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Self Assessment Module on Head and Neck Cancer

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**Image-guided Therapy Paradigm for Head and Neck Cancer**

IMRT

**1. Regarding the efficacy of IMRT vs. non-IMRT use in patients with oropharyngeal cancer:**

- a. IMRT has impact mainly on the sparing of normal tissue toxicity, but offers relatively no improvement on tumor control
- b. IMRT improves loco-regional control (LRC), but not disease specific survival (DFS)
- c. IMRT improves both loco-regional control (LRC) and disease specific survival (DFS)
- d. IMRT improves tumor control but offer no significant normal tissue protection

**The correct answer is c.**

**Reference:**

- 1) Chao, KSC, et al. Intensity-modulated radiation therapy reduces late salivary toxicity without compromising tumor control in patients with oropharyngeal carcinoma: a comparison with conventional techniques Radiotherapy and Oncology 2001, 61:275-280
- 2) Chao, KSC, et al. Intensity-modulated radiation therapy for oropharyngeal carcinoma: impact of tumor volume Int J Radiat Oncol Biol Phys 2004, 59:43-50

**Rationale:**

In a series reported by Chao *et al.* for the Washington University experience on the use of IMRT for oropharyngeal cancer, both LRC and DFS were seen to be improved as compared with non-IMRT techniques ( 2yr. LRC: IMRT vs. non-IMRT = 87.5% vs. 68.3%; 2yr. DFS: IMRT vs. non-IMRT = 73.5% vs. 58.4%). This was achieved without excessive damage to the normal tissues.

**2. Regarding IMRT for patients with oropharyngeal cancer, which of the following statements is *false*?**

- a. IMRT can improve grade 2 to 3 xerostomia compared to conventional radiation therapy
- b. IMRT improves loco-regional control (LRC) for T3-4 primary cancers as well as T1-2 tumors
- c. IMRT is advantageous only as a definitive treatment for unresected disease, but not when done after surgical resection
- d. IMRT can be used safely with chemotherapy

**The correct answer is c.**

**Reference:**

1) Chao, KSC, et. al. Intensity-modulated radiation therapy reduces late salivary toxicity without compromising tumor control in patients with oropharyngeal carcinoma: a comparison with conventional techniques *Radiotherapy and Oncology* 2001,61:275-280

2) Chao, KSC, et. al. Intensity-modulated radiation therapy for oropharyngeal carcinoma: impact of tumor volume *Int J Radiat Oncol Biol Phys* 2004, 59:43-50

**Rationale:**

In the same series reported by Chao *et al.* on the use of IMRT for T1-2 oropharyngeal cancer, IMRT achieved 92% LRC as compared to 70-90% for non-IMRT conventional treatment, as compared with non-IMRT techniques, while for T3-4 primary tumors the LRC was 87-94% for IMRT and only 30-70% for conventional technique. For normal tissue sparing effects, definitive IMRT improves late grade 2-3 xerostomia vs. conformal radiation therapy (CRT) (30% vs. 84%,  $p < 0.001$ ); likewise for post-op cases (IMRT vs. CRT = 17 vs. 77%,  $p < 0.001$ ).

**3. In a comparison study between imaging findings for GTV boundary vs. pathological analysis of the surgical specimen:**

- a. There are excellent agreement among all imaging modalities studied (CT, MRI, FDG-PET) with the surgical specimen
- b. Imaging modalities tend to overestimate the GTV volume as compared to what surgical specimen shows
- c. Imaging modalities tend to underestimate the GTV volume as compared to what surgical specimen shows
- d. FDG-PET tends to overestimate the GTV volume more than MRI or CT

**The correct answer is b.**

**Reference:**

1) *Daisne et. al.* Tumor Volume in Pharyngolaryngeal Squamous Cell Carcinoma: Comparison at CT, MR Imaging, and FDG PET and Validation with Surgical Specimen *Radiology* 233(1):93-100, 2004

**Rationale:**

In the study reported by *Daisne et al.* on the comparison between imaging findings for GTV boundary vs. pathological analysis of the surgical specimen, there was wide range of disagreement among all imaging modalities studied (CT, MRI, FDG-PET) with the surgical specimen analysis. In general, Imaging modalities tend to overestimate the GTV volume as compared to what surgical specimen shows. Of the imaging modalities, FDG-PET tends to underestimate the GTV volume more than MRI or CT.

**4. Microscopic tumor extension outside lymph node capsule can be appreciated when:**

- a. There is actual presence of tumor cells outside the capsule
- b. There is desmoplasia or associated stromal reaction
- c. There is giant cell reaction to keratin
- d. All of the above

**The correct answer is d.**

**Reference:**

1) Aisarnthanarax et al. Determining optimal clinical target volume margins in head-and-neck cancer based on microscopic extracapsular extension of metastatic neck nodes, *Int J Radiat Oncol Biol Phys* 2006, 64:678-683.

**Rationale:**

In a study reported by Apisarnthanarax *et al.* on microscopic tumor extension outside lymph node capsule, the definition of extracapsular extension (ECE) included the actual presence of tumor cells outside the capsule, a desmoplasia or associated stromal reaction, and a giant cell reaction to keratin.

**5. Regarding extracapsular extension (ECE) of tumor cells:**

- a. More than 95% ECE occurs within 5 mm of the nodal capsule
- b. Approximately 10% ECE occurs beyond 10 mm from the capsule
- c. There is a direct correlation between ECE incidence and distance from the capsule
- d. The larger the lymph node size, the higher the extent of ECE
- e. The mean ECE extent for a 1 cm size lymph node is 3 mm from the capsule

**The correct answer is a.**

**Reference:**

1) Aisarnthanarax *et al.* Determining optimal clinical target volume margins in head-and-neck cancer based on microscopic extracapsular extension of metastatic neck nodes, *Int J Radiat Oncol Biol Phys* 2006, 64:678-683.

**Rationale:**

In the report by Apisarnthanarax *et al.* on the study of extracapsular extension (ECE), 96% of the ECE seen occurred within 5 mm of the nodal capsule. None occurred beyond 10 mm. There was an inverse correlation between ECE incidence and distance from the capsule. However, there was no correlation between lymph node size and the extent of ECE: the mean ECE extent was 2.1 mm for lymph nodes < 1 cm in size, and 2.2 mm for > 1 cm size lymph nodes.

**6. When performing IMRT for head and neck cancers:**

- a. There are poor concordance rates among practitioners about the anatomic extent of tumors and normal structures
- b. It can take almost twice as long for clinicians to outline anatomic volumes for head & neck cancers than for prostate and pelvic lymph nodes
- c. There has been published consensus regarding head and neck nodal level definition and delineation
- d. All of the above

**The correct answer is d.**

**Reference:**

1) Miles, *et al.* The impact of introducing intensity modulated radiotherapy into routine clinical practice. *Radiotherapy and Oncology* 2005, 77:241

**Rationale:**

In the review by Miles *et al.* on the use of IMRT in routine clinical practice, it took clinicians a median of 2.3 hours (range: 0.7-3.5 hrs) to outline anatomic volumes for head and neck cancer, while for prostate and pelvic lymph nodes it took only 1.4 hours median (range: 0.9-2.2 hrs). The concordance rates among practitioners about the anatomic extent of tumors and normal structures are notoriously low. Thus, to ensure a uniform and consistent pattern of care, there has been published consensus regarding head and neck anatomic structure delineation, including nomenclature for the lymph nodal levels.

**7. Regarding target and normal tissue delineations for IMRT in head and neck cancers:**

- a. GTV (gross tumor volume) should trace the anatomic extents of the macroscopically detected tumor edges
- b. Various CTV (clinical target volume) levels (CTV1, CTV2, CTV3, etc.) cover what the physicians perceive as the microscopic extension of the tumor
- c. PTV (planning target volume) levels extend CTVs to cover margins for motion or set-up uncertainties
- d. Simultaneous integrated boost (SIB) aims to deliver radiation to all different PTV levels at different prescribed dosage levels at the same time during each fraction
- e. All of the above

**The correct answer is e.**

**Reference:**

1) Chao, KSC, et. al. Intensity-modulated radiation therapy for oropharyngeal carcinoma: impact of tumor volume *Int J Radiat Oncol Biol Phys* 2004, 59:43-50

**Rationale:**

In the published consensus regarding head and neck anatomic structure delineation as well as treatment target volume nomenclature, GTV (gross tumor volume) is defined as the anatomic extents of the macroscopically detected tumor edges, CTV (clinical target volume) levels (CTV1, CTV2, CTV3, etc.) should cover what the physicians perceive as the microscopic extension of the tumor, and PTV (planning target volume) levels in general should extend CTVs to cover margins for motion or set-up uncertainties. The technique of Simultaneous integrated boost (SIB) aims to deliver radiation to all different PTV levels at different prescribed dosage levels at the same time during each fraction.

**8. Regarding variations in head and neck target determination and delineation:**

- a. Variation among physicians was not a problem for the conventional non-IMRT techniques
- b. In a study of supraglottic cancer, GTV as outlined by neuroradiologists and radiation oncologists has shown a consistent rate of agreement among all specialists
- c. Knowledge-based computer-assisted contouring may help in improving the consistency in target delineation
- d. An international survey of 20 institutions has shown a fairly homogeneous practice approach when delineating CTV targets

**The correct answer is c.**

**Reference:**

1) Cooper, JS et al, An evaluation of the variability of tumor-shape definition derived by experienced observers from CT images of supraglottic carcinomas (ACRIN protocol 6658), *Int J Radat Oncol Biol Phys* 2007, 67:972-975

2) *Hong TS, Chappell RJ, Harari PM. Variations in target delineation for head and neck IMRT: An international multi-institutional study Int J Radiat Oncol Biol Phys. 60:S157, 2004*

3) *Chao, KSC et al. Reduce in Variation and Improve Efficiency of Target Volume Delineation by a Computer-Assisted System Using a Deformable Image Registration Approach Int J Radiat Oncol Biol Phys. 2007, 68:1512-1521,*

**Rationale:**

Since as early as 1970s, radiation oncologists have warned against the poor concordance rates among practitioners to identify suitable target volumes for traditional radiation treatment techniques. In a multi-center study of supraglottic cancer treatment by Cooper *et al.*, GTV as outlined by 4 neuroradiologists and 4 radiation oncologists on 20 cases based on CT images has shown a wide range of agreement (average 53%, range 0 to 82%). Another, international, survey of 20 institutions by Hong *et al.* has likewise shown a heterogeneous practice approach when delineating head and neck CTV targets. To promote uniformity in such pattern of care, knowledge-based computer-assisted contouring software has been developed to improve the consistency in target delineation.

**9. Regarding the consensus of head and neck nodal level definition and delineation:**

- a. The traditionally known anterior cervical lymphatic chain is now separated into Levels I, II, and III
- b. The traditionally known posterior cervical (spinal accessory) lymphatic chain is now categorized as Level V
- c. The supraclavicular nodes now belong to Level VI
- d. The retropharyngeal nodes are now designated as Level I nodes

**The correct answer is b.**

**Reference:**

- 1) *AJCC Cancer Staging Manual (6th Edition)*

**Rationale:**

In the recent *AJCC Cancer Staging Manual*, Level I cervical lymph node group covers the submental and submandibular nodal regions, while the traditionally known anterior cervical lymphatic chain is now separated into Levels II, III, and IV. The supraclavicular nodes now belong to Level IV. The traditionally known posterior cervical (spinal accessory) lymphatic chain is categorized as Level V. The retropharyngeal nodes do not belong to any numbered cervical nodal level.

**10. Regarding IMRT and “evidence-based” medical practice:**

- a. There are ample level I evidences in the literature supporting the beneficial role of IMRT for head and neck cancers
- b. The benefit of IMRT is largely empirical and theoretical, thus it should be avoided in the era of “evidence-based” medicine
- c. There are wide knowledge gaps in IMRT practice among all practitioners, thus it must be studied cautiously before its wide acceptance in the community
- d. The cost effectiveness of IMRT will not be a problem due to its excellent clinical outcome

**The correct answer is c.**

**Reference:**

- 1) *Chao, KSC et al. Reduce in Variation and Improve Efficiency of Target Volume Delineation by a Computer-Assisted System Using a Deformable Image Registration Approach Int J Radiat Oncol Biol Phys. 2007, 68:1512-1521,*

**Rationale:**

There are not sufficient level I evidences in the literature supporting the beneficial role of IMRT for head and neck cancers. Although the benefit of IMRT remains largely empirical and theoretical, its potential benefit in routine cancer therapy has been supported by numerous institutional reports, thus it should not be overlooked despite the recent emphasis on “evidence-based” medicine. It suffices to say that there are wide knowledge gaps in IMRT practice among all practitioners, thus the technique must be studied cautiously before its wide acceptance in the community. However, because of its high-tech nature, the

high cost of IMRT will be a source of national healthcare financial strain and thus subject to public political debate, despite its promising positive clinical outcome.

## NPC

### 11. At which location is NPC most likely to occur with high incidence?

- a. Northeast Asia (including Northern China, Japan, Korea)
- b. South America (Brazil, Columbia, Argentina, Chile)
- c. Southeastern U.S. (Florida, Caribbean Islands)
- d. Southern China and Southeast Asia (including Singapore, Philippines, Taiwan)

**The correct answer is d.**

#### **Reference:**

1) Yu MC, Yuan JM. Epidemiology of nasopharyngeal carcinoma. *Semin Cancer Biol.* 2002, 12(6):421-9,

#### **Rationale:**

NPC is a unique head and neck cancer with peculiar endemic distribution worldwide. It occurs with very high incidence in Southern China (including especially Canton or Guangdong Province and Hong Kong), where emigrants traveled to many parts of southeast Asia such as Taiwan, the Philippines, Singapore, Thailand, and even Australia. Other populations with elevated rates include the natives of Southeast Asia, the natives of the Arctic region, and the Arabs of North Africa and parts of the Middle East.

### 12. According to the WHO categorization of different histopathologic types of NPC, which of the following statements is true?

- a. Type I is typically associated with high-risk populations and younger patients
- b. Type III is linked with tobacco usage as a putative risk factor
- c. Type III pertains to nonkeratinizing squamous cell or undifferentiated carcinoma.
- d. Type III is not known to be associated with EBV viral etiology

**The correct answer is c.**

#### **Reference:**

Bray F, et al. *Cancer Epidemiol Biomarkers Prev* 2008

#### **Rationale:**

According to the WHO categorization of different histopathologic types of NPC, *Type I* is typically associated with keratinizing squamous cell, and occurs mainly in low-risk populations and older patients. It can be linked with tobacco usage as a putative risk factor. *Type II* is rare (only about 5% of all cases) and pertains to differentiated nonkeratinizing squamous cells, and has EBV and familial factors implicated as risk factors. *Type III* pertains to undifferentiated nonkeratinizing squamous cell carcinoma, and also has EBV and familial factors implicated as risk factors. It mainly affects high-risk populations as well as children.

### 13. Regarding nasopharyngeal cancer:

- a. With modern diagnostic and treatment technique, parapharyngeal tumor extension is seen to be a major critical factor in predicting outcome
- b. Metastasis rarely involves retropharyngeal nodes
- c. Retropharyngeal nodal involvement without other nodal metastasis (N0) still carries a grave prognosis similar to N2 or N3 disease
- d. Chemotherapy is beneficial for disease with any nodal involvement (N1 to N3)
- e. Cetuximab is an appropriate substitute for cytotoxic chemotherapy

**The correct answer is d.**

**Reference:**

1) Tang L, et al. Retropharyngeal lymph node metastasis in nasopharyngeal carcinoma detected by magnetic resonance imaging. *Cancer* 2009 113(2):347-354

**Rationale:**

With modern diagnostic and treatment technique, parapharyngeal tumor extension is no longer a major critical factor in predicting outcome for NPC. NPC remains a head & neck malignancy with relatively high propensity for retropharyngeal nodal spread; however, if such nodal involvement occurs without other nodal metastasis (N0), it would not carry a grave prognosis similar to N2 or N3 disease, thus can be treated as N1 disease as far as prognosis is concerned. According to the 2009 NCCN practice guidelines, chemotherapy is beneficial for disease with any nodal involvement (N1 to N3) or any T2b–T4 primary tumor with or without lymph node metastasis. Cetuximab has been found to be a beneficial radiation sensitizer in a phase III randomized trial largely for oropharyngeal cancer, but its role in substituting cytotoxic chemotherapy for NPC is not as clear.

**14. After primary radiation therapy for nasopharyngeal cancer:**

- a. Tumor response is best assessed by endoscopy examination alone
- b. Tumor response is best assessed by waiting 10 or more weeks after completion of the treatment
- c. Biopsy should be avoided due to concern of tissue break down after high dose irradiation
- d. PET-CT carries an unacceptably high rate of false positive finding, thus should be avoided for up to one year
- e. The main curative modality for salvage of local recurrence is surgical resection.

**The correct answer is b.**

**Reference:**

1) Sham JST, et al. Nasopharyngeal carcinoma. Pattern of tumor regression after radiotherapy. *Cancer* 1990 65(2):216-220

2) Chang K, Hao S, Tsang N, Ueng S, Salvage surgery for locally recurrent nasopharyngeal carcinoma—A 10-year experience *Otolaryngology - Head and Neck Surgery*, 2004, 131(4): 497-502.

**Rationale:**

After primary radiation therapy for nasopharyngeal cancer, tumor response is best assessed by waiting 10 or more weeks after completion of the treatment due to the high rate of false positivity if done too soon. To assess response, endoscopy examination as well as imaging studies using MRI or PET-CT remains useful, with tissue biopsy often as an essential step for pathologic confirmation in order to determine the need of local salvage treatment. For NPC local recurrence, salvage treatment often still incorporates further re-irradiation rather than surgical resection, although various few surgical literature have reported limited role of salvage resection (with or without post-operative radiation).

**15. Which of the following statement is true of the treatment outcome for nasopharyngeal cancer?**

- a. Globally, the cure rates in areas with high incidence are significantly lower than those in non-endemic areas, but may exhibit wide variations
- b. With older treatment technique, the 5-yr survival rate does not exceed 30 %
- c. With IMRT, the 3-year local control can exceed 90% in most published series
- d. IMRT significantly reduces late morbidity, but acute reactions are excessive
- e. SBRT has been shown to be equivalent to IMRT in local control as well as late complication rate

**The correct answer is c.**

**Reference:**

1) Gregoire, V. et al, Intensity-Modulated Radiation Therapy for Head and Neck Carcinoma Oncologist, 2007, 12(5) 555-564

**Rationale:**

Globally, the cure rates in areas with high NPC incidence are about the same as achieved in non-endemic areas (with 5-year survival rates around 40-50%), although there are wide variations. With IMRT, the 3-year local control can exceed 90% in most published series, and the overall survival rate has been reported to exceed 80-90% in 3 years (e.g. Hong Kong, MSKCC) and over 70% in 4 years (e.g. UCSF). While acute normal tissue reactions could be excessive for IMRT (especially combined with chemotherapy), whether it can significantly reduce late morbidity depends on the treatment technique which can vary widely. The use of hypofractionated SBRT, while getting popular for malignancies in the thorax and abdomen, has not been shown to be equivalent to IMRT or traditional fractionated conformal techniques as primary treatment of NPC.

HPV and Head and Neck Cancer

**16. Concerning human papilloma virus (HPV):**

- a. It is a RNA virus
- b. It has enzymes for DNA replication so does not need host's replication machinery
- c. It uses the basal, replicating keratinocytes of squamous epithelium to reproduce
- d. It has only a few subtypes, most of which are carcinogenic

**The correct answer is c.**

**Reference:**

1) McGovern SL et al. Three synchronous HPV-associated squamous cell carcinomas of Waldeyer's ring: Case report and comparison with Slaughter's model of field cancerization. Head Neck 2009, Published online prior to printing Jul 1, 2009.

**Rationale:**

Human papilloma virus (HPV) is a DNA virus with more than 120 subtypes. Only a few (13-15) subtypes are known to be carcinogenic. The HPV virus does not have enzymes for DNA replication, thus must rely on the host's replication machinery. It uses the basal, replicating keratinocytes of squamous epithelium to reproduce itself.

**17. Concerning human papilloma virus (HPV) and cancers:**

- a. Carcinogenesis due to HPV transmission is high
- b. The subtypes that cause genital warts are HPV 16/18
- c. The subtypes that cause cervical cancer are HPV 6/11
- d. HPV 31, 33, 35 are also known to be associated commonly with malignancy

**The correct answer is d.**

**Reference:**

1) Parkin DM, Bray F. The burden of HPV-related cancers. In: Bosch FX, Cuzick J et al., eds. Vaccine: HPV vaccines and screening in the prevention of cervical cancer. 2006.

**Rationale:**

While HPV is a common sexually transmitted virus, carcinogenesis due to HPV transmission is rare. About 90% of genital warts are related with HPV 6/11 infection, and about 70% of invasive cervical cancer are positive for HPV 16/18. HPV 31, 33, 35 are also known to be associated commonly with malignancy.

**18. Concerning human papilloma virus (HPV) and head & neck cancers:**

- a. The head & neck subsites affected are mainly nasopharynx and oropharynx
- b. Nearly 90% of all oropharyngeal cancers are due to HPV infection
- c. Nearly 90% of all HPV-related oropharyngeal cancers are due to HPV 16/18
- d. About half of all HPV-related oral cavity cancers are due to HPV 16/18

**The correct answer is c.**

**Reference:**

- 1) Syrjanen, KJ. HPV infections and tonsillar carcinoma J Clin Pathol (2004) 57(5):449
- 2) Syrjanen Human papillomavirus (HPV) in head and neck cancer.J Clin Virol; (2005) Mar:32 Suppl 1:S59-66.
- 3) Paz, IB et al. Human papillomavirus (HPV) in head and neck cancer. An association of HPV 16 with squamous cell carcinoma of Waldeyer's tonsillar ring.Cancer; (1997) Feb 1:79(3):595-604
- 4) Mork, J et al. Human Papillomavirus Infection as a Risk Factor for Squamous-Cell Carcinoma of the Head and Neck. NEJM (2001) Volume 344(15):1125-1131
- 5) Ritchie, JM, et al. Human papillomavirus infection as a prognostic factor in carcinomas of the oral cavity and oropharynx. International Journal of Cancer 2003 104(3): 336-34

**Rationale:**

The head & neck subsites associated with HPV induced malignancies are mainly oral cavity and oropharynx. About 25% of all oral cavity cancers and 35% of all oropharyngeal cancers are due to HPV infection. Nearly 90% of all HPV-related oropharyngeal cancers and 98% of all HPV-related oral cavity cancers are due to HPV 16/18 subtypes.

**19. Testing HPV etiology for head & neck cancers:**

- a. Keratinizing SCC with basal cell features are suggestive of HPV infection
- b. Immunohistochemistry for P16 (INK4A) correlates with HPV infection
- c. FISH plays no role in diagnosing HPV infection
- d. Nonkeratinizing SCC are rarely caused by HPV infection

**The correct answer is b.**

**Reference:**

- 1) Syrjanen, KJ. HPV infections and tonsillar carcinoma J Clin Pathol (2004) 57(5):449
- 2) Syrjanen Human papillomavirus (HPV) in head and neck cancer.J Clin Virol; (2005) Mar:32 Suppl 1:S59-66.
- 3) Paz, IB et al. Human papillomavirus (HPV) in head and neck cancer. An association of HPV 16 with squamous cell carcinoma of Waldeyer's tonsillar ring.Cancer; (1997) Feb 1:79(3):595-604
- 4) Mork, J et al. Human Papillomavirus Infection as a Risk Factor for Squamous-Cell Carcinoma of the Head and Neck. NEJM (2001) Volume 344(15):1125-1131
- 5) Ritchie, JM, et al. Human papillomavirus infection as a prognostic factor in carcinomas of the oral cavity and oropharynx. International Journal of Cancer 2003 104(3): 336-344

**Rationale:**

When testing HPV etiology for head & neck cancers, a non-keratinizing SCC with basal cell features are suggestive of HPV infection, which can be confirmed with FISH. Immunohistochemistry showing positivity for P16 (INK4A) correlates with HPV infection.

**20. Concerning HPV and head & neck cancer treatment outcome:**

- a. Positive HPV status predicts better progression free survival
- b. Positive HPV status predicts better overall survival
- c. Positive HPV status predicts better response to induction chemotherapy
- d. All of the above
- e. None of the above

**The correct answer is d.**

**Reference:**

1) Lin, JC et al. Quantification of Plasma Epstein-Barr Virus DNA in Patients with Advanced Nasopharyngeal Carcinoma. *NEJM* 2004, 350: 2461-2470

2) *Leung SF et al, Plasma Epstein-Barr Viral Deoxyribonucleic Acid Quantitation Complements Tumor-Node-Metastasis Staging Prognostication in Nasopharyngeal Carcinoma JCO, 2006 24(34):5414*

3) Fakhry C et al, Improved survival of patients with human papilloma virus-positive head and neck squamous cell carcinoma in a prospective clinical trial. *J NCI* 2008, 100(4):261-9

**Rationale:**

According to a randomized study (ECOG 2399) for oropharyngeal and laryngeal cancer treatment, a positive HPV status predicts better response to induction chemotherapy (HPV+ vs. HPV- = 82% vs. 55%, p=0.01), better progression free survival (2-yr PFS: HPV+ vs. HPV- = 86% vs. 53%, p=0.02), and better overall survival (2-yr OS: HPV+ vs. HPV- = 95% vs. 62%, p=0.005).