Head and Neck Cancer

15th Annual Comprehensive Hematology and Oncology Review Course

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Disclosures

	Cristina Rodriguez(Presenter)	**Spouse**
Institutional Research Funding	AstraZeneca Ayala Bristol Myers Squibb Cue Biopharma Kura Merck Prelude Therapeutics Sanofi Aventis Seagen	Acerta Pharma BV Astrazeneca Bayer Beigene De Novo Biopharma Incyte Corporation Merck Sharp and Dohme Corp. Pharmacyclics Portola Pharmaceuticals
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I. Mucosal Squamous Cell Carcinomas

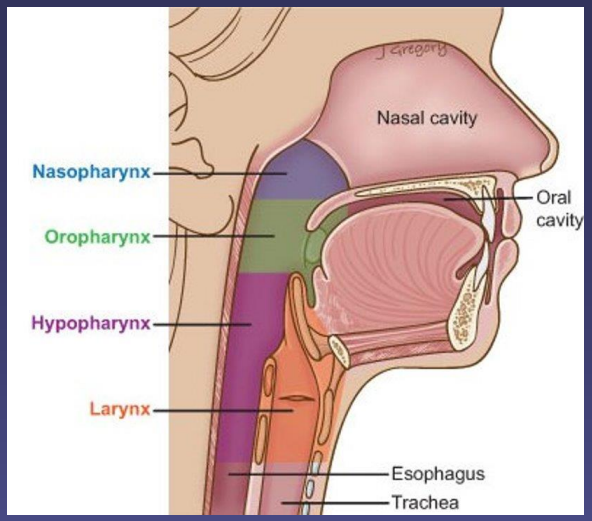
- anatomy epidemiology and pathogenesis
- staging
- treatment by subset
  - locally advanced disease
    - unresectable/organ preservation
    - postoperative therapy
  - metastatic disease

II. Thyroid Cancer

III. Salivary Gland Cancer

Part I

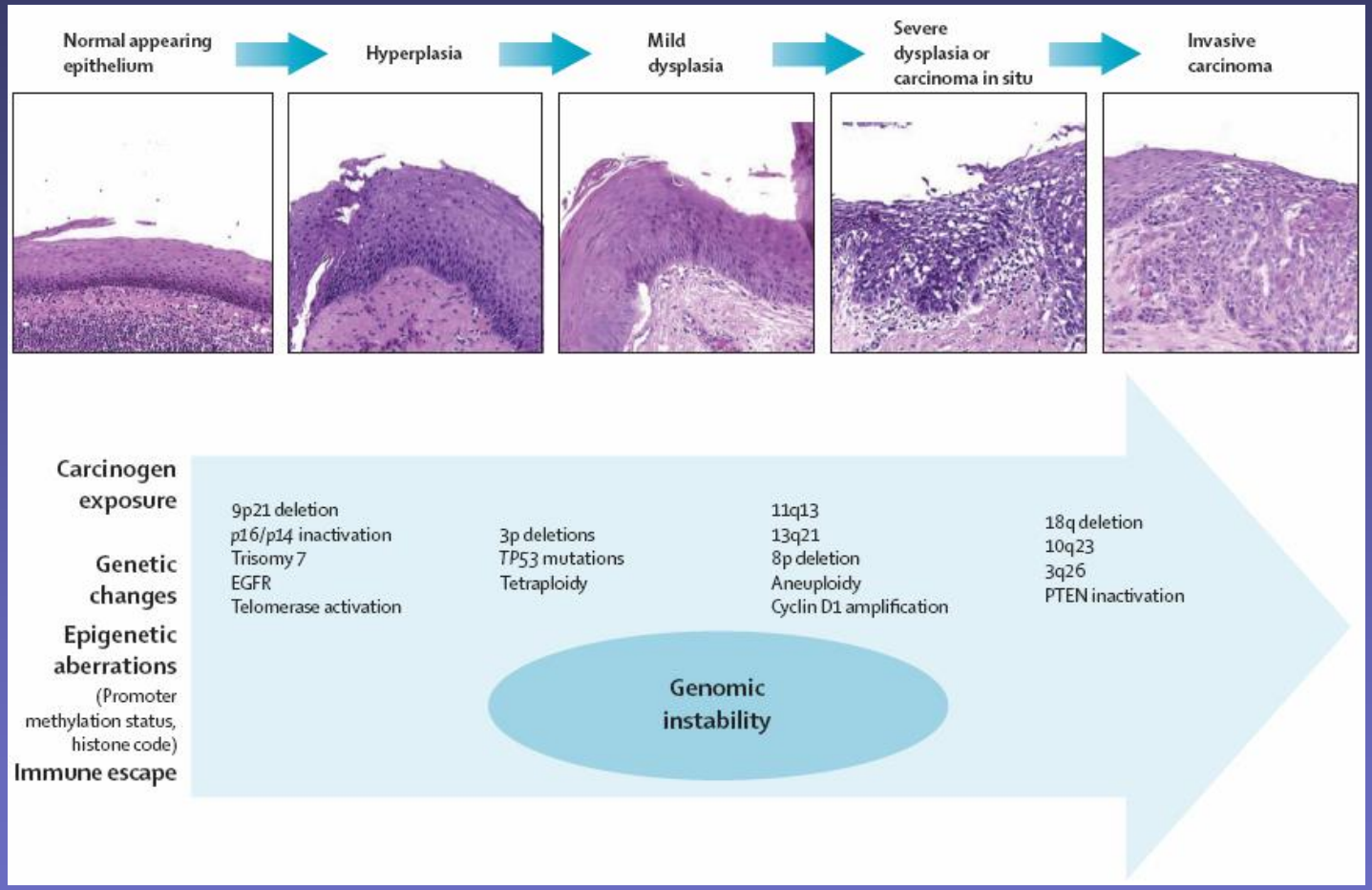
Mucosal squamous cell carcinomas of the head and neck



Pathogenesis

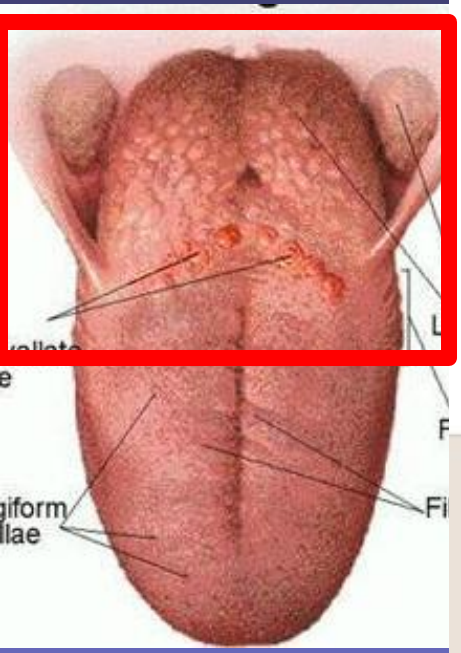
1. **Tobacco and alcohol**
   - oral cavity, larynx, hypopharynx
   - declining in incidence
   - economic and racial disparity
2. **Viral exposure**
   - HPV in oropharynx, increasing incidence
   - EBV in nasopharyx

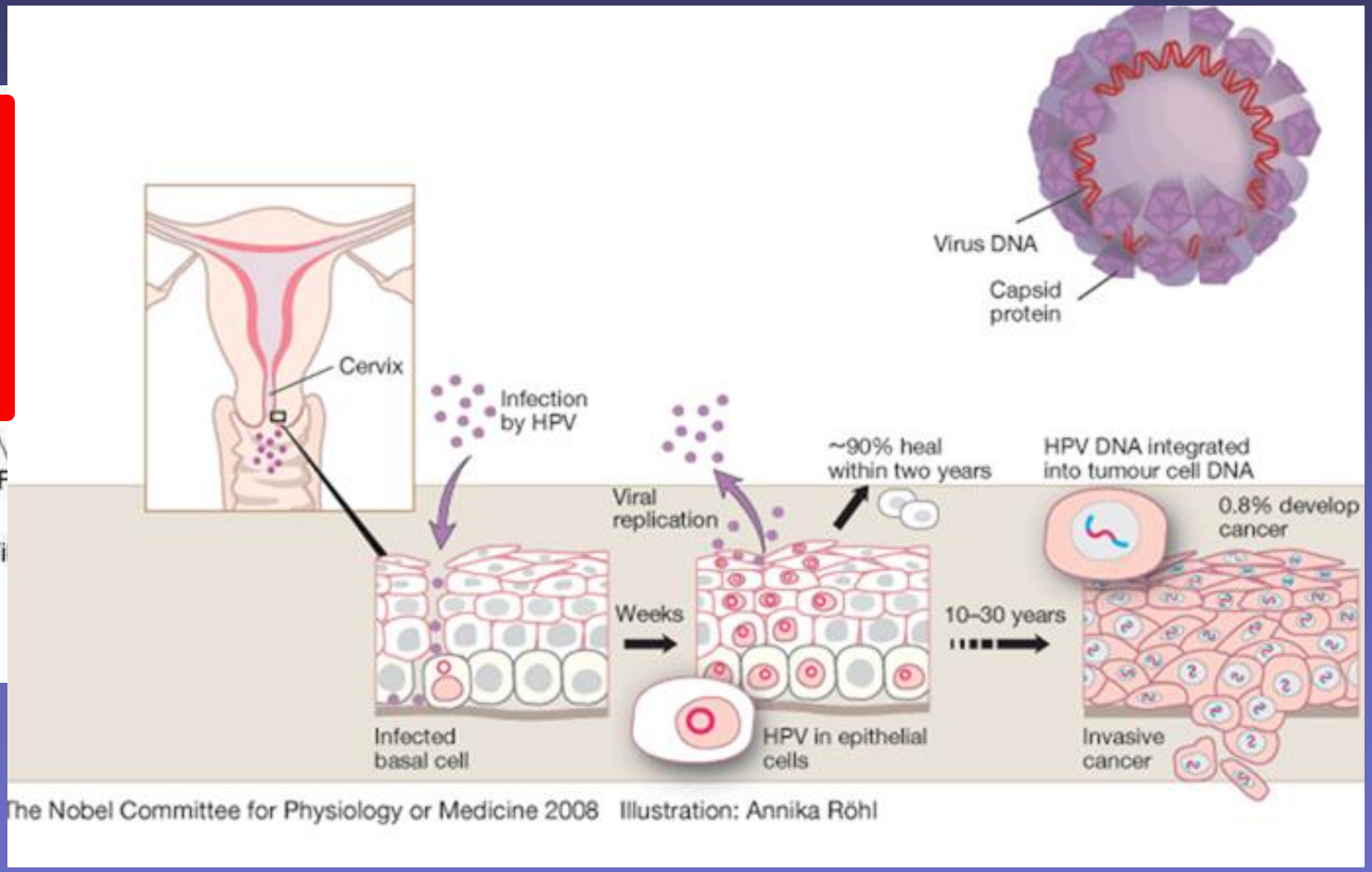
Tobacco and Alcohol



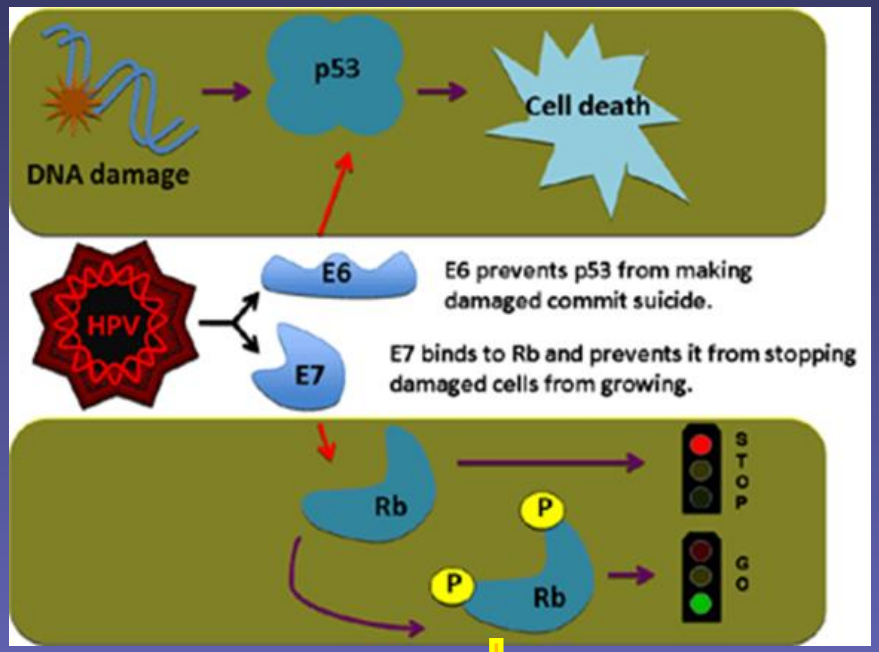
Argiris et al. Lancet. 2008 May 17;371(9625):1695-709.

The oropharynx and HPV16

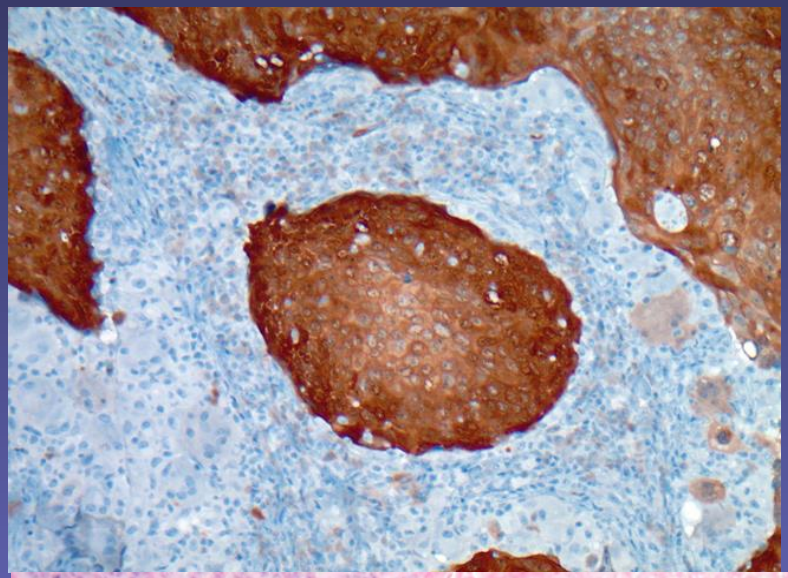


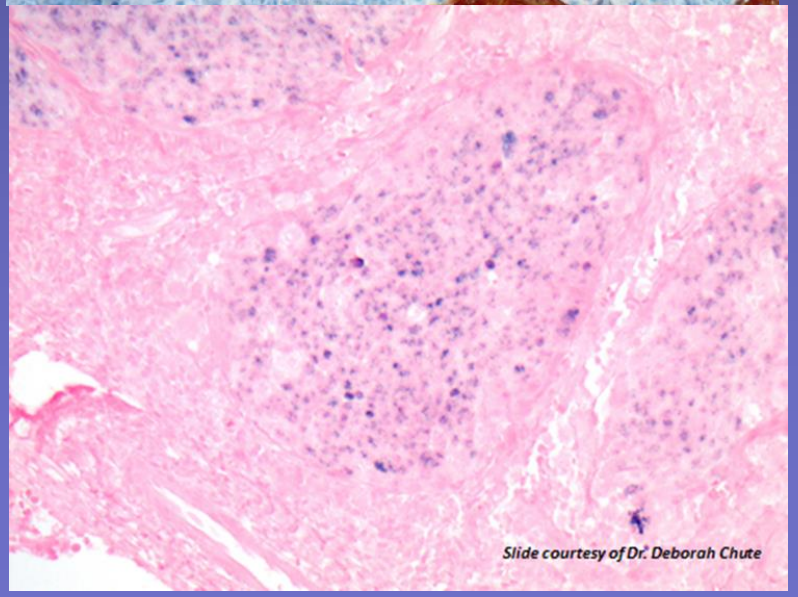


HPV and p16



p16 upregulation





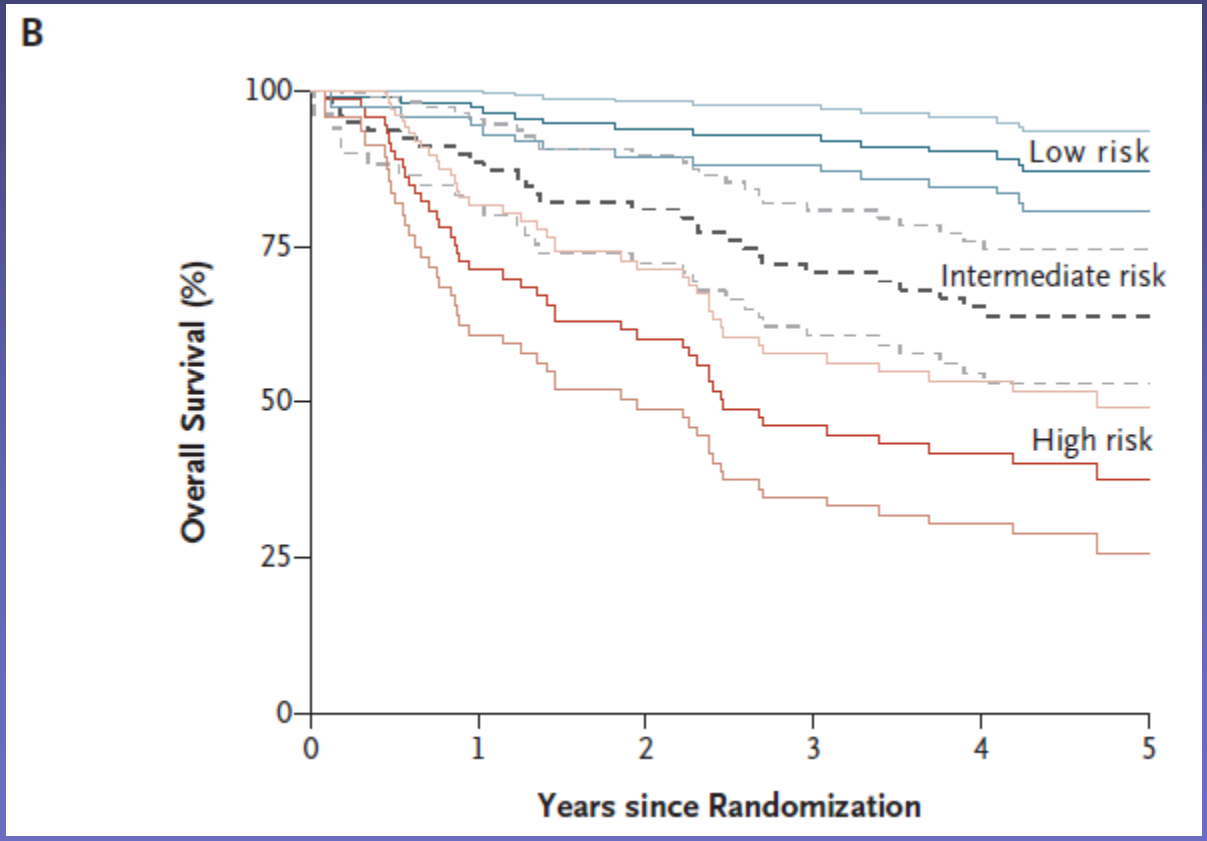
http://genetics.thetech.org/ask/ask359

HPV+ OPC vs HPV- HNSCC

- Demographically distinct
  - Lower median age, caucasian males
  - Sexual risk factors
  - Minimal comorbidity
- Tumor characteristics
  - p53/Rb WT
  - Cystic LAD, BOT/Tonsil primaries
- Clinical behavior
  - Improved prognosis
  - Second primaries uncommon

HPV+ OPC is heterogenous

RTOG 0129



Ang KK et al. N Engl J Med. 2010 Jul 1

Key points on HPV+OPC

- IHC for p16 is highly correlated with HPV-positivity ***in the oropharynx***
- Completion of HPV+ clinical trials have established standards of care
- Treatment de-escalation remains a research question in active investigation

Staging

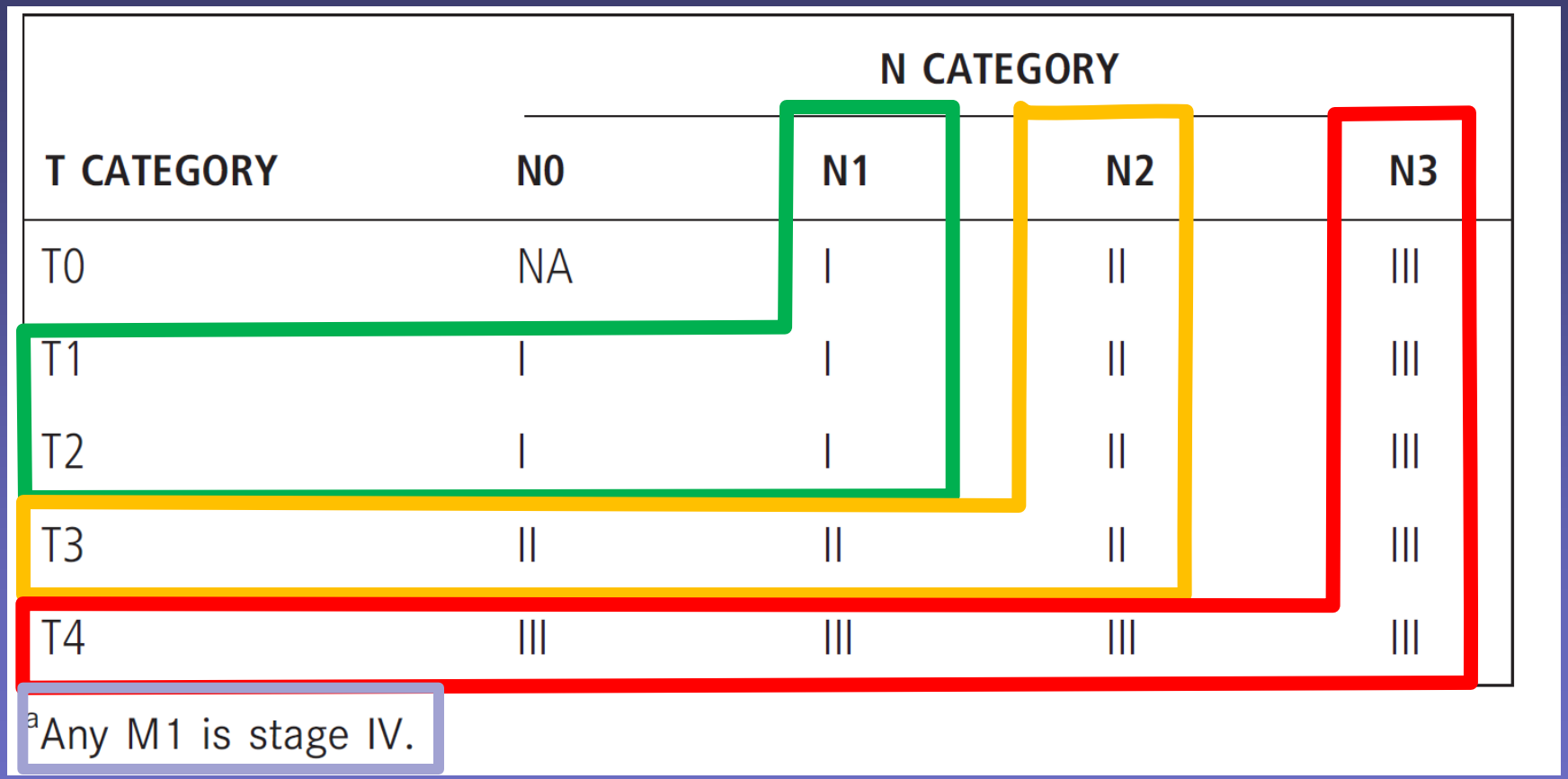
- General Principles:
  - T1-2 lesions small
  - T4 lesions invade into surrounding structures
  - N3 >6cm nodes
- Unknown primaries (Tx)
  - Occur in 10-13% of cases
  - Curable
- **HPV related OPC is now staged separately**

STAGING: AJCC v. 8
NonHPV related

Stage I	T1	N0	M0	15% new diagnoses Surgery or XRT with curative intent 70% or greater 5 year Overall Survival
Stage II	T2	N0	M0	
Stage III	T3 T1-3	N0 N1	M0 M0	75% of new diagnoses Curable with multimodality therapy Usually chemotherapy + XRT 30-50% 5 year over all survival
Stage IVA	T4a T1-4a	N0-1 N2	M0 M0	
Stage IVB	T4b Any T	Any N N3	M0 M0	
Stage IVC	Any T	Any N	M1	10% new diagnoses Incurable, median survival <1 yr

AJCC Cancer Staging Manual, Eighth Edition 2016

STAGING: AJCC v. 8
HPV related OP Cancer



T CATEGORY	N CATEGORY N0	N1	N2	N3
T0	NA	I	II	III
T1	I	I	II	III
T2	I	I	II	III
T3	II	II	II	III
T4	III	III	III	III

[a]Any M1 is stage IV.

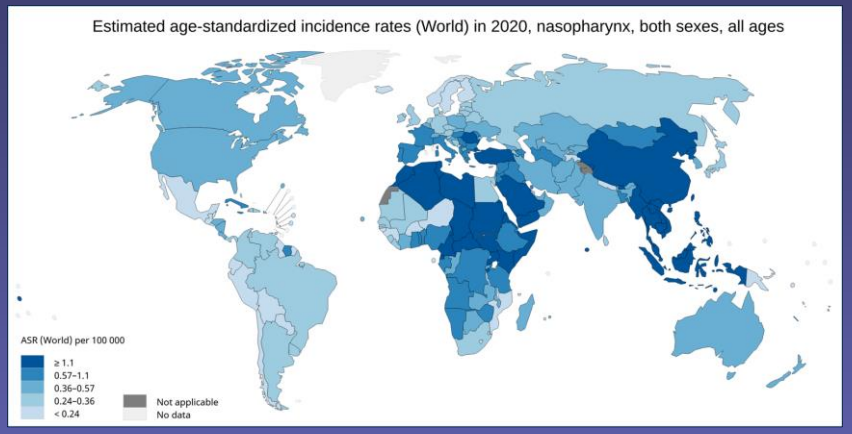
AJCC Cancer Staging Manual, Eighth Edition 2016

Locally Advanced Disease

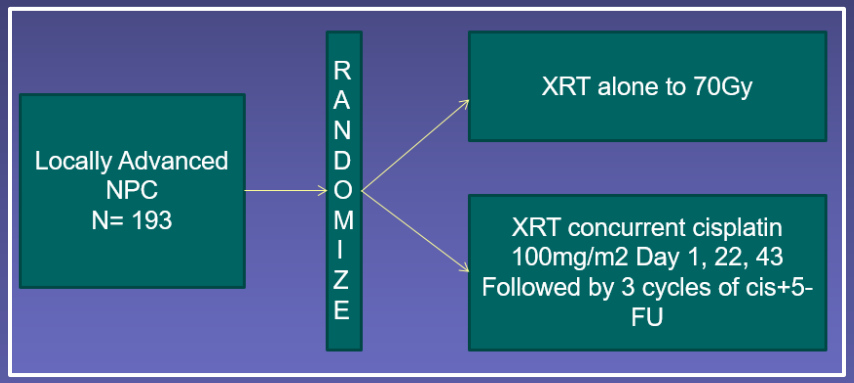
- Curative intent approach is possible
  - Surgery (**preferred for oral cavity**)
  - Radiation
  - Chemotherapy : NOT curative
- Multidisciplinary assessment is critical
- Functional outcome/ long term QOL

Organ Preservation: Nasopharyngeal Carcinoma (NPC)

- Epidemiologically distinct
- EBV associated
- Unresectable at diagnosis
- Classic presentation:
  - Middle ear effusions in adults
  - Level V (post triangle) LAD



NPC: Intergroup 0099



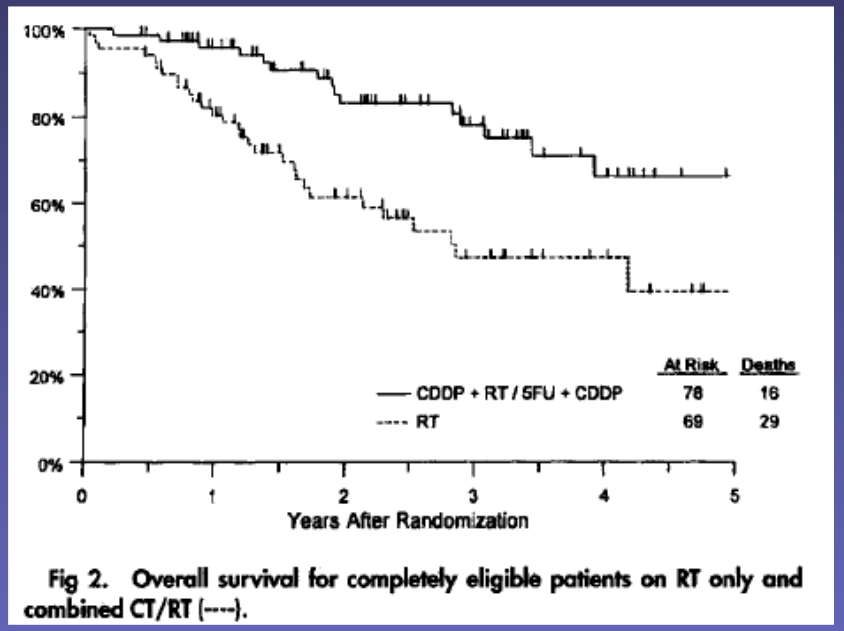


Fig 2. Overall survival for completely eligible patients on RT only and combined CT/RT (----).

- PFS and OS advantage to experimental arm
- Endemic area Phase III studies comparing CRT to CRT + adj cisFU negative

Al- Sarraf. J Clin Oncol 16:1310-1217 1998

Locally Advanced NPC: systemic therapy strategies

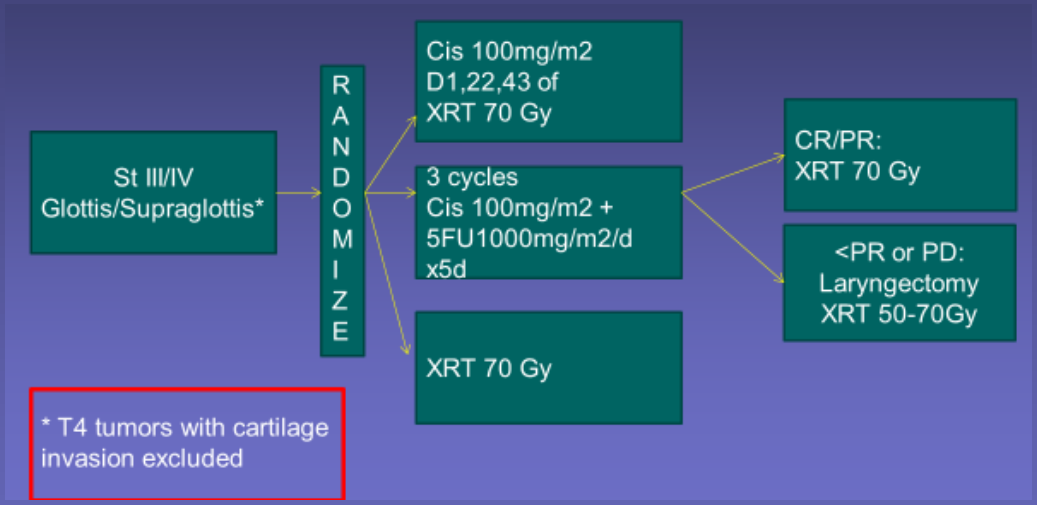
Therapeutic Strategy	Stage	Evidence
Weekly cisplatin + XRT[1]	II-IVB	OR/Toxicity similar
Neoadjuvant gem+cis followed by cisXRT[2]	Stage III-IVB Heavy nodal burden	RFS and distant FFS benefit
Adjuvant capecitabine post cisXRT[3]	III-IVA	FFS and OS Benefit

[1]Lee et al. Ann Oncol 2015 Oct 1
[2]Zhang et al. N Engl J Med. 2019 May 31
[3]Chen et al. Lancet 2021 Jun 4

Organ Preservation: Laryngeal Carcinoma

- Laryngectomy was historical standard of care
- VA Larynx Trial (NEJM 1991)
  - Randomized phase III study
  - surgery vs. chemo followed by XRT for PR/CR
  - 64% in experimental arm had successful organ preservation
  - OS similar, attributed to successful surgical salvage

Landmark Studies in Organ Preservation: Larynx Ca RTOG 91-11



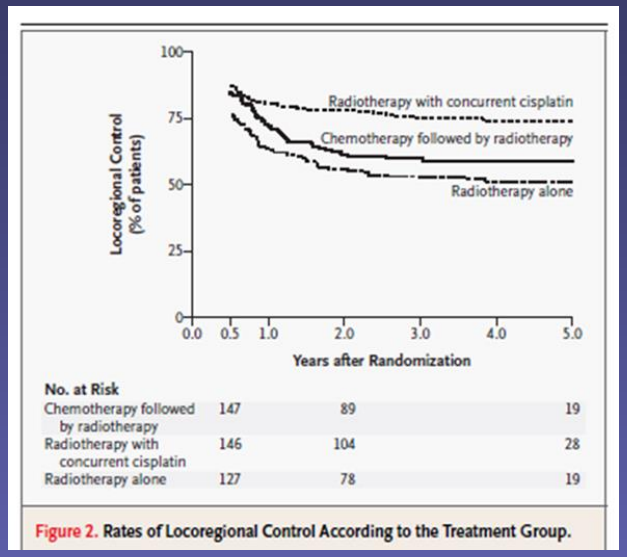


Figure 2. Rates of Locoregional Control According to the Treatment Group.

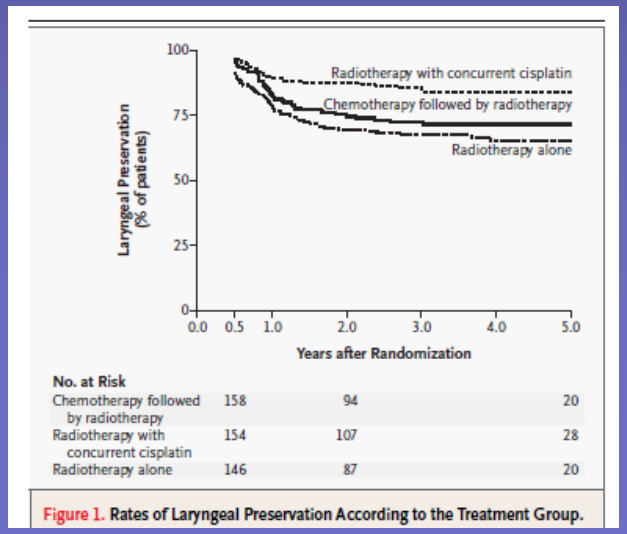


Figure 1. Rates of Laryngeal Preservation According to the Treatment Group.

Forastiere AA et al. NEJM. 2003; 22(349) 2091-98.

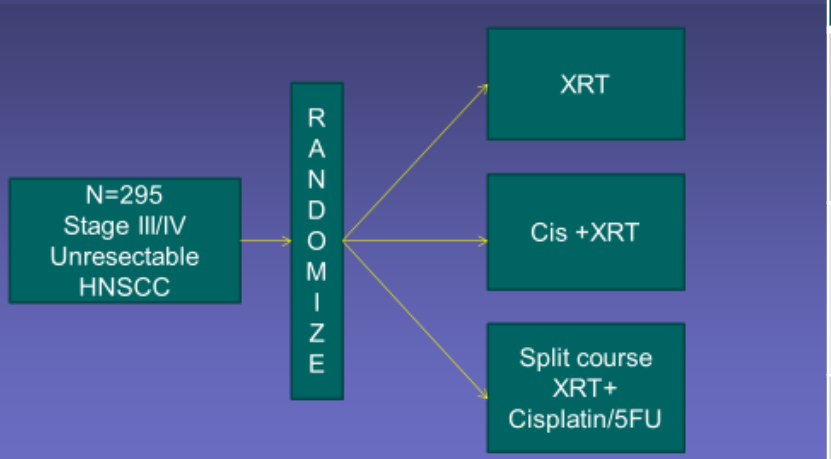
Landmark Studies in Organ Preservation: RTOG 91-11

- Significantly higher Gr ≥3 toxicities in chemoXRT vs XRT
- Distant metastasis decreased in groups receiving chemotherapy
- OS not different among treatment groups
  - Success of salvage surgery
- Long term results reported in 2013
  - Results hold up with 6.9 years median F/U

Forastiere AA et al. NEJM. 2003; 22(349) 2091-98.

Forastiere A et al. J Clin Oncol. 2013 Mar 1;31(7):845-52.

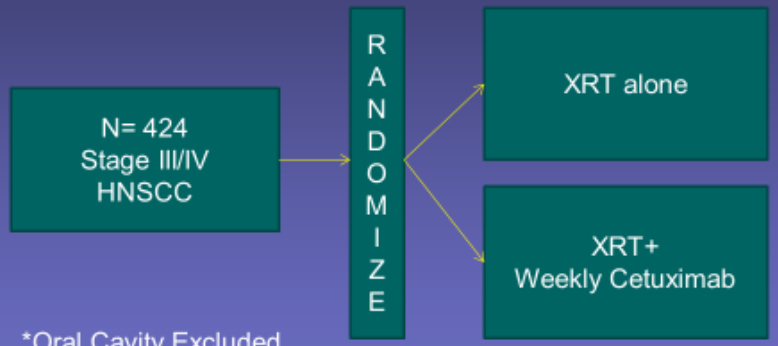
Organ Preservation: Intergroup Study



	Arm A XRT	Arm B cisXRT	Arm C splitXRT
OS (3yr)	23%	**37% A vs B p=0.14**	27%
DSSurvival (3yr)	33%	**51% A vs B p=0.01**	41%
Distant Failure	17.9%	21.8%	19.1%
Toxicity	51%	**85% A vs B p<.0001**	**72% A vs C P<.0001**

Adelstein et al. J Clin Oncol, 2003; 21(1):92-8.

Organ Preservation with cetuximab: Bonner Study



	XRT alone	XRT+ Cetux	p Value
LRCl(3yr)	34%	**47%**	p<.01
PFS(3yr)	31%	**37%**	p=.04
OS(3yr)	45%	**55%**	p=.05
Gr ≥3 toxicity	52%	56%	ND

Bonner JA. NEJM 2006:354:567-78.

Landmark Studies in Organ Preservation:
Bonner Study

- 60% had oropharynx primaries
  –Subsequent HPV testing lower magnitude of benefit in HPV- OPC
- No impact on distant metastatic failure rate
- No identifiable biomarker for response
- Control arm not regarded as standard of care
  – RTOG 1016 with published showing inferiority compared to cis+XRT in HPV+ population

Bonner JA. NEJM 2006:354:567-78.

Rosenthal et al. J Clin Oncol. 2016 Apr 20;34(12):1300-8

Alternative cisplatin dosing in definitive setting

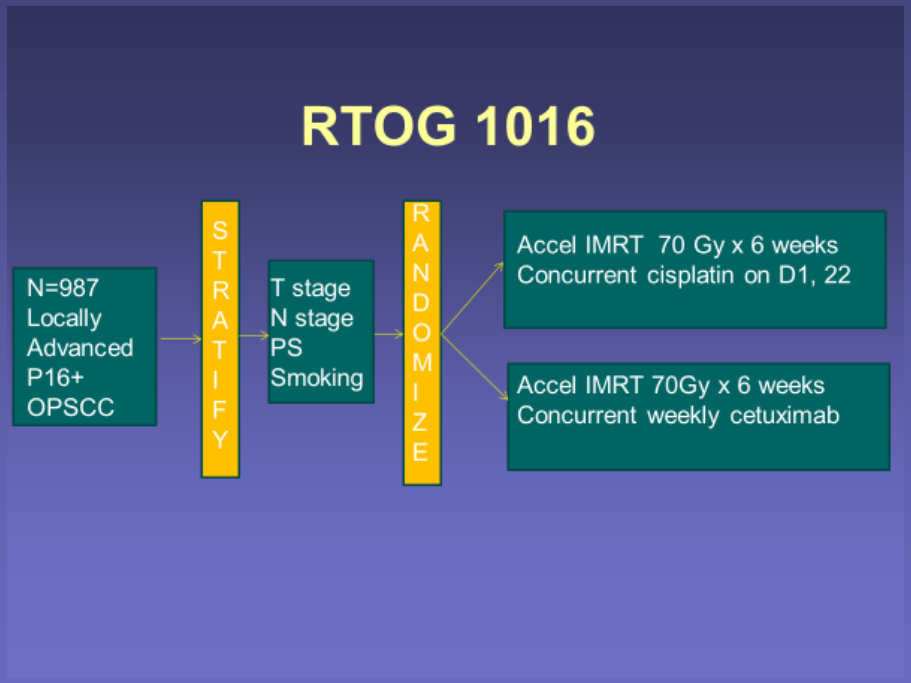
ASCO 2022 #6004

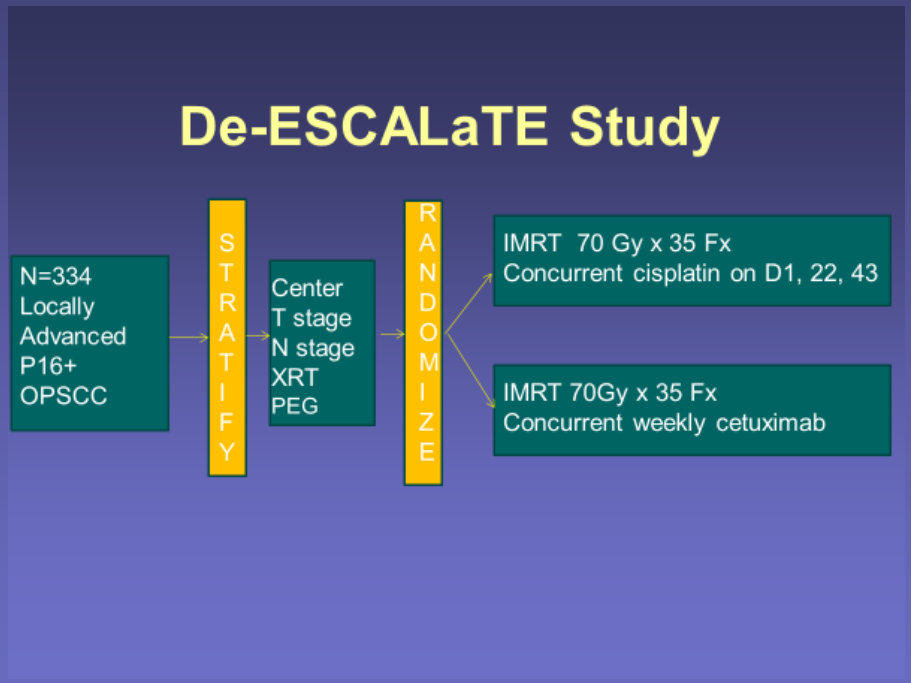
- Concert phase III study (India)
  - Weekly 40mg/m2 vs Bolus 100mg/m2 in definitive XRT setting
- Primary endpoint: LRC at 2 years
- Patient population (N=278)
  - p16 positive in 5-8%
  - 20% with PS 2
- 2D radiation therapy, majority with delays/interruptions

Alternative cisplatin dosing in definitive setting

- 2 yr LRC similar 56% (bolus) vs 60% (weekly)
- Similar median OS in mos: 30 (bolus) vs 25 (weekly)
- Toxicity favors weekly arm:
  - Grade 3 mucositis, myelosuppression, renal, vomiting
- Health care utilization metrics favor weekly arm
  - Reduced need for IVF, hospitalization, treatment interruption

Organ Preservation: Oropharyngeal Carcinoma

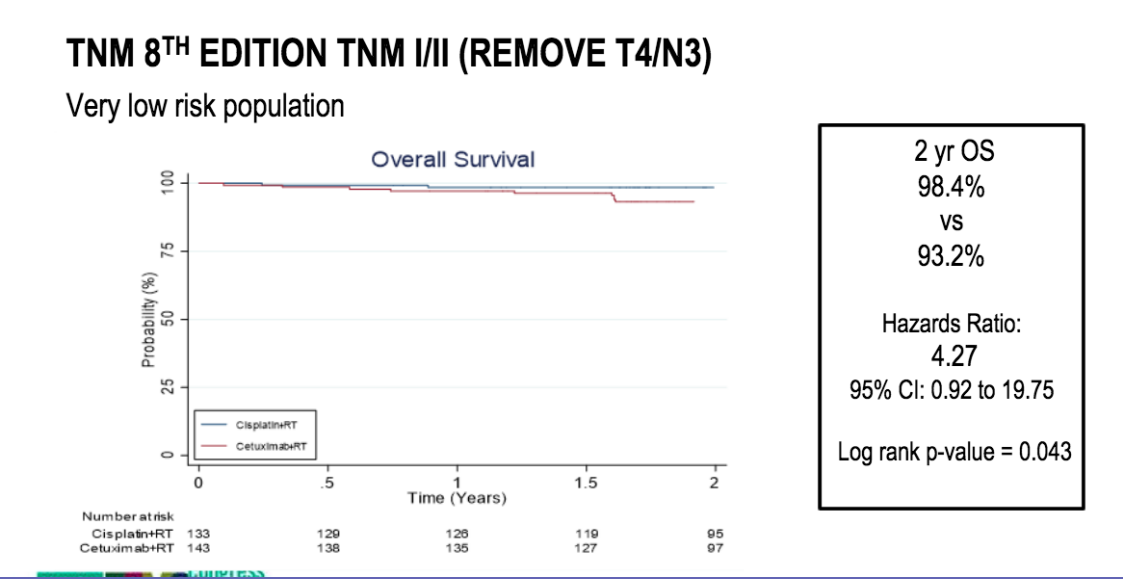




Gillison et al. Lancet.2019 Jan 5;393(10166):40-50
Mehanna et al. Lancet. 2019 Jan 5;393(10166):51-60

Phase III clinical trials in HPV + OPC

- Both trials"
  - CisplatinXRT superior OS, LRC
  - No difference in acute/late tox
  - T score higher in cisXRT in 1016



De-escalation remains a research question in HPV+ OPC

Gillison et al. 2019 Jan 5;393(10166):40-50
Mehanna et al. Lancet. 2019 Jan 5;393(10166):51-60

Alternative cisplatin dosing for definitive XRT in p16+ OPC

- TROG 12.01
  - Randomized phase III of good risk p16+ OPC
  - cisplatin 40mg/m2 XRT to cetuximab XRT
  - N=189
  - Primary endpoint: symptom severity
  - FFS superior in cisplatin arm, OS similar
  - No difference in primary endpoint

[3]Rischin et al. Int J Radiat Oncol Biol Phys 2021 Nov 15;111(4):876-886.

Functional Imaging after definitive chemoradiation

- Planned neck dissections (ND) post chemoXRT was SOC for N3 or bulky N2b disease
- PET-NECK randomized 564 pts to ND vs. surveillance with PET-CT 12wk post chemoXRT
- Necks with nonPETavid LNs <1cm observed in exp arm
- Less NDs done in exp arm, no difference in OS

Mehanna et al. N Engl J Med. 2016 Apr 14;374(15):1444-54

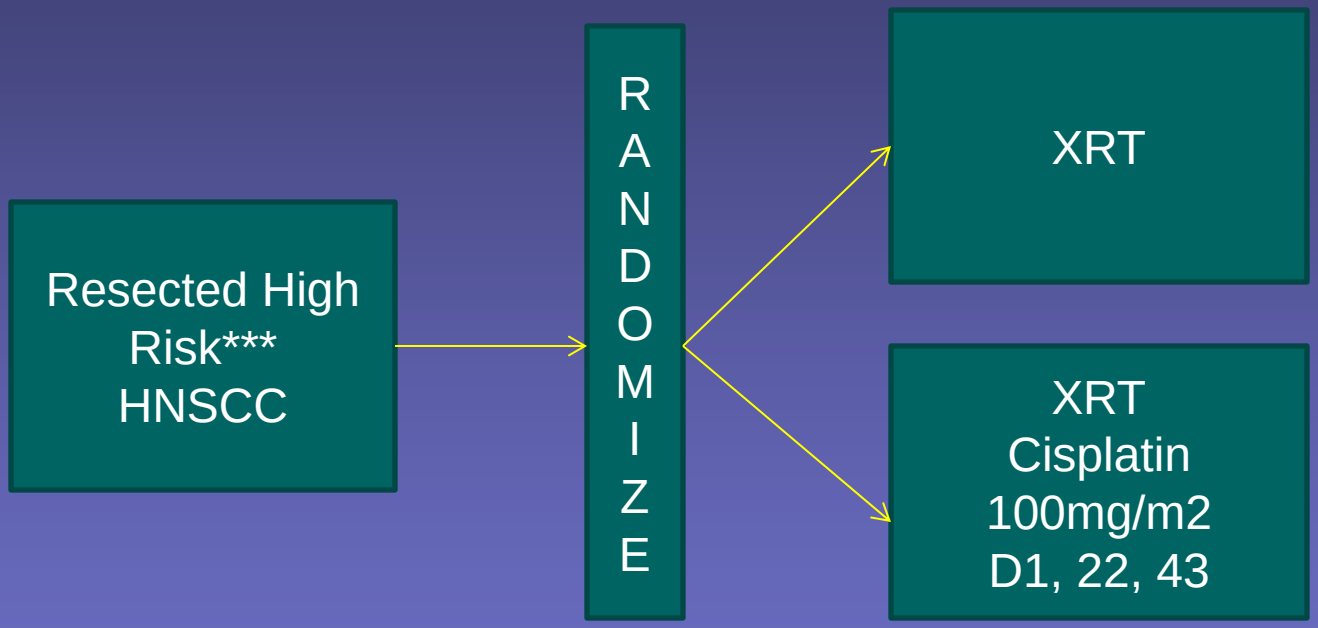
KEY POINTS: Locally advanced disease

- Organ preservation/unresectable disease
  - Concurrent cisXRT supported by RTOG 91-11, Intergroup, RTOG 1016, DE-ESCALaTE, Intergroup 099
  - Weekly cisXRT supported by CONCERT trial in predominantly p16- population
  - CetuximabXRT is inferior to cisXRT in the HPV+OPC
  - Neoadjuvant gem/cis for NPC with nodal burden
- PET-CT can be used to guide need for neck dissection post XRT

More KEY POINTS: Locally advanced disease

- A multidisciplinary approach is essential
- Patient selection is critical
  - Not everyone is meant for nonsurgical treatment approach
  - Remember exclusion criteria in organ preservation studies
- Deescalation in HPV+ remains a research question

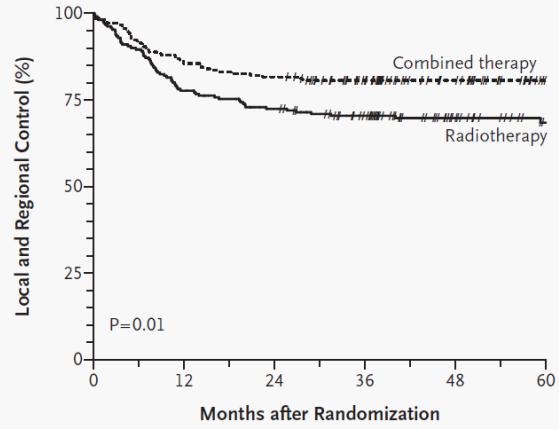
Postoperative therapy RTOG and EORTC studies



*** Eligibility criteria varied in 2 studies

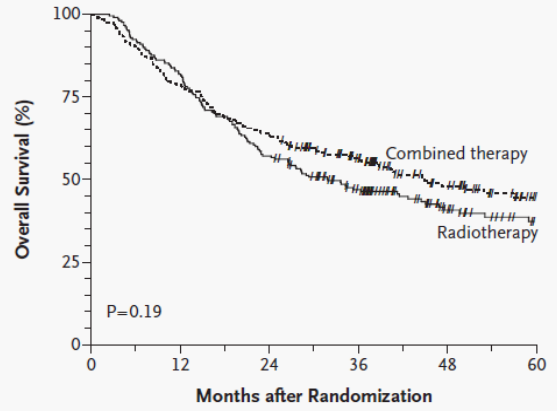
Bernier et al. N Engl J Med. 2004;350(19):1945
Cooper et al. N Engl J Med. 2004;350(19):1937

RTOG 9501



No. at Risk			
Combined therapy	206	123	26
Radiotherapy	210	108	24

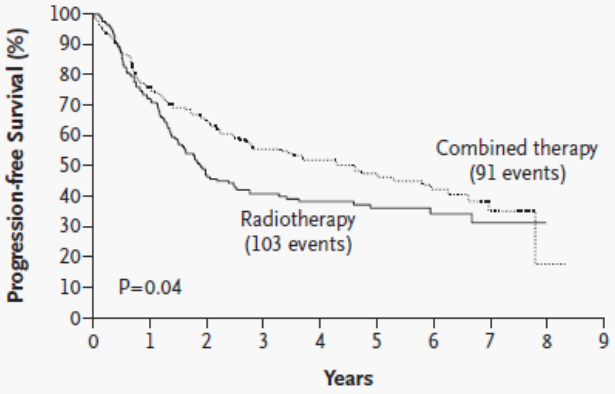
Figure 1. Rates of Local and Regional Control.



No. at Risk			
Combined therapy	206	132	27
Radiotherapy	210	120	26

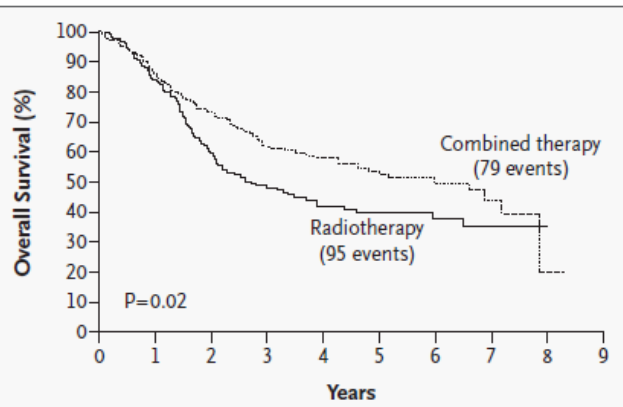
Figure 3. Kaplan–Meier Estimates of Overall Survival.
Overall survival did not differ significantly between groups (P=0.19 by the log-

EORTC 22931



No. at Risk									
Radiotherapy	167	119	73	57	45	30	18	9	0
Combined therapy	167	125	105	85	66	42	29	10	1

Figure 1. Kaplan–Meier Estimates of Progression-free Survival.



No. at Risk									
Radiotherapy	167	139	93	68	49	31	19	9	0
Combined therapy	167	141	118	93	72	47	33	11	1

Figure 2. Kaplan–Meier Estimates of Overall Survival.

Pooled Analysis

Overall survival advantage to Cisplatin + XRT for

- Positive surgical margin
- Extracapsular extension

LRC, PFS benefit confirmed

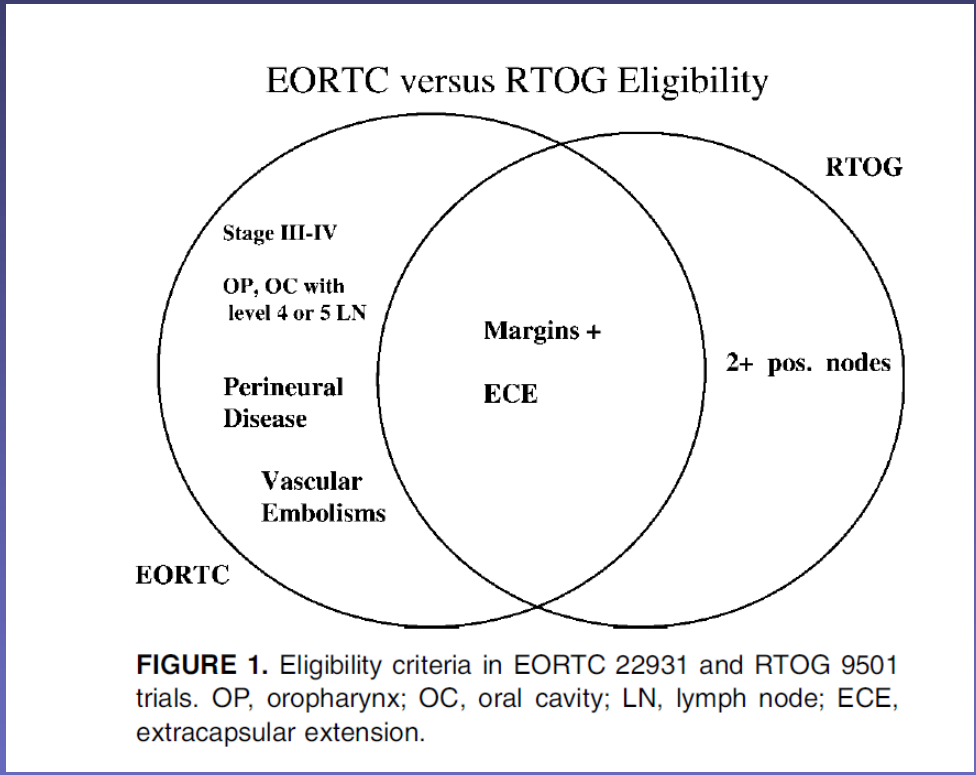


FIGURE 1. Eligibility criteria in EORTC 22931 and RTOG 9501 trials. OP, oropharynx; OC, oral cavity; LN, lymph node; ECE, extracapsular extension.

Bernier et al. Head Neck. 2005 Oct;27(10):843-50.

Alternative cisplatin dosing + XRT in postoperative setting

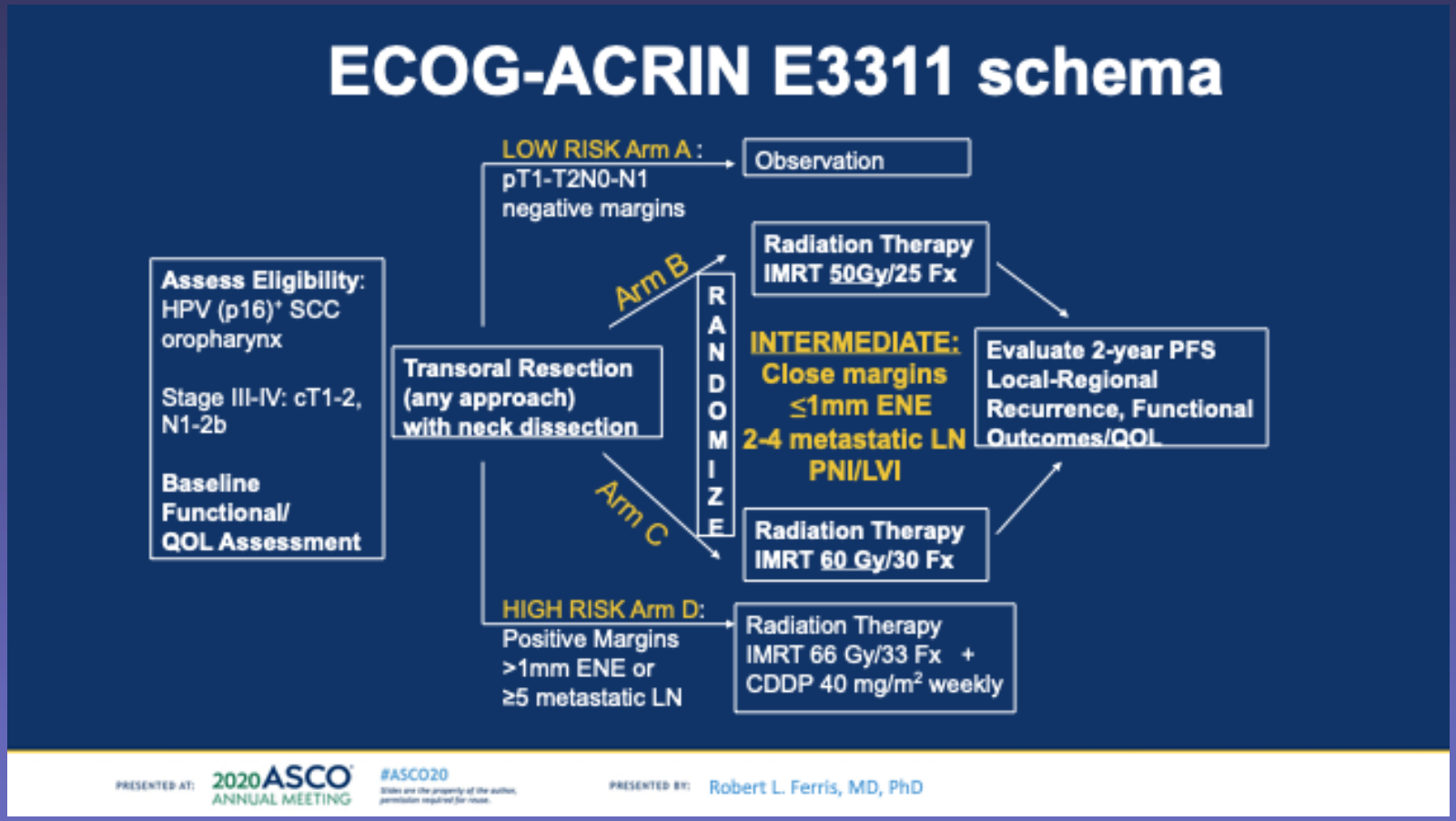
- Randomized phase III study of 30mg/m2 vs 100mg/m2
  - Indian population, mostly adjuvant post resection
  - Inferior LRC with weekly

***Noronha, et al JCO 2018*.**

- Randomized phase III study of 40mg/m2 vs 100mg/m2
  - Japanese study in adjuvant setting for high risk disease
  - Weekly dosing non-inferior

Kiyota et al. JCO 2022

Postop treatment in HPV+ OPC



- Arm B met 2 yr PFS threshold, will be compared to nonsurgical therapy

KEY POINTS: postoperative therapy

- High Risk pathologic features that benefit from concurrent cis+XRT:
  - Positive margins
  - Extracapsular nodal extension
- Most data is with 100mg/m2 on days 1,22, 43 of therapy
  - If weekly cisplatin given, use 40mg/m2

The Cisplatin Ineligible Patient

- Historically excluded from studies
- This is changing

Trial	N	Intervention	Primary endpoint/Results
NCT02707588[1] GORTEC 2015-01 PembroRad	133	Pembrolizumab/XRT vs Cetuximab/XRT	2 yr LRC Similar in both arms (60% vs 59%)
NCT02999087[2] GORTEC REACH	277	Avelumab/cetuximab/XRT vs Cetuximab/XRT	2 yr PFS Similar in both arms (44% vs 31%)
NCT03258554 NRG-HN004	523	Durvalumab/XRT vs Cetuximab/XRT	2 yr PFS Similar in both arms (51% vs 66%)
ASCO 2022 ABSTRACT 6003	356	XRT vs docetaxel XRT in both definitive and postoperative setting	2 yr DFS and OS superior with weekly docetaxel

[1]Bourhis et al. ESMO 2021
[2]Tao et al. ESMO 2020
[3]Patil et al. ASCO 2022

Noncisplatin concurrent regimens in definitive XRT

Trial	N	Intervention	Exp Arm Results	Exp arm Toxicities
GORTEC 9401[1,2]	226	Carboplatin/5FU/XRT vs. XRT	OS DFS superior	Mucositis/Skin/Nutrition/Heme toxicity worse
GORTEC 2007-01[3]	406	Carboplatin/5FU/Cetuximab/XRT Vs. Cetuximab XRT	PFS and LRC superior OS similar	LFT elevation, leucopenia, PEG, hospitalizations worse
Bonner IMCL9815[4]	253	Cetuximab/XRT vs. XRT	OS and LRC superior	More rash and infusion reactions

[1]Calais et al. J Natl Cancer Inst 1999
[2]Denis et al. J Clin Oncol 2004
[3]Tao et al. J Clin Oncol 2018
[4]Bonner et al. N Eng J Med 2006

Other Considerations

- Supportive care during curative intent therapy is critical to success
  - Frequent OTVs with MD/APP
  - Infusion space for IVF
  - Access to enteral nutrition/PEG
  - Speech and swallowing therapy before/during/after
  - Tobacco cessation

Ongoing Clinical Investigation: Themes

- Therapeutic intensification
  - Incorporation of IO agents into standard of care chemoXRT, including neoadjuvant and maintenance PD1
- Therapeutic deintensifcation for HPV+
  - Upfront surgical approaches
  - IO + XRT in NRG HN005
- Cisplatin ineligible pts

Clinical Investigation: definitive therapy

Trial	Treatment Population	N	Intervention
KEYNOTE-412[1]	LAHNSCC (HPV+ for select stages/primary sites)	780	Pembro + cis + RT vs. placebo + cis + RT
JAVELIN HN100[2]	LAHNSCC HPV- HNSCC (HPV+ for select stages/primary sites)	640	Avel + chemoRT vs chemoRT alone
IMSTAR-HN[3]	Stage III/IV p16- OPC, L, HP, OC	276	Neoadjuvant nivo, surgery, and adj chemoRT + adj nivo ± ipi vs SOC surgery + chemoRT
KEYNOTE-689[4]	Resectable stage III/IVa L, HP, OC, p16-OPC Stage III p16+ OPC	600	Pembro prior to surgery/with adj chemoRT vs surgery
IMvoke010[5]	LAHNSCC treated with curative-intent therapy	400	Atezo vs placebo after chemoRT
KEYCHAIN[6]	LAHNSCC p16+ OPC, L, OC	114	Cis + RT vs pembro + RT
HN005[7]	Locally advanced good risk p16+ OPC	711	Cis 70GyRT vs Cis 60GyRT vs Nivo 60GyRT

1. NCT03040999. 2. NCT02952586. 3. NCT03700905. 4. NCT03765918. 5. NCT03452137
6. NCT03383094 7. *NCT03952585*

Metastatic Disease

- Poor prognosis, survival measured in months (longer for HPV+ patients)

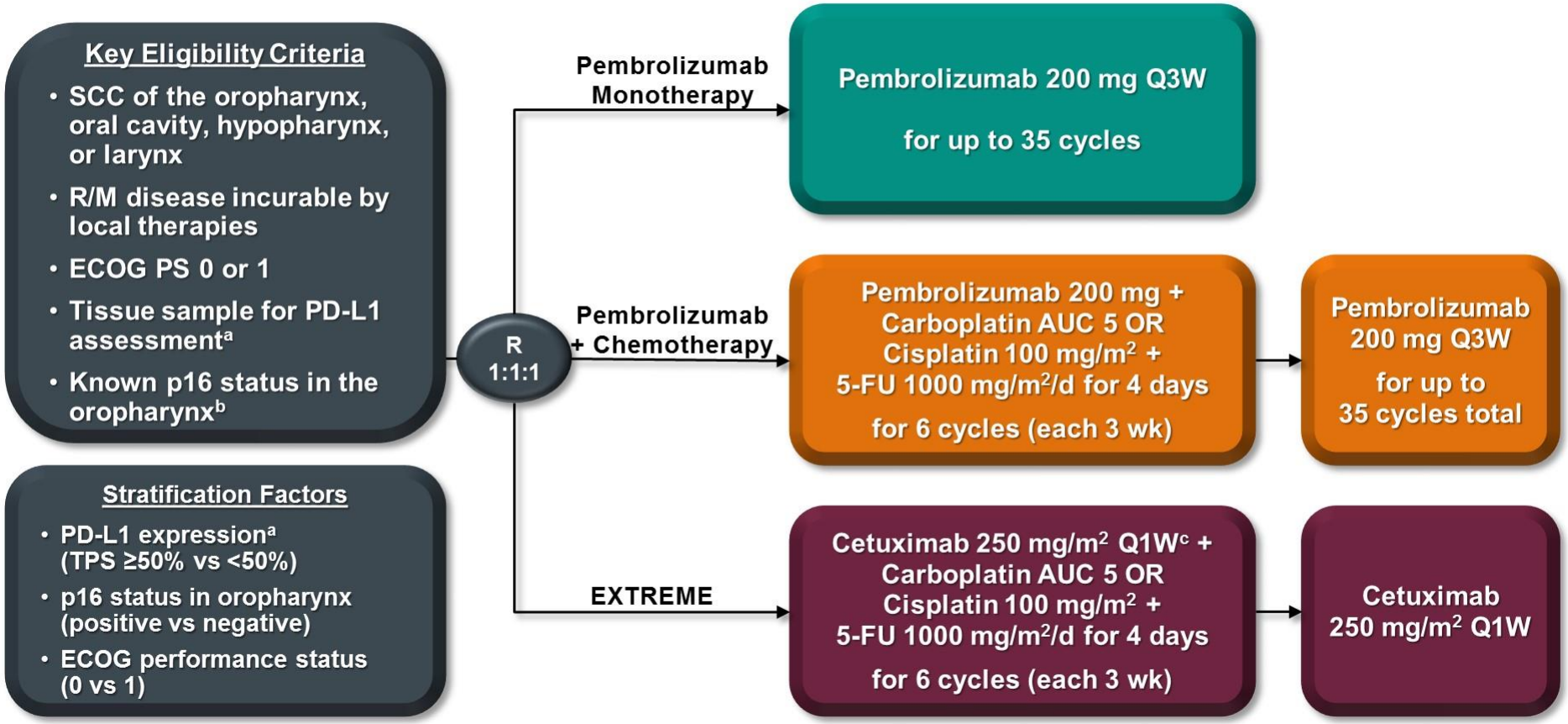
- Multiple active single agents

- Combination vs. single agent chemotherapy trials largely negative except for 2008 EXTREME study:

    - 1st line R/M: cetuximab+PF vs PF
    - OS: 10.1 vs 7.4 mo (p=0.04)

PD1 inhibitor in First Line R/M Setting

KEYNOTE-048 Study Design (NCT02358031)



[a]Assessed using the PD-L1 IHC 22C3 pharmDx assay (Agilent). TPS = tumor proportion score = % of tumor cells with membranous PD-L1 expression.
[b]Assessed using the CINtec p16 Histology assay (Ventana); cutpoint for positivity = 70%. [c]Following a loading dose of 400 mg/m^2.

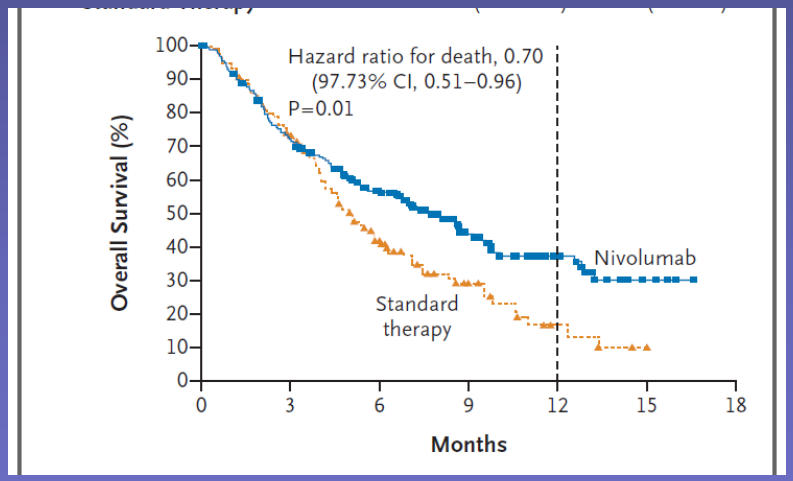
Pembrolizumab in 1st line R/M HNSCC: Keynote 48

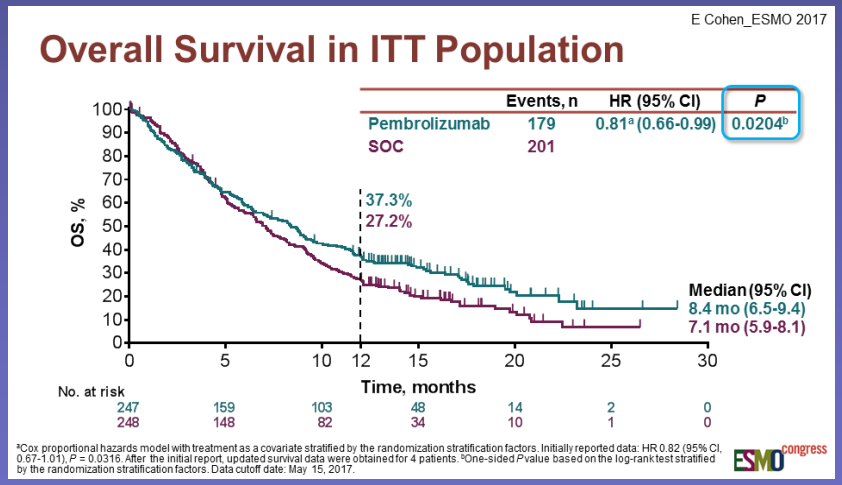
- In CPS≥1, Pembro mono vs EXTREME
  - OS 12.3 vs 10.4 m (p=0.0008)
  - Gr≥3 AE 17% vs. 70%
  - ORR 19%, DoR 23.4 m vs 4.5

- All-comers Pembro+Chemo vs EXTREME
  - OS 13 vs 10.7 m (p=0.0008)
  - Gr≥3 AE 72% vs 70%
  - ORR 36% DoR 6.7m vs 4.3

PD1 inhibitors: second line (post-cisplatin)

- Two similarly designed trials
  - Checkmate 141 nivo vs clinician choice
  - Keynote-40 pembro vs clinician choice
- PDL1 expression agnostic





Ferris, et al. NEJM 2016 Nov 10
Cohen et al. Lancet 2019 Jan 12

Phase III clinical trials in 1st line R/M NPC

Trial	Treatment Arms	Results in PD-L1 arm	High Grade AEs	ORR/mDOR
JUPITER -02[1]	GC + placebo vs GC + toripalimab	PFS and OS advantage	89% vs 89.5%	66.4% (5.7 mo) 77.4% (10 mo)
CAPTAIN-1ST[2]	GC + placebo vs GC + camrelizumab	PFS advantage	91% vs 94%	80.6 (5.6 mo) 87.3% (8.5 mo)
RATIONALE-309[3]	GC + placebo vs GC + tislelizumab	PFS advantage	80.9% VS 81.8%	55.3 (6.1 mo) 69.5 (8.5 mo)

[1]Mai et al. Nat Med 2021
[2]Yang et al. Lancet Oncology 2021
[3]Yang et al. Cancer Cell 2023

KEY POINTS: Metastatic Disease

- Non NPC
  - PembroPFu prolongs OS vs EXTREME
  - Pembro mono prolongs OS in CPS≥1
  - Nivo and Pembro prolong OS in plat treated R/M vs (independent of PDL1 or HPV status)
- NPC
  - Gem+Cis+PD1 improves OS vs. GemCis

Future landscape of head and neck cancer therapy

- Deescalation in good risk HPV
  - Upfront surgical resection vs lower dose XRT
- Immune checkpoint combinations in R/M
- Cellular therapeutics in R/M
- Integration of immune checkpoint inhibitors into curative intent therapy
- Epidemiologic changes with prophylactic vaccines
- ctDNA, cHPVDNA in LA and R/M disease

Part II
Thyroid Cancer

Thyroid Cancer Review

- **Differentiated Thyroid Cancer**
  - Papillary (85%) and Follicular (5%)
  - Familial in 3-9% (AFP,Cowden's, Werner's)

- **Medullary thyroid Cancer (5%)**
  - Parafollicullar C cells, produce calcitonin
  - Familial (less common, MEN2) or Sporadic (majority)
  - RET

- **Anaplastic thyroid Cancer**
  - Elderly patients, rapid growth, airway compromise
  - Evolved from prior differentiated cancers

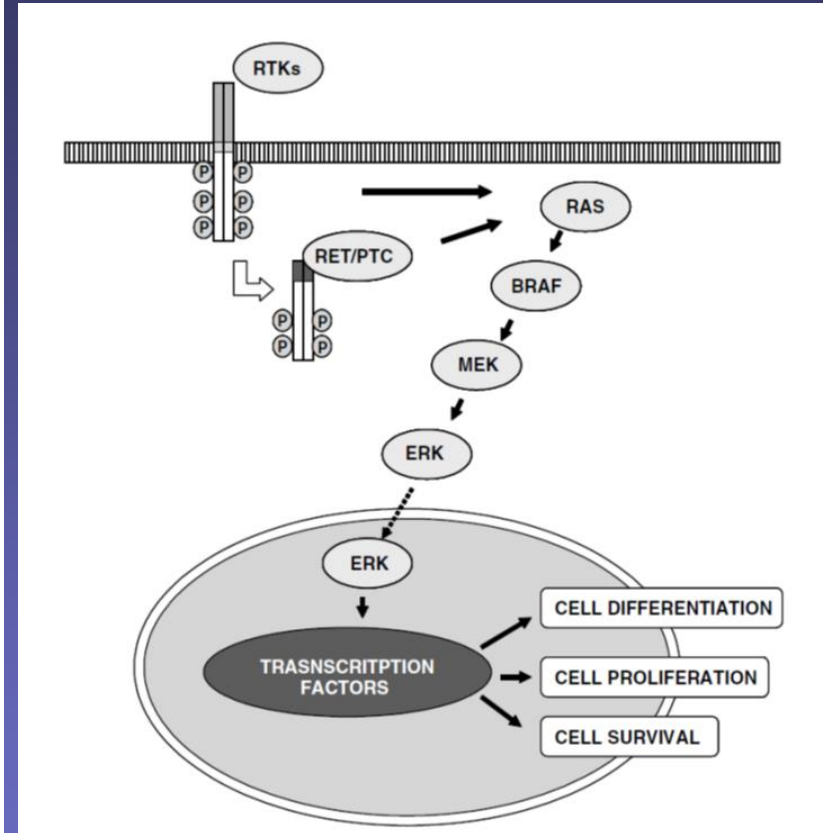
The historical role of the medical oncologist

	Agent	N	Histology	Objective Response Rate	Overall Survival
Gottleib, 1974	doxorubicin	30	All	11 (37%)	Responding patients: 11 months
Shimaoka, 1985	Doxorubicin vs cisplatin & doxorubicin	92	All	7 (17%) vs. 11 (26%)	< 24 months
Williams, 1986	Doxorubicin and cisplatin	22	All	2 (9%)	NR
Ain, 2000	Paclitaxel	20	ATC	10 (53%)	Median OS: 25 weeks

Kondo T et al. Nat Rev Cancer. 2006 Apr;6(4):292-306.

Molecular targets in Thyroid Cancers

Tumor type	*Prevalence (%)*
Papillary carcinoma	
BRAF	45
RET/PTC	20
RAS	10
TRK	<5
Follicular carcinoma	
RAS	45
PAX8-PPARγ	35
PIK3CA	<10
PTEN	<10
Medulllary carcinoma	
Familial forms of *RET*	>95
Sporadic *RET*	50
Poorly differentiated carcinoma	
RAS	35
β-Catenin (*CTNNB1*)	20
TP53	20
BRAF	15
Anaplastic carcinoma	
TP53	70
β-Catenin (*CTNNB1*)	65
RAS	55
BRAF	20



MAPK signaling pathway

Nikiforov YE. Mod Pathol. 2008 May;21 Suppl 2:S37-43

FDA approved TKIs in RAIR DTC

Agent/Line	Target	Evidence	ORR	PFS	OS	AEs
Lenvatinib[1] *FIRST LINE*	VEGF, BRAF, FGFR, RET, KIT	R Ph III vs. Placebo SELECT (N=392)	**64.8%** vs 1.5% (p<0.001)	18.3 vs 3m (p<0.001)	NS	75.9% vs 9.9%
Sorafenib[2] *FIRST LINE*	VEGF, BRAF, RET RAF, PDGFR	R Ph III vs. Placebo DECISION (N=417)	**12.2%** vs 0.5%	10.8 vs. 5.8m (p<0.0001)	NS	37.2 vs 26.3%
Cabozantinib[3] *SECOND LINE*	VEGFR2, AXL, MET, RET	Phase III COSMIC-311 N=187	**15%** vs 0	Not reached vs. 1.9 mo	NS	64% vs 37%

[1]Schlumberger et al. N Engl J Med. 2015 Feb 12;372(7):621-30.
[2]Brose et al. Lancet. 2014 Jul 26;384(9940):319-28.
[3]Brose at al. Lancet 2021

Mutation specific approved TKIs in nonMTC

Agent	Target	Evidence	ORR	PFS	OS	AEs
Selpercatinib[1]	RET	Ph1/2 N=19	79%	1 yr 92%	NR	Mostly Gr1/2
Pralsetinib[2]	RET	Phase I/2 N=20	89%	1 yr 81%	1 yr 91%	Gr1/2
Entrectinib[3]	NTRK	Ph1 N=121(all tumors)	54%	NR	NR	Gr1/2
Larotrectinib[4]	NTRK	Ph1 N=29 (all thyroid)	71%	2 yr 69%	2 yr 76%	Gr1/2

[1]Wirth et al NEJM 2020
[2]Subbiah et al. Lancet Diab Endo 2021
[3]Doebele AACR 2020
[4]Waguespack EurJ Endo 2022

FDA approved TKIs in MTC

Agent	Target	Evidence	ORR	PFS	OS	AEs
Vandetanib[1]	RET VEGF EGFr	R Ph III vs.Plac ZETA (N=331)	45% vs 13% (p<0.01)	NR vs 19.3 m (p<0.01)	NR	GI: 56 vs 26%
Cabozantinib[2]	RET MET VEGF	R Ph III vs. Plac EXAM (N=330) noXover	28% vs 0%	11.2 vs. 4m (p<0.0001)	NS	Gr3 69% vs 33%
Selpercatinib[3]	RET	Phase I/2 N=143	71%	NR	NR	Most Gr1/2

Pralsetinib FDA indication withdrawn 7/2023

[1]Wells, et al. J Clin Oncol. 2012 Jan 10;30(2):134-41.
[2]Elisei et al. J Clin Oncol. 2013 Oct 10;31(29):3639-46.
[3]Wirth et al. N Eng J Med 2020

Anaplastic Thyroid Cancer

- Often unresectable and metastatic at diagnosis
- Very poor prognosis
- Local control and QOL are priorities Radiation often concurrent with chemotherapy often used to achieve treatment goals
- Paclitaxel has a response rate of ~50%

BRAF and MEK inhibition

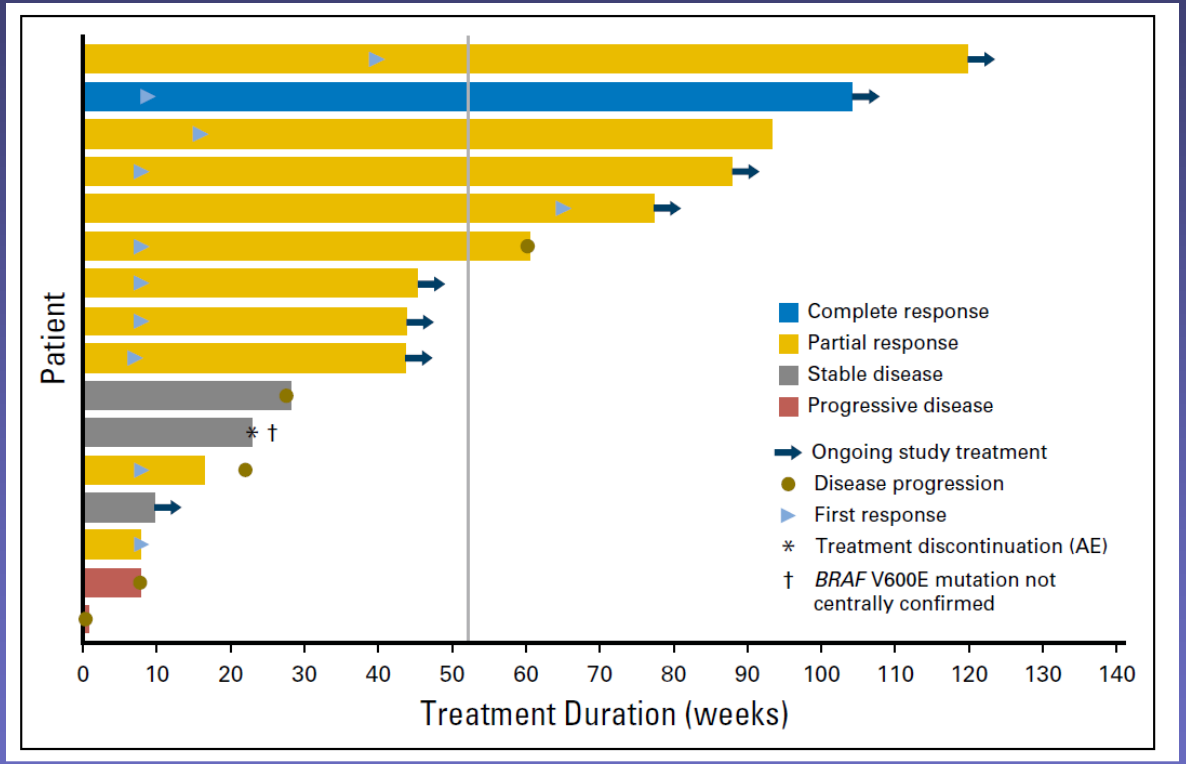
Phase I experience with dabrafenib/trametinib

N= 16 pts +BRAFV600E

Responses in 11 (69%)

80% previously treated with XRT

FDA approved



Subbiah et al. J Clin Oncol. 2018 Jan 1;36(1):7-13

Key Points: Thyroid Cancer

- Independent of mutational status
  - RAI refractory differentiated thyroid cancer
    - Lenvatinib and sorafenib
  - Medullary Thyroid Cancer
    - Vandetanib and cabozantinib
- RET and NTRK specific TKIs for DTC and MTC
- Anaplastic thyroid cancer
  - Recognize and attempt local control
  - Test for BRAF V600E

Part III
Salivary Gland Cancer

Salivary Gland Cancers

- Uncommon (5% of head and neck CA)
- Diverse histology (2017 WHO)
  - Most common: adenoid cystic (ACC), mucoepidermoid carcinoma, adenocarcinoma
- Variable clinical behavior
  - Indolent subtypes such as ACC
- Molecular profiling
  - Secretory Carcinoma (*ETV6-NTRK3* fusion)

Salivary Gland Cancer: Local or Locally advanced

- Surgical resection of localized disease
- Postoperative radiation therapy in high risk disease
  - Data to support Neutron Radiation
  - Photon radiation also extensively studied and reported in postoperative setting
  - Concurrent chemoradiation being studied in RTOG 1008

Salivary Gland Cancer: Metastatic

- No current standard of care
  - Small trials with heterogeneous population
    - Low response rates, stable disease
    - Contemporary experience with single agent paclitaxel gemcitabine-cisplatin, carboplatin-paclitaxel
- Clinical trials preferred

Salivary Gland Cancer: Metastatic

- On label/tumor agnostic approvals
  - Entrectinib in NTRK mutant sal gland cancer
  - Selpecatinib in RET mutant sal gland cancer
  - Traztuzumab deruxtecan in Her2+
- Off label prospective data
  - Lenvatinib in adenoid cystic (15%ORR)
  - Androgen deprivation in AR+ sal gland cancer
  - Pembro in PDL1>1% (10% ORR


Thank you!
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HN chemoXRT on treatment visits

- Weekly appointments for labs/chemo/hydration
- APP or MD see patients weekly
- APP to see patient in week 1 and week 2 post chemoXRT with labs/hydration
- APP to see patient 1 month post XRT
    - Evaluate for PEG removal
    - Discontinue pain medications/nausea meds
    - Evaluate for depression

HN LTFU Plan

YEAR 1

3 mo post XRT
- MD
- Scope
- CT Neck/Chest

6 mo post XRT
- APP/scope

9 mo post XRT
-APP/scope

12 mo postXRT
- MD
- Scope
- CT chest/neck
- Screening TSH

YEAR 2

15, 18 and 21 mos post XRT
-APP/scope

24 mo postXRT
- MD
- Scope
- CT chest/neck

YEAR 3-5

30 mos post XRT
-APP/scope

3, 4, 5 yrs postXRT
- MD
- Scope
- CT chest/neck

HN LTFU Plan – Retreat Discussion

YEAR 1

3 mo post XRT
- Med onc/ ? Rad onc
- Scope
- Baseline Scan: CT Neck/Ches
- ? PET/CT for chemoXRT patients

6 mo post XRT
- APP/scope
- CT Neck – should we do med onc or rad onc for review?

9 mo post XRT
-APP/scope

12 mo postXRT
- Med onc
- Scope
- CT chest/neck
- Screening TSH

YEAR 2

15 mos post XRT
-APP/scope

18
-APP/scope
- CT Neck - Neck – should we do med onc or rad onc for review?

21 mos post XRT
-APP/scope

24 mo postXRT
- Med onc
- Scope
- CT chest/neck

YEAR 3-5

30 mos post XRT
-APP/scope

3 years postXRT
- Med onc
- Scope
- CT chest/neck

4, 5 yrs postXRT
- med onc
- Scope