HPV positive Ca Oropharynx

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Regional Cancer Centre

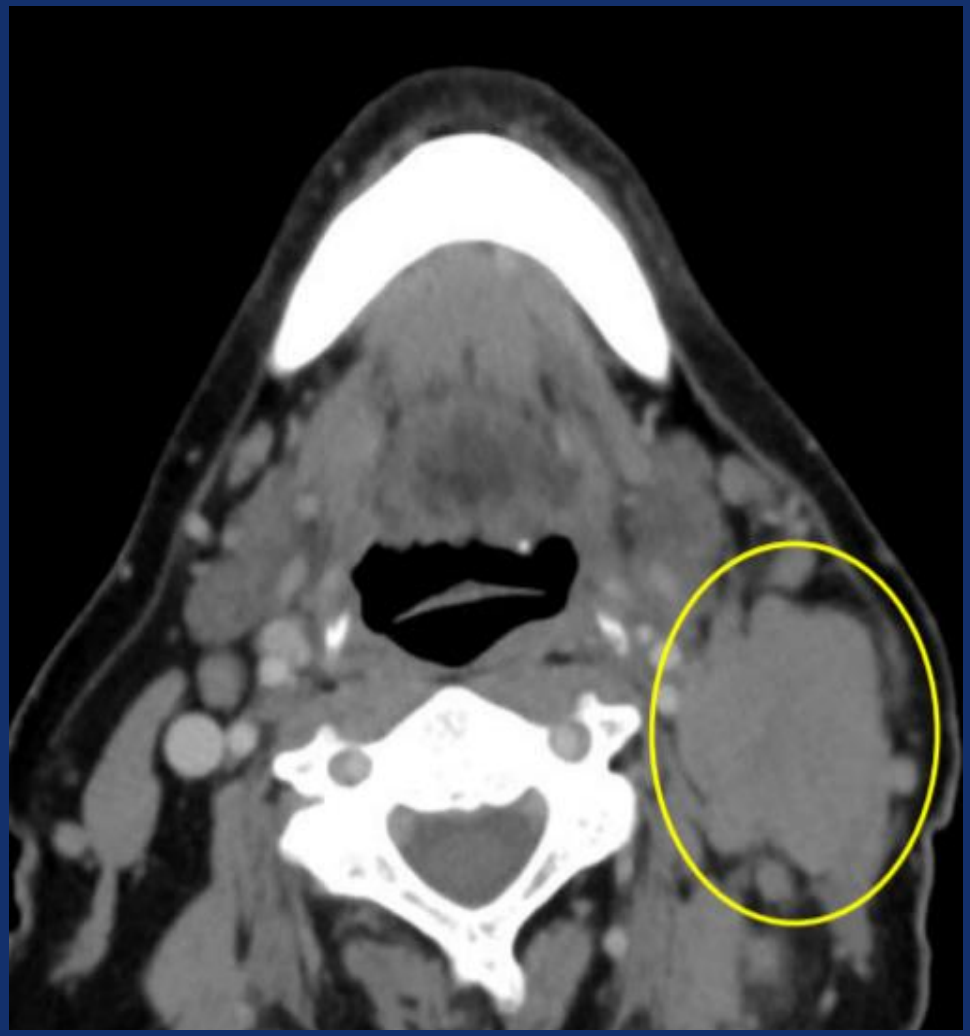
Trivandrum, Kerala

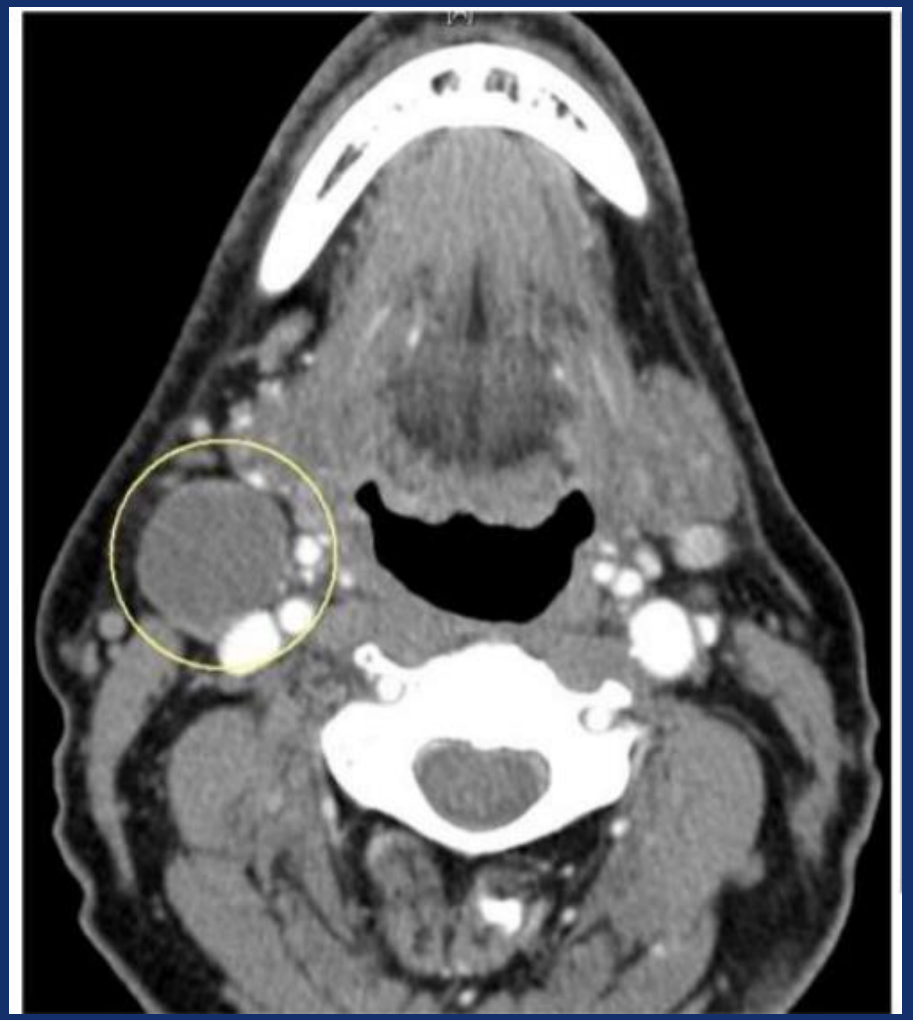
Contents

- **Clinical presentation**
- Why a new disease entity?
- New staging system
- Current status of de intensification protocols
- Future directions

Feature	HPV-negative	HPV-positive
Age	Above 60 years	Middle-aged
Risk factors	Tobacco +/- alcohol	Sexual behaviour
Field cancerization	yes	Unknown
Predilection site	None	Oropharynx
T stage	Higher T Stage	Lower T Stage
Nodal status	Lower	Higher
TP53 mutations	Frequent	Infrequent
Histology	Insitu changes	Basaloid/poorly diff

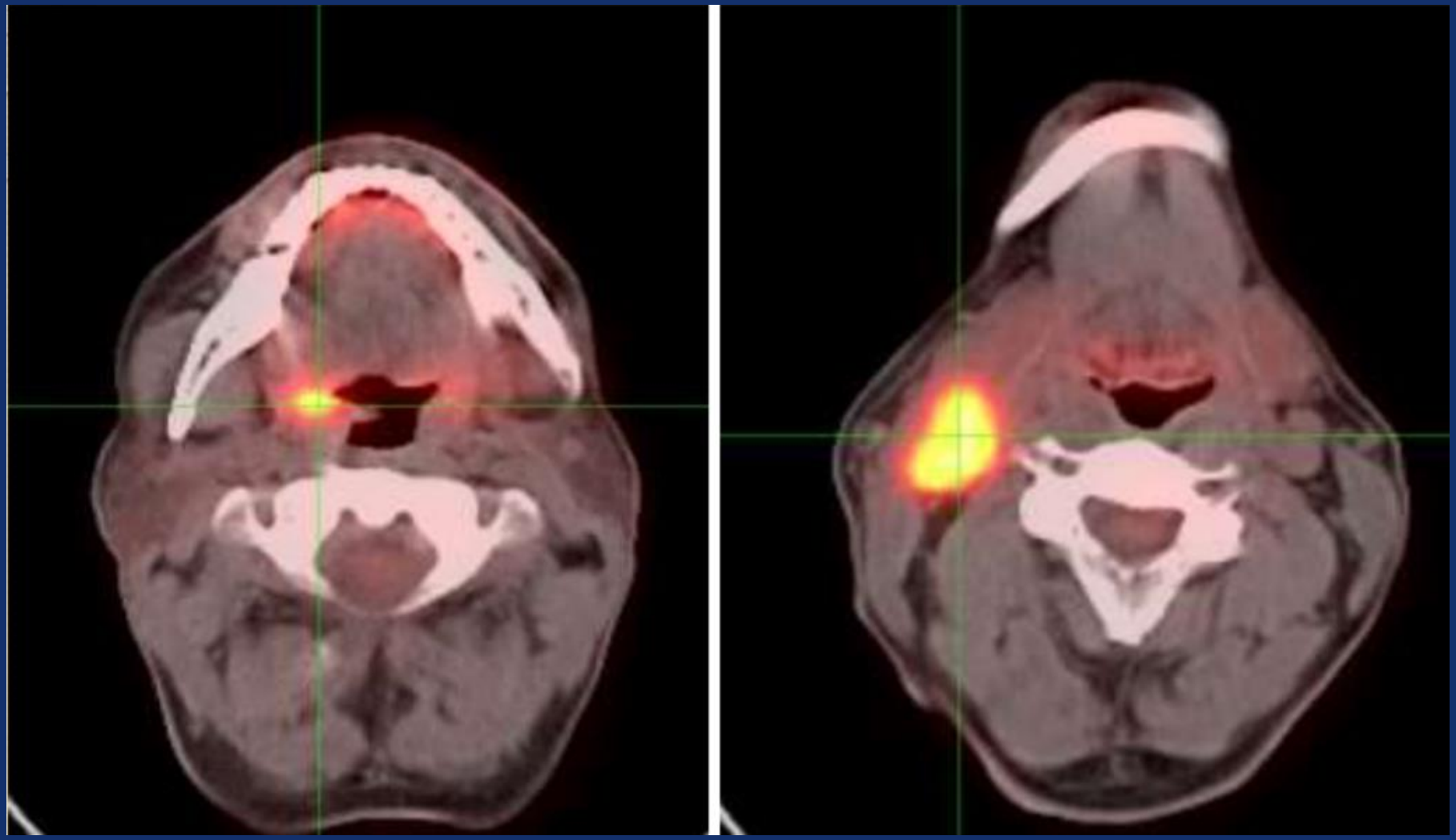
Gillison ML et al. JAMA 2012;307:693-703.





No primary or small primary

Work up for MUO

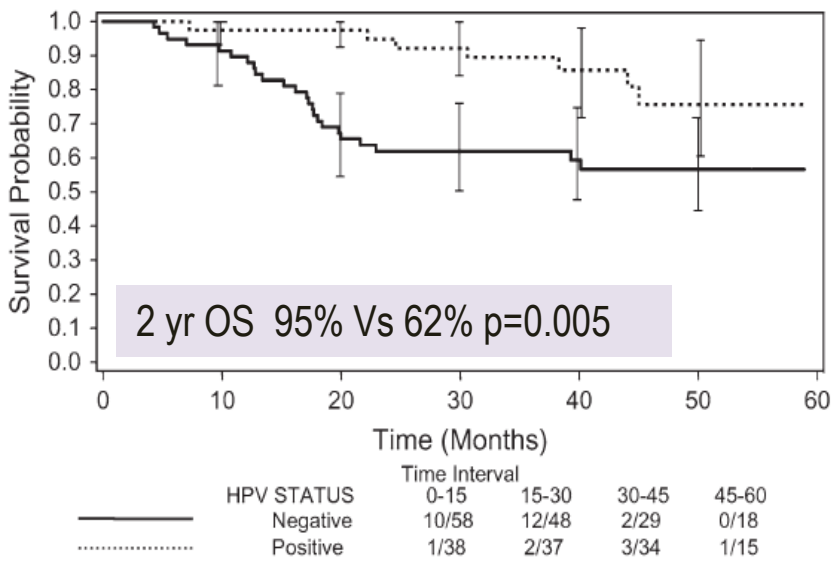


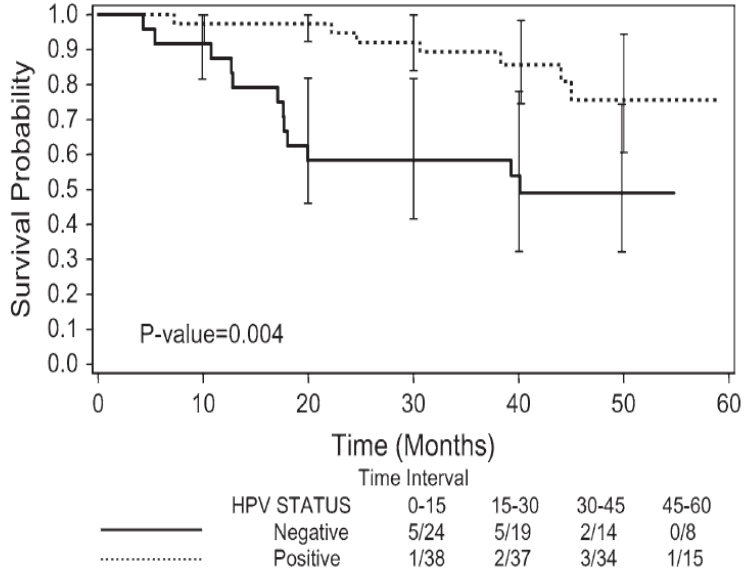
ARTICLE

Phase II Trial
ECOG2399
N=96
38/96- HPV positive

Improved Survival of Patients With Human Papillomavirus–Positive Head and Neck Squamous Cell Carcinoma in a Prospective Clinical Trial

Carole Fakhry, William H. Westra, Sigui Li, Anthony Cmelak, John A. Ridge, Harlan Pinto, Arlene Forastiere, Maura L. Gillison





2 cycles of IC→CCRT 70Gy/35Fr.Ca Oropharynx and Ca Larynx, Median FU 39.1 months .

J Natl Cancer Inst 2008;100:261–269

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

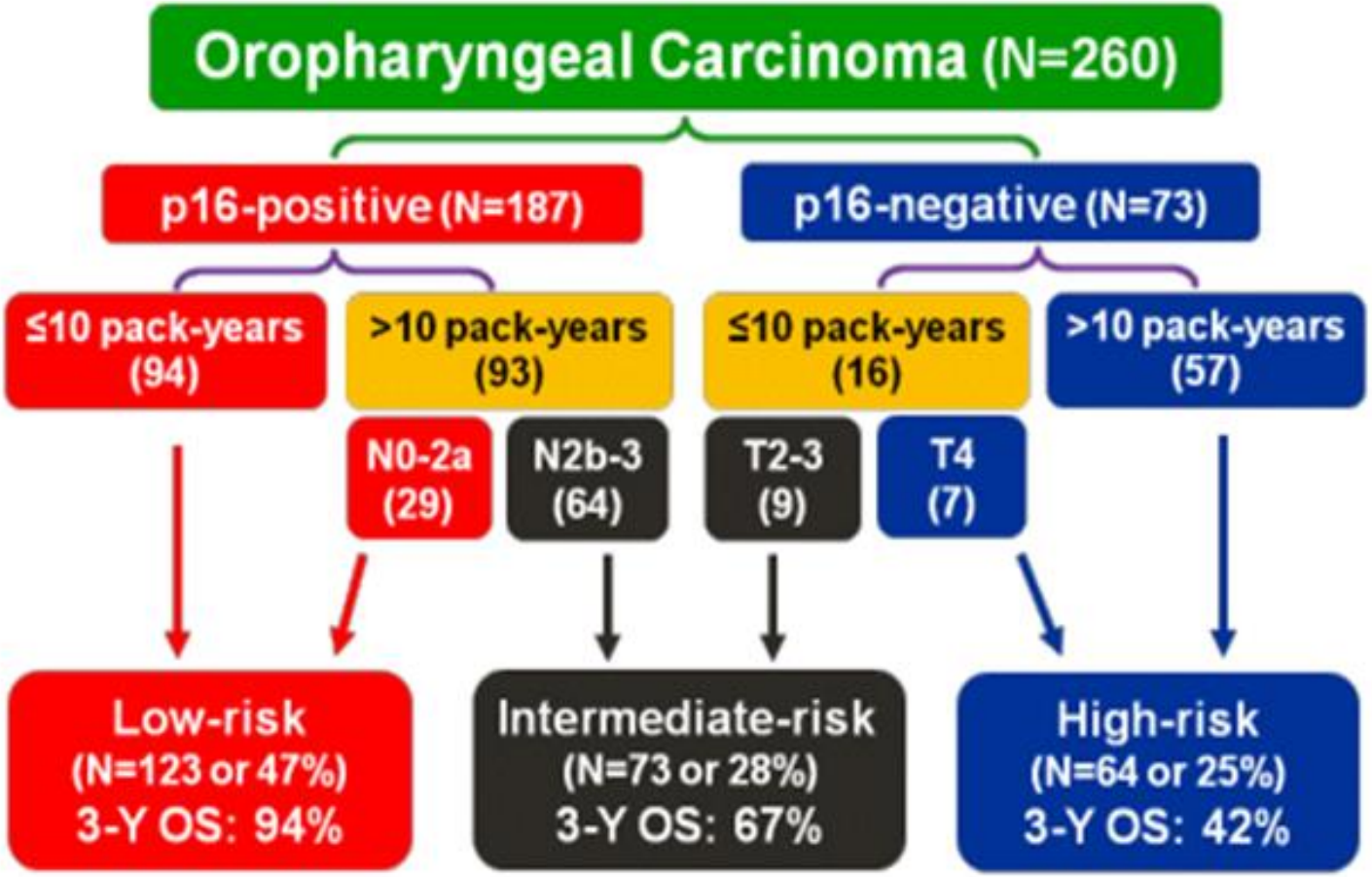
Human Papillomavirus and Survival of Patients with Oropharyngeal Cancer

K. Kian Ang, M.D., Ph.D., Jonathan Harris, M.S., Richard Wheeler, M.D., Randal Weber, M.D., David I. Rosenthal, M.D., Phuc Felix Nguyen-Tân, M.D., William H. Westra, M.D., Christine H. Chung, M.D., Richard C. Jordan, D.D.S., Ph.D., Charles Lu, M.D., Harold Kim, M.D., Rita Axelrod, M.D., C. Craig Silverman, M.D., Kevin P. Redmond, M.D., and Maura L. Gillison, M.D., Ph.D.

Prognostic Implications of HPV in Oropharyngeal Cancer

Douglas R. Lowy, M.D., and Karl Munger, Ph.D.

N Engl J Med 2010; 363:1576

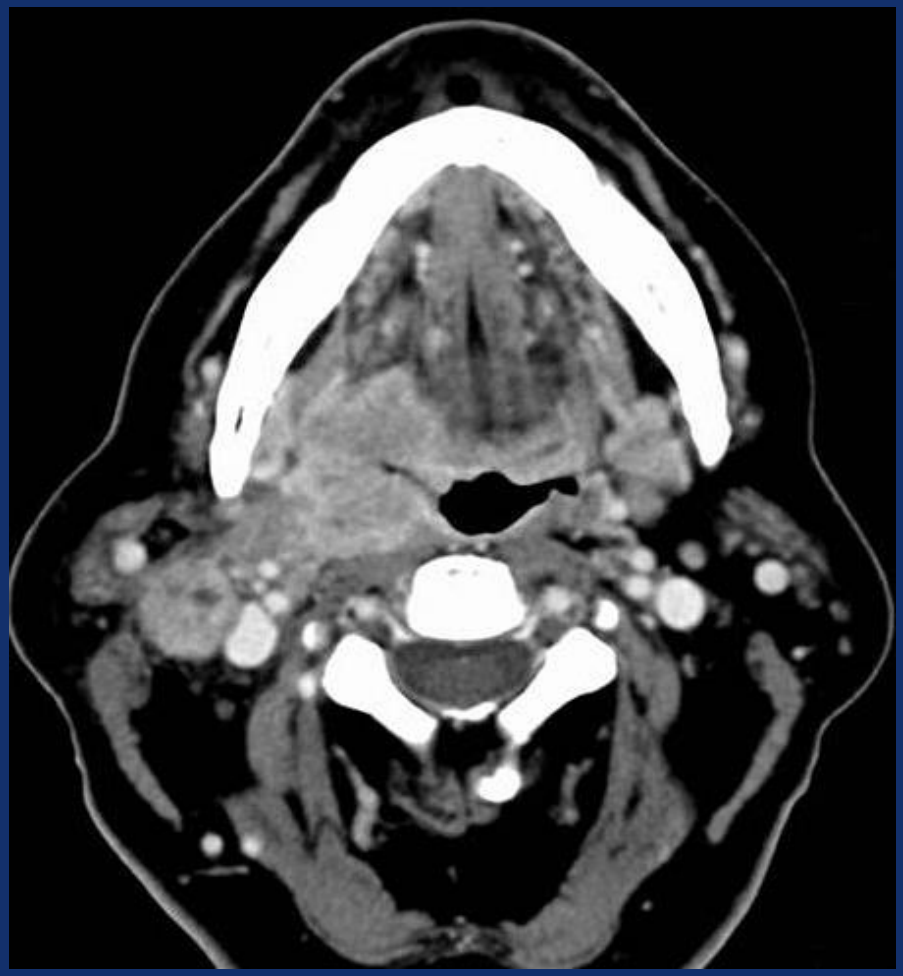


N Engl J Med 2010; 363:1576

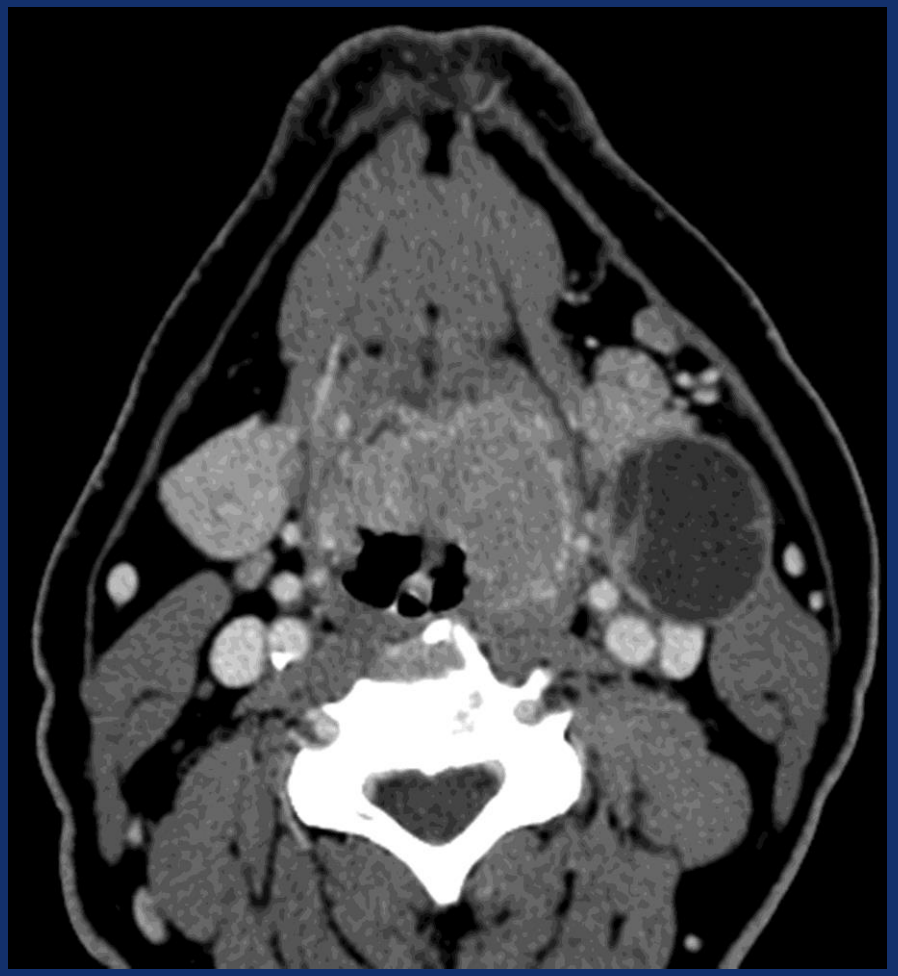
HPV and better H&N Cause-specific survival

Study	N pts	Subsite	% Hpv	Rx	HR
Fahkry,08 ECOG 2399	96	Oroph+Lar	40	IndCT +CTRT	0.36
Lassen,09 DAHANCA 05	135	H &N	22	RT(100%)	0.44
Rischin,10 TROG 02.02	172	Oroph	57	CTRT	0.36
Posner,11 TAX 324	111	Oroph	50	Ind +CTRT	0.20
Gillison,12 RTOG 9003	190	Oroph	39	RT	Nrp<0/001
Ang,10 RTOG 0129	323	Oroph	64	CTRT	0.42
Lassen,11 DAHANCA 6 & 7	769	H&N	-	RT	0.54

HPV-ve T2N1 Stage III

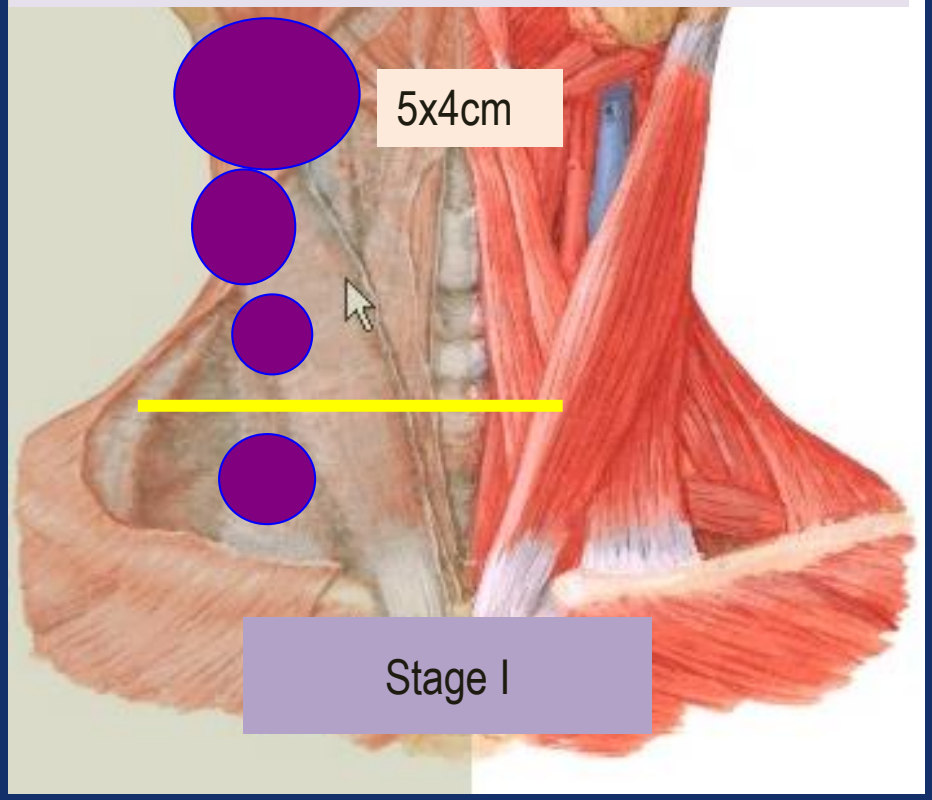


HPV+ve T2N1- Stage I

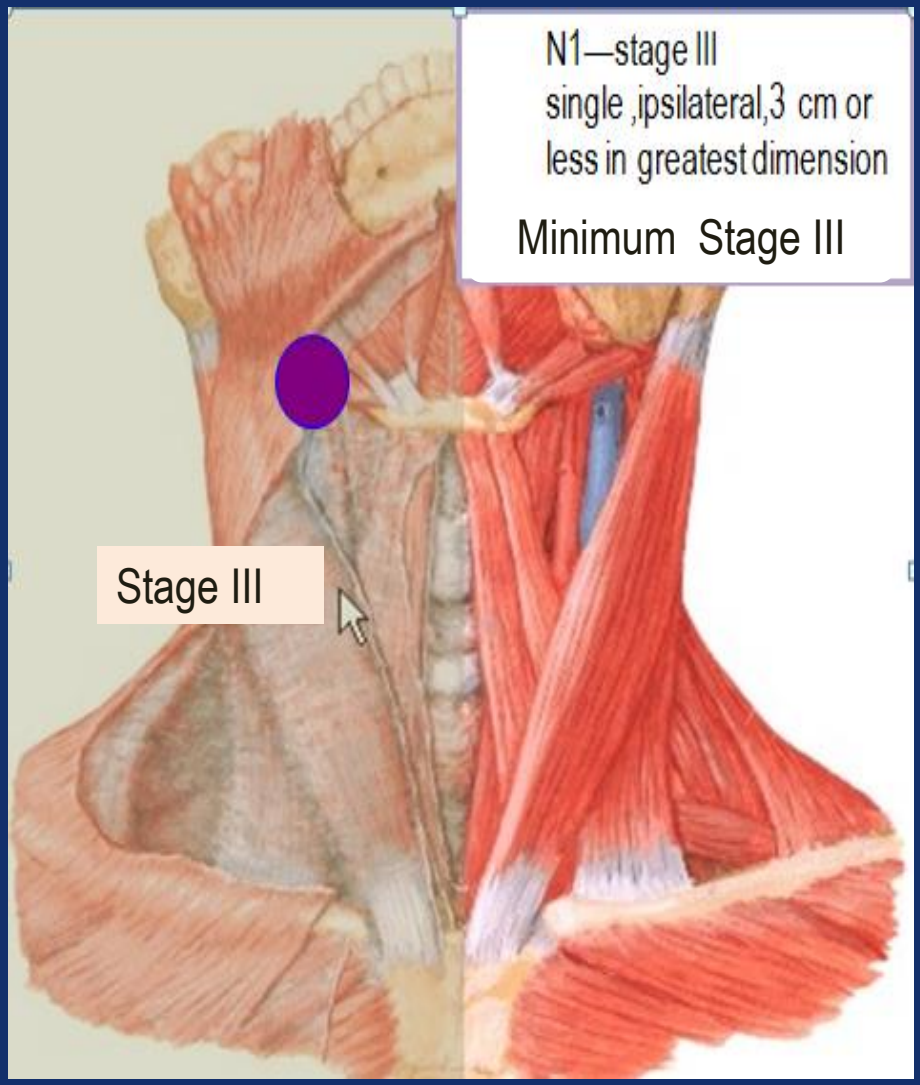


HPV positive

Nodal stage –N1 (Single or Multiple,Ipsilateral,if not more than 6 cm)- up to T-T2, Stage I(Lower border of cricoid is not included)



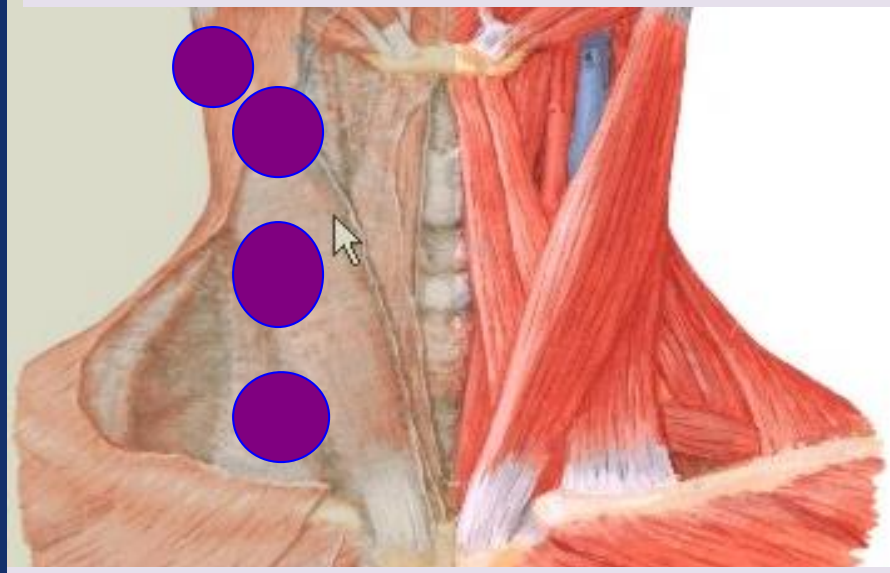
HPV -Ve



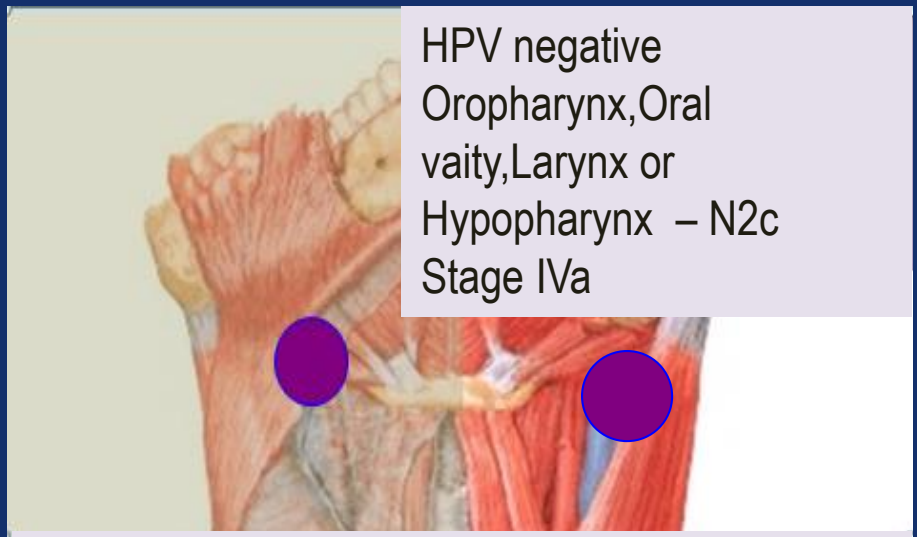
Nodal Staging

HPV positive- Nodal stage –N1 (Single or Multiple,Ipsilateral,if not more than 6 cm)- Stage I

HPV negative Oropharynx,Oral vaity,Larynx or Hypopharynx -N2b
Stage IVa



Nasopharynx–N3(Any node below lower border of cricoid cartilage) – Stage IVa

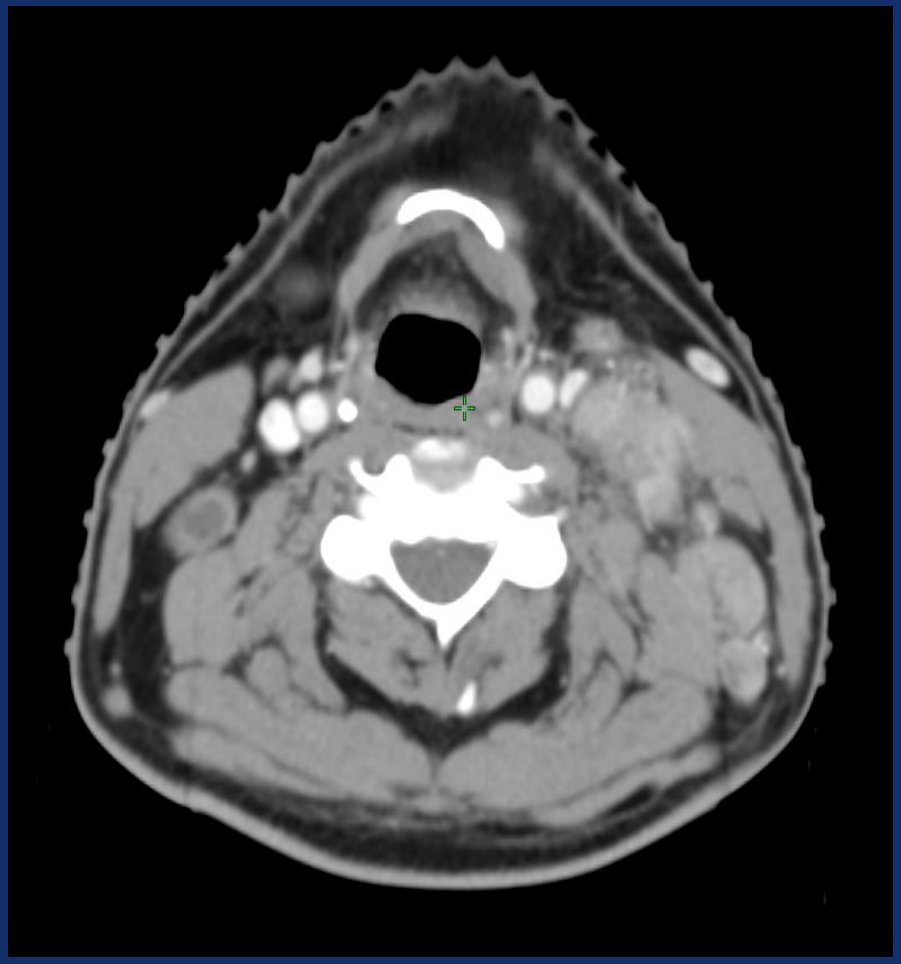


HPV negative Oropharynx,Oral vaity,Larynx or Hypopharynx – N2c
Stage IVa

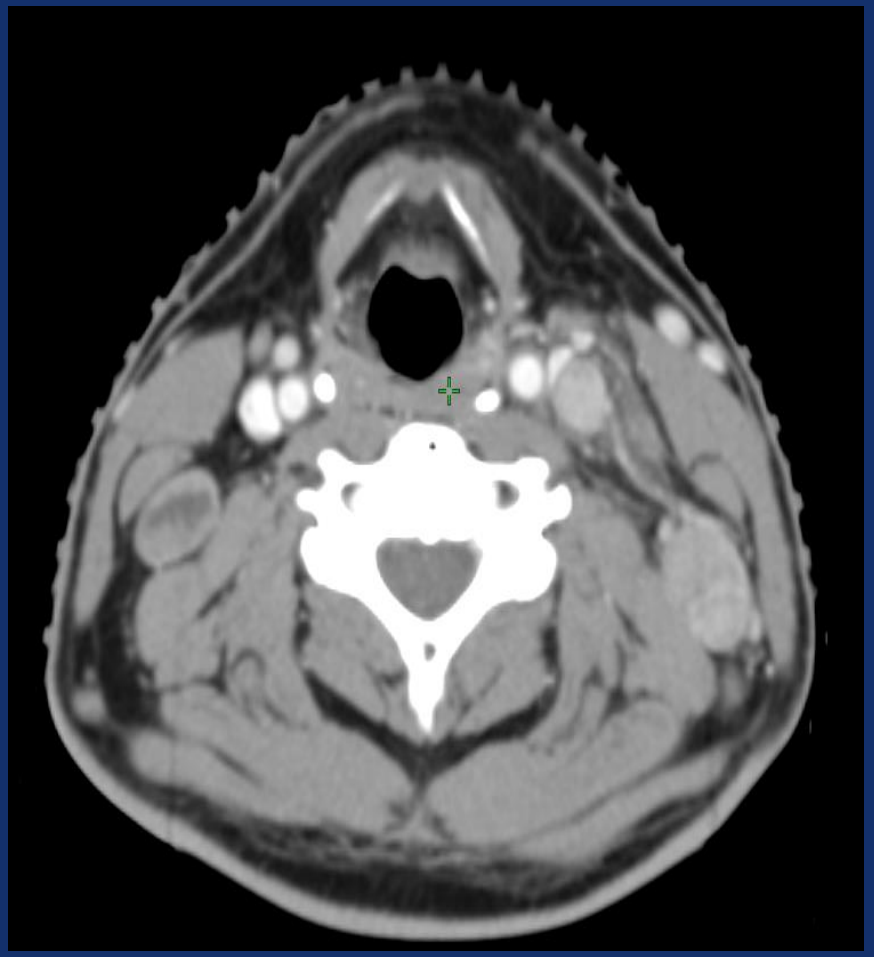
HPV positive – N2. Bilateral (Single or multiple).No sub classification for N2. (if not more than 6 cm) – Stage II

Ca Nasopharynx–N2 Bilateral (if not more than 6 cm)
Stage III

HPV Positive -T2N2-Stage II



HPV Negative,N2c,Stage IVa

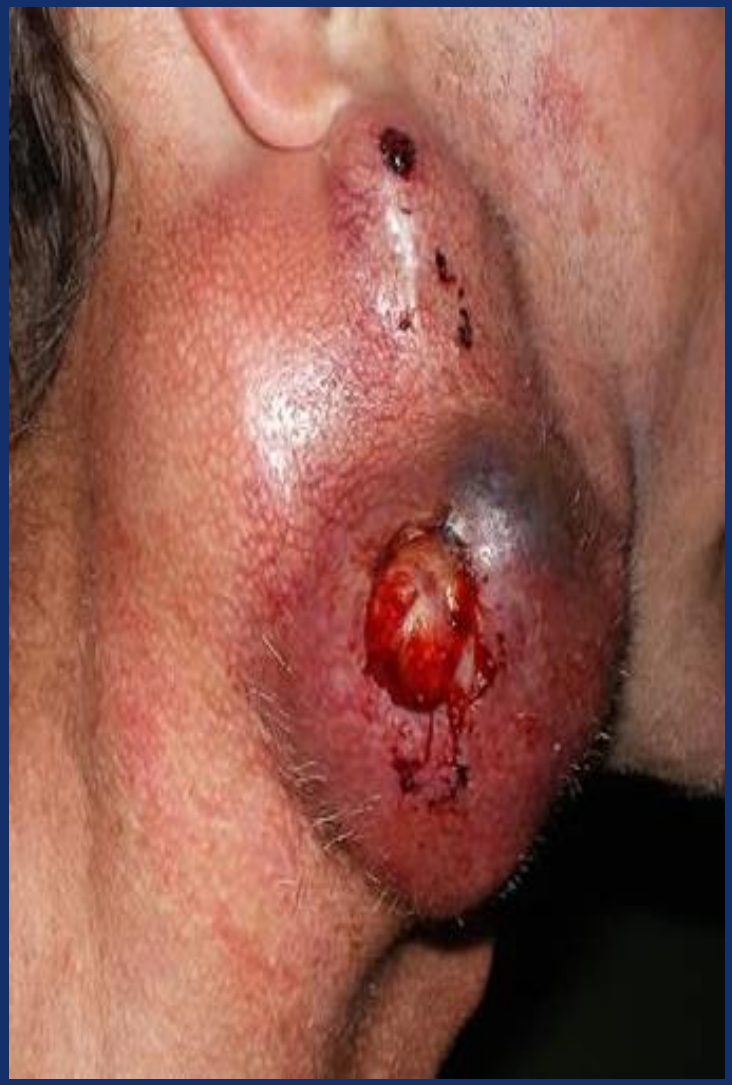


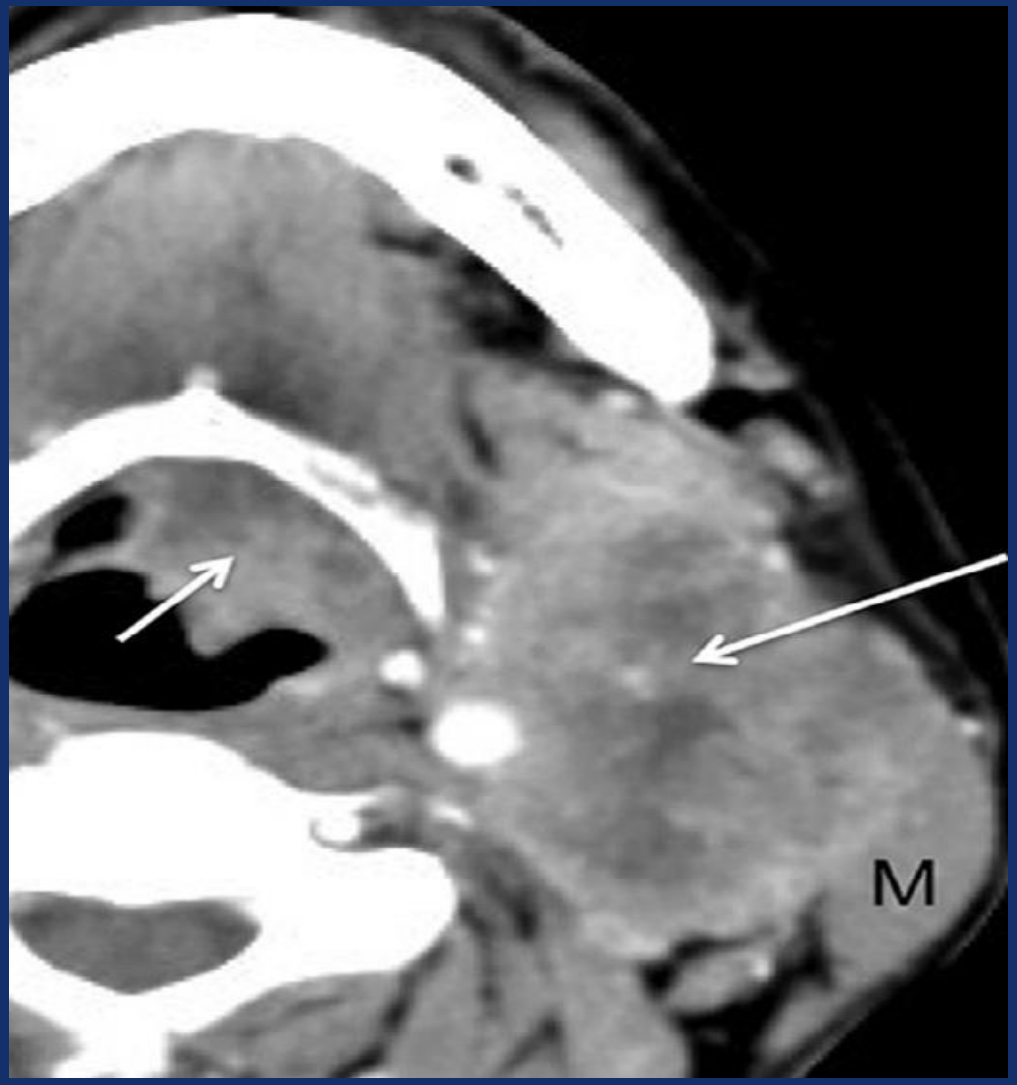
Nodal staging- HPV +ve

N CATEGORY	N CRITERIA
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	One or more ipsilateral lymph nodes, none larger than 6 cm
N2	Contralateral or bilateral lymph nodes, none larger than 6 cm
N3	Lymph node(s) larger than 6 cm

No ENE

N3b /Stage IVb or N3 Disease/Stage III?





Oropharynx p16 Positive tumors

Clinical

Stage I	T1,T2	N0,N1	M0
Stage II	T1,T2	N2	M0
	T3	N0,N1,N2	M0
Stage III	T1-T4	N3	M0
	T4	Any N	M0
Stage IV	Any T	Any N	M1

Human Papillomavirus Testing in Head and Neck Carcinomas

Arch Pathol Lab Med. 2018;142:559–597

Guideline From the College of American Pathologists

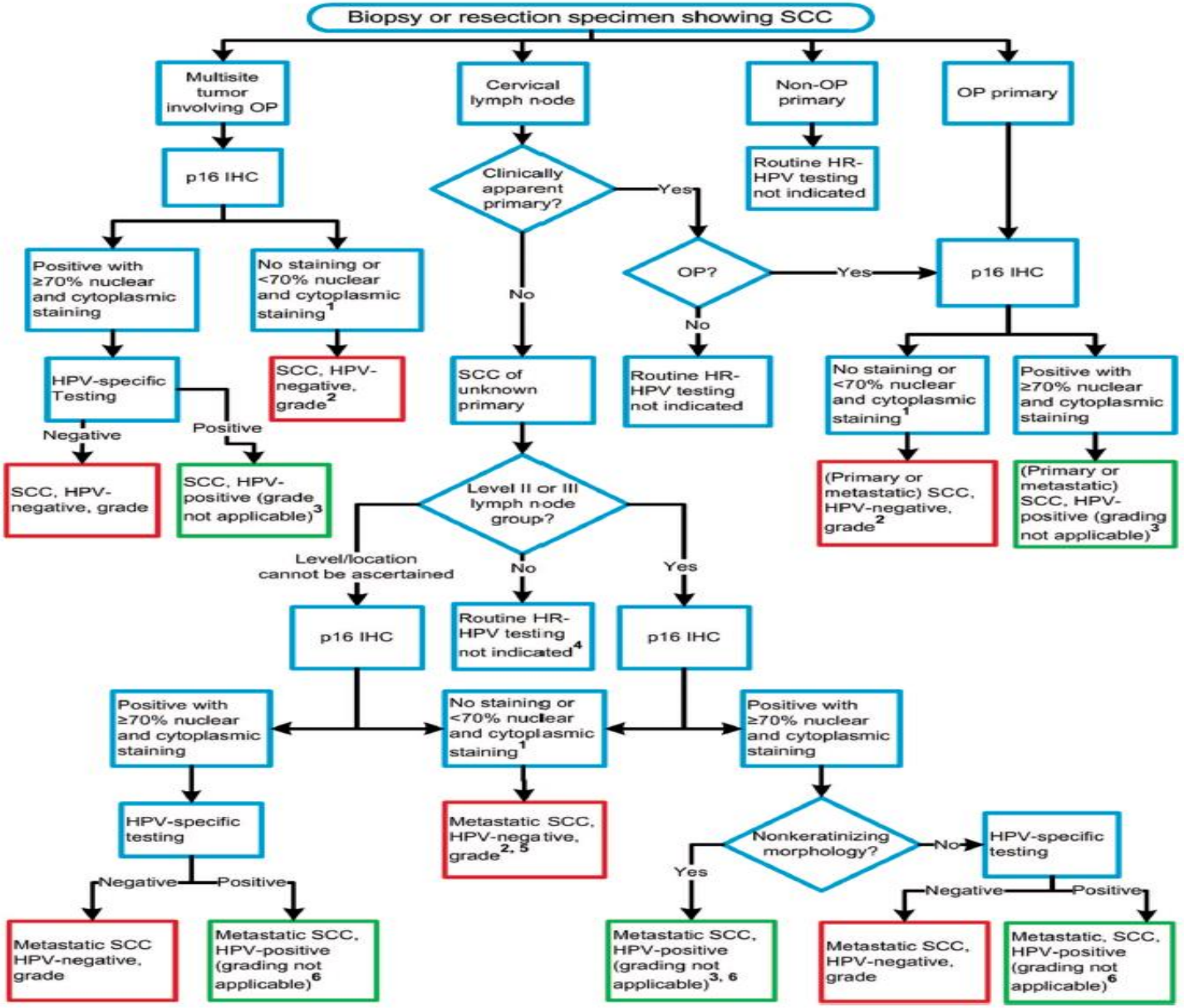
James S. Lewis Jr, MD; Beth Beadle, MD, PhD; Justin A. Bishop, MD; Rebecca D. Chernock, MD; Carol Colasacco, MLIS, SCT(ASCP); Christina Lacchetti, MHSc; Joel Todd Moncur, MD, PhD; James W. Rocco, MD, PhD; Mary R. Schwartz, MD; Raja R. Seethala, MD; Nicole E. Thomas, MPH, CT(ASCP)^{CM}; William H. Westra, MD; William C. Faquin, MD, PhD

Guideline Summary

Human Papillomavirus Testing in Head and Neck Carcinomas: ASCO Clinical Practice Guideline Endorsement Summary of the CAP Guideline

Volume 14 / Issue 10 / October 2018

Carole Fakhry, Christina Lacchetti, and Bayardo Perez-Ordonez



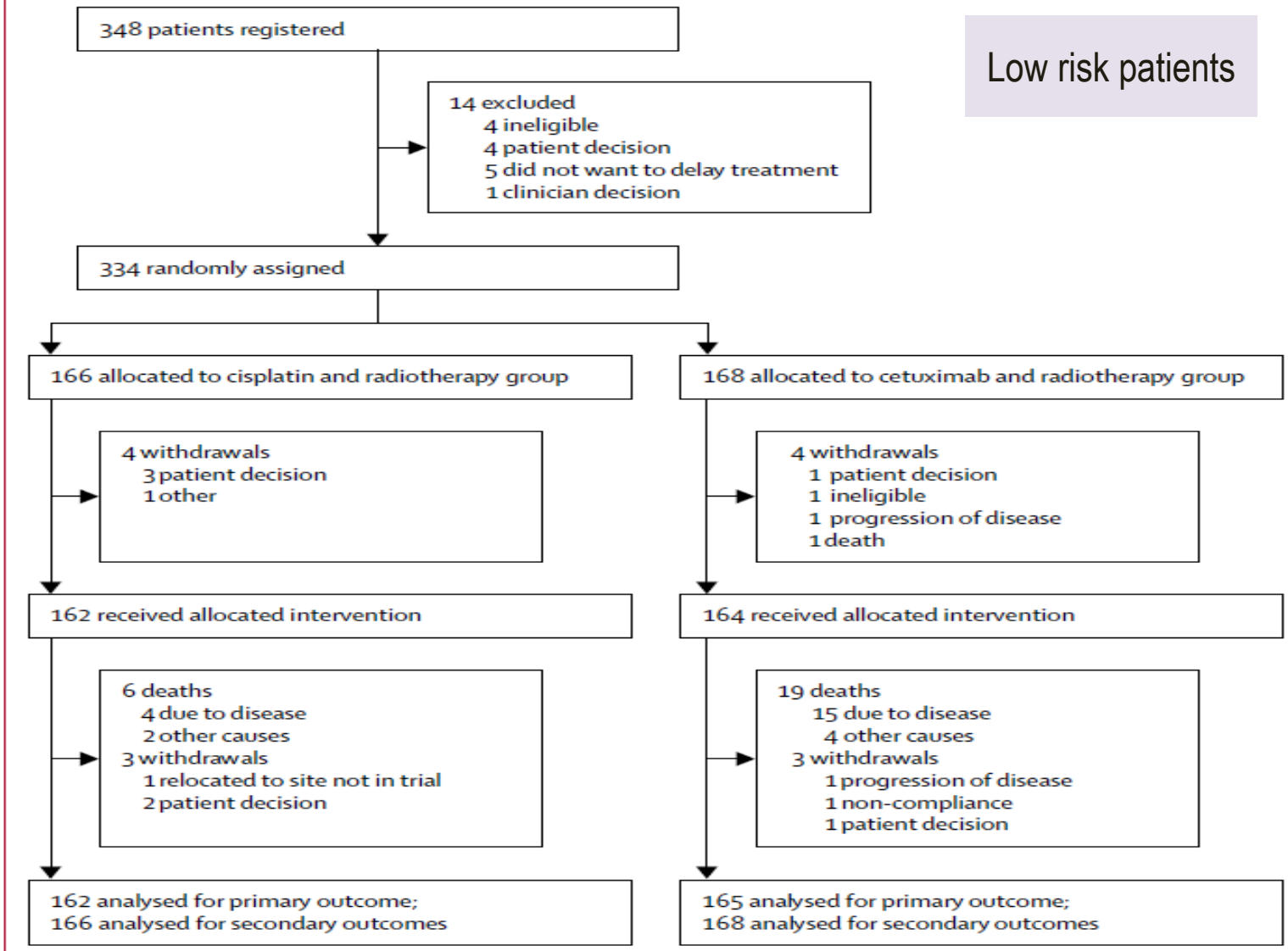
Arch Pathol Lab Med. 2018;142:559–597

Radiotherapy plus cisplatin or cetuximab in low-risk human papillomavirus-positive oropharyngeal cancer (De-ESCALaTE HPV): an open-label randomised controlled phase 3 trial

Hisham Mehanna, Max Robinson, Andrew Hartley, Anthony Kong, Bernadette Foran, Tessa Fulton-Lieuw, Matthew Dalby, Pankaj Mistry, Mehmet Sen, Lorcan O'Toole, Hoda Al Booz, Karen Dyker, Rafael Moleron, Stephen Whitaker, Sinead Brennan, Audrey Cook, Matthew Griffin, Eleanor Aynsley, Martin Rolles, Emma De Winton, Andrew Chan, Devraj Srinivasan, Ioanna Nixon, Joanne Grumett, C René Leemans, Jan Buter, Julia Henderson, Kevin Harrington, Christopher McConkey, Alastair Gray, Janet Dunn, on behalf of the De-ESCALaTE HPV Trial Group*

Radiotherapy plus cetuximab or cisplatin in human papillomavirus-positive oropharyngeal cancer (NRG Oncology RTOG 1016): a randomised, multicentre, non-inferiority trial

Maura L Gillison*, Andy M Trotti*, Jonathan Harris, Avraham Eisbruch, Paul M Harari, David J Adelstein, Erich M Sturgis, Barbara Burtness, John A Ridge, Jolie Ringash, James Galvin, Min Yao, Shlomo A Koyfman, Dukagjin M Blakaj, Mohammed A Razaq, A Dimitrios Colevas, Jonathan J Beitler, Christopher U Jones, Neal E Dunlap, Samantha A Seaward, Sharon Spencer, Thomas J Galloway, Jack Phan, James J Dignam, Quynh Thu Le



Low risk patients

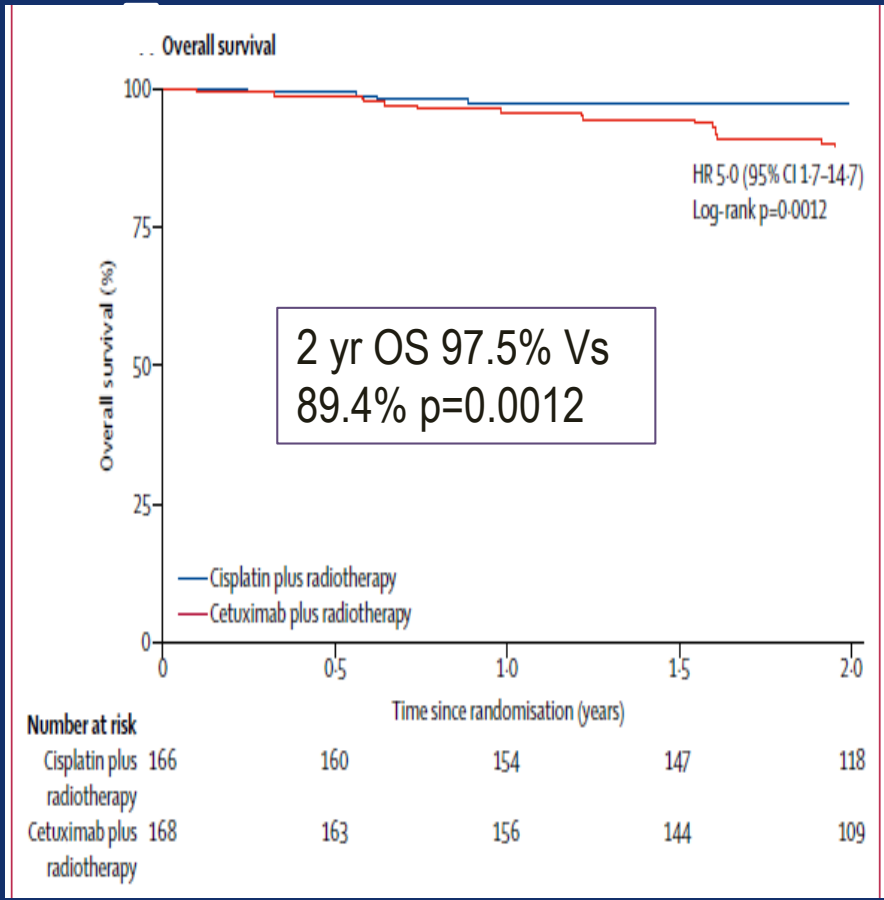
Lancet 2019; 393: 51–60

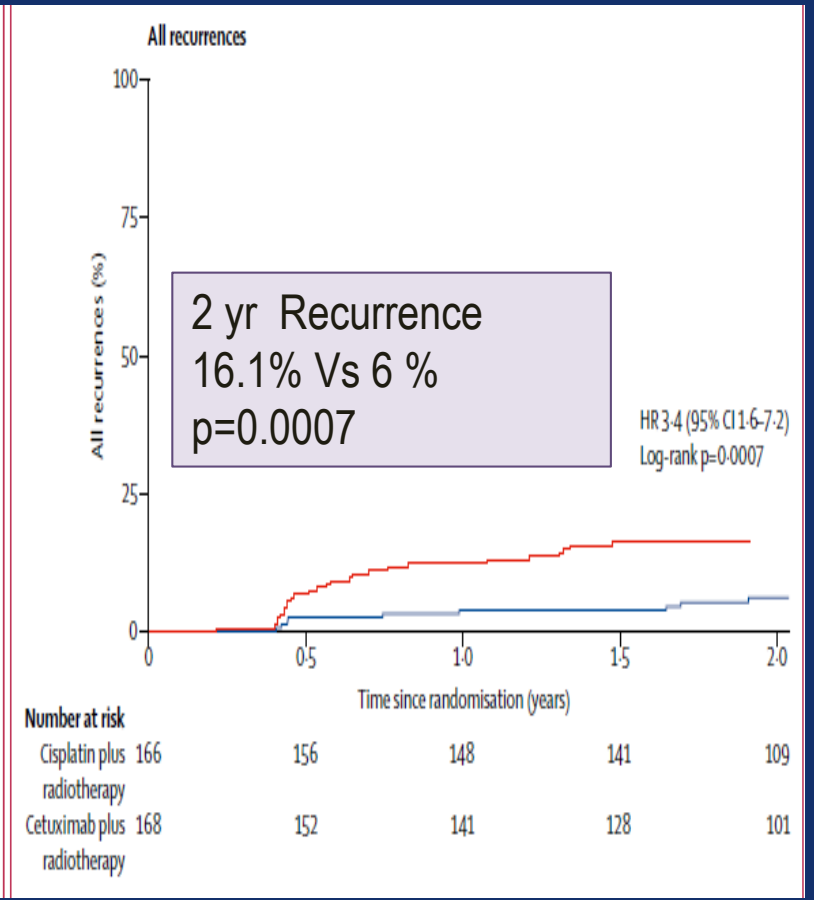
Toxicity- Primary end point

	Cisplatin plus radiotherapy (95% CI)	Cetuximab plus radiotherapy (95% CI)	p value
Primary outcome			
Overall			
Grade 3–5	4·81 (4·23–5·40)	4·82 (4·22–5·43)	0·98
All grades	29·15 (27·33–30·97)	30·05 (28·26–31·85)	0·49
Secondary outcomes			
Acute short-term toxicities			
Grade 3–5	4·43 (3·88–4·97)	4·35 (3·84–4·86)	0·84
All grades	19·96 (18·81–21·12)	20·35 (19·18–21·52)	0·64
Severe late toxicities			
Grade 3–5	0·41 (0·29–0·54)	0·48 (0·30–0·67)	0·53
All grades	9·44 (8·53–10·34)	9·87 (9·02–10·72)	0·49

Lancet 2019; 393: 51–60

Results- Median follow up 22 months



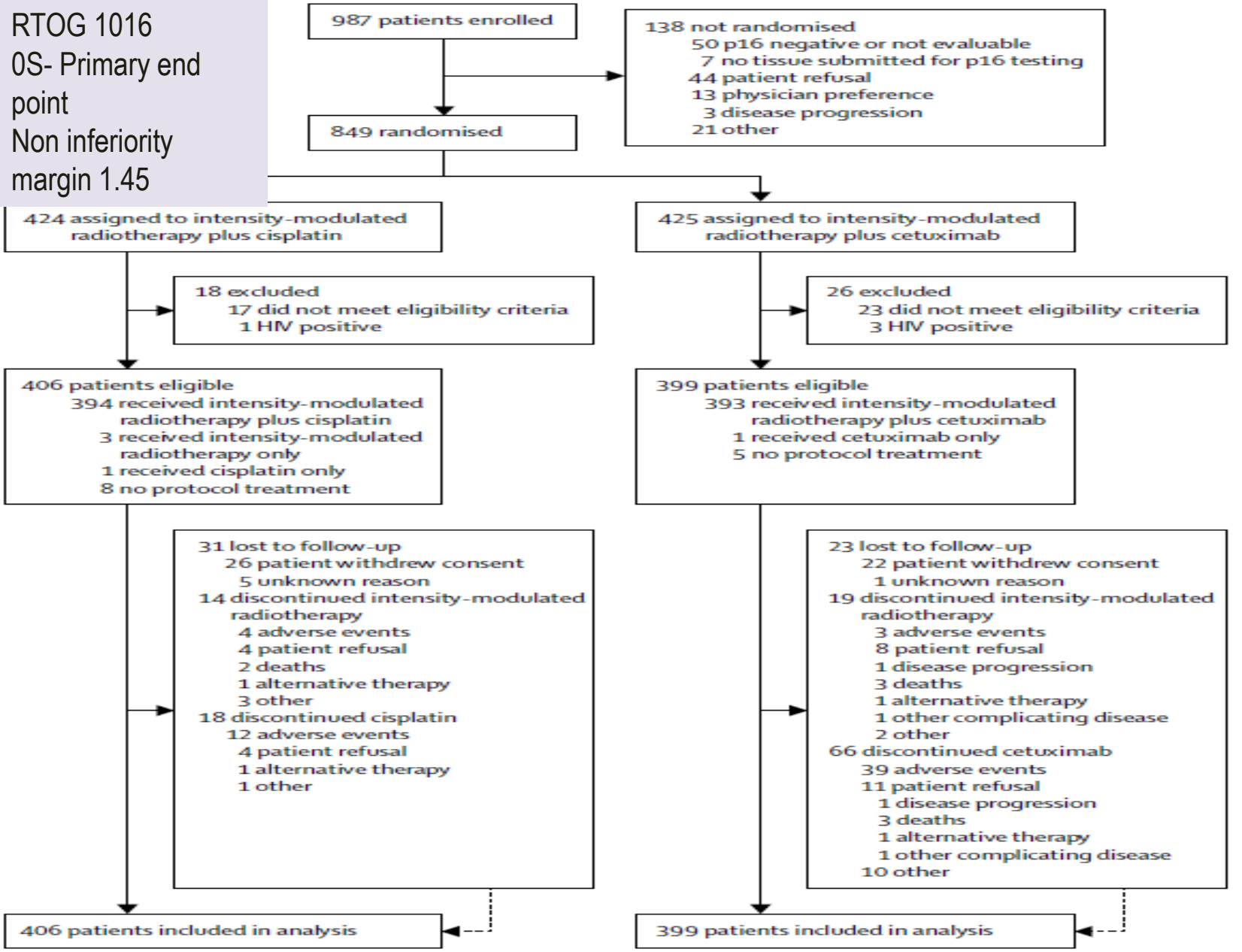


Lancet 2019; 393: 51–60

Conclusions – De- ESCALaTE (low risk)

- HPV positive disease have good prognosis
- There was no difference toxicity between the two arms
- Better OS and less recurrence -with CDDP plus RT
- CDDP plus RT remains standard of care in low risk HPV +ve Disease

RTOG 1016
0S- Primary end point
Non inferiority margin 1.45

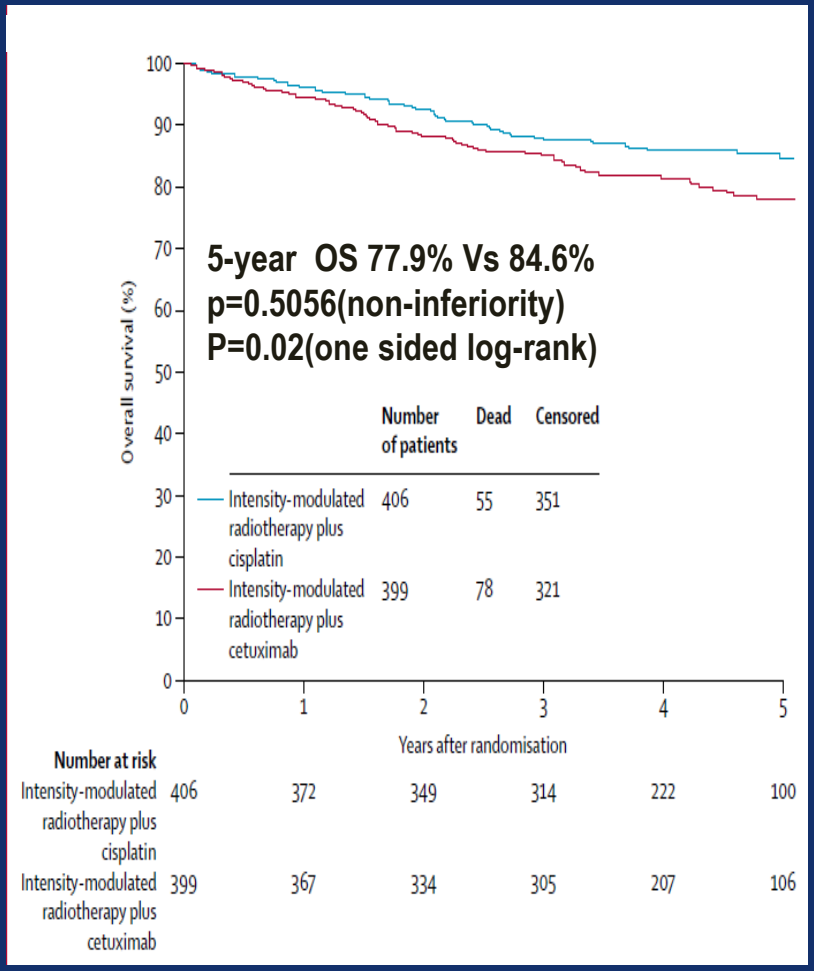


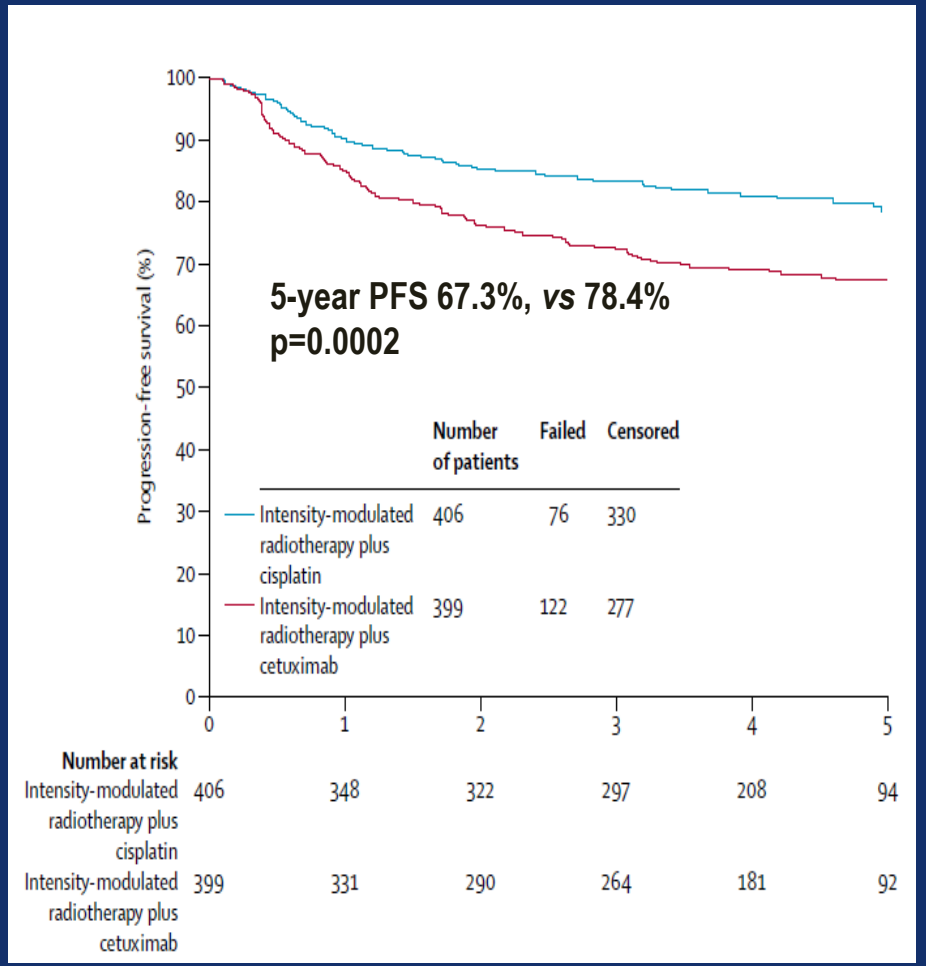
Lancet 2019; 393: 40–50

	Intensity-modulated radiotherapy plus cisplatin	Intensity-modulated radiotherapy plus cetuximab	p value
Acute period patient total	398	394	--
Early death	6 (1·5%)	6 (1·5%)	1·0000
Grade 3–4 overall	325 (81·7%)	305 (77·4%)	0·1586
Grade 3–4 anaemia	11 (2·8%)	0	0·0009*
Grade 3–4 hearing impaired	12 (3·0%)	1 (0·3%)	0·0032*
Grade 2–3 dry mouth	198 (49·7%)	211 (53·6%)	0·2872
Grade 3–4 dysphagia	149 (37·4%)	126 (32·0%)	0·1171
Grade 3–4 mucositis oral	165 (41·5%)	182 (46·2%)	0·1974
Grade 3 nausea	76 (19·1%)	32 (8·1%)	<0·0001*
Grade 3–4 vomiting	48 (12·1%)	16 (4·1%)	<0·0001*
Grade 3 fatigue	23 (5·8%)	17 (4·3%)	0·4178
Grade 3–4 dermatitis radiation	32 (8·0%)	49 (12·4%)	0·0462
Grade 3–4 lymphocyte count decreased	68 (17·1%)	69 (17·5%)	0·9252
Grade 3–4 neutrophil count decreased	61 (15·3%)	2 (0·5%)	<0·0001*
Grade 3 weight loss	31 (7·8%)	23 (5·8%)	0·3241
Grade 3–4 white blood cells decreased	48 (12·1%)	0	<0·0001*
Grade 3–4 anorexia	89 (22·4%)	61 (15·5%)	0·0144*
Grade 3–4 dehydration	61 (15·3%)	24 (6·1%)	<0·0001*
Grade 3–4 hyponatremia	21 (5·3%)	4 (1·0%)	0·0008*
Grade 3–4 acute kidney injury	13 (3·3%)	1 (0·3%)	0·0017*
Grade 3–4 pharyngeal mucositis	54 (13·6%)	40 (10·2%)	0·1535
Grade 3–4 rash acneiform	1 (0·3%)	37 (9·4%)	<0·0001*
Grade 3–4 pain (all terms)	58 (14·6%)	50 (12·7%)	0·4694
Mean raw T-score	3·19	2·35	<0·0001*
Late period patient total	383	375	--
Grade 3–4 overall	78 (20·4%)	62 (16·5%)	0·1904
Grade 3–4 hearing impaired	24 (6·3%)	8 (2·1%)	0·0060*
Grade 2–3 dry mouth	123 (32·1%)	126 (33·6%)	0·6991
Grade 3–4 dysphagia	17 (4·4%)	23 (6·1%)	0·3318
Grade 3 weight loss	17 (4·4%)	11 (2·9%)	0·3366
Grade 3–4 osteonecrosis of jaw	8 (2·1%)	3 (0·8%)	0·2234
Grade 3–4 pain (all terms)	5 (1·3%)	8 (2·1%)	0·4154
Mean raw A-score	0·38	0·27	0·1189

Lancet 2019; 393: 40–50

Median follow up 4.5 yrs





Lancet 2019; 393: 40–50

Comparison

RTOG 1016	De- ESCALaTE
Low risk and intermediate	Only low risk
Primary end point – OS	Primary end point -Toxicity
More long term follow up 4.5 yrs	Median follow up 22 months
Number of patients-987	Number of patients -348
Difference in toxicity	No difference in toxicities
OS better with CDDP plus RT	OS better with CDDP plus RT

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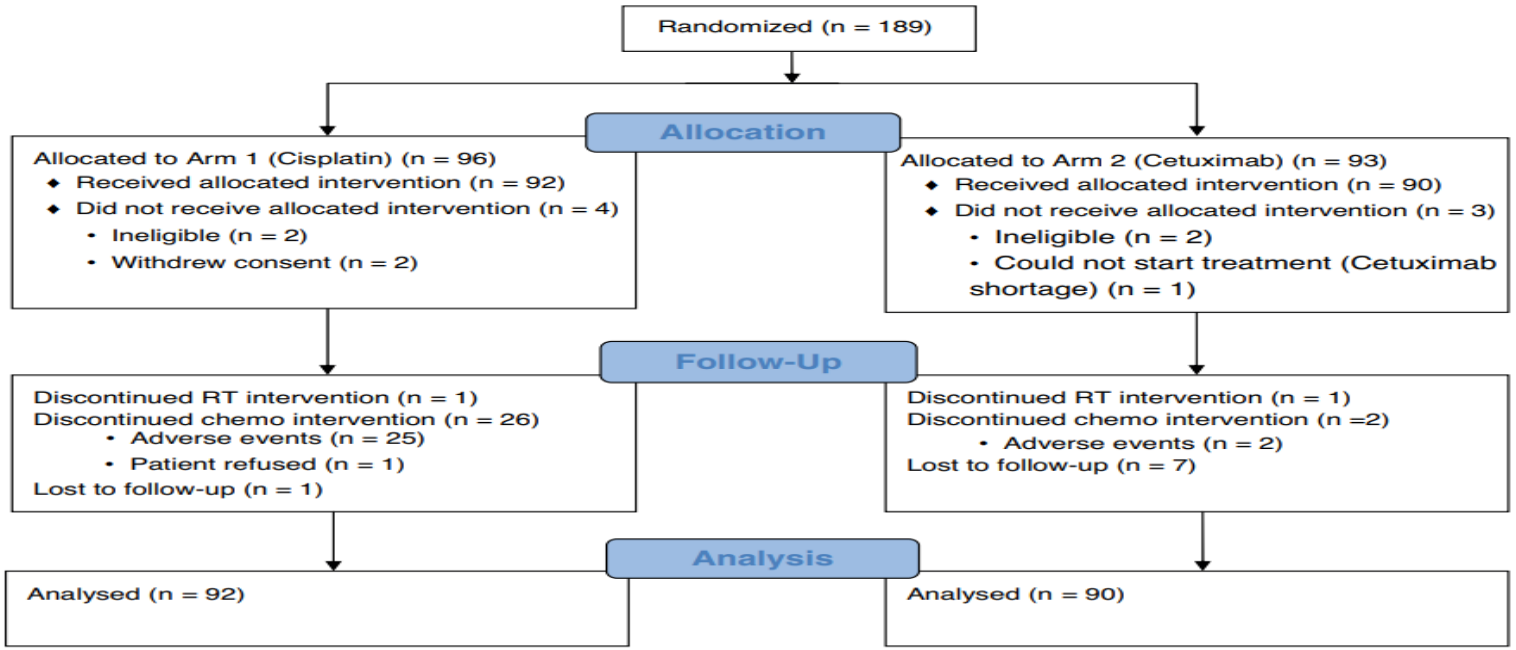
Clinical Investigation

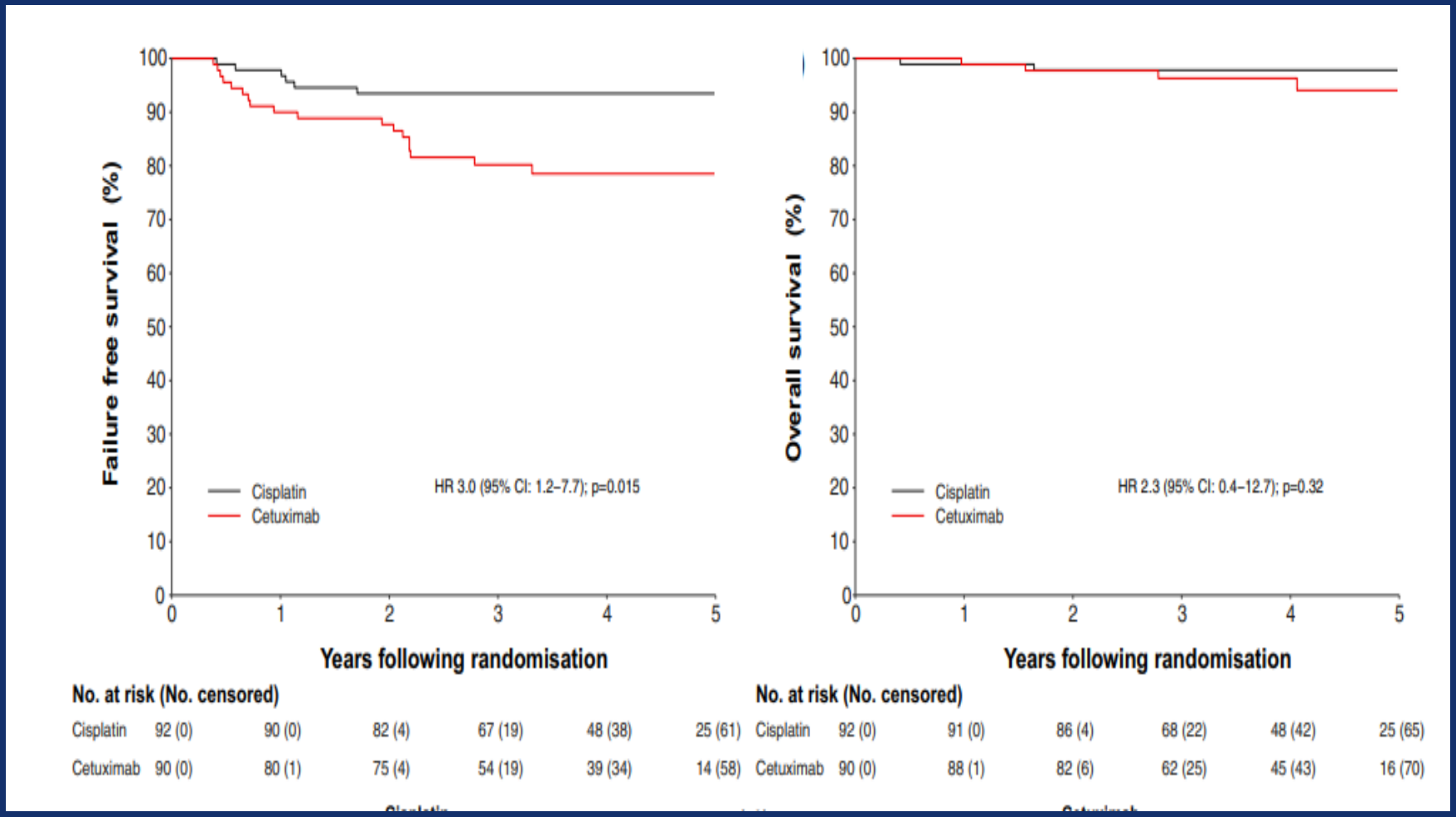
Randomized Trial of Radiation Therapy With Weekly Cisplatin or Cetuximab in Low-Risk HPV-Associated Oropharyngeal Cancer (TROG 12.01) — A Trans-Tasman Radiation Oncology Group Study

Danny Rischin, MD,[*,†] Madeleine King, PhD,[‡] Lizbeth Kenny, MBBS,[§,‖] Sandro Porceddu, MD,[‖,#] Christopher Wratten, MBBS,[**] Andrew Macann, MBChB,[††] James E. Jackson, MBBS,[‡‡] Mathias Bressel, MSc,[§§] Alan Herschtal, PhD,[§§] Richard Fisher, PhD,[§§] Tsien Fua, MBBS,[‖‖] Charles Lin, MBBS,[§] Chen Liu, MBBS,[‖‖] Brett G.M. Hughes, MBBS,[‖,##] Margaret McGrath, MBBS,[***] Lachlan McDowell, MBBS,[†,‖‖] and June Corry, MD[†††,‡‡‡]



Int J Radiation Oncol Biol Phys, Vol. 111, No. 4, pp. 876–886, 2021

Efficacy..



Int J Radiation Oncol Biol Phys, Vol. 111, No. 4, pp. 876–886, 2021

VOLUME 35 · NUMBER 5 · FEBRUARY 10, 2017

JOURNAL OF CLINICAL ONCOLOGY

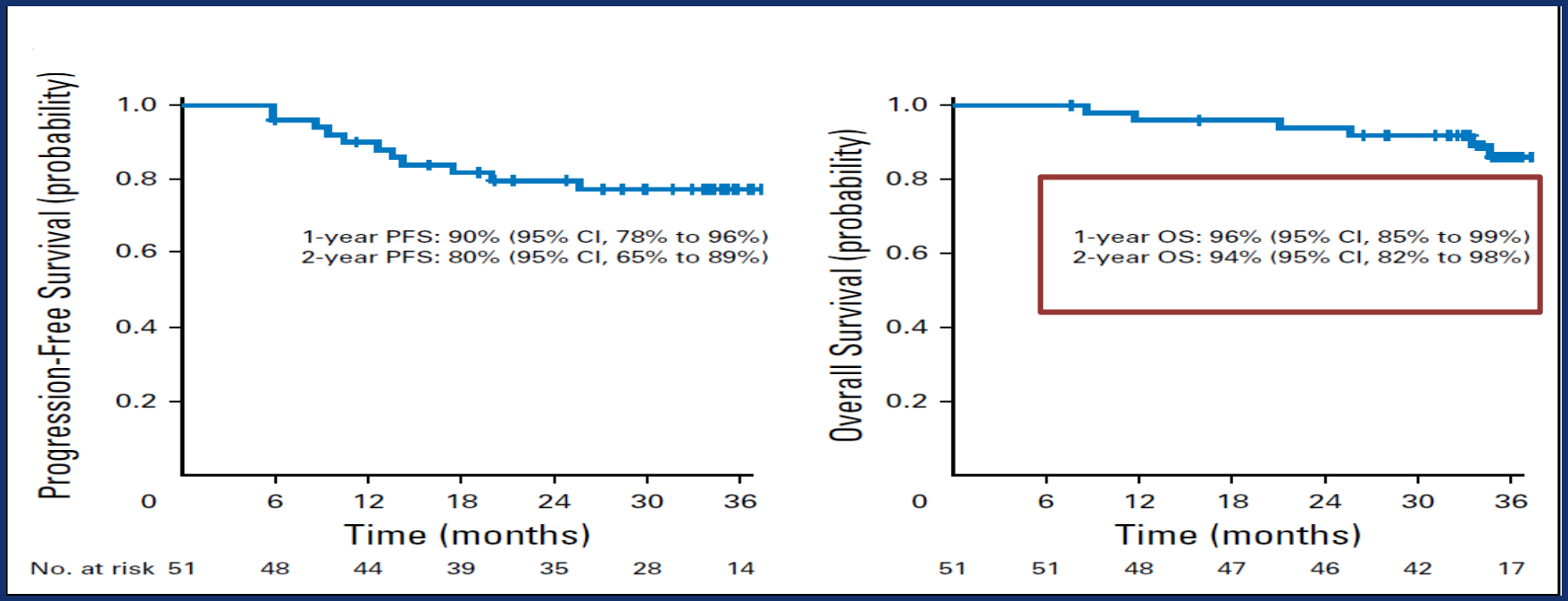
ORIGINAL REPORT

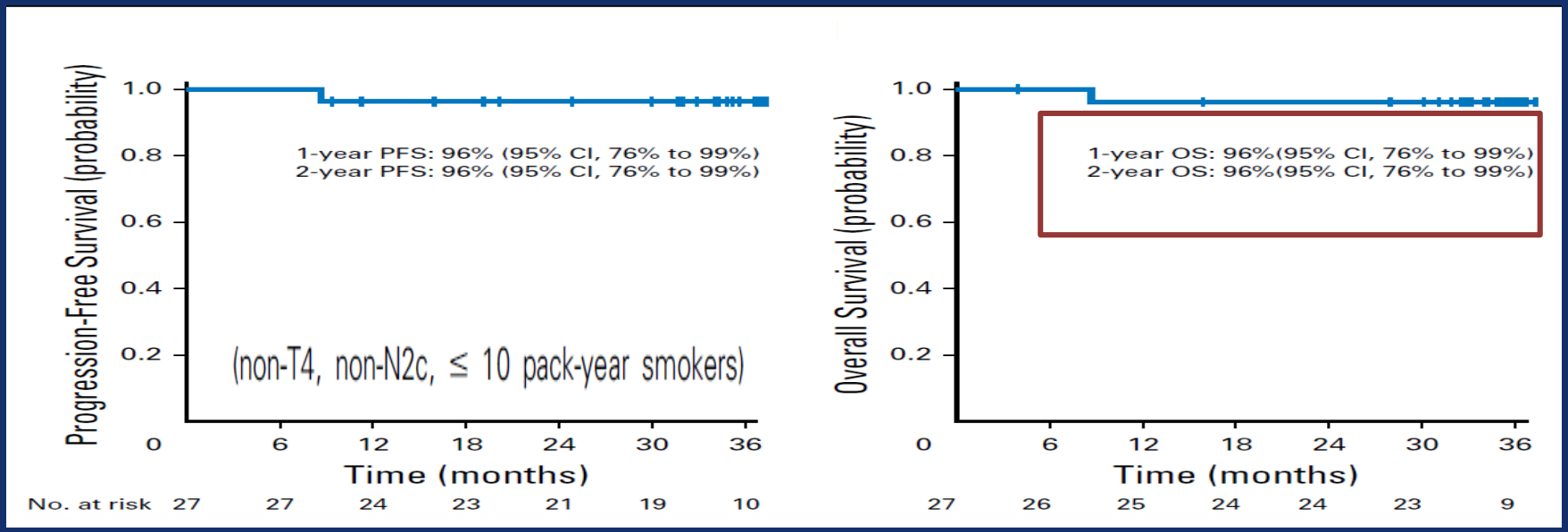
E1308: Phase II Trial of Induction Chemotherapy Followed by Reduced-Dose Radiation and Weekly Cetuximab in Patients With HPV-Associated Resectable Squamous Cell Carcinoma of the Oropharynx— ECOG-ACRIN Cancer Research Group

Shanthi Marur, Shuli Li, Anthony J. Cmelak, Maura L. Gillison, Weiqiang J. Zhao, Robert L. Ferris, William H. Westra, Jill Gilbert, Julie E. Bauman, Lynne I. Wagner, David R. Trevarthen, Jahagirdar Balkrishna, Barbara A. Murphy, Nishant Agrawal, A. Dimitrios Colevas, Christine H. Chung, and Barbara Burtness

INDUCTION CT (Pacli +CDDP+C225) X 1-3

CR		PR/SD	
54Gy/27# 5days a week +		69.3Gy/33# 5days a week +	
C225 x 6 weeks		C225 x 7 weeks	
N=80 , Primary end point – 2 yr PFS			





J Clin Oncol 35:490-497.

The Quarterback Trial: A Randomized Phase III Clinical Trial Comparing Reduced and Standard Radiation Therapy Doses for Locally Advanced HPV Positive Oropharynx Cancer

- Phase III
- Stage III & IV patients
- Primary end point: -PFS
- Secondary end point – LRC and OS
- 3 cycles of Induction Chemotherapy TPF
- Patients who achieve CR or PR

RANDOMIZE

IMRT- 70Gy/35 fr+ Concurrent Carboplatin weekly

IMRT- 56 Gy/28 fr+ Concurrent Carboplatin weekly

PI: Marshall Posner, M.D, Mount Sinai Hospital , NY

https://clinicaltrials.gov/ct2/show/NCT01706939

International Journal of Radiation Oncology biology • physics
www.redjournal.org

Clinical Investigation

Phase 2 Trial of De-intensified Chemoradiation Therapy for Favorable-Risk Human Papillomavirus—Associated Oropharyngeal Squamous Cell Carcinoma

Bhishamjit S. Chera, MD,*,† Robert J. Amdur, MD,‡,§
Joel Tepper, MD,*,† Bahjat Qaqish, PhD,†,|| Rebecca Green, MSW,*
Shannon L. Aumer, MA,# Neil Hayes, MD, MPH,†,¶ Jared Weiss, MD,†,¶
Juneko Grilley-Olson, MD,†,¶ Adam Zanation, MD,#
Trevor Hackman, MD,# William Funkhouser, MD,**
Nathan Sheets, MD,†† Mark Weissler, MD,#
and William Mendenhall, MD‡,§

T0-3 and N0-2. N=44

RT: 60 Gy IMRT + Weekly Cisplatin 30 mg/m2

Primary endpoint: Complete Response

Median FU – 14 months

CR: 98% for primary and 84% for nodal sites.

Cons

They included early stage cases

Short follow up

Planned Neck dissection

Int J Radiation Oncol Biol Phys, Vol. 93, No. 5, pp. 976–985, 2015

De-intensification of Radiation and Chemotherapy for Low-Risk HPV-related Oropharyngeal SCC: Follow-up Study

- Phase II
- IMRT, 60 Gy at 2 Gy/fx.
- Weekly chemotherapy regimens are Cisplatin 30 to 40 mg/m2 (first choice), Cetuximab 250mg/m2 (second choice), Carboplatin AUC 1.5 and paclitaxel 45 mg/m2 .
- Chemotherapy will not be given to patients with T0-2 N0-1 disease, ≤ 10 pack years smoking history.
- Neck dissection based on PET/CT done 10-16 weeks

PI	Bhishamjit Chera, MD	University of North Carolina

https://clinicaltrials.gov/ct2/show/NCT02281955

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ORIGINAL ARTICLE

Annals of Oncology 30: 297–302, 2019
doi:10.1093/annonc/mdy522
Published online 27 November 2018

OPTIMA: a phase II dose and volume de-escalation trial for human papillomavirus-positive oropharyngeal cancer

T. Y. Seiwert[1†], C. C. Foster[2†], E. A. Blair[3], T. G. Karrison[4], N. Agrawal[3], J. M. Melotek[2], L. Portugal[3], R. J. Brisson[5], A. Dekker[1], S. Kochanny[1], Z. Gooi[3], M. W. Lingen[6], V. M. Villaflor[7], D. T. Ginat[8], D. J. Haraf[2] & E. E. Vokes[1*]

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Primary end point:2 yr PFS
N=62
IC- Carboplatin plus nab –paclitaxel

Low risk patients
(≤ T3, ≤ N2b ≤ 10 pack-year history)

High risk patients
(≥T4, ≥ N2c , ≥ 10 pack-year history)

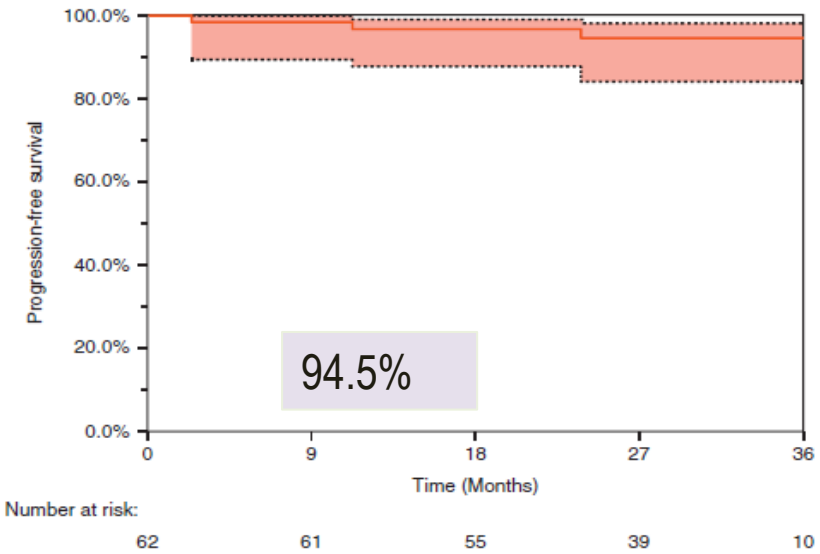
→ ICX3 →

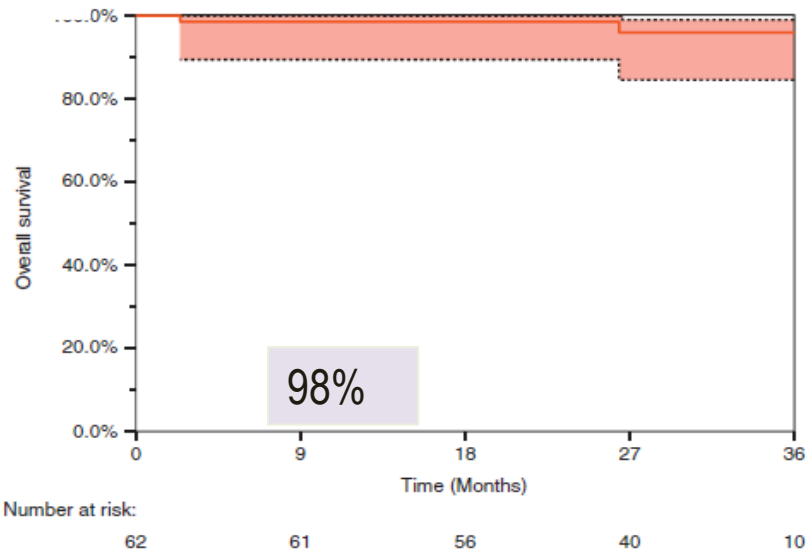
Low-risk patients with 50% response received 50 (Gy)/25 RT (RT50)

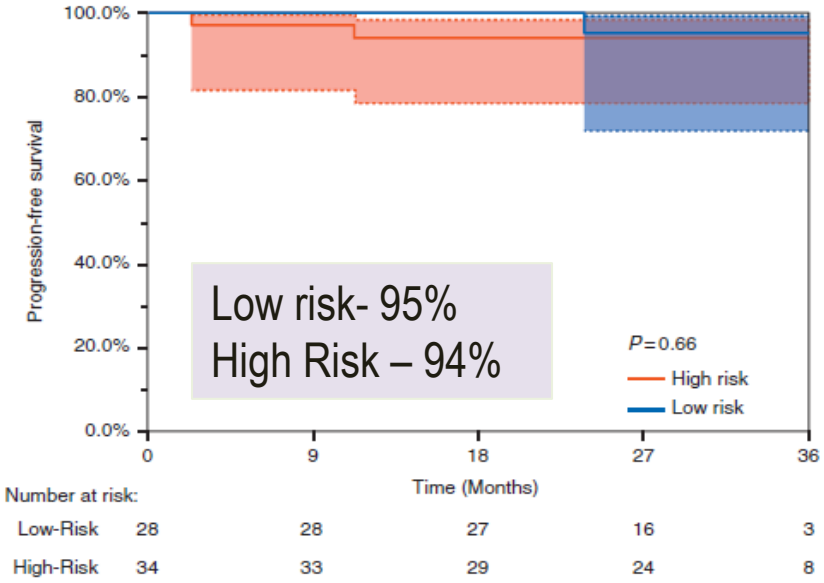
low-risk patients with 30%–50% response or high-risk patients with 50% response received 45 Gy CRT (CRT45)

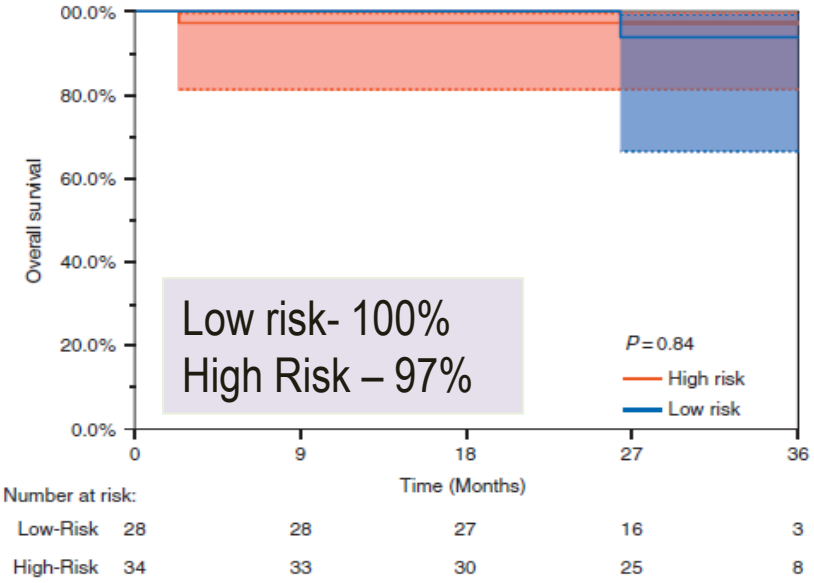
Patients with lesser response received standardof-care 75 Gy CRT (CRT75)

Annals of Oncology 30: 297–302, 2019



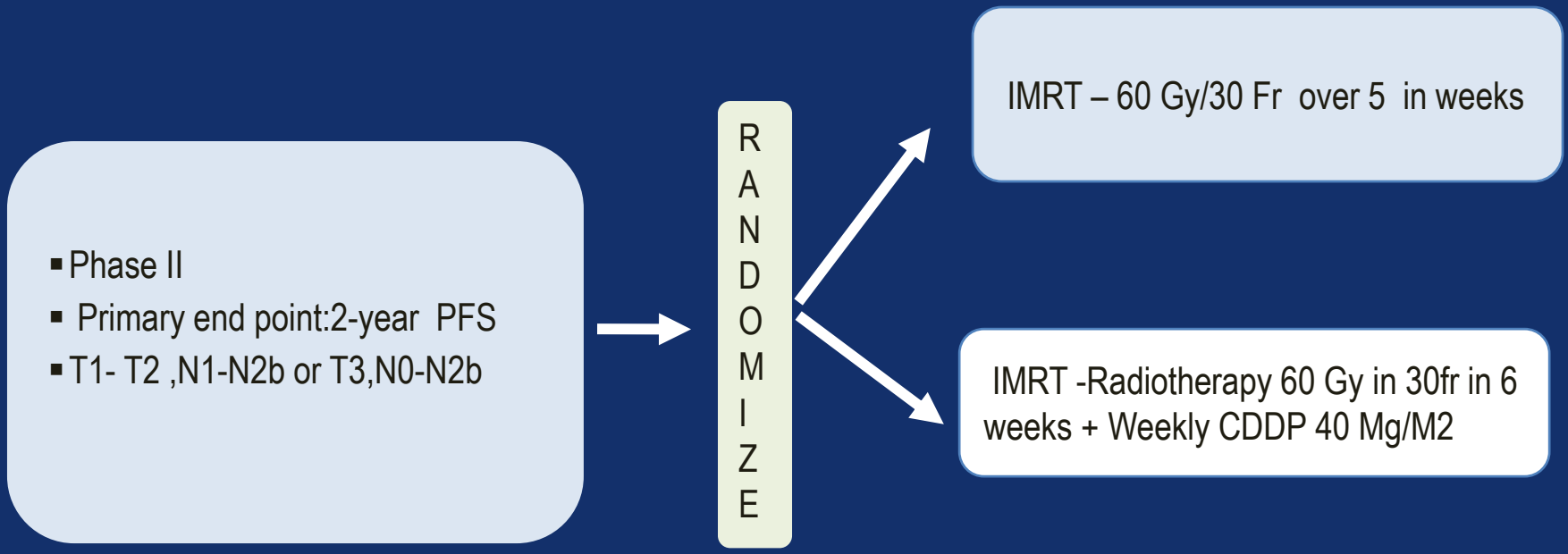






Annals of Oncology 30: 297–302, 2019

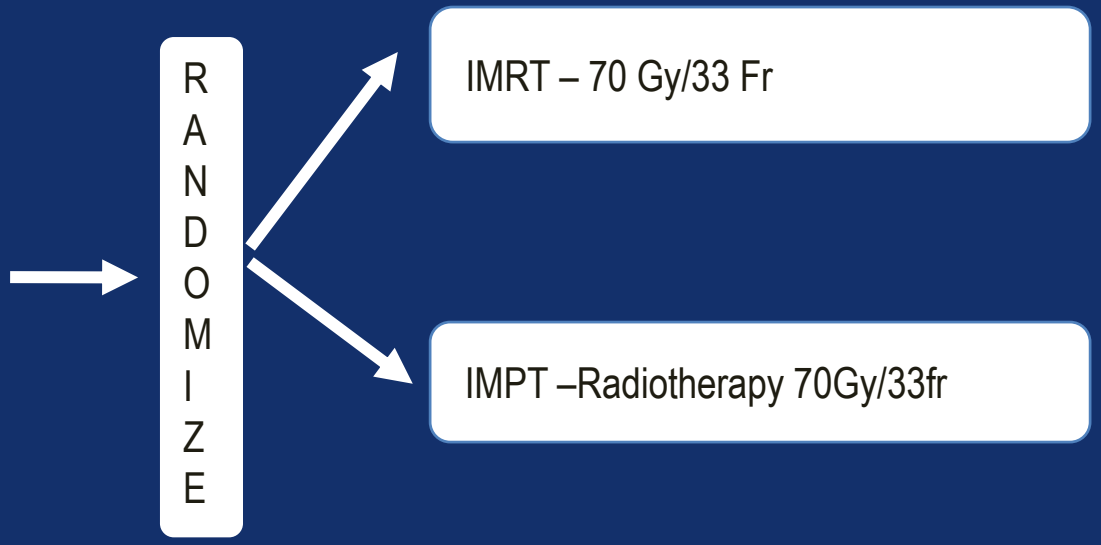
Reduced-Dose Intensity-Modulated Radiation Therapy With or Without Cisplatin in Treating Patients With Oropharyngeal Cancer-HN002 Phase II Trial



https://clinicaltrials.gov/ct2/show/NCT02254278

IMPT Versus IMRT for the Treatment of Ca Oropharynx

- Squamous Cell Carcinoma of the oropharynx (American Joint Committee on Cancer (AJCC) v7Stage III-IV A,B)
- Phase II/III
- Chemotherapy at the discretion of the Physician
- Rates and severity of late grade 3-5 toxicity between two arms



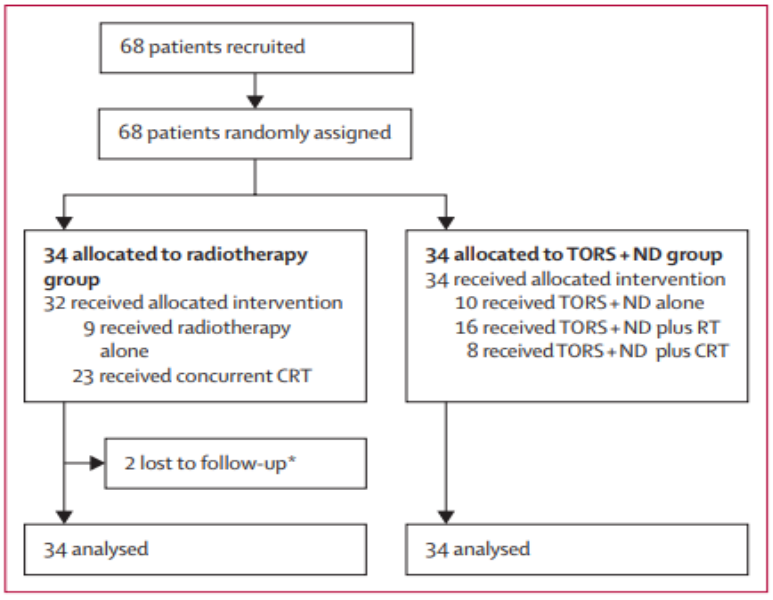
Steven J. Frank, MD M.D. Anderson Cancer Center

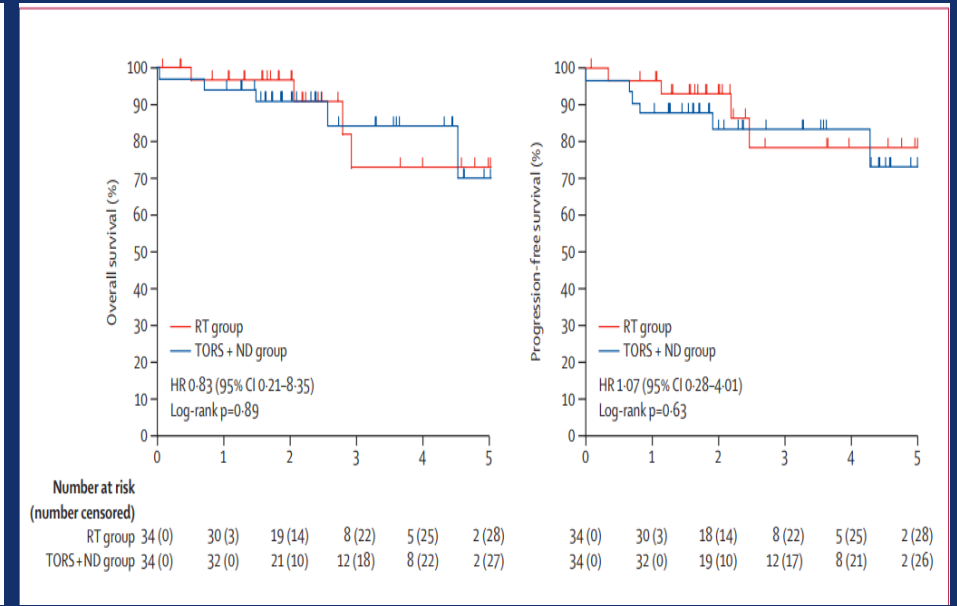
https://clinicaltrials.gov/ct2/show/NCT01893307

The primary endpoint -swallowing-related QOL at 1 year based on MD Anderson Dysphagia Inventory (MDADI) score

Radiotherapy versus transoral robotic surgery and neck dissection for oropharyngeal squamous cell carcinoma (ORATOR): an open-label, phase 2, randomised trial

Anthony C Nichols, Julie Theurer, Eitan Prisman, Nancy Read, Eric Berthelet, Eric Tran, Kevin Fung, John R de Almeida, Andrew Bayley, David P Goldstein, Michael Hier, Khalil Sultanem, Keith Richardson, Alex Mlynarek, Suren Krishnan, Hien Le, John Yoo, S Danielle MacNeil, Eric Winquist, J Alex Hammond, Varagur Venkatesan, Sara Kuruvilla, Andrew Warner, Sylvia Mitchell, Jeff Chen, Martin Corsten, Stephanie Johnson-Obaseki, Libni Eapen, Michael Odell, Christina Parker, Bret Wehrli, Keith Kwan, David A Palma





Lancet Oncol 2019; 20: 1349–59

1 year Efficacy results

	1 year				Clinically meaningful decline*		
	RT group	TORS + ND group	Effect estimate (95% CI)	p value†	RT group	TORS + ND group	p value
Total (primary endpoint)	86·9 (11·4)	80·1 (13·0)	6·7 (0·2 to 13·2)	0·042	7/27 (26%)	11/27 (41%)	0·25
Global	89·6 (15·1)	79·3 (22·6)	10·3 (0·2 to 20·4)	0·046	6/27 (22%)	14/27 (52%)	0·024
Emotional	88·8 (12·0)	81·3 (12·5)	7·4 (0·9 to 14·0)	0·027	5/27 (19%)	13/27 (48%)	0·021
Functional	89·9 (11·5)	86·5 (12·0)	3·4 (−2·9 to 9·6)	0·28	7/27 (26%)	9/26 (35%)	0·49
Physical	83·1 (14·1)	75·3 (16·5)	7·9 (−0·3 to 16·0)	0·058	12/27 (44%)	16/27 (59%)	0·28
Composite (total score excluding global score)	86·7 (11·4)	80·2 (13·1)	6·5 (0·0 to 13·1)	0·049	6/27 (22%)	11/27 (41%)	0·14

Data are presented as mean (SD) unless otherwise stated. RT=radiotherapy. TORS + ND=transoral robotic surgery and neck dissection. *Defined as a decrease of at least 10 points. †p values adjusted for stratification by p16 status (post-hoc analysis): total (p=0·054), global (p=0·071), emotional (p=0·040), functional (p=0·29), physical (p=0·064), and composite (p=0·062).

Lancet Oncol 2019; 20: 1349–59

RT vs Surgery in Early OPC

Radiotherapy	Surgery (TORS/TLM)+/-Adjuvant Treatment
Established approach	Under evaluation
Functional outcomes better	Minimally invasive and less disfiguring No external incision/scar
HPV status is prognostic	Outcomes independent of HPV status
Applicable in all patients	Requires good oral access Patient selection is very important
Can be done in tumors in close proximity to critical structures	Reconstruction may be an issue
IMRT can potential reduce toxicity and late dysphagia	Clearance with negative margins may be an issue
RP Nodes cannot be excised	Most patients need Adjuvant RT +/- chemo
No steep learning curve	Required

Surgery

- ADEPT - Phase III
- ECOG 3311- Phase II
- PATHOS- Phase II

Post Operative Adjuvant Therapy De-intensification Trial for Human Papillomavirus-related, p16+ Oropharynx Cancer (ADEPT)

- Transoral resection of their T1-4a oropharynx primary to a negative margin, and a neck dissection(s).
- ECS in their nodal metastasis

N= 496

RANDOMIZE

IMRT -Radiotherapy 60 Gy in 30fr

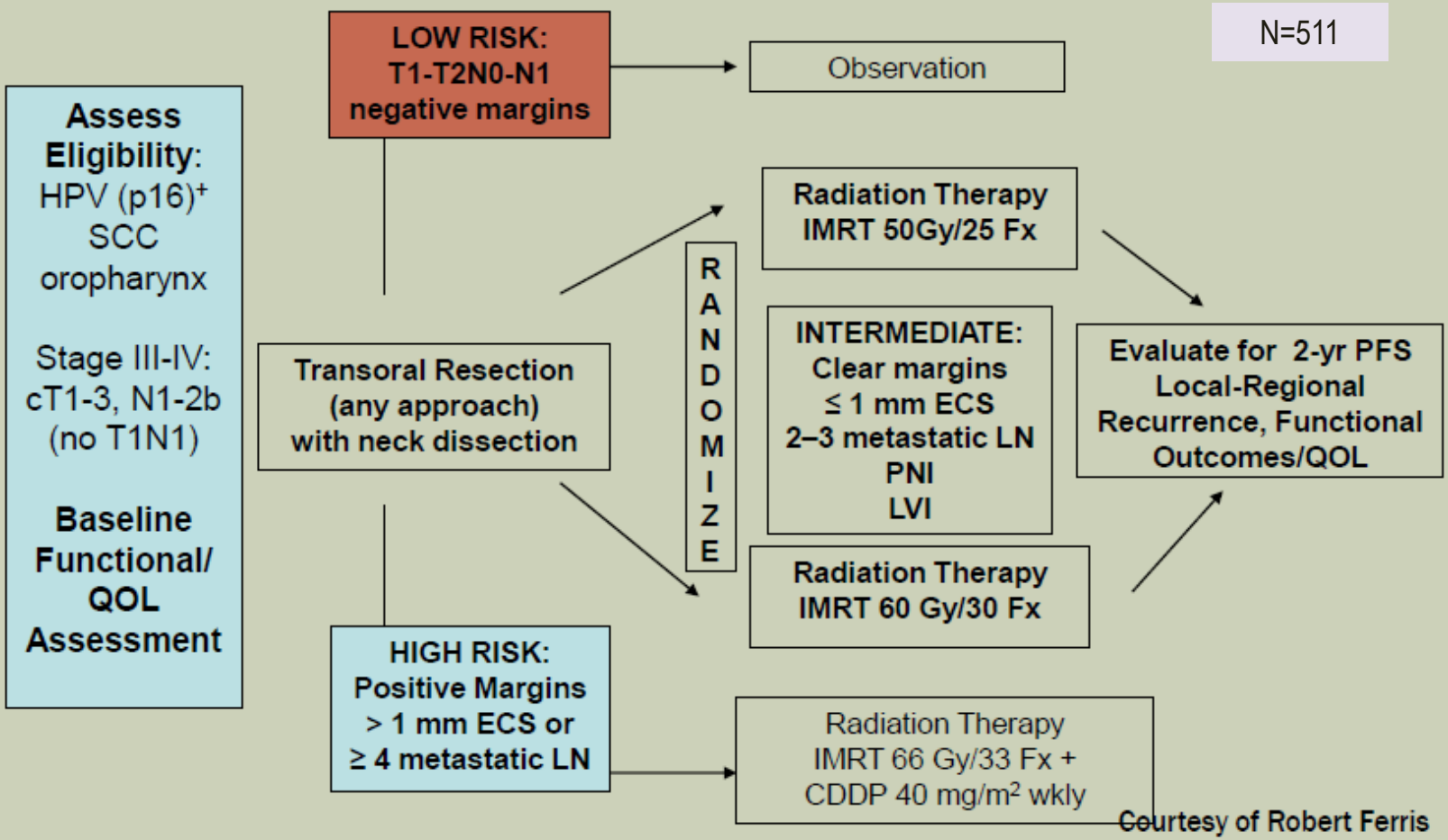
IMRT- Radiotherapy 60 Gy in 30fr + Weekly CDDP 40 Mg/M2

Primary endpoints
- 1.Disease-free survival (DFS)
- 2.Locoregional control

Secondary end points
- ✓ Distant metastasis rates
- ✓ Disease specific survival
- ✓ Cumulative incidence of complications/acute toxicity
- ✓ Function and quality of life (QOL)

https://clinicaltrials.gov/ct2/show/NCT01687413

ECOG 3311 P16+ Trial – Low Risk OPSCC: Personalized Adjuvant Therapy Based on Pathologic Staging of Surgically Excised HPV+ Oropharynx Cancer



https://clinicaltrials.gov/ct2/show/NCT01898494

Results – Median follow up 35 months

3-year PFS

- 96.9% for Arm A
- 94.9% for Arm B
- 93.5% for Arm C
- 90.7% for Arm D

Primary TOS and reduced PORT retained outstanding oncologic outcome at 35 months follow up

ASCO 2021 Abstract 6010

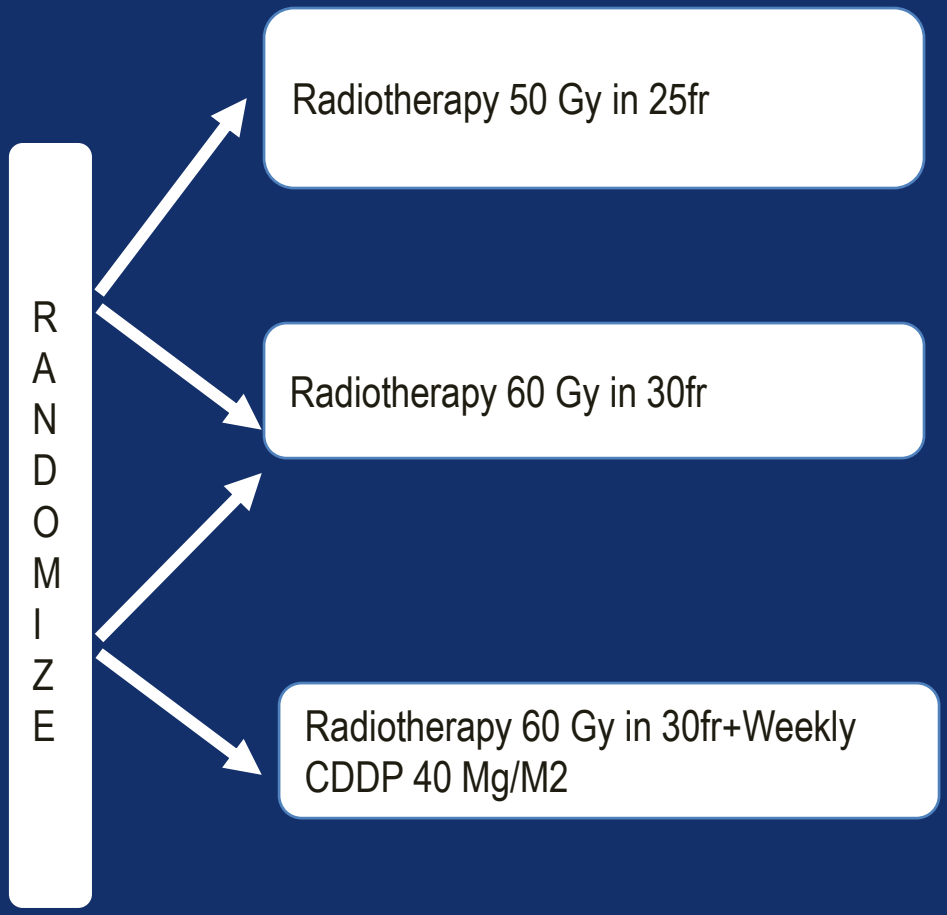
PATHOS

- Phase II Trial

Intermediate risk patients

High risk patients

N=242
Primary end point – Swallowing dysfunction



https://clinicaltrials.gov/ct2/show/NCT02215265

Conclusions

- Replace Cisplatin with Cetuximab – 3 Negative Phase III trials
- NACT →Decreased RT doses – Positive Phase II, Phase III underway
- CTRT with decreased RT and chemo doses- 2 Positive Phase II, Phase II underway
- Omitting Chemotherapy- HN002 Phase II Trial
- Protons instead of Photons- IMRT Vs IMPRT Phase II trial underway
- Less invasive surgery (TORS)- One Phase III and 1 Phase II trials underway

Ipilimumab, Nivolumab, and Radiation Therapy in Treating Patients With HPV Positive Advanced Oropharyngeal Squamous Cell Carcinoma

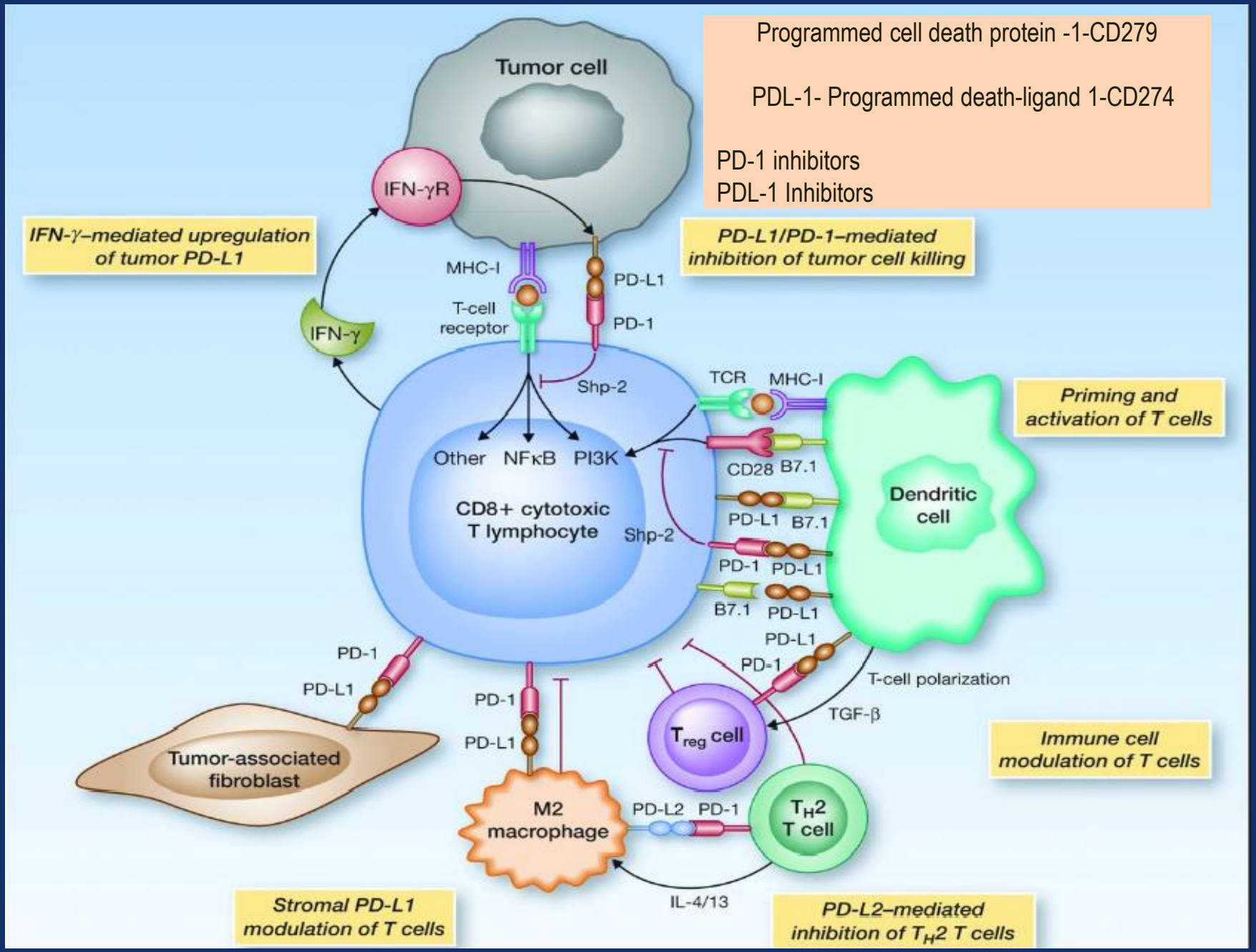
- A phase II study
- T1N2, T2N1-2, and T3N0-2 HPV-related OPSCC
- Ipilimumab and anti-PD-1 (Nivolumab) in combination with RT 60Gy/30r

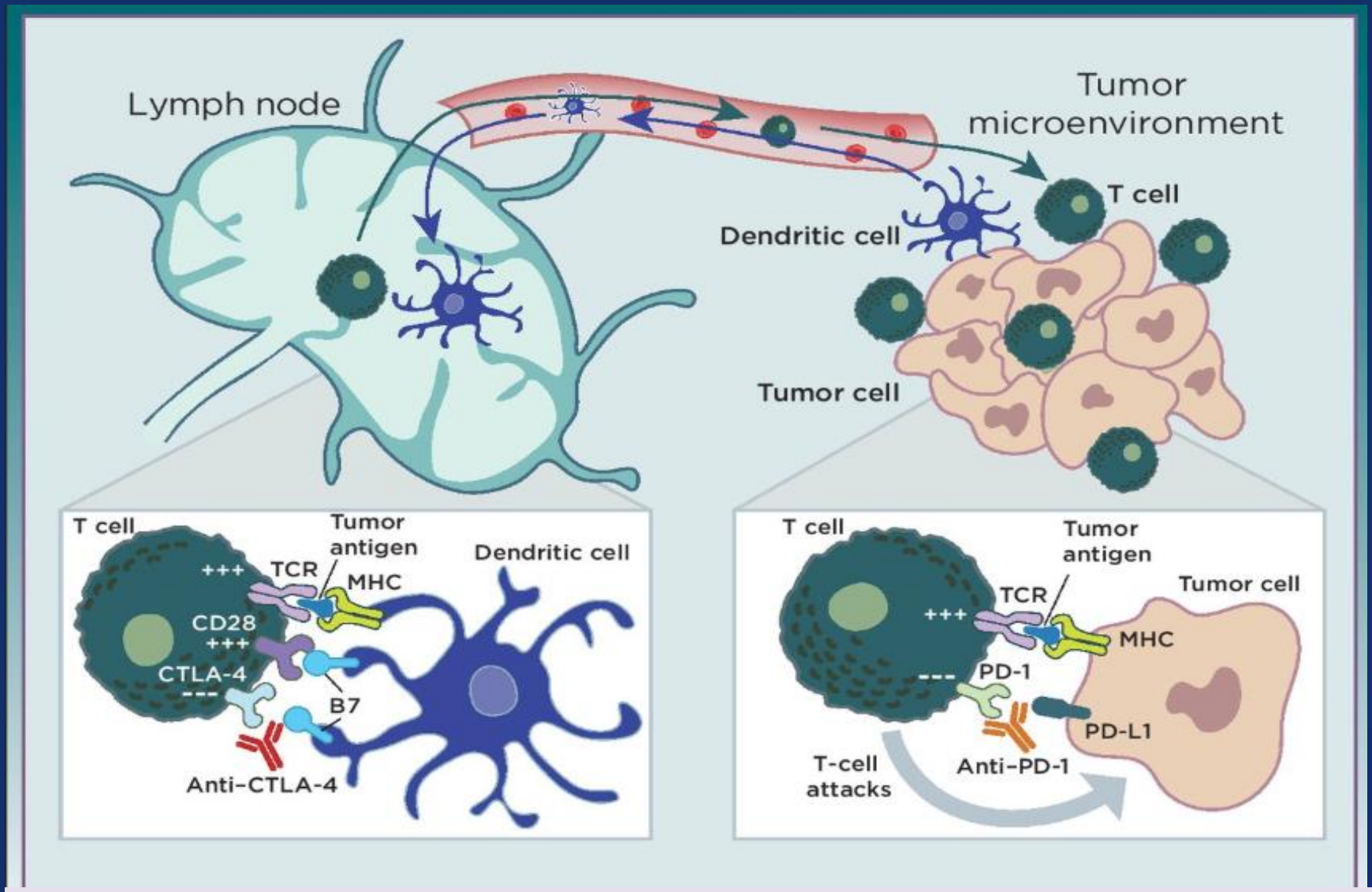
https://clinicaltrials.gov/NCT03799445.

Programmed cell death protein -1-CD279

PDL-1- Programmed death-ligand 1-CD274

PD-1 inhibitors
PDL-1 Inhibitors





T-cell activation by ipilimumab (anti-CTLA-4, site of action in the periphery/lymph nodes) and nivolumab (anti-PD-1, site of action in the tumor microenvironment). MHC, major histocompatibility complex; TCR, T-cell receptor.

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2021
Cancer of the Oropharynx (p16 [HPV]-positive)

NCCN Guidelines Index
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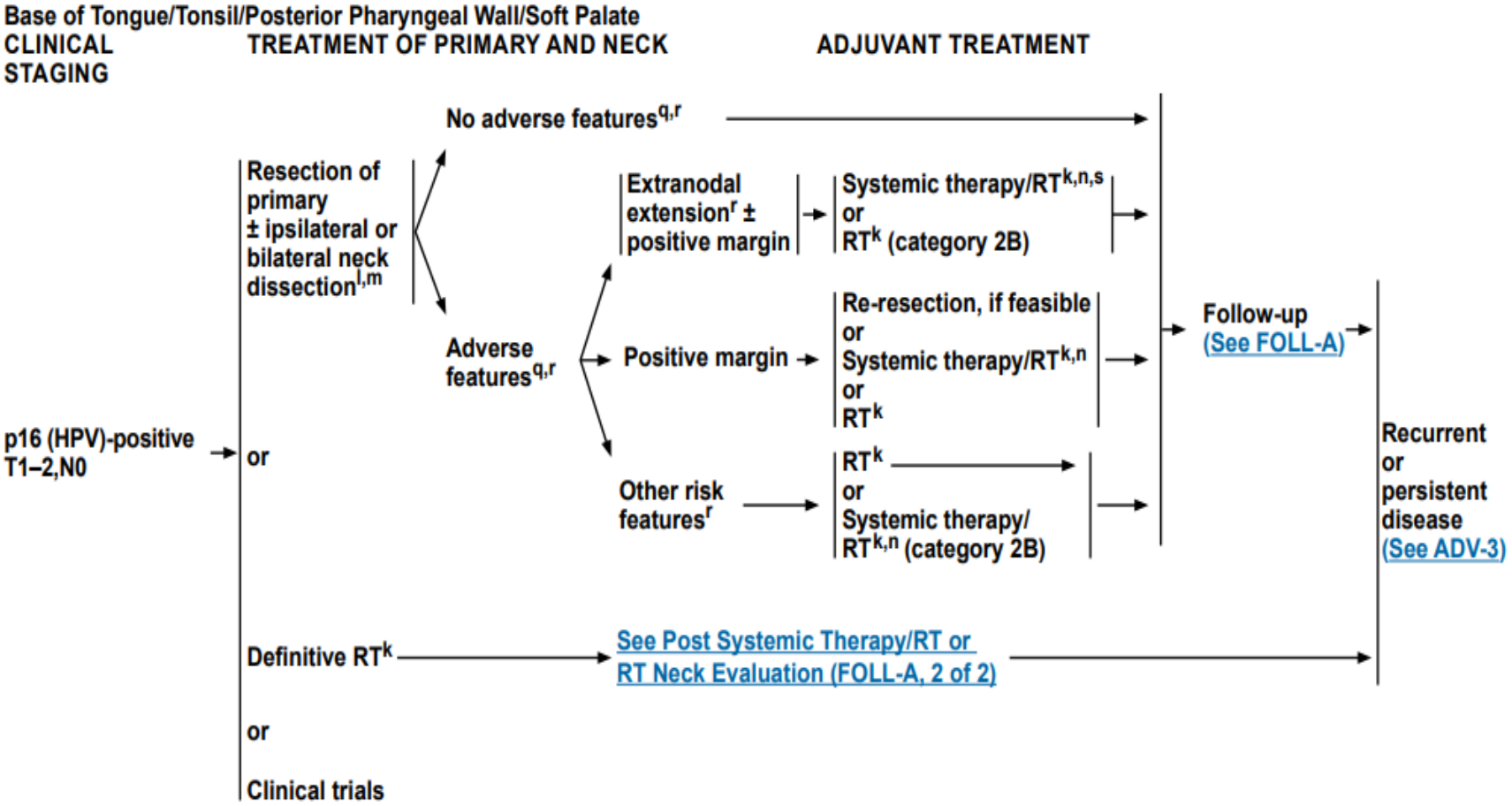
Discussion

Base of Tongue/Tonsil/Posterior Pharyngeal Wall/Soft Palate



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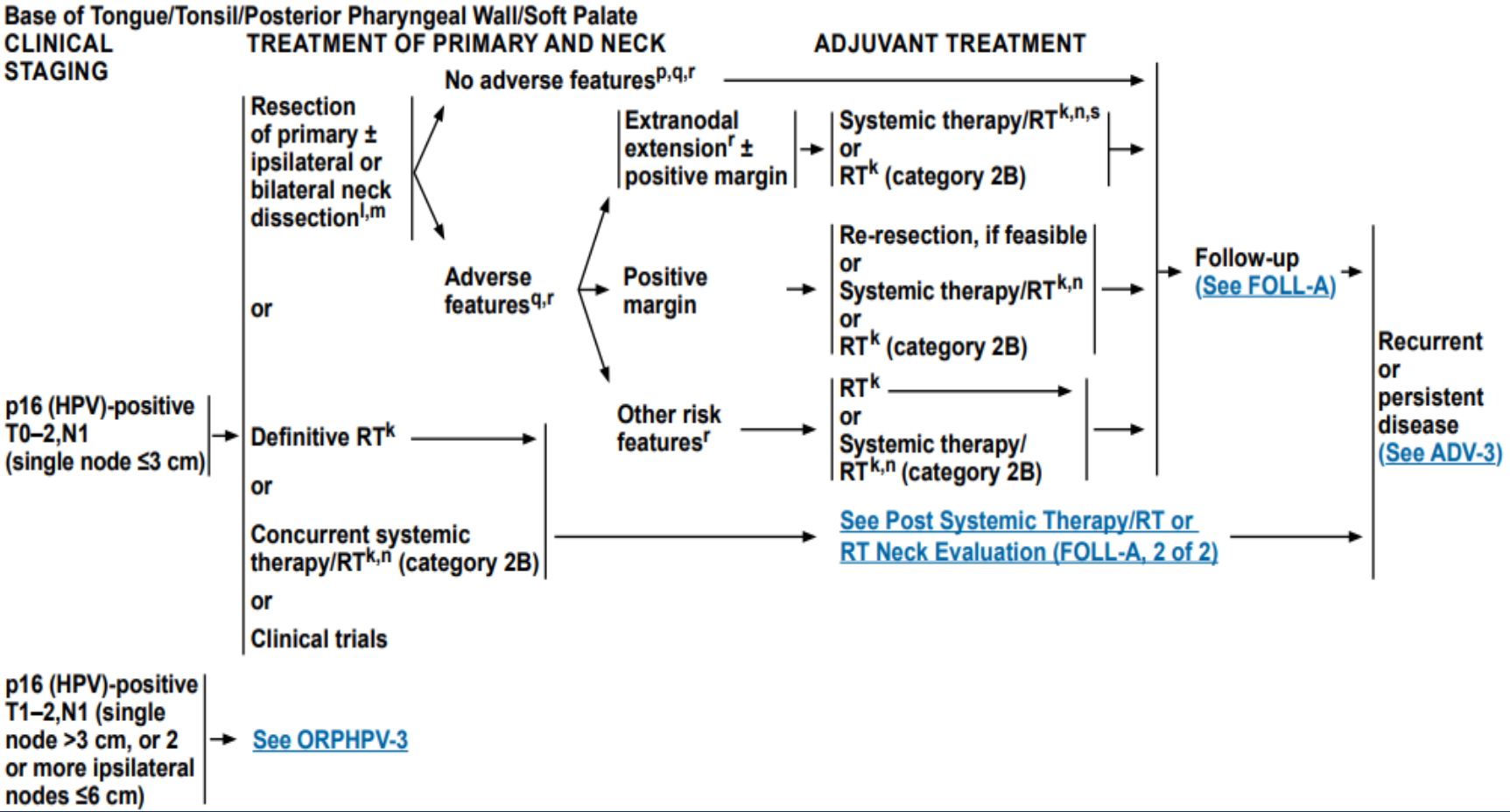

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CLINICAL STAGING

p16 (HPV)-positive T0–2,N1 (single node >3 cm, or 2 or more ipsilateral nodes ≤6 cm), or T0–2,N2 or T3,N0–2

TREATMENT OF PRIMARY AND NECK

- Concurrent systemic therapy/RT[k,n,t] → See Post Systemic Therapy/RT or RT Neck Evaluation (FOLL-A, 2 of 2) → Recurrent or persistent disease (See ADV-3)

or

- Resection of primary and ipsilateral or bilateral neck dissection[l,m,t]
  - unilateral cN0–3 → Resection of primary, neck dissection[l]
  - bilateral cN2–3 → Resection of primary and bilateral neck dissection[l]

  → No adverse features[q,r] → Follow-up (See FOLL-A)

  → Adverse features[q,r]
  - Extranodal extension and/or positive margin → Systemic therapy/RT[k,n,s]
  - Other risk features[q,r] → RT[k] or Consider systemic therapy/RT[k,n]

  → Recurrent or persistent disease (See ADV-3)

or

- Induction chemotherapy[n,p] (category 3) followed by RT[k] or systemic therapy/RT[k,n] → See Post Systemic Therapy/RT or RT Neck Evaluation (FOLL-A, 2 of 2) → Recurrent or persistent disease (See ADV-3)

or

- Clinical trials

ADJUVANT TREATMENT

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2021
Cancer of the Oropharynx (p16 [HPV]-positive)

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Base of Tongue/Tonsil/Posterior Pharyngeal Wall/Soft Palate

CLINICAL STAGING

p16 (HPV)-positive
T0–3,N3
or
T4,N0–3

TREATMENT OF PRIMARY AND NECK

- Concurrent systemic therapy/RT[k,n] (preferred) → See Post Systemic Therapy/RT or RT Neck Evaluation (FOLL-A, 2 of 2) → Recurrent or persistent disease (See ADV-3)

or

- Resection of primary and ipsilateral or bilateral neck dissection[l,m,t]
  - cN0–3 (unilateral) → Resection of primary, neck dissection[l]
  - cN2–3 (bilateral) → Resection of primary and bilateral neck dissection[l]

  → No adverse features[q,r] → Follow-up (See FOLL-A)

  → Adverse features[q,r]
  - Extranodal extension and/or positive margin → Systemic therapy/RT[k,n,s]
  - Other risk features[q,r] → RT[k] or Consider systemic therapy/RT[k,n]

  → Recurrent or persistent disease (See ADV-3)

or

- Induction chemotherapy[n,p] (category 3) followed by RT[k] or systemic therapy/RT[k,n] → See Post Systemic Therapy/RT or RT Neck Evaluation (FOLL-A, 2 of 2) → Recurrent or persistent disease (See ADV-3)

or

ADJUVANT TREATMENT

Further reading ....

Chapter

Human Papillomavirus Associated Oropharyngeal Carcinoma- Diagnosis and Management

Mullangath Prakasan Aparna, Ravi Rejnish Kumar, Malu Rafi, Geethu Babu, Pradeep Naveen Kumar, Kunnambath Ramadas and Kainickal Cessal Thommachan*
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