

高雄榮民總醫院 下咽癌診療原則

[2016年第1版]

頭頸癌治療團隊制訂

提醒您：此份診療原則為本院關於癌症診斷與治療之參考指引。臨床應用上可能會依照個人情況而有所調整。歡迎與您的醫師討論。

與上一版的差異

- 化療藥物Regimen及給予方式單純化
- 強調surgery在positive margin或residual disease狀態的角色
- 加入Up-front neck dissection作為advanced N status的起始治療選擇
- 加入Neck sonography及PET scan為clinical image staging之輔助參考依據

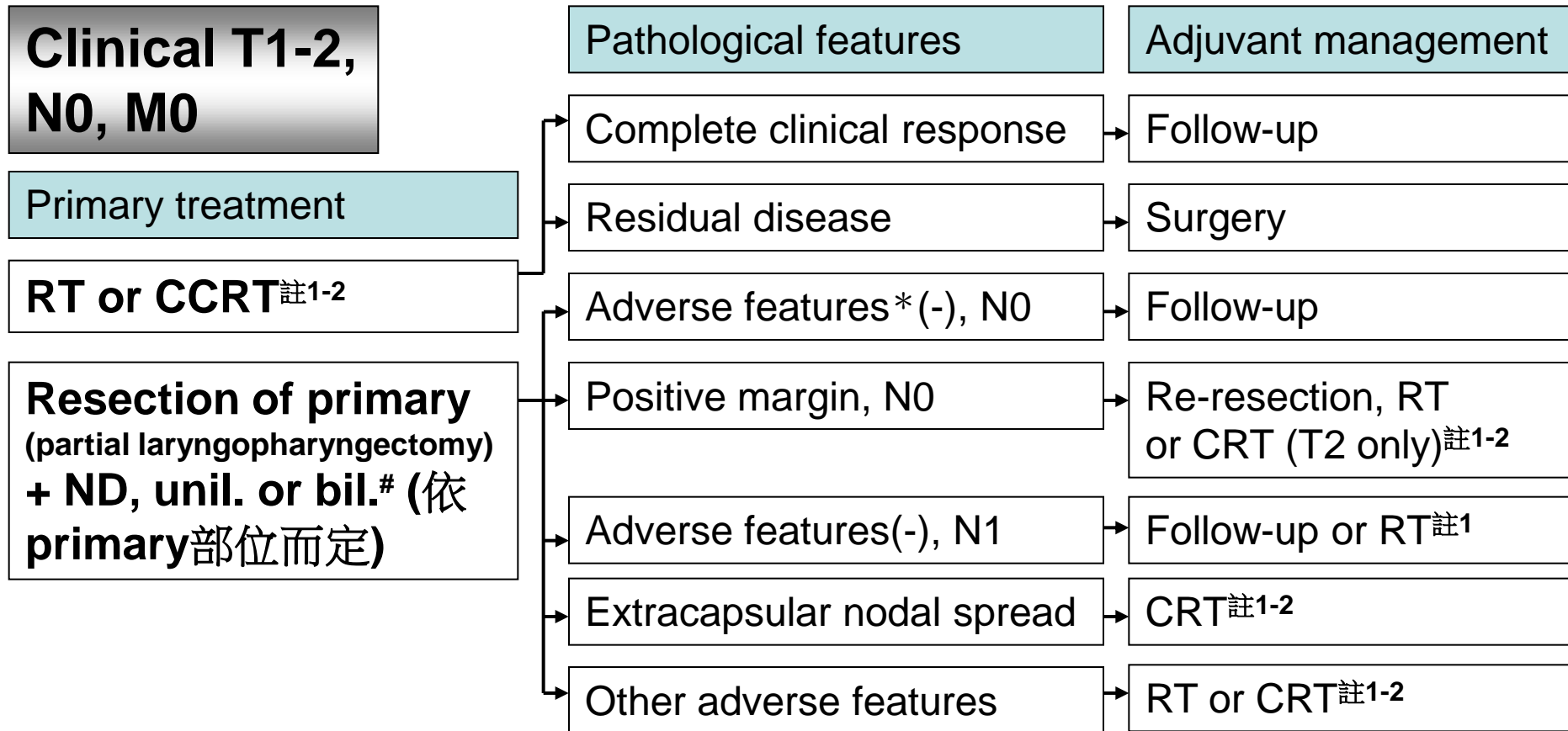
Carcinoma of Hypopharynx

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| WORK-UP | STAGING & TREATMENT | FOLLOW-UP |
|--|--|--|
| <ul style="list-style-type: none">• <u>History & PE</u>• <u>Biopsy & Pathology</u>• <u>Image</u><ul style="list-style-type: none">→ MRI or CT of H & N→ Chest X-ray→ Bone scan→ Abd. Sono→ ± Neck Sono→ ± PET scan• <u>Dental evaluation</u><ul style="list-style-type: none">→ Panorex→ ± teeth extraction• <u>Multidisciplinary consultation</u> | <ul style="list-style-type: none">• <u>[T1-2, N0, M0]</u> <i>詳見 Page 2</i>• <u>[T1-3, N1-3, M0]</u> <i>詳見 Page 3</i>• <u>[T4a, resectable T4b, any N, M0]</u> <i>詳見 Page 4</i>• <u>Inoperable status</u> <i>詳見 Page 5</i> | <ul style="list-style-type: none">• <u>[Post-Tx within 6 months]</u><ul style="list-style-type: none">→ Every month: PE→ Baseline MRI or CT• <u>[0.5-3 years after Tx]</u><ul style="list-style-type: none">→ Every 3 months: PE→ Every 1 year: H & N MRI or CT, CxR, Bone scan & Abd. Sono, ± Neck Sono• <u>[3-5 years after Tx]</u><ul style="list-style-type: none">→ Every 4-6 months: PE• <u>[5 years later after Tx]</u><ul style="list-style-type: none">→ Every 6-12 months: PE |

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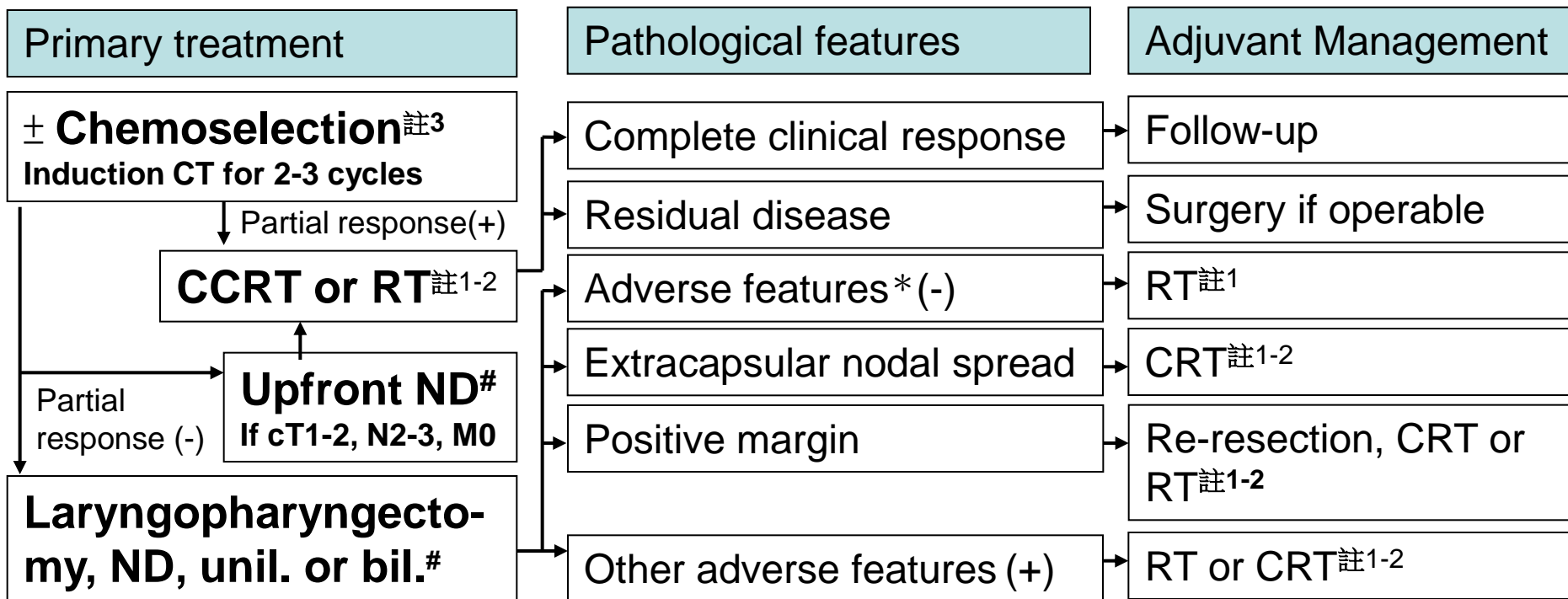
#Bilateral ND was suggested if the primary site is the posterior pharyngeal wall or the postcricoid area.

*Adverse features : Extracapsular nodal spread, positive or close margins, N2 or N3 nodal disease, nodal disease in levels IV or V, perineural invasion, lymphovascular invasion.

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**Clinical T1-3,
N1-3, M0**



Neck dissection level 依 primary 部位及 cN status 而定。

* Adverse features : Extracapsular nodal spread, positive margins, N2 or N3 nodal disease, nodal disease in levels IV or V, perineural invasion, lymphovascular invasion.

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**Clinical T4a,
resectable T4b,
any N, M0**

Primary treatment

**Laryngopharyngectomy, ND, unil. or bil.#
(Preferred if applicable)**

↑ Partial response(-)

± **Chemoselection**^{註3}
Induction CT for 2-3 cycles

↓ Partial response(+)

CCRT or RT^{註1-2}

Pathological features

Adverse features* (-)

Extracapsular nodal spread

Positive margin

Other adverse features

Complete clinical response

Residual disease

Adjuvant Management

RT^{註1}

CRT^{註1-2}

Re-resection, CRT or
RT^{註1-2}

RT or CRT^{註1-2}

Follow-up

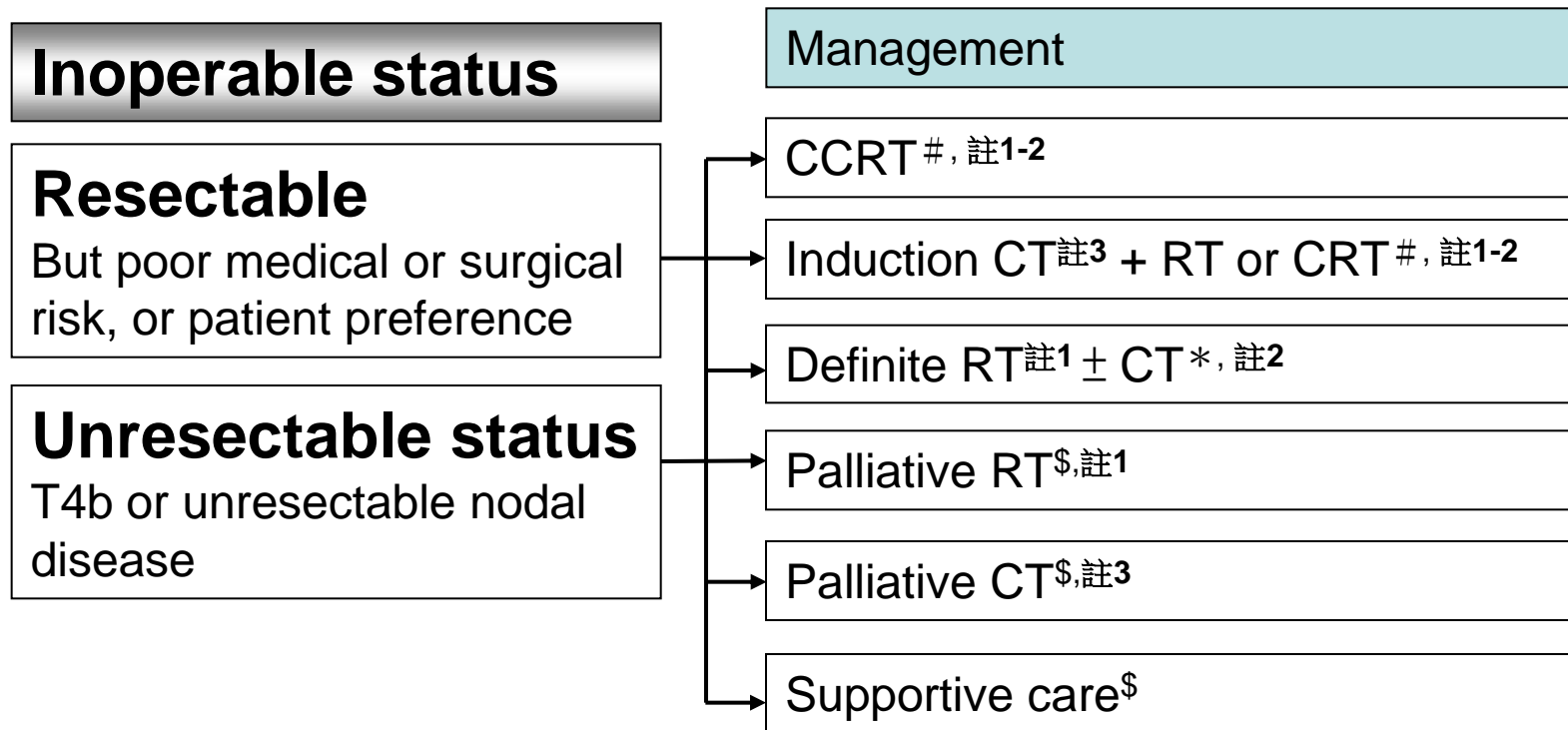
Surgery if operable

Neck dissection level 依primary部位及cN status而定。

* Adverse features : Extracapsular nodal spread, positive margins, N2 or N3 nodal disease, nodal disease in levels IV or V, perineural invasion, lymphovascular invasion.

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ECOG Performance Status 0-1 註5

* ECOG Performance Status 2

\$ ECOG Performance Status 3

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註1

Principles of Radiotherapy

Definitive Radiotherapy

- Primary and gross adenopathy : 66 - 74 Gy (1.8-2.0 Gy/fraction)
- Neck uninvolved nodal stations : 44 - 64 Gy (1.6-2.0 Gy/fractions)

Postoperative Radiotherapy

- Preferred interval between operation and radiotherapy is ≤ 6 weeks.
- Primary : 60-66 Gy (1.8-2.0 Gy/fraction)
- Neck involved nodal stations : 60 - 66 Gy (1.8-2.0 Gy/fraction)
- Neck uninvolved nodal stations : 44 - 64 Gy (1.6-2.0 Gy/fraction)

CCRT or RT

- RT alone if : old age, impaired renal function, poor condition or refused chemotherapy

Palliative RT

- Indicated in : relieve local symptoms, prevent debilitation such as spinal cord compression and pathological fracture, achieve durable locoregional control.

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註2

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Principles of Chemotherapy

Concurrent with RT

Regimen 1: q3w CDDP ± Cetuximab^{註4} + RT

- Cisplatin (80-100mg/ m²) q3w during R/T
- Cetuximab(400mg/ m²) loading dose first week, then Cetuximab(250mg/ m²) maintain dose D1 + Cisplatin (80-100mg/ m²) q3w D2 during R/T

Regimen 2: Weekly CDDP ± Cetuximab^{註4} + RT

- Cisplatin (30-40mg/ m²) weekly during R/T
- Cetuximab(400mg/ m²) loading dose first week, and then Cisplatin (30-40mg/ m²) weekly D1 + Cetuximab(250mg/ m²) maintain dose D2 during R/T

Regimen 3: q3w Carboplatin ± Cetuximab^{註4} + RT

- Carboplatin (AUC x 5mg) q3w during R/T
- Cetuximab(400mg/ m²) loading dose first week, then Cetuximab(250mg/ m²) maintain dose D1 + Cisplatin (80-100mg/ m²) q3w D2 during R/T

Regimen 4: Weekly Cetuximab^{註4} + RT

- Cetuximab(400mg/ m²) loading dose first week, then Cetuximab(250mg/ m²) maintain dose during RT

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註3

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Regimens of Chemotherapy

Induction, salvage or adjuvant, 建議2-3cycles

Regimen 1: q3-4 weeks CDDP ± F ± weekly Cetuximab^{註4}

- Cisplatin(80-100mg/m²) D1
- Fluorouracil (5-FU) (600-1000mg/m²) D2-D5
- Cetuximab(400mg/m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Regimen 2: P ± F q3-4 weeks ± weekly Cetuximab^{註4}

- Cisplatin (20mg/ m²) D1-D5
- Fluorouracil (5-FU) (600-1000mg/m²) D1-D5
- Cetuximab(400mg/m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

Regimen 3: q3-4 weeks Carboplatin ± F ± weekly Cetuximab^{註4}

- Carboplatin (AUC x 5mg) D1
- Fluorouracil (5-FU) (600-1000mg/m²) D2-D5
- Cetuximab(400mg/ m²) loading dose first week, then weekly Cetuximab (250mg/ m²)

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註3

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Regimens of Chemotherapy

Induction, salvage or adjuvant, 建議2-3cycles

Regimen 4: q3-4 weeks T + P ± F ± weekly Cetuximab^{註4}

- Taxotere(60 mg/ m²) D1
- Cisplatin(60-75 mg/ m²) D1
- Fluorouracil (5-FU) (600-750mg/m²) D2-D5
- Cetuximab (400mg/ m²) loading dose first week, then Cetuximab (250mg/ m²) maintain dose

Regimen 5: weekly Cetuximab^{註4}

- Cetuximab (400mg/ m²) loading dose first week, then Cetuximab (250mg/ m²) maintain dose

Regimen 6: oral Fluorouracil

- Ufur cap (tegafur 100mg+uracil 224mg) 2# TID
(Salvage or palliative CT中作為取代iv-formed 5-FU之替代藥物)

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特殊用藥健保給付規定

Taxotere

- 頭頸部癌，限局部晚期且無遠端轉移之頭頸部鱗狀細胞癌且無法手術切除者。
- 與Cisplatin 及5-FU 併用，作為放射治療前的引導治療，限使用四個療程。

Cetuximab

- 限與放射線療法合併使用於局部晚期之口咽癌、下咽癌及喉癌患者，且符合下列條件之一：
 1. 年齡 ≥ 70 歲
 2. $Ccr < 50ml/min$
 3. 聽力障礙者 (聽力障礙定義為500Hz、1000Hz、2000Hz 平均聽力損失大於25 分貝)
 4. 無法耐受platinum-based 化學治療。
- 使用總療程以接受8 次輸注為上限。
- 需經事前審查核准後使用。

Carboplatin

- 限腎功能不佳 ($CCr < 60$) 或曾作單側或以上腎切除之惡性腫瘤患者使用。

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註5

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Eastern Cooperative Oncology Group (ECOG) Performance Status

| Grade | Description | Suggestion |
|-------|---|---------------|
| 0 | Normal activity fully ambulatory (無症狀) | 按照標準化療評估及療程。 |
| 1 | Symptoms, but nearly fully ambulatory (有症狀，完全步行，但對生活無影響) | 按照標準化療評估及療程。 |
| 2 | Some bed time, but needs to be in bed less than 50% of normal daytime (躺在床上的時間<50%) | 按照標準化療評估及療程。 |
| 3 | Needs to be in bed more than 50% of normal daytime (躺在床上的時間>50%) | 可視情況考慮停止化學治療。 |
| 4 | Unable to get out of bed (長期完全臥床) | 建議停止化學治療。 |
| 5 | Dead | |

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References

1. NCCN Clinical Practice Guidelines in Oncology – Head and Neck Cancers Version 1. 2015
2. AJCC (American Joint Committee on Cancer) Manual for Staging of Cancer, 7th ed, Greene, FL, Page, DL, Fleming, ID, et al (Eds), Springer-Verlag, New York 2010.
3. Iro, H, Waldfahner, F. Evaluation of the newly updated TNM classification of head and neck carcinoma with data from 3247 patients. *Cancer* 1998; 83:2201.
4. Peter AP, Michael EC, Greg D, et al. Up-front neck dissection followed by concurrent chemoradiation in patients with regionally advanced head and neck cancer. *Head Neck*. 2012;34:1798-1803
5. Bradley, PJ, MacLennan, K, Brakenhoff, RH, Leemans, CR. Status of primary tumour surgical margins in squamous head and neck cancer: prognostic implications. *Curr Opin Otolaryngol Head Neck Surg* 2007; 15:74.
6. Brockstein, B, Vokes, EE. Concurrent chemoradiotherapy for head and neck cancer. *Semin Oncol* 2004; 31:786.
7. Nair, MK, Sankaranarayanan, R, Padmanabhan, TK. Evaluation of the role of radiotherapy in the management of carcinoma of the buccal mucosa. *Cancer* 1988; 61:1326.
8. Hong, WK, Bromer, RH, Amato, DA, et al. Patterns of relapse in locally advanced head and neck cancer patients who achieved complete remission after combined modality therapy. *Cancer* 1985; 56:1242.
9. Forastiere, AA, Metch, B, Schuller, DE, et al. Randomized comparison of cisplatin plus fluorouracil and carboplatin plus fluorouracil versus methotrexate in advanced squamous-cell carcinoma of the head and neck: A Southwest Oncology Group study. *J Clin Oncol* 1992; 10:1245.
10. Jacobs, C, Lyman, G, Velez-Garcia, E, et al. A phase III randomized study comparing cisplatin and fluorouracil as single agents and in combination for advanced squamous cell carcinoma of the head and neck. *J Clin Oncol* 1992; 10:257.
11. Rowland KM, Taylor SG, O'Donnell MR et al. Cisplatin and 5-FU infusion chemotherapy in advanced recurrent cancer of the head and neck: An Eastern Cooperative Oncology Group pilot study. *Cancer Treat Rep* 1986; 70: 461-464.
12. Vermorken JB, Remenar E, van Herpen C, Gorlia T, Mesia R, Degardin M, Stewart JS, Jelic S, Betka J, Preiss JH, et al. Cisplatin, fluorouracil, and docetaxel in unresectable head and neck cancer. *N Engl J Med*. 2007 Oct 25; 357(17):1695-704
13. Posner MR, Hershock DM, Blajman CR, Mickiewicz E, Winkvist E, Gorbounova V, Tjulandin S, Shin DM, Cullen K, Ervin TJ, et al. Cisplatin and fluorouracil alone or with docetaxel in head and neck cancer. *N Engl J Med*. 2007 Oct 25; 357(17):1705-1