Original Article

Radical treatment of locally advanced head and neck cancer with concurrent chemo radiation-cisplatin versus carboplatin: A randomized comparative phase III trial

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ABSTRACT

Context: Concurrent chemoradiation with cisplatin is a standard approach for definitive management of locally advanced head and neck squamous cell carcinoma (LAHNSCC). Carboplatin, though a platinum group of drug, is generally well-tolerated compared to cisplatin. **Aim:** The aim is whether carboplatin can be a substitute of cisplatin with equivalent response and with less toxicity profile. **Settings and Design:** Single institutional prospective randomized phase III study. **Materials and Methods:** Between January 2011 and August 2012, 100 patients LAHNSCC with normal comorbidities were included. The patients in Arm A received injection carboplatin (AUC 6) 3 weeks along with external beam radiotherapy (EBRT) dose 66-70 Gy in conventional fractionation and Arm B received injection cisplatin (100 mg/m^2) 3 weeks with same EBRT schedule. Detailed clinical examination along with biopsy for residual or recurrent disease, CT scan of head and neck were done to assess the response, toxicities, and disease-free survival (DFS) in follow-up. **Statistical Analysis Used:** SPSS version 17 used for statistical calculation. For categorical variables, Chi-Square and Fisher Exact tests were used. For continuous variables, independent samples *t* test were used with 95% CI. Kaplan-Meier survival analysis was used for comparing the DFS. **Results:** Overall response rate (CR + PR) were 76.9% in Arm A and 63.6% in Arm B ($P = 0.06$, non-significant). Statistically significant acute skin ($P = 0.003$), mucosa ($P = 0.003$), and upper GI ($P = <0.0001$) toxicities were found more in cisplatin arm compared to carboplatin arm except acute haematological toxicities. **Conclusions:** It can be concluded that carboplatin is non-inferior in response with statistically significant less toxicities when compared with cisplatin.

Key words: Cisplatin, carboplatin, locally advanced head and neck squamous cell carcinoma

INTRODUCTION

Squamous cell carcinoma of the head neck is predominantly a locoregional disease and the primary treatment methods are radiotherapy and surgery. Nonetheless, even the most effective radiotherapy regimens result in local control rate of 50-70% and disease-free survivals (DFS) of 30-40%. The aim of therapy in the treatment of locoregionally advanced squamous cell carcinomas of head and neck are cure, organ preservation, control the morbidities associated with therapy, and improvement in quality of life.

Concurrent chemoradiation with cisplatin has become a standard approach for organ function preservation for resectable disease (where surgery followed by radiotherapy give same result) and for definitive management of unresectable head and neck squamous cell carcinoma[1-3] not only to increase locoregional control but also decrease distal failure.

Carboplatin, though a platinum group of drug, is generally well tolerated than cisplatin. The favorable toxicity profile and similar mechanisms of action make it tempting to substitute carboplatin for cisplatin. But, till date there are no studies that compare the response and toxicity pattern between the two drugs used as radio sensitizer.

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The aims and objectives of this study are to compare the efficacy of radiation with either carboplatin or cisplatin and to assess toxicities and DFS in locally advanced head and neck cancer.

MATERIALS AND METHODS

From January 2011 to August 2012, 100 patients with LASCCHN were initially enrolled for inclusion in the study. Eligibility criteria were patients with (i) age more than 18 years up to 65 years, (ii) Histologically confirmed primary squamous cell carcinoma of head and neck (excluding nasopharyngeal and oral cavity cancer), (iii) patient should have stage III or non-metastatic stage IV (any T, N 1-3, M0, or T3-4, N0M0), (iv) patient should have ECOG performance status ≤2, (v) all patients must be medically suitable for concurrent chemo radiotherapy, (vi) no previous history of treatment of cancer, (vii) patient must sign informed consent prior to study entry, (viii) routine blood reports like complete hemogram, renal function test (Creatinine clearance ≥50 ml/minute), and liver function test within normal range. Ten patients were left out of study after failing the eligibility criteria. The remaining 90 patients were randomized for study; in ratio of 1:1 allocation using computer-generated random numbers. The accruals of all patients were completed within the stipulated 6 months after initiation of study. Another 7 patients were left out of study, 2 ($n = 2$) of whom failed to comply with the treatment guidelines due to socioeconomic conditions, another 2 died within the study period due to cerebrovascular accidents not completing the treatment ($n = 2$), and remaining 3 voluntarily left the study ($n = 3$). So at the end of study, only 83 patients were eligible for analysis with 39 patients in Arm A (carboplatin-containing chemoradiation) and 44 patients in Arm B (cisplatin-containing chemoradiation). Before the inception of the study, an application was submitted to the Institutional Ethics Committee (IEC). IEC, after proper scrutiny and detailed deliberation, approved the research proposal.

Patients were randomly assigned in two different arms. Patients in Arm A received external beam radiotherapy (EBRT) with dose of 66-70 Gy in 1.8-2 Gy/fraction, single fraction per day, 5 fractions per week, along with injection carboplatin (Dose AUC 6 on Day 1, Day 22, and Day 43) and in Arm B patients received 66-70 Gy EBRT in 1.8-2 Gy/fraction, single fraction per day, 5 fractions per week, along with injection cisplatin (Dose 100 mg/m^2 on Day 1, Day 22, and Day 43).

RADIOTHRERAPY

EBRT was given using megavoltage equipment with Cobalt-60, energy 1.17 Mev, 1.33 Mev (average 1.25 MeV). The minimum Source-Surface Distance (SSD) was 80 cm. All patients received pre and post radiation dental check-up. Parallel opposed radiation portals with separate fields for low neck nodal irradiation were given and off-cord field placed after 45 Gy with standard immobilization technique and conventional 2-D treatment planning.

AFTER COMPLETION OF TREATMENT

Interpretation of response and DFS

Patients were followed-up, first at 6-8 weeks after completion of treatment and thereafter, at 1-3 monthly intervals based on detailed ENT examination and contrast-enhanced CT scan of head and neck. Biopsy was taken from any suspicious clinical and/or radiological residual disease of primary site and/or nodal area. Patients were then categorized as per RECIST criterion[4] as having complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD).

Radiation-induced toxicity - acute and late toxicity

Patients were evaluated for toxicity weekly during radiation and thereafter in each follow-up and graded according to the RTOG Acute and Chronic Radiation Morbidity Criteria.[5] Toxicities that appeared after 6 months are regarded as late toxicity and if they occurred during treatment or up to 6 months following treatment are regarded as acute toxicity.

Statistical analysis

Statistical analysis was done using SPSS version 17. For categorical variables, Chi-Square and Fisher Exact tests were used, while for continuous variables, the mean and SD were compared using independent samples t test with 95% CI. All tests were 2-tailed and $P < 0.05$ were taken as significant. Kaplan-Meier survival analysis with Log rank test was used for comparing the DFS.

RESULTS

Baseline profiles i.e., distribution of patients and tumour characteristics in terms of age distribution, sex distribution, creatinine clearance, performance status, primary site [Table 1], tumour (T) status, nodal (N) status, stage were similar in the two groups.

Table 1: Site specific occurrence

Primary site	Group			
	Concurrent carboplatin with RT (n=39)		Concurrent cisplatin with RT (n=44)	
Oropharynx	19	48.72%	20	45.45%
Larynx	11	28.21%	12	27.27%
Hypopharynx	9	23.08%	12	27.27%

P=0.906

The average age in Arm A ($n = 39$) was 53.5 ± 1.5 years (range 29-65 years), while for patients in Arm B ($n = 44$) the average age was 52.0 ± 1.3 years (range 33-65 years), $P = 0.441$. 89.74% of patients in Arm A and 86.36% patients in Arm B were males, $P = 0.743$.

Response evaluation

The response assessment was evaluated at 8 weeks post-treatment using RECIST criteria. Overall response rate (CR + PR) were 76.9% in Arm A and 63.6% in Arm B.

Chi-Square test analysis showed non-significant statistical difference in response rates between the 2 treatment arms [Table 2].

Comparison of toxicity profile

The acute grade 2 and grade 3 skin toxicity assessed by RTOG Acute Morbidity Scoring were significantly high in cisplatin arm than carboplatin arm (grade 2 31.82% vs. 10.26% and grade 3 22.73% vs. 15.38) which is statistically significant ($P = 0.003$). Combined grade 2 and grade 3 mucositis were 25.64% and 65.9% in Arm A and Arm B, respectively, ($P = 0.003$) i.e., radiation along with cisplatin was associated with increased skin toxicity and mucositis. Acute grade 2 salivary gland toxicity (XEROSTOMIA) was 40.9% and 33.33% in Arm A and Arm B, respectively ($P = 0.450$). Combined acute grade 2 and grade 3 nausea and vomiting 70.46% were in the cisplatin arm and 12.82% in the carboplatin arm. RTOG acute haematological toxicity grade 2 and grade 3 were more commonly seen in carboplatin arm than cisplatin arm [Table 3].

Combined late grade 2 and grade 3 skin toxicity were 10.26% and 56.82% in Arm A and Arm B, respectively, ($P = < 0.0001$) and grade 1 mucosal toxicity were 25.64% and 50% in Arm A and Arm B respectively ($P = 0.031$). Combined late grade 2 and grade 3 salivary gland toxicity (XEROSTOMIA) were 20.51% and 31.82% in Arm A and Arm B, respectively ($P = 0.647$) i.e., radiation along with cisplatin was associated with increased late skin and mucosal toxicity [Table 4].

With a mean follow-up of 12.7 months, the DFS using Kaplan-Meier survival analysis was comparable and not statistically different in carboplatin arm when compared with standard cisplatin arm. Log rank test $P = 0.456$ [Tables 5-7 and Figure 1].

Table 2: Response assessment comparison between two groups, *P*=0.06

Response (RECIST)	Group			
	Carboplatin (*n*=39)		Cisplatin (*n*=44)	
Complete response	20	51.3%	10	22.7%
Partial response	10	25.6%	18	40.9%
Stable response	5	12.8%	10	22.7%
Progressive disease	4	10.3%	6	13.6%

Table 3: Grades of acute toxicity using RTOG toxicity scheme

Site-specific grades of acute toxicities	Group				*P*
	Concurrent carboplatin with RT (*n*=39)		Concurrent cisplatin with RT (*n*=44)		
Skin					
G0	10	25.64%	4	9.09%	0.0030
G1	19	48.72%	11	25.0%	
G2	4	10.26%	14	31.82%	
G3	6	15.38%	10	22.73%	
G4	0	0%	5	11.36%	
Mucosa					
G0	10	25.64%	6	13.64%	0.0030
G1	19	48.72%	9	20.45%	
G2	8	20.51%	20	45.45%	
G3	2	5.13%	9	20.45%	
Salivary gland					
G1	25	64.1%	23	52.27%	0.450
G2	13	33.33%	18	40.91%	
G3	1	2.56%	3	6.82%	
Upper G.I.					
G0	7	17.95%	0	0%	<0.0001
G1	27	69.23%	11	25.0%	
G2	5	12.82%	21	47.73%	
G3	0	0%	10	22.73%	
G4	0	0%	2	4.55%	
Hematological					
G0	0	0%	3	6.82%	<0.0001
G1	3	7.69%	24	54.55%	
G2	18	46.15%	15	34.09%	
G3	16	41.03%	1	2.27%	
G4	2	5.13%	1	2.27%	

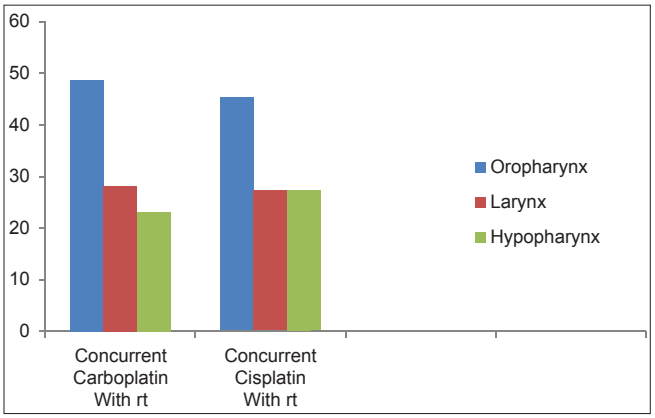

Figure 1: Site-specific occurrence of tumour

DISCUSSION

Locally advanced head and neck cancer is usually associated with a poor prognosis because of high recurrence rate.[6,7] The combination of chemotherapy and radiation may improve the local control and survival rate because of the additive or synergistic effect of chemo radiation[8] and to eradicate systemic micrometastasis up to 30% in some patients at high-risk (i.e., patients with large tumors, node

Table 4: Grades of late toxicity using RTOG toxicity scheme

Grades of late toxcities	Group				*P*
	Concurrent carboplatin with RT (*n*=39)		Concurrent cisplatin with RT (*n*=44)		
Skin					
G0	18	46.15%	8	18.18%	<0.0001
G1	17	33.59%	11	25.0%	
G2	4	10.26%	14	31.82%	
G3	0	0%	11	25.0%	
Mucosa					
G0	26	66.67%	15	34.09%	0.0314
G1	10	25.64%	22	50.0%	
G2	2	5.13%	4	9.09%	
G3	1	2.56%	3	6.82%	
Salivary gland					
G0	5	12.82%	4	9.09%	0.647
G1	26	66.67%	25	56.82%	
G2	7	17.95%	12	27.27%	
G3	1	2.56%	2	4.55%	
G4	0	0.00%	1	2.27%	

Table 5: DFS between two arms

Group	Total *N*	*N* of Events	Censored	
			N	Percent
Carboplatin	20	12	8	40.0
Cisplatin	10	5	5	50.0
Overall	30	17	13	43.3

Table 6: Mean for survival time

Group	Mean			
	Estimate	Std. Error	95% Confidence Interval	
			Lower bound	Upper bound
Carboplatin	12.244	1.058	10.170	14.318
Cisplatin	13.400	1.594	10.276	16.524
Overall	12.717	0.875	11.002	14.431

Table 7: Overall comparisons

	Chi-Square	Df	Sig.
Log rank (mantel-cox)	0.557	1	0.456

Test of equality of survival distributions for the different levels of group

involvement in the lower neck)[9] but may be associated with severe toxicity which can sometimes be life-threatening also.

French meta-analysis (MACH-NC), based on individual patient data, published by Pignon *et al*. in 2000[10] and updated in 2004;[11] showed that adding chemotherapy to radiotherapy in locally advanced disease: (1) improved overall survival by 5% at 5 years with any chemotherapy association or timing of association; (2) overall survival is improved by 8% at 5 years if a concomitant association is employed; (3) neoadjuvant chemotherapy followed by radiotherapy alone is less effective than concomitant association; (4) a benefit is evident if cisplatin is used in the combined approach; (5) polychemotherapy does not appear to be better than monochemotherapy; (6) the benefit is less evident in patients over 70 years.

In 1987, the Radiation Therapy Oncology Group (RTOG) first reported results from a phase II trial testing radiation and concurrent high-dose cisplatin (100 mg/m^2 given every 3 weeks during radiation therapy). A complete response rate of 71% was reported.[12]

High-dose cisplatin regimens are more toxic. The high emetogenic potential of cisplatin at doses above 50 mg/m^2 may be a consideration for patients who have risk factors for chemotherapy-induced nausea and vomiting.

Carboplatin, the second-generation platinum drug, possesses all of the radiopotentiation properties of cisplatin but has a different metabolites and side-effect profile. Carboplatin is generally well tolerated than cisplatin, with less nausea and vomiting but with more frequent hematologic toxicities. The favorable toxicity profile and similar mechanisms of action make it tempting to substitute carboplatin for cisplatin. The clinical CR rate reported in phase II studies with concomitant carboplatin and radiation therapy (single daily fraction) is in the range of 65-70%, which is similar to the clinical CR rate reported with cisplatin and radiation therapy.[13]

Although the National Comprehensive Cancer Network generally prefers cisplatin-based regimens for locoregionally advanced head and neck cancers as primary treatment, for concurrent chemoradiation, and for postoperative chemo radiation[14] data from several clinical trials have suggested that the two platinum agents may, in fact, be interchangeable in certain settings.[15-17] Till date there is no head-to-head trial to identify response rate, toxicity, and DFS difference between concurrent chemoradiation with carboplatin with concurrent cisplatin in locally advanced squamous cell head and neck carcinoma.

In our study, in the carboplatin arm, CR rate was 51.3% and PR rate was 25.6%, i.e., overall response rate of 76.9% [Table 2]. We cannot compare this with previous experiences due to lack of evidences. In cisplatin arm, CR rate was 22.7% and PR rate was 40.9%, i.e., overall response rate of 63.6%. The difference in these two arms were 13.3% but ANOVA analysis showed non-significant statistical difference in response rates among the two treatment arms ($P \sim 0.06$) [Table 2].

In our study, radiation along with cisplatin was associated with increased grade 3 skin (for acute 22.73% vs 15.38% and for late 25.0% vs 0%), mucosal (acute-20.45% vs 5.13% and for late 6.83% vs 2.53%) and late grade 2 salivary gland toxicity (27.27% vs 17.95%) than Carboplatin [Tables 3 and 4]. Again incidence of combined grade 2 and 3 nausea and vomiting were 12.82% and 70.46% in Arm A (carboplatin-containing arm) and Arm B

(cisplatin-containing arm), respectively ($P < 0.0001$) [Table 3]. These indicate that radiation with carboplatin was associated with significantly lesser incidence of nausea and vomiting. So in contrast to cisplatin IV hydration pretreatment and post-treatment are not necessary in patients receiving carboplatin. However, patients should still be instructed to maintain adequate oral hydration.

But incidences of grade 2 RTOG acute haematological toxicity were 46.15% in Arm A a 34.09% in Arm B which is statistically significant ($P < 0.0001$) [Table 3]. Myelosuppression is significant and dose-limiting with carboplatin. Dose-dependent cumulative toxicity is more severe in elderly patients. Thrombocytopenia is most commonly observed usually by day 21.

With a mean follow-up of 12.7 months, there were equivalent recurrence rate in patients in Arm A [mean survival time in months −12.2 ± 1.05, 95% Confidence Interval (CI) 10.17-14.32] and Arm B (mean survival time in months −13.4 ± 1.6, 95% CI 10.28-16.52). Kaplan-Meier survival analysis showed non-significant difference in DFS between these two arms (Log rank test 0.456) [Tables 5-7, Figure 2].

So, it can be said that response-wise radiation with carboplatin is similar to chemoradiation with cisplatin and after a mean follow-up of 12.7 months; there is no significant difference in DFS between them, though chemoradiation with cisplatin causes higher incidence of both acute and late skin, mucosal, salivary gland toxicity, and nausea and vomiting. Carboplatin, along with radiation, is associated with higher incidence of hematological toxicity.

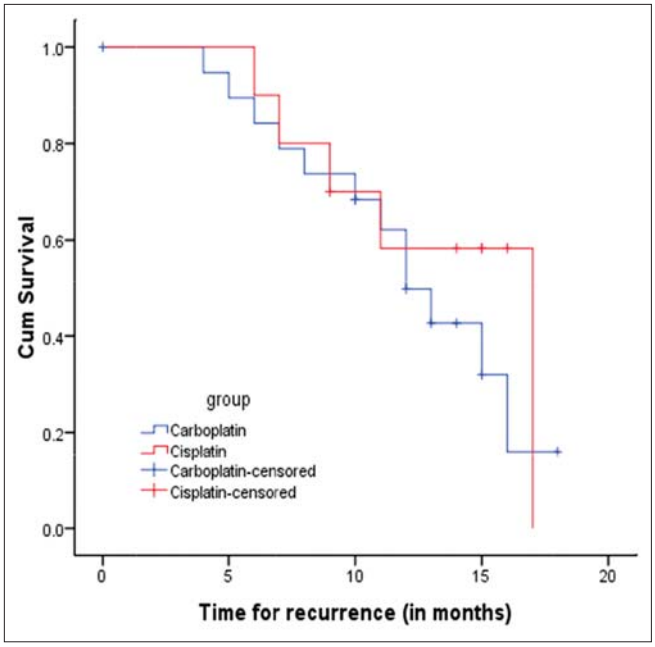

Figure 2: Kaplan-Meier survival analysis of DFS between two arms

However, there were several pitfalls of the study.

1. Our sample size was small, only 83 patients and it was not statistically powered, so any conclusion cannot be applicable to the entire head and neck cancer population
2. Usually head and neck carcinoma recurrence occur within 24 months, more so in first 12 months post-treatment. In our study, entire study period was 20 months including patient accrual, intervention, and assessment, and median survival of patients were 12.7 months in both treatment arms (maximum follow-up period of 16.5 months), the exact incidence of toxicity, tumour recurrence, and DFS among patients achieved CR could not be computed
3. In analysis, contributing factors such as anaemia, duration of treatment interruption, deterioration of nutritional status with fall in QOL, were not adjusted for assessing the response rate and DFS
4. We used 2D conformal radiotherapy planning. A 3D conformal radiotherapy planning would have resulted in better parotid sparing in both arms
5. Locally advanced head and neck cancer in Indian population is probably different from those of the Western World, establishing the basic concept of pharmacogenomics and its impact on cancer.

Other advantage of carboplatin is that it is convenient to use (to be given over 1 hr, no need of indoor admission of patient for pre- and posthydration in contrast to cisplatin). Although it causes increased incidence of haematological toxicity these are often tolerable and controlled with proper supportive management without prolongation of overall treatment time. Whereas, cisplatin chemoradiation causes increased acute toxicity, overall duration of radiation gets prolonged by a few days to weeks in some cases, and moreover all the cycles of cisplatin cannot be administered in some cases which may turn into somewhat poorer response. Although these issues were not addressed in this study, but should be considered in larger studies to measure the actual therapeutic gain.

CONCLUSIONS

So, this study concludes that carboplatin, along with radiation, is non-inferior in response to concurrent chemoradiation with cisplatin in the treatment of locally advanced head and neck cancer. Carboplatin causes lower incidence of both acute and late skin, mucosal and salivary gland toxicity, and nausea and vomiting in comparison to chemoradiation with cisplatin without interruption of treatment though it is associated with higher incidence of haematological toxicity.

Further studies with larger sample size and longer follow-up period are required for establishing this observation.

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REFERENCES

1. Burri RJ, Lee NY. Concurrent chemotherapy and radiotherapy for head and neck cancer. Expert Rev Anticancer Ther 2009; 9:293-302.
2. Forastiere AA, Goepfert H, Maor M, Pajak TF, Weber R, Morrison W, *et al*. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. N Engl J Med 2003;349:2091-8.
3. Adelstein DJ, Li Y, Adams GL, Wagner H Jr, Kish JA, Ensley JF, *et al*. An intergroup phase III comparison of standard radiation and two schedules of concurrent chemoradiotherapy in patients with unresectable squamous cell head and neck cancer. J Clin Oncol 2003;21:92-8.
4. Therasse P, Arbuck SG, Eisenhauer EA, Wanders J, Kaplan RS, Rubinstein L, *et al*. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. J Natl Cancer Inst 2000;92:205-16.
5. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys 1995;31:1341-6.
6. Al-Sarraf M. Treatment of locally advanced head and neck cancer: Historical and critical review. Cancer Control 2002;9:387-99.
7. Tupchong L, Scott CB, Blitzer PH, Marcial VA, Lowry LD, Jacobs JR, *et al*. Randomized study of preoperative versus postoperative radiation therapy in advanced head and neck carcinoma: Long-term follow-up of RTOG study 73-03. Int J Radiat Oncol Biol Phys 1991;20:21-8.
8. Lawrence TS, Blackstock AW, McGinn C. The mechanism of action of radiosensitization of conventional chemotherapeutic agents. Semin Radiat Oncol 2003;13:13-21.
9. Brizel DM, Esclamado R. Concurrent chemoradiotherapy for locally advanced, nonmetastatic, squamous cell carcinoma of the Head and Neck: Consensus, controversy and conundrum. J Clin Oncol 2006;24:2612-7.
10. Argiris A. Update on chemoradiotherapy for head and neck cancer. Curr Opin Oncol 2002;14:323-29.
11. Bourhis J, Amand C, Pignon JP. Update of MACH.NC (Metaanalysis of chemotherapy in Head and Neck Cancer) database focused on concomitant chemotherapy. Proc Am Soc Clin Oncol 2004:22;488.
12. Marcial VA, Pajak TF, Mohiuddin M, Cooper JS, al Sarraf M, Mowry PA, *et al*. Concomitant cisplatin chemotherapy and radiotherapy in advanced mucosal squamous cell carcinoma of the head and neck. Long-term results of the Radiation Therapy Oncology Group study 81-17. Cancer 1990;66:1861-8.
13. Al-Sarraf M, Hussein M. Head and neck cancer: Present status and future prospects of adjuvant chemotherapy. Cancer Invest 1995;13:41-53.
14. National Comprehensive Cancer Network. Clinical practice guidelines in oncology: Head and neck cancer v. 1.2007. Available from www.nccn.org. [Last accessed on 2008 May 30].
15. Chitapanarux I, Lorvidhaya V, Kamnerdsupaphon P, Sumitsawan Y, Tharavichitkul E, Sukthomya V, *et al*. Chemoradiation comparing cisplatin versus carboplatin in locally advanced nasopharyngeal cancer: Randomized, non-inferiority, open trial. Eur J Cancer 2007;43:1399-406.
16. Bourhis J, Rivera F, Mesia R, Awada A, Geoffrois L, Borel C, *et al*. Phase I/II study of cetuximab in combination with cisplatin or carboplatin and fluorouracil in patients with recurrent or metastatic squamous cell carcinoma of the head and neck. J Clin Oncol 2006;24:2866-72.
17. Baselga J, Trigo JM, Bourhis J, Tortochaux J, Cortés-Funes H, Hitt R, *et al*. Phase II multicenter study of the antiepidermal growth factor receptor monoclonal antibody cetuximab in combination with platinum-based chemotherapy in patients with platinum-refractory metastatic and/or recurrent squamous cell carcinoma of the head and neck. J Clin Oncol 2005;23:5568-77.

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