PILOT STUDY OF CONCURRENT CHEMO-RADIOThERAPY FOR ADVANCED NASOPHARYNGEAL CARCINOMA
(Forum for Nuclear Cooperation in Asia)

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LEAD AGENCY:

FORUM FOR NUCLEAR COOPERATION IN ASIA
PROJECT BRIEF DESCRIPTION

• Non-randomized phase I-II trial.
• Concurrent chemo-radiotherapy
  standard radiotherapy
  weekly chemotherapy.
• chemotherapy may act or give synergistic effect w/ RT by sensitizing tumor cells.
OBJECTIVES:

• GENERAL:
  Evaluate the acute & late toxicity of patients w/ NPC treated w/ standard RT concurrent w/ weekly chemotherapy.

• SPECIFIC:
  Determine the efficacy of the treatment regimen as to response rate, duration of response & time-to-tumor progression or recurrence.
SIGNIFICANCE OF THE STUDY:

• 6th most common cancer among Filipinos.
• With improved RT techniques, local control has also improved.
• With chemotherapy, 3 year survival has improved from 46% to 76%.
• Incidence of distant failure reduced from 35% to 13%.
BRIEF LITERATURE REVIEW:

• NPC is both radio & chemo sensitive.

• RADIOTHERAPY:
  - used as single modality for cure.
  - highly curable in early stage.
  - poor outcome in advance stages.
  - good local control.
BRIEF LITERATURE REVIEW:

CHEMOTHERAPY:
- undefined role.
- taken as experimental.
- adjuvant & neo adjuvant chemo is not conclusive to benefit the patient.
BRIEF LITERATURE REVIEW:

COMBINED CHEMORADIOTHERAPY:
- concurrent chemoradiotherapy improves survival in advance NPC.
- too toxic if given in large amount.
- some chemotherapeutic regimen are too toxic & has unacceptable morbidity.
BRIEF LITERATURE REVIEW:

• Improved survival in cervical cancer is an attractive proposition in NPC.
• Weekly chemotherapy potentially cause continued enhancement of RT effect to tumor cells.
• Easier to increase or adjust in presence of acute complications.
• This regimen is a common practice in cervix cancer management.
BRIEF LITERATURE REVIEW:

Why concurrent chemoradiotherapy?
- acts synergistically with radiation by sensitizing cell to RT.
- chemotherapy synchronizes cells into a more radiation sensitive phase and potentiate the effect of RT.
RESEARCH METHODOLOGY

- Non-randomized phase I/II trial in Asia and Southeast Asian multi-center study:
- Participating countries:
  - Vietnam (2 centers)
  - Malaysia (2 centers)
  - Indonesia
  - Philippines
  - Korea
  - China
  - Thailand
  - Japan
RESEARCH METHODOLOGY

Conduct of study:

This study will be conducted according to Good Clinical Practice guidelines and Declaration of Helsinki.
RESEARCH METHODOLOGY

• Evaluation before treatment:
  • Medical history & PE
  • ENT evaluation
  • Biopsy/histopathology report
  • CXR, CT scan of post-nasal space up to thoracic inlet. (MRI & bone scan optional.)
  • Nutritional & dental assessment
  • Blood chemistries
RESEARCH METHODOLOGY

• Treatment protocol: Concurrent chemoradiotherapy

• RT: Standard fractionation (1.8 to 2 Gy/day for 6.5 to 7.5 weeks).

• Chemotherapy: weekly cisplatinum at 30 mg/m², IV infusion.
RESEARCH METHODOLOGY

- **Prophylactic medications:**
- **Radiotherapy** = dental clearance & oral fluoride prophylaxis.
- **Chemotherapy** = dexamethasone p.o. given 2 days prior to start of chemo, routine hydration and anti-emetics.
RESEARCH METHODOLOGY

Target population:

ONLY THREE PATIENTS IN THE PHILIPPINES
INCLUSION CRITERIA:
Age range (20 - 70 y.o.)
Biopsy proven WHO type 2 or 3, NPC
Stage III, IVA & IVB (TNM 1997)
No distant metastases
No previous history of cancer except stage 0 carcinoma of cervix or basal cell carcinoma.
RESEARCH METHODOLOGY

INCLUSION CRITERIA:

WHO performance status 0-2
WBC > 3,500/L
Platelet count > 100,000/L
Hemoglobin > 10 gm/dL
Crea clearance > 6ml/min
Patients should be accessible to follow-up.
RESEARCH METHODOLOGY

EXCLUSION CRITERIA:

WHO type I NPC
Stage IV C
WHO performance status > 3
History of cancer within 5 years except for skin cancer & CIS of cervix.
Previous RT to head and neck.
RESEARCH METHODOLOGY

EXCLUSION CRITERIA:

– severe concomitant medical illness like uncontrolled diabetes or hypertension.
– Concurrent chemotherapy or investigational therapy.
– pregnancy and/or lactation
– patients who are unlikely to follow-up.
PATIENT ASSESSMENT

During treatment:
- weekly assessment for toxicity.
- toxicity grading according to standard NCICTC/WHO criteria.
- toxicity evaluation shall include the skin, mucosa, nausea, vomiting and weight loss.
Stopping rule:

- WBC < 3,000/mm$^3$
- Platelet count < 75,000/mm$^3$
- Fever > 38 $^\circ$C
- Performance status: 3-4
- Grade 3 nausea
Stopping rule:

When patients develop grade 3-4 non-hematological toxicities (mucositis), chemotherapy or radiotherapy should be interrupted according to institutional policy.
CRITERIA FOR DISCONTINUATION OF TREATMENT

• Progressive disease (PD)
• Very serious acute toxicities:
  - grade 4 non-hematological toxicities.
  - septic shock due to hematologic toxicities.
  - treatment related death.
• denial or withdrawal of the protocol treatment.
CRITERIA FOR DISCONTINUATION OF TREATMENT

• Interruption of radiotherapy more than 3 weeks.
• Cases that are judged to be difficult to continue the protocol treatment by the responsible physician.
PATIENTS’ PROFILE

- 3 patients enrolled in the study.
- Age ranged from 46 – 62 years old.
- All are males.
- Filipino
CASE 1:

• I. C., 46 years old.
• Chief complaint - blurring of vision.
  - bilateral rectus muscle palsy.
• Biopsy of the nasopharyngeal mass:
  - poorly differentiated squamous cell CA.
CASE 1:

- CT scan of the nasopharynx:
  - soft tissue fullness in the left side of nasopharynx with blunting of the torus tobarius.
  - Fossa of Rossenmuller obliterated.
- CT scan of the brain and orbit:
  - negative
CASE 1:

- Metastatic work-up: all are negative.
- Clinical and radiologic diagnosis/staging: poorly differentiated NPCA stage 1VA (T4N1Mx).
CASE 2:

R. F., 62 years old.

Chief complaint - bilateral neck mass.

Biopsy of the right supraclavicular mass:

- large cell undifferentiated CA
- LCA (-), Cytokeratin (+)
CASE 2:

CT Scan of the nasopharynx / neck:
- soft tissue fullness on the right side of nasopharynx extending to the oropharynx with attenuation of ipsilateral parapharyngeal space.
- enlarged lymph nodes both internal jugular, supraclavicular, posterior cervical, submandibular.
CASE 2:

- Metastatic work-up: negative
- Clinical and radiologic staging: undifferentiated NPCA stage 1VB (T2bN3bMx)
CASE 3:

- H.R., 56 year old male
- Chief complaint - bilateral neck mass
  - bilateral rectus muscle palsy
- Biopsy of the neck mass:
  - Undifferentiated CA
  - Cytokeratin( -), LCA ( + )
CASE 3

CT Scan of the Nasopharynx/ Neck/ Head
- Soft tissue fullness obliterating the NP extending to posterior nasal cavity, sphenoid, ethmoid, clivus, prepontine cisterns.
- Enlarged lymph nodes in the internal jugular chain, posterior cervical spaces.
CASE 3:

- Metastatic work-up: negative
- Clinical and radiologic diagnosis: undifferentiated NPCA stage 1VB (T4N3bMx).
RESULTS:

All of the 3 patients completed the prescribe dose of chemoradiotx EXCEPT for the 3rd patient with interruption on the 6th week for 1 week because of grade 3 mucositis.
## TOXICITY INTRA-CHEMORT

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FOLLOW-UP:

CT Scan due for: Case 1 - Dec. 2003
Case 2 - Jan. 2004
Case 3 - Mar. 2004
MARAMING SALAMAT PO!