

BC Cancer Protocol Summary for Combined Chemotherapy (CARBOplatin and Fluorouracil) and Radiation Treatment for Locally Advanced Squamous Cell Carcinoma of the Head and Neck

Protocol Code

HNLACAFRT

Tumour Group

Head and Neck

Contact Physician

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ELIGIBILITY:

- Stage III or IV (T2-4, N1-3, M0) squamous cell carcinoma of the oral cavity or oropharynx including head and neck primary unknown with cervical lymphadenopathy
- ECOG performance status 0, 1, 2
- Weight loss less than or equal to 20% in preceding 3 months if ECOG 0 or 1
- Weight loss less than or equal to 15% in preceding 3 months if ECOG 2
- Suitable for radical irradiation
- Not eligible for concomitant boost irradiation, or expectation that patient unable to attend clinic for boost irradiation
- ENT assessment pretreatment required

EXCLUSIONS:

- Neutropenia, absolute neutrophil count less than $1.5 \times 10^9/L$
- Thrombocytopenia, platelet count less than $100 \times 10^9/L$
- Renal insufficiency with creatinine greater than 120 micromol/L or Creatinine clearance less than or equal to 50 mL/min
- Bilirubin greater than 1.5 x upper limit of normal

RELATIVE CONTRAINDICATIONS:

- Pre-existing motor or sensory neuropathy greater than grade 2

STAGING:

- Chest X-ray, CT scan of the head and neck
- Bone scan is not mandatory except in patients who complain of bone pain or chest pain, or who have an elevated serum calcium or alkaline phosphatase
- Imaging of the abdomen by CT or U/S is not mandatory except in patients who complain of abdominal pain, or who have an elevated AST or ALT
- CT scan of the brain is warranted only in patients who have signs or symptoms to suggest brain metastasis

SUPPORTIVE CARE:

- Prior to initiation of treatment, patients will be referred for consultation to Dentistry and Nutrition Services
- Placement of a feeding gastrostomy tube prior to treatment is encouraged if there has been significant weight loss (ie, greater than 10% from baseline)
- Standard oral hygiene during treatment (sodium bicarbonate mouth rinse, nystatin/fluconazole for fungal infections, antibiotics for documented infections)

TESTS:

- Baseline: CBC & diff, platelets, creatinine, bilirubin, ALT, ALP
- Before each cycle: CBC & diff, platelets, creatinine, bilirubin, ALT, ALP
- 4-8 weeks post-treatment: CT neck, reassessment by ENT

PREMEDICATIONS:

- ondansetron 8 mg PO 30 minutes pre-CARBOplatin
- dexamethasone 8 mg PO 30 minutes pre-CARBOplatin, then 4 mg po 6 to 8 hours post-chemo, then 4 mg po BID x 2 days

Chemotherapy:

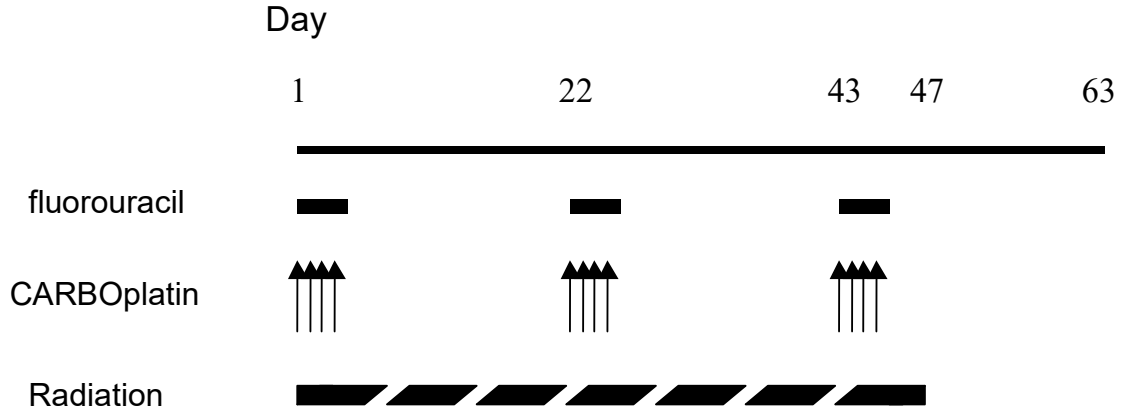
Drug	Dose	BC Cancer Administration Guideline
CARBOplatin	70 mg/m ² /day x 4 days (days 1 to 4)	IV in NS 100 to 250 mL over 30 minutes
fluorouracil	600 mg/m ² /day for 4 days (total dose = 2,400 mg/m ² over 96 h)	IV in D5W to a total volume of 480 mL by continuous infusion at 5 mL/h via appropriate infusor device*

*Inpatients: 600 mg/m² /day in D5W 1,000 mL by continuous infusion daily over 24 h for 4 days

- **Every 21 days for three cycles**
- **Chemotherapy is only to be administered if concurrent with radiation;** if there is a significant delay in delivery of cycle 2, scheduling with radiation may result in omission of the third cycle

Radiation:

- **7,000 cGy in 35 fractions** (treatment daily M- F, no planned interruptions)



DOSE MODIFICATIONS:

1. Hematological:

ANC (x 10⁹/L)		Platelets (x 10⁹/L)	Dose
greater than or equal to 1.5	and	greater than or equal to 100	100%
1.0 to less than 1.5	or	75 to 99	75%
less than 1.0	or	less than 75	Delay one week

2. Renal dysfunction:

Creatinine (micromol/L)	Dose
less than or equal to 120	100%
greater than 120	Delay one week

3. Gastrointestinal:

Grade	Dysphagia or stomatitis	Dose
0 to 2		100%
3	Requiring [initiation of] feeding tube, IV hydration or hyperalimentation	Delay until improvement and proceed at 75% to 100%
4	Complete obstruction (cannot swallow saliva); ulceration with bleeding not induced by minor trauma or abrasion or perforation	Discontinue

Weight loss from baseline	Dose
less than or equal to 10%	100%
greater than 10%	75% if hyperalimentation instituted, otherwise discontinue

4. Skin:

Grade	Palmar-plantar erythrodyesthesia	Dose
0 to 2	No interference with function	100%
3	Skin changes with pain, interfering with function	75%

- 5. Neuropathy:** Dose modification or discontinuation of CARBOplatin and/or fluorouracil may be required (see BC Cancer Drug Manual).
- 6. Hepatic Dysfunction:** Omit fluorouracil if Bilirubin greater than 85 micromol/L unless secondary to biliary obstruction (see BC Cancer Drug Manual).

PRECAUTIONS:

- 1. Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively.
- 2. Palmar-plantar erythrodyesthesia:** May require discontinuation of fluorouracil. Treatment with 50 or 150 mg of pyridoxine daily has been associated with reversal of the syndrome.
- 3. Neurotoxicity:** Both CARBOplatin and fluorouracil are rarely neurotoxic. Both drugs may have to be discontinued if functionally important neuropathy and/or cerebellar dysfunction develops.
- 4. Ototoxicity:** CARBOplatin is mildly ototoxic but its use must be cautioned in individuals with existing hearing loss.
- 5. Mutagen:** Both CARBOplatin and fluorouracil are mutagenic. Women of childbearing age must practice an appropriate form of contraception while being treated.
- 6. Drug Interactions:** The following medications may interact or increase toxicity of Fluorouracil; cimetidine, metronidazole, thiazide diuretics. The following medications may interact or increase toxicity of CARBOplatin; phenytoin, warfarin, aminoglycosides (see BC Cancer Drug Manual).

- 7. Myocardial ischemia and angina occurs rarely in patients receiving fluorouracil or capecitabine.** Development of cardiac symptoms including signs suggestive of ischemia or of cardiac arrhythmia is an indication to discontinue treatment. If there is development of cardiac symptoms patients should have urgent cardiac assessment. Generally re-challenge with either fluorouracil or capecitabine is not recommended as symptoms potentially have a high likelihood of recurrence which can be severe or even fatal. Seeking opinion from cardiologists and oncologists with expert knowledge about fluorouracil or capecitabine toxicity is strongly advised under these circumstances. The toxicity should also be noted in the patient's allergy profile.

RADIATION TREATMENT VOLUME AND DOSE:

A combination of lateral opposed fields, anterior and lateral wedged fields, or several beam-directed fields, will be used for the primary tumour site at the discretion of the radiation oncologist. Total dose to the primary and involved lymph nodes will be 70 Gy in 35 fractions. Efforts should be made to have dose heterogeneity within +/- 5% of prescribed dose in the target volume. There should be a margin of at least 2 cm (GTV to block edge) around the primary tumour and involved nodes. Treatment energy may be cobalt, 4MV, or 6 MV. Spinal cord block should be introduced (usually after 40 Gy) to limit total dosage to spinal cord to less than 45 Gy. CT planning is encouraged (but not mandatory).

A single anterior (A-P) field will be used to treat the neck below the fields for the primary tumour. A midline block (about 2 cm wide) may be used to shield the spinal cord. When there is/are positive node(s) in the lower neck, an additional posterior field (ie. AP / PA fields) may be necessary to deliver a supplemental dose to the positive node(s). If clinically uninvolved posterior neck nodes are treated, they should be treated to a minimum dosage of 44Gy using electrons of appropriate energy after the spinal cord block. If there is a planned neck dissection for nodes greater than 3 cm, then the dose to the lymph node(s) may be limited to 50 Gy.

Oral tongue and floor of mouth

- The fields should include the primary tumour, submandibular and upper jugular nodes.
- Irradiation of the posterior chain is not indicated unless there are clinically involved positive cervical nodes.

Anterior tonsillar pillar, retromolar trigone, and oropharynx

- The ipsilateral posterior cervical nodes must be irradiated if the primary tumour is T3 or T4.
- Both ipsilateral and contralateral posterior cervical nodes may be irradiated if there are clinically positive nodes in the anterior chain.
- Radiation of contralateral lymph nodes should be considered if the primary lesion extends to the base of tongue or palate.

Lower neck

- A single anterior lower neck field will be used to treat the neck and the supraclavicular fossa below the primary fields. For treatment of the clinically uninvolved lower neck and supraclavicular nodes, the dose prescription should be at least 44 Gy in 2 Gy fractions prescribed to 3 cm depth. A midline block may be used to shield spinal cord. Where there is/are positive node(s) in the lower neck, an additional posterior field may be necessary to deliver supplemental dose to the positive node(s).
- The lower border of the field will be just below the clavicle or 1 cm below the clavicle when there are positive nodes in the supraclavicular fossa.
- If a patient has involved supraclavicular lymph nodes, a "mediastinal T field" may be used. The upper mediastinum is included in the low anterior neck field. The lateral limbs of the "T" extend to 1 cm below the clavicle and the central portion of the field extends another 5 cm inferior.

Neck Dissection

- If a neck dissection is planned for lymph nodes greater than 3 cm, then the dose to the lymph node(s) may be limited to 50Gy

PRECAUTIONS:

1. Spinal cord:

Dose to the spinal cord should be kept below 45 Gy.

*** please see Appendix I for information to be included in the Radiation Oncology treatment completion dictation**

Call Drs. Cheryl Ho or Christopher Lee or tumour group delegate at (604) 877-6000 or (604) 930-4064 with any problems or questions regarding this treatment program.

REFERENCES:

Calais G, Alfonsi M, Bardet E, et al. Randomized trial of radiation therapy versus concomitant chemotherapy and radiation therapy for advanced-stage oropharynx carcinoma. J Natl Cancer Inst 1999;91:2081-6.

APPENDIX I: RADIATION TREATMENT COMPLETION DICTATION GUIDELINES

1. Total dose / fractions delivered to primary tumour, involved nodes, and uninvolved nodes. Total elapsed time (in days). Treatment interruption(s)? - if yes, why?

2. Comment on the following according to the RTOG Acute radiation morbidity scoring criteria:

	[0]	[1]	[2]	[3]	[4]
Skin	no change over baseline	follicular, faint or dull erythema / epilation / dry desquamation / decreased sweating	tender or bright erythema, patchy moist desquamation / moderate edema	confluent, moist desquamation other than skin folds, pitting edema	ulceration, hemorrhage, necrosis
Mucous Membrane	no change over baseline	injection / may experience mild pain not requiring analgesic	patchy mucositis which may produce an inflammatory serosanguinous discharge / may experience moderate pain requiring analgesia	confluent fibrinous mucositis / may include severe pain requiring narcotic	ulceration, hemorrhage, necrosis
Salivary Gland	no change over baseline	mild mouth dryness / slightly thickened saliva / may have slightly altered taste such as metallic taste / these changes not reflected in alteration in baseline feeding behaviour, such as increased use of liquids with meals	moderate to complete dryness / thick, sticky saliva / markedly altered taste	-----	acute salivary gland necrosis
Pharynx/ Esophagus	no change over baseline	mild dysphagia or odynophagia / may require topical anesthetic or non-narcotic analgesics/ may require soft diet	moderate dysphagia or odynophagia / may require narcotic analgesics/ may require puree or liquid diet	severe dysphagia or odynophagia with dehydration or weight loss greater than 15% from pre-treatment baseline, requiring feeding tube, iv fluids or hyperalimentation	complete obstruction, ulceration, perforation, fistula
Larynx	no change over baseline	mild or intermittent hoarseness / cough not requiring antitussive / erythema of mucosa	persistent hoarseness but able to vocalize / referred ear pain, sore throat, patchy fibrinous exudate or mild arytenoid edema not requiring narcotic / cough requiring antitussive	whispered speech, throat pain or referred ear pain requiring narcotic / confluent fibrinous exudate, marked arytenoid edema	marked dyspnea, stridor or hemoptysis with tracheostomy or intubation necessary

3. Comment on weight loss according to the Common Toxicity Criteria (CTC):

	[0]	[1]	[2]	[3]	[4]
Weight Loss	less than 5.0%	5.0 - 9.9%	10.0 - 19.9%	greater than or equal to 20%	-----