Phase II Study of Concurrent Chemoradiotherapy for Inoperable (Bulky) Stage III (A/B) Non-Small Cell Lung Cancer (NSCLC) : A Preliminary Report

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Abstract

We designed a phase II study to determine the feasibility and toxicity of concomitant radiotherapy and Paclitaxel/Carboplatin followed by adjuvant chemotherapy of the same regimen in patients with newly diagnosed inoperable stage III A/B non-small cell lung cancer. Patients were irradiated with a total dose of 66 Gy. Weekly courses of Paclitaxel 45 mg/m^2 and Carboplatin AUC 2 were administered intravenously during the irradiation period. After completion of concurrent chemoradiotherapy, adjuvant chemotherapy with Paclitaxel 175 mg/m^2 and Carboplatin AUC 6 intravenously every 3 weeks for 4 cycles were given. Since March 1998, 15 patients have been enrolled. All patients were assessable for efficacy and toxicity after concurrent chemoradiotherapy. Eleven patients were assessable for efficacy and toxicity after adjuvant chemotherapy. After concomitant chemoradiotherapy, complete response (CR) was documented in 2 of 15 (13%). Partial response (PR) was documented in 9 of 15 (60%). After completion of adjuvant chemotherapy in 11 patients, the overall response rate was 91 per cent. (18% CR, 73% PR). There were 8 per cent gr. 3-4 neutropenia which occurred during adjuvant chemotherapy. Concomitant Paclitaxel/Carboplatin and radiotherapy are promising modalities in the treatment of inoperable stage III A/B non-small cell lung cancer.

Key word : Lung Cancer, Inoperable Non-Small Cell Lung Cancer, Concomitant (Concurrent) Chemoradiotherapy

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In locally advanced stages IIIA and IIIB of non-small cell lung cancer (NSCLC), locoregional treatment alone with surgery or radiotherapy results in 5-year survival rates of 15 per cent and 5 per cent, respectively[1,2]. However, radiation therapy has been used conventionally for the treatment of such patients based, in part, on two historical randomized studies that used low-energy orthovoltage equipment, with one showing marginal benefit[3] and the other no survival benefit[4]. Prospective randomized study to evaluate the efficacy of megavoltage, high-dose radiotherapy was performed by the Southeastern Cancer Study Group (SECSG), however, this treatment has not been demonstrated to produce clinically meaningful survival advantage[5].

Efforts to improve these results have included dose escalation and altered dose-fractionation schedules[6] and combined chemoradiation approaches[7,8]. With incorporation of cisplatin-based chemotherapy regimens in the combined modality programs, promising survival results were reported that have been further substantiated by randomized trials[9,10]. Relatively high rates of local and systemic relapse, however, suggest the need for further refinement of treatment. Cisplatin-containing chemotherapy regimens, however, have led to only marginal improvements in survival of patients with advanced disease[11]. Paclitaxel has yielded response rates of 21 per cent and 25 per cent in advanced NSCLC with 1-year survival rates of 41 per cent and 38 per cent in separate phase II studies[12,13]. The paclitaxel-carboplatin combination is active in advanced NSCLC with an objective response rate of 62 per cent and the 1-year survival rate is 54 per cent[14]. Paclitaxel appears to potentiate the effects of ionizing radiation at low concentrations[15] and possesses a sequence-dependent positive interaction with platinum compounds[16].

On the basis of these data and the encouraging preliminary results employing paclitaxel plus carboplatin and concurrent radiation therapy for patients with stages IIIA or IIIB NSCLC[17], we have undertaken this phase II multiinstitutional study to further define the toxicities and efficacy of this chemoradiation regimen.

PATIENTS AND METHOD

Criteria for Eligibility

Patients with histologically or cytologically proof of a newly diagnosed single, primary bronchogenic non-small cell lung cancer were eligible. A biopsy with histology was preferred, but cytology alone was allowed. Histology or cytology from involved mediastinal or supraclavicular lymph nodes alone was allowed if a separate distal primary lesion was clearly evident on radiographs. Patients with two or more parenchymal lesions on the same or opposite sides of the lung were ineligible. Eligible patients had either stage IIIA, with bulky single-level or multi-level ipsilateral N2 disease on CT scan, with at least one node documented to be positive by either fine needle aspiration or mediastinoscopy, or IIIB disease with pathologically documented N3 nodes or T4 lesions (except malignant pleural or pericardial effusion). Performance status was WHO 0 or 1. Age between 18 and 70 years was accrued.

The staging evaluation included history and physical examination; blood chemistry including LDH, alkaline phosphatase, SGOT or SGPT, bilirubin, albumin and calcium; chest X-ray; computed tomographic (CT) scan of the chest and upper abdomen involving the liver, adrenals, and a bone scan to exclude metastatic disease. Biopsy aspiration cytology was required to confirm the benign diagnosis of CT abnormalities. Abnormalities seen on bone scan had to be further evaluated by appropriate plain radiographs or by aspiration cytology or both in order to rule out metastatic disease. All patients had to have either a measurable or evaluable tumor by chest X-ray or CT scan. Patients who received any prior chemotherapy, radiotherapy or surgical resection for the purpose of treatment of lung cancer were ineligible. White blood cell count at least 4,000 cell/mm^3, platelet count within normal limit, serum bilirubin, SGOT less than 1.5 times of upper normal limit, and calculated creatinine clearance at least 40 ml/min were required.

Patients who had medical illnesses, such as recent myocardial infarction, active angina, unstable heart rhythms, clinically evident congestive heart failure and peptic ulcer, which were not adequately controlled with appropriate therapy were not enrolled. Symptomatic peripheral neuropathy was an exclusion criteria. Pregnant or lactating women were ineligible. No prior malignancy was allowed except for adequately treated basal cell or squamous cell skin cancer, *in situ* cervical cancer, or other cancers for which the patient has been disease free for five years. All patients gave written informed consent in accordance with institutional guidelines.

Treatment

During concomitant chemoradiotherapy, patients received paclitaxel 45 mg/m^2 intravenous infusion in 1-3 hours and carboplatin AUC of 2 intravenously infusion in $^1/_2$ - 3 hours every week for 6 cycles. Adjuvant chemotherapy was started at 4 weeks after completion of concomitant treatment. Patients received paclitaxel 175 mg/m^2 intravenous infusion in 1-3 hours and carboplatin AUC of 6 intravenous infusion in $^1/_2$ -3 hours every 3 weeks for 4 cycles. The conventional premedication were given prior to paclitaxel administration. The area under the concentration-time curve (AUC) was calculated from calculated glomerular filtration rate (GFR).

Radiation therapy was delivered simultaneously on the first day of chemotherapy. The irradiated volume included the primary tumor, the ipsilateral and contralateral hilar and the mediastinum. Radiation therapy was delivered initially to the large volume (45 Gy) followed by a boost to the total tumor dose of 66 Gy. In case of no clinical supraclavicular lymph node involvement, this area was not included in the RT field. If CT scan showed paratracheal lymph nodes, supraclavicular lymph node enlargement or upper lobe lesions, then the supraclavicular areas were included in the radiation therapy port.

Chemotherapy dose was reduced to 50 per cent if there was grade 2 neutropenia and/or grade 2 thrombocytopenia. The treatment was omitted in cases of severe neutropenia or thrombocytopenia. G-CSF was not routinely used. The treatment was definitely discontinued when the treatment was delayed more than 2 weeks or when the patient developed progressive disease or due to any reason at the discretion of the attending physician.

Treatment evaluation

During concomitant therapy, physical examination and toxicity assessment were performed weekly. Complete blood count, platelet count, BUN, creatinine and electrolytes were also determined weekly. After completion of chemoradiotherapy, these assessments were done prior to each adjuvant chemotherapy cycle. Liver function test was determined after completion of concomitant treatment, after completion of adjuvant treatment and when indicated. Chest X-ray was done at the middle period of concomitant therapy and after the completion of adjuvant chemotherapy. CT scan was done to evaluate the lesions at 4 weeks after the completion of concomitant treatment and 4 weeks after the last cycle of adjuvant chemotherapy. Patients who received at least 3 cycles of adjuvant chemotherapy were assessed for response. Patients who completed the treatment protocol or had to discontinue the treatment due to any reasons were followed until disease progression. Then they were monitored until death.

RESULTS

Patient Characteristics

Since March 1998, fifteen patients have been enrolled. They were registered by six institutions. Patient characteristics are listed in Table 1. The median age was 57 years (range, 39 to 70). Thirteen patients were male. The performance status was 0 in 5 (33%) and 1 in 10 (67%). The histology was squamous cell carcinoma in 7 (46%), adenocarcinoma in 6 (40%), large cell carcinoma in 1 (7%) and unclassified cell type in 1 (7%). There were 7 patients (46%) with stage IIIA disease and 8 patients (54%) with stage IIIB disease. For stage IIIA patients, four patients had T3N2 disease, two patients had T3N1 disease and one had T2N2

Table 1. Patient characteristics.

Characteristics	N	%
Sex: Male	13	87
Female	2	13
Cell type:		
Squamous cell carcinoma	7	46
Adenocarcinoma	6	40
Large cell carcinoma	1	7
Unclassified	1	7
Differentiation:		
Well differentiated	3	20
Poorly differentiated	7	46
Undifferentiated	1	7
Unknown	4	27
Staging : IIIA	7	46
IIIB	8	54
Performance status: 0	5	33
1	10	67
Weight loss:		
None	6	40
less than 5%	1	7
5% or more	5	33
Unknown	3	20

Table 2. Response.

Response	After concomitant chemoradiotherapy	After adjuvant chemotherapy
Complete response (CR)	2 (13%)	2 (18%)
Partial response (PR)	9 (60%)	8 (73%)
Stable disease (SD)	3 (20%)	-
Progressive disease (PD)	1 (7%)	1 (9%)
Overall response rate	11 (73%)	10 (91%)

disease. For stage IIIB patients, one patient had T4N3 disease, four patient had T4N2 disease, one had T3N3 disease and two had T2N3 disease. Five patients (33%) had at least 5 per cent weight loss before the study enrollment.

Response to treatment

All patients were assessed for responses and toxicity after completion of concomitant chemoradiotherapy. Variation of concurrent chemotherapy courses was due to radiation schedule of each patient. Response rates are demonstrated in Table 2. Complete response was documented in 2 patients (13%). There were 9 partial responders (60%). Three patients (20%) had minor response or stable disease. The other one (7%) developed progressive disease and treatment was discontinued.

Eleven out of fifteen patients were assessed after completion of treatment protocol because one patient was under treatment with less than 3 cycles of adjuvant chemotherapy, one had to discontinue the treatment due to progressive disease and the other developed a new primary cancer on his tongue. The last patient who achieved complete response after concomitant chemoradiotherapy died from pneumonia and the autopsy revealed Aspergillosis but no residual cancer was detected (pathological complete response). Of the eleven patients who completed the adjuvant therapy, there were 2 complete response (18%) and 8 partial response (73%). The overall response rate increased from 73 per cent after concomitant chemoradiotherapy to 91 per cent after completion of adjuvant chemotherapy. Only one patient who had stable disease after concomitant treatment developed progressive disease after completion of the treatment protocol. The response of each individual patient is demonstrated in Table 3.

Table 3. Response of individual patients.

Patient No.	Response		
	Concurrent chemoradiotherapy	Adjuvant chemotherapy	End result
1	PD	NA[a]	PD
2	PR	PR	PR
3	MR	PR	PR
4	PR	NA[b]	PR
5	CR	NA[c]	CR
6	pCR[1]	NA[d]	pCR
7	PR	pCR[2]	pCR
8	PR	PR	PR
9	PR	PR	PR
10	MR	PR	PR
11	PR	PR	PR
12	PR	PR	PR
13	PR	CR	CR
14	PR	CR	CR
15	SD	PD	PD

* Assessment was performed after at least 3 cycles of adjuvant chemotherapy

a Progressive disease after completion of concurrent chemoradiotherapy

b New primary cancer after concurrent chemoradiotherapy

c Less than 3 cycle of adjuvant chemotherapy administration

d Death from aspergillosis after concurrent chemoradiotherapy

1 Autopsy result

2 Pathological result of surgical specimen after completion of adjuvant chemotherapy

CR = complete response, pCR = pathological complete response,
PR = partial response, MR = minor response,
SD = stable disease, PD = progressive disease,
NA = not assessable

Toxicity

Toxicity was assessed during concomitant chemoradiotherapy and during adjuvant chemotherapy. Toxicities are listed in Table 4. Chemotherapy had to be delayed in 22 courses with a median duration of treatment delay of 6 days.

Esophagitis was a common toxicity especially during concomitant chemoradiotherapy. There were 32 per cent esophagitis which were mostly grade 1-2. Only 1 per cent of the total cycles given resulted in grade 3 esophagitis and there was no grade 4 esophagitis. Grade 3 stomatitis occurred in only one patient who necessitated feeding *via* nasogastric tube. No nutritional support *via* parenteral route was needed.

Myelosuppression was acceptable. Grade 4 neutropenic events were 5 per cent and grade 3 of only 3 per cent. There was no febrile neutropenic

Table 4. Toxicity.

Toxicity	Concomitant chemoradiotherapy (%)	Adjuvant chemotherapy (%)	Overall (%)
Anemia gr.1-2	31	56	38
Anemia gr.3-4	-	6	2
Neutropenia gr.1-2	10	22	13
Neutropenia gr.3-4	-	28	8
Thrombocytopenia gr.1-2	-	3	1
Thrombocytopenia gr.3-4	1	-	1
Esophagitis gr.1-2	36	19	32
Esophagitis gr.3-4	1	-	1
Stomatitis gr.1-2	11	31	17
Stomatitis gr.3-4	-	3	1
Nausea/vomiting gr.1-2	17	25	19
Anorexia gr.1-2	28	78	32
Anorexia gr.3-4	1	-	1
Constipation gr.1-2	17	25	19
Diarrhea gr.1-2	7	9	8
Arthralgia gr.1-2	9	59	23
Myalgia gr.1-2	13	56	24
Paresthesia gr.1-2	32	84	46
Fatigue gr.1-2	34	63	42
Fatigue gr.3-4	-	3	1
Alopecia gr.1-2	17	81	34
Non-neutropenic fever	5	16	8

episode. G-CSF was given prophylactically in 4 per cent. Median absolute neutrophil count (ANC) was 3,390 cells/mm^3. Grade 4 anemia occurred in 2 per cent. No greater than grade 2 anemia was noted in 38 per cent. Median hemoglobin level was 11.7 g/dl. Thrombocytopenia was rarely observed. Only 1 per cent grade 2 and 1 per cent grade 3 thrombocytopenic events occurred. Median platelet count was 253,000 /mm^3.

Gastrointestinal side effect was tolerable. There was 19 per cent grade 1-2 nausea/vomiting, 32 per cent grade 1-2 anorexia, 1 per cent grade 3 anorexia, 19 per cent grade 1-2 constipation and 8 per cent grade 1-2 diarrhea. Grade 1-2 arthralgia occurred in 23 per cent. Grade 1-2 myalgia was observed in 24 per cent. There was 46 per cent grade 1-2 paresthesia. No grade 3-4 arthralgia, myalgia or paresthesia was observed. Fatigue occurred in 42 per cent but only 1 per cent was greater than grade 2. There was 8 per cent non-neutropenic fever.

DISCUSSION

Concomitant chemoradiotherapy offers an alternative strategy for combined therapy because it can provide both local and distant control simultaneously. Chest irradiation effectively palliates many symptoms of intrathoracic NSCLC and induces objective tumor regression about half the time, but is associated with 5-year survival and potential cure in only 5 per cent or fewer patients[18]. Increasing doses of irradiation are associated with higher rates of tumor regression and better local tumor control, but not with improved survival due to occult distant metastases[19]. Distant metastatic cancer is the principal barrier to improve outcome after radiotherapy of locally advanced NSCLC. Arriagada et al[20] treated patients with three monthly cycles of adjuvant chemotherapy after high-dose radiotherapy. Distant metastases occurred less often in the combination-treatment group, although this did not lead to improvement in survival. Schaake-Koning et al[9] reported a randomized trial showing that survival was significantly increased among patients with inoperable, nonmetastatic NSCLC when they were treated with radiotherapy and cisplatin daily compared with radiotherapy alone. The improvement in survival was due to improved control of local disease from the addition of cisplatin to radiotherapy in a concurrent fashion. The West Japan Lung Cancer Group conducted a phase III trial that compared sequential to concurrent chemoradiation using mitomycin, vindesine, and cisplatin (MVP) chemotherapy

among 320 patients with stage III NSCLC and showed a survival advantage with the concurrent arm, with median survival times (MSTs) of 16.5 *versus* 13.3 months, respectively (p = 0.047)[21].

Combined chemoradiation therapy is now considered a standard of care for patients with stage IIIA or IIIB NSCLC who are not candidates for surgical resection. Various agents have been used either sequentially or concurrently in clinical trials of combined chemoradiotherapy for NSCLC. Choy et al[22] assessed concurrent paclitaxel/carboplatin plus thoracic radiation followed by consolidation paclitaxel/carboplatin in patients with stage IIIA/B NSCLC, the survival rates at 24 months was 38.3 per cent with a median overall survival of 20.5 months. Grade 3 or 4 esophagitis was the primary toxicity observed in this trial, with an incidence of 46 per cent and 2 out of 39 patients developed late esophageal toxicity with stricture at 3 and 6 months post treatment. Lau et al[23] are currently evaluating paclitaxel administered twice weekly plus carboplatin and concurrent thoracic radiation in patients with stage IIIA/B NSCLC followed by consolidation paclitaxel / carboplatin to those who respond or have stable disease. The overall response rate was 59 per cent, with 12 per cent complete response (CR) rate which is promising. The results of these trials suggest that paclitaxel doses of 45 mg/m^2/wk plus carboplatin doses of 100 mg/m^2/wk or dosed to a target area under the concentration-timed curve (AUC) of 2 mg/ml•min per week can be combined with thoracic radiation therapy in patients with locally advanced, unresectable NSCLC for the best therapeutic index. In a planned randomized trial to be conducted by RTOG (RTOG 98-01)[24], the cytoprotective effects of amifostine will be evaluated with concurrent paclitaxel / carboplatin and thoracic radiation. An Eastern Cooperative Oncology Group randomized phase III study (E-2597)[25] is comparing standard daily thoracic radiation with hyperfractionated accelerated radiation therapy after induction chemotherapy with paclitaxel and carboplatin[25].

Although there is no single standard combined-modality regimen for the treatment of locally advanced, unresectable NSCLC, the results of these ongoing and planned trials may elucidate the effects that sequencing chemotherapy and thoracic radiation have on response and survival in patients with locally advanced stage III disease. In this study, we incorporated a newer, more active radiation-enhancing chemotherapeutic agent in the management of NSCLC in a concurrent modality setting to determine whether local and distal disease control could further improve.

This preliminary phase II study of paclitaxel, carboplatin and radiation therapy showed an overall response rate of 91 per cent. The low incidence of grade 3 or 4 esophageal toxicity in this study when compared with the report by Choy et al[22] is unexplained and considered to be an almost identical treatment regimen. Six different university-based or teaching-based hospitals participated in this trial. A randomized study will be necessary to fully evaluate the usefulness of these findings. The hope for the immediate future is to define an effective and optimal regimen that can be administered concurrently with radiation therapy and results in improved local and systemic control in patients with regionally advanced NSCLC.

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REFERENCES

1. Mountain CF. A new international staging system of lung cancer. Chest 1986: 225-33.
2. Mountain CF. Prognostic implications of the International Staging System for Lung Cancer. Semin Oncol 1988; 15: 236-45.
3. Roswit B, Patno ME, Rapp R, et al. The survival of patients with inoperable lung cancer: A large-scale randomized study of radiation therapy versus placebo. Radiology 1968; 90: 688-97.
4. Durrant KR, Ellis F, Black JM, et al. Comparison of treatment policies in inoperable bronchial carcinoma. Lancet 1971; 1: 715-9.
5. Johnson DH, Einhorn LH, Bartolucci A, et al. Thoracic radiotherapy does not prolong survival in patients with locally advanced, unresectable non-small cell lung cancer. Ann Intern Med 1990; 113 : 33-8.
6. Cox JD, Azarnia N, Byhardt RW, et al. A randomized phase I/II trial of hyperfractionated radiation therapy with total doses of 60.0 Gy to 79.2 Gy: Possible survival benefit with $\geq$ 69.6 Gy in favorable patients with Radiation Therapy Oncology Group stage III non-small-cell lung carcinoma: Report of Radiation Therapy Oncology Group 83-11. J Clin Oncol 1990; 8: 1543-55.
7. Ihde DC. Chemotherapy combined with chest irradiation for locally advanced non-small cell lung cancer. Ann Intern Med 1991; 115: 737-9.
8. LeChevalier T, Arriagada R, Quoix E, et al. Radiotherapy alone versus combined chemotherapy and radiotherapy in nonresectable non-small cell lung cancer: First analysis of a randomized trial in 353 patients. J Natl Cancer Inst 1991; 83: 417-23.
9. Schaake-Koning C, van den Bogaert W, Dalesio O, et al. Effects of concomitant cisplatin and radiotherapy on inoperable non-small-cell lung cancer. N Engl J Med 1992; 326: 524-30.
10. Sause WT, Scott C, Taylor S, et al. Radiation Therapy Oncology Group (RTOG) 88 - 08 and Eastern Cooperative Oncology Group (ECOG) 4588: Preliminary results of a phase III trial in regionally advanced, unresectable non-small-cell lung cancer. J Natl Cancer Inst 1995; 87: 198-205.
11. Rapp E, Pater JL, Willan A, et al. Chemotherapy can prolong survival in patients with advanced non-small cell lung cancer: Report of a Canadian multi-center randomized trial. J Clin Oncol 1988; 6: 633-41.
12. Chang AY, Kim K, Glick J, et al. Phase II study of Taxol, merbalone and piroxantrone in stage IV non-small cell lung cancer: The Eastern Cooperative Oncology Group results. J Natl Cancer Inst 1993; 85: 388-94.
13. Murphy WK, Fossella F, Winn RJ, et al. Phase II study of taxol in patients with untreated advanced non-small cell lung cancer J Natl Cancer Inst 1997; 85: 384-8.
14. Langer CJ, Leighton JC, Comis RL, et al. Paclitaxel and carboplatin in combination in the treatment of advanced non-small-cell lung cancer: A Phase II toxicity, response, and survival analysis. J Clin Oncol 1995; 13: 1860-70.
15. Tishler RB, Geard R, Hall EJ, et al. Taxol sensitizes human astrocytoma cells to radiation. Cancer Res 1992; 52: 3495-7.
16. Rowinsky EK, Gilbert MR, McGuire WP, et al. Sequences of taxol and cisplatin: A phase I and pharmacologic study. J Clin Oncol 1991; 9: 1692-703.
17. Choy H, Akerley W, Safran H, et al. Paclitaxel plus carboplatin and concurrent radiation therapy for patients with locally advanced non-small cell lung cancer. Semin Oncol 1996; 23 : 117-9.
18. Ihde DC, Minna JD. Non-small cell lung cancer. Part II: Treatment. Curr Probl Cancer 1991; 15: 105-54.
19. Perez CA, Pajak TF, Rubin P, et al. Long-term observations of patterns of failure in patients with unresectable non-oat cell carcinoma of the lung treated with definitive radiotherapy. Reported by the Radiation Therapy Oncology Group. Cancer 1987; 59: 1874-81.
20. Arriagada R, Le Chevalier T, Quoix E, et al. Chemotherapy effect on locally advanced non-small cell lung carcinoma: a randomized study on 353 patients. Int J Radiat Oncol Biol Phys 1990; 19: 195 (abstract).
21. Furuse K, Fukuoka M, Takada H, et al. A randomized phase III study of concurrent versus sequential thoracic radiotherapy in combination with mitomycin, vindesine, and cisplatin in unresectable stage III non-small-cell lung cancer. Proc Am Soc Clin Oncol 1997; 16: 459a, 1 (abstr).
22. Choy H, Akerley W, Safran H, et al. Multiinstitutional Phase II Trials of paclitaxel, carboplatin, and concurrent radiation therapy for locally advanced non-small-cell lung cancer. J Clin Oncol 1998; 16: 3316-22.
23. Lau D, Leigh B, Gandara D, et al. Weekly carboplatin, twice-weekly paclitaxel, and thoracic radiation followed by carboplatin / paclitaxel for stage III non-small cell lung cancer. Semin Oncol 1999; 26 (Suppl 2): 70 (abstr).
24. RTOG-98-01 protocol. Current Clinical Trials Oncology: Phase III randomized study of amifostine mucosal protection in patients with favorable performance inoperable stage II, IIIA, or IIIB non-small cell lung cancer receiving sequential induction and concurrent hyperfractionated radiotherapy with paclitaxel and carboplatin.

25. E-2597 protocol. Current Clinical Trials Oncology: Phase III randomized study of induction paclitaxel and carboplatin followed by standard radiotherapy vs hyperfractionated accelerated radiotherapy for patients with unresectable stage IIIA, or IIIB non-small cell lung cancer.

การรักษามะเร็งปอดชนิดนอน-สมอลล์ เซลล์ ระยะที่สาม A/B ที่ไม่สามารถผ่าตัดได้ ด้วยเคมีบำบัดพร้อมกับรังสีรักษา : รายงานเบื้องต้น

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เป็นการศึกษาถึงประสิทธิภาพและผลข้างเคียงของการรักษาผู้ป่วยโรคมะเร็งปอดชนิด non-small cell ระยะที่ 3 A/B ที่ไม่สามารถผ่าตัดได้ ด้วยเคมีบำบัด Paclitaxel/Carboplatin พร้อมกับรังสีรักษาและตามด้วยเคมีบำบัดสูตรเดียวกัน ผู้ป่วยได้รับ Paclitaxel 45 มิลลิกรัมต่อพื้นที่ผิวหนึ่งตารางเมตร และ Carboplatin คำนวณขนาดโดยใช้พื้นที่ใต้ concentration-time curve (AUC) เท่ากับ 2 ทางเส้นเลือดดำ สัปดาห์ละหนึ่งครั้ง พร้อมกับรังสีรักษาขนาดทั้งหมด 66 Gy หลังจากได้รับรังสีรักษาครบแล้ว ผู้ป่วยจะได้รับ Paclitaxel 175 มิลลิกรัมต่อพื้นที่ผิวหนึ่งตารางเมตร และ Carboplatin AUC เท่ากับ 6 ทางเส้นเลือดดำ ทั้งหมด 4 ครั้ง แต่ละครั้งห่างกัน 3 สัปดาห์ ตั้งแต่เดือนมีนาคม 2541 ผู้วิจัยประเมินประสิทธิภาพและผลข้างเคียงของผู้ป่วยที่ได้รับการรักษาด้วยเคมีบำบัดพร้อมกับรังสีรักษาครบจำนวน 15 ราย และผู้ป่วยที่ได้รับการรักษาด้วยเคมีบำบัดต่อจนครบจำนวน 11 ราย หลังการรักษาด้วยเคมีบำบัดพร้อมกับรังสีรักษาครบ มีการตอบสนองชนิด complete response 2 ราย (13%) และ partial response 9 ราย (60%) หลังการรักษาด้วยเคมีบำบัดต่อจนครบ มีการตอบสนองทั้งหมด 91% (18% CR, 73% PR) มีภาวะ neutropenia ระดับรุนแรง 8% ซึ่งเกิดขึ้นในระหว่างการรักษาด้วยเคมีบำบัดหลังรังสีรักษาครบ สรุปว่า การรักษาผู้ป่วยโรคมะเร็งปอดชนิด non-small cell ระยะที่ 3 A/B ที่ไม่สามารถผ่าตัดได้ ด้วยเคมีบำบัด Paclitaxel/Carboplatin พร้อมกับรังสีรักษา เป็นวิธีการรักษาที่มีประสิทธิภาพ

คำสำคัญ : มะเร็งปอด, นอน-สมอลล์ เซลล์ ที่ผ่าตัดไม่ได้, เคมีบำบัดพร้อมกับรังสีรักษา

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