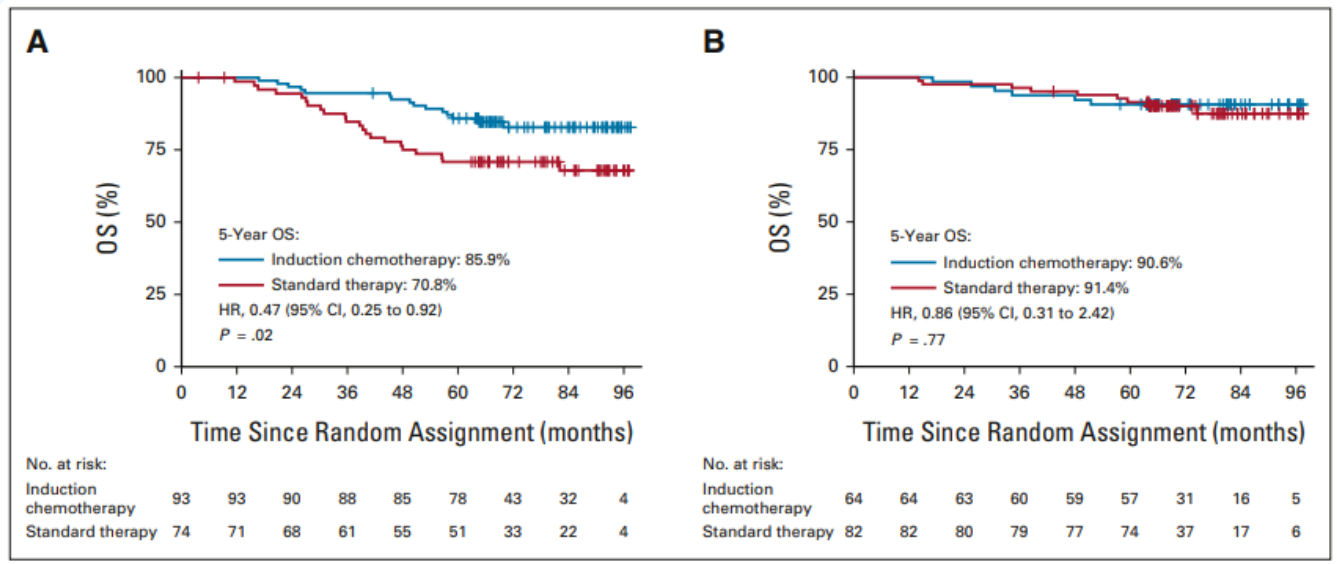

FIG 2. Kaplan-Meier survival curves for OS in the two treatment groups stratified by different pretreatment cell-free EBV DNA loads: (A) ≥ 4,000 and (B) < 4,000 copies/mL. HRs and 95% CIs were calculated using an unstratified Cox proportional hazards model. Plus symbols indicate censored data. EBV, Epstein-Barr virus; HR, hazard ratio; OS, overall survival.

Induction radiotherapy?

"Quad-shot" RT: 14-15 Gy over 4 fractions

- 2x/day (6h separation) x 2 days
- palliative
- if response, can continue monthly (usually cap around Gy in the low 40s)
- studies looking at quad-shot+something are ongoing (e.g. NCT04454489 - +pembro)

Resources

HemOnc.org entry

NCCN Guidelines

PathologyOutlines

notes

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