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The Randomized Study Comparing the Efficacy and Safety of Radio-chemotherapy plus Adjuvant Chemotherapy (CCRT) vs. Neo-adjuvant Chemotherapy plus Radio-chemotherapy (NAC-RT) for Locally Advanced Nasopharyngeal Cancer

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INTRODUCTION

- Nasopharyngeal cancer is sensitive to radiotherapy and chemotherapy[1]. Chemotherapy has been combined with radiotherapy in an attempt to increase local-regional control, decrease distant metastasis, and improve survival of patients with advanced nasopharyngeal carcinoma[2].
- We have developed a randomized trial comparing the efficacy and safety of radio-chemotherapy plus adjuvant chemotherapy (CCRT) versus neo-adjuvant chemotherapy plus radio-chemotherapy (NAC-RT) in locally advanced nasopharyngeal cancer.

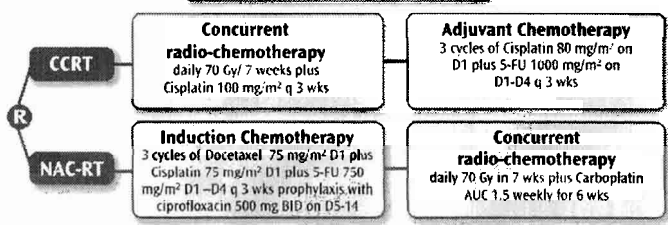
RESEARCH DESIGN AND METHODS

Inclusion criteria: Patient age 16 - 65 years with histologically-proven squamous cell nasopharyngeal carcinoma (WHO type II and III), locally advanced stage and ECOG performance status 0-1. All patients had adequate hematological, renal and hepatic function. Patients who were accessible for study treatment and follow-up schedule and signed study-specific consent form.

Exclusion criteria: Patients who had prior or concomitant malignant tumors (except for curatively treated skin basal cell carcinoma and/or carcinoma in situ of the uterine cervix), history of previous irradiation into the treatment field, evidence of metastatic disease (Bone scan and liver ultrasound show no evidence of metastasis), serious active infection (including HIV+) or other serious underlying medical condition that would impair the ability of the patient to receive protocol treatment. Patients who were pregnant or breast-feeding conditions or sensory hearing loss prior to treatment.

Study Treatment: Patients who met eligible criteria were centrally randomized to two treatment arms, CCRT or NAC-RT, treatment regimens were shown in Figure 1.

Figure 1: Treatment regimens



RESULTS

Between October 2009 to December 2011, a total of 175 patients were enrolled. There were 87 patients randomized to CCRT group while 88 patients were in NAC-RT group. Their baseline characteristics are presented in Table 1.

Table 1: Baseline Characteristics*

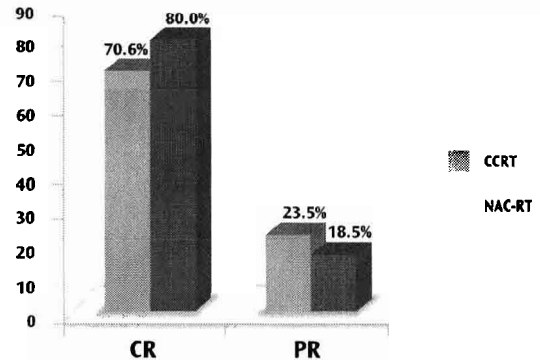
Patient Characteristic	CCRT (N=87)	NAC-RT (N=88)
Age (years)(Mean ± SD)	46.35 ± 10.44	43.14 ± 11.01
Male (%)	59.8	72.7
ECOG 0 (%)	73.6	83.0
Stage (%)		
•II	16.1	12.5
•III	42.5	37.5
•IV	41.4	50.0
Histological grading (%)		
•Undifferentiated	52.9	48.9

*No statistically significant difference, p-value < 0.05

Efficacy

- As of Mar 30th, 2012, 50% of patients (88 of 175) completed treatment, among those, the evaluation showed the number of patients with no evidence of disease was higher in NAC-RT group but no statistically significant (85.2% vs. 76.5%, p-value 0.346).
- The 1-year progression-free survival rate in the CCRT group was 91.8% and was 89.3% in the NAC-RT group (p-value 0.905).

Figure 2: Patients Response at completed treatment period



*Per-Protocol Population; CCRT 34 patients and NAC-RT 54 patients
CR; Complete Response, PR; Partial Response

Safety

- The grade 3 and 4 treatment-related adverse events were **mucositis/stomatitis and nausea/vomiting that were two times higher** in the CCRT group, p-value 0.002 and 0.062, respectively.
- There was no statistically significant difference in hematologic adverse events between groups, details were shown in Table 2.

able 2: Hematologic and Non-hematologic toxicities*

Toxicities	CCRT (N=87)		NAC-RT (N=88)	
	Grade 1-2	Grade 3-4	Grade 1-2	Grade 3-4
Non-hematologic				
•Diarrhea	98.9	1.1	98.9	1.1
•Mucositis/ Stomatitis †	71.3	28.7	89.8	10.2
•Nausea/ Vomiting	79.3	20.7	89.8	10.2
•Allergic reactions	100.0	0.0	100.0	0.0
Hematologic (%)				
•Thrombocytopenia	100.0	0.0	98.9	1.1
•Neutropenia	77.0	23.0	67.0	33.0
•Anemia	97.7	2.3	97.7	2.3
•Leukopenia	77.0	23.0	81.8	18.2

*Intention-To-Treat Population; CCRT 87 patients and NAC-RT 88 patients
†Statistically significant difference, p-value < 0.05

CONCLUSION

Neo-adjuvant chemotherapy with docetaxel plus cisplatin and 5-fluorouracil followed by concurrent radio-chemotherapy was tolerable and provide well control of disease. Complete prospective studies can better establish the efficacy of this treatment regimen to current favored protocols.

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