Whither HPV-related Oropharynx Cancer?

Surgery and Adjuvant Therapy considerations

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Grand Rounds, Greater Baltimore Medical Center
February 5th 2016

“whither” : “to what place or state” (OED, Mirriam-Webster)
Whither HPV-related Oropharynx Cancer?

Surgery and Adjuvant Therapy considerations

Disclosures

Elsevier (Text book Royalties)

Karl Storz (Airfare to teach course, 2015)
Adjuvant Therapy in HPV OPSCC

- Current Rx paradigms (surgical + adj. non-surgical)
- Adjuvant therapy in HPV-OPSCC - so what?
- Current, Guideline-based practice +/- evidence
- HPV OPSCC – specific adjuvant therapy - evidence?
- Clinical trials: current, vs. evidence-based
Oropharynx cancer

Chaturvedi et al JCO 2011
Adjuvant Therapy in HPV-OPSCC

Transoral Surgery and Neck dissection
T1N2bM0 p16+SCC (R) G-P sulcus
Swallowing Function After Transoral Laser Microsurgery (TLM) ± Adjuvant Therapy for Advanced-Stage Oropharyngeal Cancer

Jason T. Rich, MD; Jingxia Liu, PhD; Bruce H. Haughey, MBChB

N=118, p16+ 87%
Adjuvant Therapy in HPV-OPSCC

Transoral Robotic Surgery for Oropharyngeal Cancer
Long-term Quality of Life and Functional Outcomes

Peter T. Dziegielewski, MD, FRCSC; Theodoros N. Teknos, MD; Kasim Durmus, MD; Matthew Old, MD; Amit Agrawal, MD; Kiran Kakarala, MD; Anna Marcinow, MD; Enver Ozer, MD


after TORS. Speech, eating, social, and overall scores continued to drop and bottomed out at 3 months post TORS. This timeframe coincides with XRT and/or CRT treatment, during which patients face many challenges with the acute toxic effects of adjuvant treatment. Functional outcomes and HRQOL.
Toxicity Burden: CRT vs. RT

Bentzen & Trotti, JCO 2007
Distribution of FOSS scores by type of adjuvant therapy (N=202)

Differences in median FOSS scores: No adj. vs. adj Rx (p=0.012); No adj vs. CRT (p=0.0006)

Haughey et al, Head Neck 2011
17% excluded (medial RPN’s or post.ph wall +)
Late toxicity yet to be determined (pharyngeal branches of the vagus 60-70 Gy exp)
Cost Considerations in the Treatment of Oropharyngeal Squamous Cell Carcinoma

Eric J. Moore, MD¹, Michael L. Hinni, MD², Kerry D. Olsen, MD¹, Daniel L. Price, MD¹, Rebecca R. Laborde, PhD¹, and Jared C. Inman, MD²

T3N0 p16 + SCC rt tonsil retropharyngeal node dissection
Adjuvant Therapy in HPV OPSCC

SO WHAT?

TOXICITY

...primum non nocere.. (Hippocrates)

COST

US spends two-and-a-half times the OECD average

Total health expenditure per capita, public and private, 2010 (or nearest year)

Source: OECD Health Data 2012.

1. In the Netherlands, it is not possible to clearly distinguish the public and private share related to investments.
2. Total expenditure excludes investment. Information on data for Israel: http://dx.doi.org/10.1787/88893315467.
NCCN Guidelines Version 1.2015
Cancer of the Oropharynx

Base of tongue/tonsil/posterior pharyngeal wall/soft palate

CLINICAL STAGING

TREATMENT OF PRIMARY AND NECK

Definitive RT

Complete clinical response

Residual disease

Salvage surgery

or

Transoral or open resection of primary ± ipsilateral or bilateral neck dissection

No adverse features

Adverse features

Positive margin

Other risk features

Complete clinical response

Residual disease

Salvage surgery

ADJUVANT TREATMENT

Systemic therapy/RT (category 1)

Re-resection or RT

or

Consider systemic therapy/RT (for T2 only)

Consider systemic therapy/RT

Follow-up

Recurrent or Persistent Disease

Extracapsular spread ± positive margin

(Systemic therapy/RT (category 1))

Multimodality clinical trials

1See Principles of Radiation Therapy (ORPH-A).
2See Principles of Surgery (SURG-A).
3See Principles of Systemic Therapy (CHEM-A).

Adverse features: extracapsular nodal spread, positive margins, pT3 or pT4 primary, N2 or N3 nodal disease, nodal disease in levels IV or V, perineural invasion, vascular embolism (lymphovascular invasion) (See Discussion).

Consider re-resection to achieve negative margins, if feasible.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
**POSTOPERATIVE:**

**RT**
- Preferred interval between resection and postoperative RT is ≤6 weeks.

**PTV**
- High risk: Adverse features such as positive margins (See footnote i on ORPH-3).
  - 60–66 Gy (2.0 Gy/fraction); daily Monday–Friday in 6–6.5 weeks
  - Low to intermediate risk: sites of suspected subclinical spread
  - 44–50 Gy (2.0 Gy/fraction) to 54–63 Gy (1.6–1.8 Gy/fraction)

**POSTOPERATIVE CHEMORADIATION**
- Concurrent single-agent cisplatin at 100 mg/m² every 3 weeks is recommended.7-10

Either IMRT or 3-D conformal RT is recommended for cancers of the oropharynx in order to minimize dose to critical structures, especially the parotid glands.

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1 See Radiation Techniques (RAD-A) and Discussion.

4 Suggest 44–50 Gy in 3D conformal RT and sequentially planned IMRT or 54–63 Gy with IMRT dose painting technique (dependent upon dose per fraction).


Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
The Role of Postoperative Chemoradiation for Oropharynx Carcinoma: A Critical Appraisal of the Published Literature and National Comprehensive Cancer Network Guidelines

Parul Sinha, MBBS, MS; Jay F. Piccirillo, MD, FACS, CPI; Dorina Kallogjeri, MD, MPH; Edward L. Spitznagel, PhD; and Bruce H. Haughey, MBChB, MS, FACS, FRACS

**TABLE 4.** Reported Relative Effect Size, Calculated Absolute Effect Size, and Number Needed to Treat for Benefit With the Addition of Chemotherapy to Adjuvant Radiation

<table>
<thead>
<tr>
<th>Study</th>
<th>Reported Relative Effect Size: HR/95% CI</th>
<th>No./Total No. of Patients (%)</th>
<th>Rate [95% CI], %</th>
</tr>
</thead>
<tbody>
<tr>
<td>RTOG 9501: Cooper 2004*</td>
<td>39% Reduced risk of locoregional recurrence: 0.61/0.41–0.91</td>
<td>64/210 (30)</td>
<td>11 [3–19]</td>
</tr>
<tr>
<td>EORTC 22931: Bernier 2004*</td>
<td>25% Reduced risk of disease progression/ death: 0.75/0.56–0.99</td>
<td>103/167 (62)</td>
<td>7 [–3 to 18]</td>
</tr>
<tr>
<td>Collaborative analysis: Bernier 2005*</td>
<td>42% Reduced risk of locoregional recurrence: 0.58/exact 95% CI not reported</td>
<td>116/377 (31)</td>
<td>12 [6–18]</td>
</tr>
</tbody>
</table>

**Abbreviations:** ARR, absolute risk reduction; CER, control event rate; CI, confidence interval; CRT, chemoradiation; EER, experimental event rate; EORTC, European Organization for Research and Treatment of Cancer; HR, hazard ratio; NNT, number needed to treat; RT, radiation; RTOG, Radiation Therapy Oncology Group.

**NNH:**

For every 3 patients who received adjuvant CRT, 1 patient suffered severe acute and late toxicity.
**TABLE 2. Summary of the Salient Observations From the Literature Appraisal**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Lack of human papillomavirus or p16 status in both trials</td>
</tr>
<tr>
<td>2</td>
<td>Heterogeneous study population: different subsites, unequal distribution of subsites within radiation and chemoradiation arms</td>
</tr>
<tr>
<td>3</td>
<td>Failure to describe the tumor (T) and lymph node (N) classification of tumors</td>
</tr>
<tr>
<td>4</td>
<td>Exclusion after randomization</td>
</tr>
<tr>
<td>5</td>
<td>Inconsistencies in numerical data</td>
</tr>
<tr>
<td>6</td>
<td>Failure to present both absolute and relative effect sizes</td>
</tr>
<tr>
<td>7</td>
<td>Use of unplanned subgroup analyses in treatment recommendations for extracapsular spread and/or positive margins</td>
</tr>
<tr>
<td>8</td>
<td>Failure to perform appropriate multivariable analyses</td>
</tr>
<tr>
<td>9</td>
<td><strong>Long-term RTOG 9501 study:</strong> Absent adjuvant chemotherapy treatment effect in all eligible patients and in the oropharynx cancer subgroup; missing cause of death for study patients and unexplained, high mortality in the chemoradiation arm; inconsistencies in numerical data</td>
</tr>
<tr>
<td>10</td>
<td>Ineffectiveness of chemoradiation versus radiation on distant metastasis; no reduction in distant metastasis rate reported in the adjuvant chemoradiation versus radiation arm for either of the 2 trials or for the long-term RTOG 9501 study</td>
</tr>
</tbody>
</table>
Adjuvant Therapy in HPV OPSCC

- No evidence in that currently supports the guideline - recommended *radiation fields* or *doses* of either *RT* or systemic therapy, *specific to HPV OPSCC*, in the adjuvant setting.
WHAT IS THE CURRENT EVIDENCE FOR ADJUVANT THERAPY IN HPV OPSCC?
How much adjuvant Rx is enough?

Haughey, Hinni, Salassa et al,
Update: TLM for p16+ OPSCC (n=214, STL)

Recurrence more frequent without adjuvant, but salvageable (DSS): Unpublished update

Recurrence

- No Adj = 7/44 (16%)
- Adj. = 14/170 (8%)
- Adj. = 11/170 (6%)

Disease-specific survival

- None = 2/44 (4.5%)
- Adj. = 11/170 (6%)

p = 0.055

p = 0.971
n=171 p16 positive cases

Matched Study: WUSM and MC
(T class and node no.)
109 pairs
5.5% vs.22% (p< 0.001)

<table>
<thead>
<tr>
<th></th>
<th>T1-2</th>
<th>T3-4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>18 (62%)</td>
<td>11 (38%)</td>
<td>29</td>
</tr>
<tr>
<td>Adj. Rx</td>
<td>98 (69%)</td>
<td>44 (31%)</td>
<td>142</td>
</tr>
</tbody>
</table>

p=0.208

p=0.208
Local Control: T1 & T2

Kaplan Meier curves in T1-T2 patients with and without RT to primary
T3&4: Local Control

Kaplan Meier curves in T3-T4 patients with and without RT to primary
Radiotherapeutic Management of Cervical Lymph Node Metastases From an Unknown Primary Site

Stephanie M. Perkins, MD; Christopher R. Spencer, MD; Rebecca D. Chernock, MD; Bruce H. Haughey, MB, ChB; Brian Nussenbaum, MD; Douglas R. Adkins, MD; David I. Kuperman, MD; Wade L. Thorstad, MD

Mucosal “failure”

Comp = 1 (5%)

Ipsi = 2 (10%) (N.S.)

(25 comp, 21 lpsi)

Figure 4. Overall survival grouped by comprehensive radiation treatment (COMP) vs ipsilateral (IPS). Filled circles indicate censored events.
De-intensification of adjuvant therapy from study period 2001-2006 to 2007-2012
Eliminating Radiation Therapy to the Pathologic Node-Negative Neck Does Not Increase the Risk of Regional Recurrence: **A Prospective Phase 2 Trial**


- A total of 69 patients were needed to achieve 83% power to demonstrate with 90% confidence the equivalence of eliminating the pN0 neck compared to bilateral irradiation.

- Median follow up = 34 mo

- There were no recurrences (/72) in the un-irradiated pN0 neck (95% CI, 0%-4.2%).

- *Int Jnl Rad Onc*: November 2015, 93, 3, PpS70-S71
Extracapsular Spread in Head and Neck Carcinoma: Impact of Site and Human Papillomavirus Status

Cancer  Month 00, 2013

Jessica H. Maxwell, MD, MPH; Robert L. Ferris, MD, PhD; William Gooding, MS; Diana Cunningham, MS; Vikas Mehta, MD; Seungwon Kim, MD; Eugene N. Myers, MD; Jonas Johnson, MD; and Simion Chiosea, MD

DSS in p16+ OP (n=76)

DSS in p16- OP (n=57)
Extracapsular Spread and Adjuvant Therapy in Human Papillomavirus-Related, p16-Positive Oropharyngeal Carcinoma

n=152, p16 IHC+ ONLY

Cancer 2012
Transoral Laser Microsurgery (TLM) ± Adjuvant Therapy for Advanced Stage Oropharyngeal Cancer: Outcomes and Prognostic Factors

Jason T. Rich, MD; Simon Milov, MD; James S. Lewis, Jr., MD; Wade L. Thorstad, MD; Douglas R. Adkins, MD; Bruce H. Haughey, MBChB

67 ECS + 10 margin +ve “high risk” cases: Recurrences = 3% for RT alone, 7.4% for CRT(ns)

Overall Survival

Disease-specific Survival

\[ P = < 0.75 \]

\[ P = < 0.41 \]
Soft tissue metastasis in p16-positive oropharynx carcinoma: Prevalence and association with distant metastasis

Parul Sinha a, James S. Lewis Jr. a,b, Dorina Kallogjeri a,c, Brian Nussenbaum a, Bruce H. Haughey a,*

a Otolaryngology-Head and Neck Surgery, Washington University School of Medicine, St. Louis, MO, USA
b Pathology and Immunology, Washington University School of Medicine, St. Louis, MO, USA
c Clinical Outcomes Research, Washington University School of Medicine, St. Louis, MO, USA
What about Soft Tissue Metastasis (STM), the **highest** pathological grade of ecs?
Adjuvant Therapy in HPV-OPSCC

**T1/2**

- CRT (22)
- RT (11)

- Time from TOS (months): 0, 12, 24, 36, 48, 60, 72, 84, 96, 108

- Distant metastasis-free survival: 1.0, 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.2, 0.1

- p = 0.629

**T3/4**

- RT (6)
- CRT (13)

- Time from TOS (months): 0, 12, 24, 36, 48, 60, 72, 84, 96, 108

- Distant metastasis-free survival: 1.0, 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.2, 0.1

- p = 0.502

Fig. 7. Kaplan–Meier estimates for distant-metastasis-free survival after TOS for patients with STM by types of adjuvant therapy within the (A) T1–T2 (n = 33), and (B) T3–T4 (n = 19) groups. TOS = transoral surgery; STM = soft tissue metastasis; RT = radiation; CRT = chemoradiation.
High metastatic node number, not extracapsular spread or N-classification is a node-related prognosticator in transorally-resected, neck-dissected p16-positive oropharynx cancer

Parul Sinha a, Dorina Kallogjeri a,b, Hiram Gay c, Wade L. Thorstad c, James S. Lewis Jr. a,d, Rebecca Chernock a,d, Brian Nussenbaum a, Bruce H. Haughey a,*

a Otolaryngology-Head and Neck Surgery, Washington University School of Medicine, St. Louis, MO, United States
b Clinical Outcomes Research, Washington University School of Medicine, St. Louis, MO, United States
c Radiation Oncology, Washington University School of Medicine, St. Louis, MO, United States
d Pathology, Washington University School of Medicine, St. Louis, MO, United States
Impact of metastatic node number ≤4 vs. >4 (N=704)
Sinha P. et al: High metastatic node number, not extracapsular spread or N-classification, is a node-related prognosticator in transorally resected, neck-dissected p16-positive oropharynx cancer

Oral Oncology 2015 May;51(5):514-20

Fig. 4. Kaplan Meier estimates for Disease-specific survival by adjuvant therapy type (RT = Radiotherapy, CRT = Chemoradiotherapy) for patients with, (A) less than 5 nodes and, (B) ≥ 5 nodes.
After controlling for all other variables, no difference in survival was seen between patients treated with surgery with adjuvant radiation versus surgery with adjuvant chemoradiation ($p = .6306$). In the HPV-positive subgroup, no difference was seen in patients treated with surgery with adjuvant radiation versus surgery with adjuvant chemoradiation ($p = .4707$). Similarly, in the HPV-negative
TABLE 3. Multivariable

<table>
<thead>
<tr>
<th>Variables</th>
<th>HR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approach</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transoral</td>
<td>Ref</td>
<td>1.293–7.385</td>
<td>.0111</td>
</tr>
<tr>
<td>Open</td>
<td>3.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Extranodal extension</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Ref</td>
<td>0.536–2.335</td>
<td>.7644</td>
</tr>
<tr>
<td>Yes</td>
<td>1.119</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HPV</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Negative</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Mucosal margins</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Free of carcinoma</td>
<td>Ref</td>
<td>1.101–5.766</td>
<td>.0287</td>
</tr>
<tr>
<td>Positive</td>
<td>2.519</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Perineural invasion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Ref</td>
<td>0.514–2.529</td>
<td>.7466</td>
</tr>
<tr>
<td>Yes</td>
<td>1.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Smoking status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤10 pack-years</td>
<td>Ref</td>
<td>0.616–2.751</td>
<td>.4894</td>
</tr>
<tr>
<td>&gt;10 pack-years</td>
<td>1.302</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>T classification</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1/T2</td>
<td>Ref</td>
<td>0.983–4.595</td>
<td>.0555</td>
</tr>
<tr>
<td>T3/T4</td>
<td>2.125</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

rent chemoradiation. With the recent emphasis on treatment deintensification for HPV-positive patients, transoral surgery with postoperative radiotherapy alone may be an effective strategy to pursue based on these results. On the
Adjuvant Therapy in HPV OPSCC
Summary of what (we think) we know (Level 3)

- **High T-classification** and **high met. node number**, rather than ECE are “high risk.”

- Radiation plans **do not need to include primary resection bed** for unknown primary, T1/2, negative margins.

- pN0 necks **do not benefit from adding RT**.

- **No apparent benefit** to OS, DSS, even in the new “high risk” clinical presentations, **to addition traditional platinum-based systemic therapy**
How will the existing adjuvant therapy trials in HPV-OPSCC help us?
ECOG 3311

ECOG 3311 p16⁺ trial schema

ASSOCIATE

Assess Eligibility: HPV (p16)⁺
SCC oropharynx
Stage III-IV: cT1-2, N1-2b
Baseline Functional/QOL Assessment

LOW RISK: T1-T2N0-N1 negative margins

- Observation
- Radiation Therapy IMRT 50Gy/25 Fx

INTERMEDIATE: Clear/close margins <1mm ECS 2-4 metastatic LN PNI, LVI

- Radiation Therapy IMRT 60 Gy/30 Fx
- Radiation Therapy IMRT 66 Gy/33 Fx + CDDP 40 mg/m² weekly

HIGHER RISK: Positive Margins >1mm ECS or ≥5 metastatic LN

- Evaluate 2-year PFS Local-Regional Recurrence, Functional Outcomes/QOL

Accrual goal = 377
The ADEPT* Trial

*“Adjuvant, De-escalation, Extracapsular spread, P16-positive, Transoral”*
PATHOS (Postoperative adjuvant treatment for HPV-positive tumours)

Randomized, multicentre, phase II

HPV positive OPC T1-3 N1-N2b

Transoral resection (TLM/TORS) of primary + neck dissection

Pathology assessment

Group A: No RT.

Group B: Randomize
- 50Gy in 25# *
- 60Gy in 30# *

Group C: Randomize
- 60Gy in 30# *
- 60Gy in 30# + cisplatin *

Group A: no adverse pathological risk factors (no adjuvant treatment recommended).
Group B: T3, N2, perineural invasion, vascular invasion.
Group C: nodal extracapsular spread (ECS), close (1-5mm) or positive (<1mm) primary tumour margins, with negative marginal biopsies.

Primary endpoint phase II – swallowing function at 12m; future phase III – overall survival
Prognostic Factors and Survival Unique to Surgically Treated p16+ Oropharyngeal Cancer

Bruce H. Haughey, MBChB, FRACS, FACS; Parul Sinha, MBBS, MS

Laryngoscope, 122:S13-S33, 2012

N=171, 48% BOT

Disease-Specific Survival

Disease-Free Survival
Distribution of FOSS scores by type of adjuvant therapy (N=202)

Differences in median FOSS scores: No adj. vs. adj Rx (p=0.012); No adj vs. CRT (p=0.0006)

Haughey et al, Head Neck 2011
67 ECS + 10 margin +ve “high risk” cases: Recurrences = 3% for RT alone, 7.4% for CRT(ns)
How much adjuvant therapy is enough?

Disease-free survival

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Update: TLM for p16+ OPSCC (n=214, STL)

Recurrence more frequent without adjuvant, but salvageable (DSS): Unpublished update

- Recurrence:
  - None: 7/44 (16%)
  - Adj.: 14/170 (8%)
- Disease-specific survival:
  - None: 2/44 (4.5%)
  - Adj.: 11/170 (6%)

p = 0.055

p = 0.971
Comparisons with non-surgical: HPV-related

- Ang et al 2010: n=216 p16+, 3yr PFS=74% (T2,35%, T3/4,65%)
- Huang et al, 2015: 3yr OS=~80%, n=573p16+

- T1,2 = 55%
- T3,4 = 45%
Haughey & Sinha L’scope (2012)
N=171 p16+ OP, 3yr OS= 94%, 5yr 91% (T1,2 =67%, T3,4=33%)
Unknown Primary
Occult lesion in rt. Palatine tonsil
Video: TLM for unknown primary

59 YEAR OLD WHITE MALE
T2N2M0 Stage III Primary

Transoral Resection Surgery
Lingual & Submandibular Resillectomy

Bruce H Haughey MBChB  FACS  FRACS
Kimbrough Professor & Director
Head & Neck Surgical Oncology
Washington University in St. Louis
Management of human papillomavirus–related unknown primaries of the head and neck with a transoral surgical approach

Evan M. Graboyes, MD, Parul Sinha, MBBS, MS, Wade L. Thorstad, MD, Jason T. Rich, MD, Bruce H. Haughey, MBChB, MS, FRACS

- n=65
- Primary detection rate: 89% (N=58)
- Median FU=33.5 months, (3.7 - 131.2)
- Both 3- & 5-year DSS=98%; OS=97%

Graboyes E, Sinha P, Thorstad W., Rich JT, Haughey BH
Head and Neck, online 2014
To demonstrate that de-intensified therapy (radiation only) following resection is not inferior to chemoradiation adjuvant therapy.
T1N2bM0 p16+ SCC (R) G-P sulcus
CD8+ tumour-infiltrating lymphocytes in relation to HPV status and clinical outcome in patients with head and neck cancer after postoperative chemoradiotherapy: A multicentre study of the German cancer consortium radiation oncology group (DKTK-ROG)  

Panagiotis, B et al *Int. Jnl of Cancer* 2015
DSS by Node no. & Adjuvant Rx

(n=220 HPV+, IFHNOS
abstract:unpubl.)

< 5 nodes (n=183)
- CRT (55)
- RT (82)
- None (46)

p=0.445

≥ 5 nodes (n=37)
- CRT (20)
- RT (15)
- None (2)

p=0.027
Whither HPV-related oropharyngeal squamous carcinoma?

Surgery and adjuvant therapy considerations