BC Cancer Protocol Summary for Combined Chemotherapy CISplatin and Radiation Treatment for Locally Advanced Squamous Cell Carcinoma of the Head and Neck

Protocol Code:	*HNLAPRT*
Tumour Group:	*Head and Neck*
Contact Physicians:	*Dr.Cheryl Ho, Medical Oncology* *Dr. Frances Wong, Radiation Oncology (FVCC)* *Dr. Christopher Lee, Medical Oncology (FVCC)*

ELIGIBILITY:

- Stage III-IV squamous cell carcinoma of the of the head and neck including unknown primary
- ECOG performance status 0, 1, 2
- Suitable for radical irradiation
- Patients with nasopharyngeal carcinoma of the head and neck or nasopharyngeal carcinoma of unknown primary who are able to tolerate the standard option of CISplatin 100 mg/m^2 q3wk, may receive HNLAPRT as an option.

EXCLUSIONS:

- Renal insufficiency, creatinine clearance less than 45 mL/min
- Contraindication to CISplatin (i.e marked hearing loss, intolerance to fluid load, neuropathy, inadequate blood counts)

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)

- pilocarpine (SALAGEN®) tablets may be used during radiation (usual dose 5 mg PO tid)
- amifostine should NOT be used until evaluation by the BC Cancer Head and Neck Tumour Group

TESTS:

- Baseline: CBC & diff, platelets, serum creatinine, ALT, alkaline phosphatase, LDH, bilirubin, sodium, potassium, BUN, magnesium, albumin, calcium, phosphate.
- Before each cycle: CBC & diff, platelets, serum creatinine, sodium, potassium, calcium, albumin, magnesium.
- If clinically indicated: bilirubin, phosphate.

PREMEDICATIONS:

- **dexamethasone** 12 mg PO or IV 30 to 60 minutes pre-CISplatin and then 4 mg PO/IV every 12 hours x 6 doses
- **ondansetron** 8 mg PO/IV 30 to 60 minutes pre-CISplatin, then 8 mg PO/IV every 12 hours x 6 doses
- **aprepitant** 125 mg PO 30 to 60 minutes pre-CISplatin on day 1, then 80 mg PO daily on day 2 and 3 **OR netupitant-palonosetron** 300 mg-0.5 mg PO 30 to 60 minutes pre-CISplatin (ondansetron is not given pre- or post- chemotherapy if netupitant-palonosetron is given)
- **lorazepam** 1 mg SL every 4 to 6 hours prn for nausea, sleep or restlessness
- **prochlorperazine** 10 mg PO every 4 to 6 hours prn for nausea
- **diphenhydrAMINE** 25-50 mg PO/IV every 4 to 6 hours prn

TREATMENT:

Chemotherapy:

Drug	Dose	BC Cancer Administration Guideline
CISplatin	100 mg/m^2	IV in NS 1000 mL with mannitol 30 g and potassium chloride 10 mEq over 2 h

- **Every 21 days for up to three cycles**
- **Chemotherapy is only to be administered if concurrent with radiation**

Hydration:

Pre-CISplatin:	D5W-1/2NS 1000 mL with potassium chloride 20 mEq plus magnesium sulphate 2 g over 1 h.
Post-CISplatin:	D5W-1/2NS 1000 mL with potassium chloride 20 mEq plus magnesium sulphate 2 g at 500 mL/h for 2 h.

Alternative hydration for inpatients:

Pre-CISplatin:	D5W-1/2NS 1000 mL with potassium chloride 20 mEq plus magnesium sulphate 2 g IV over 3 h. Prior to beginning **CISplatin**, urine output must be greater than or equal to 300 mL in 3 h. May repeat prehydration x 1000 mL to ensure urine output greater than 300 mL in 3 h. If urine output not adequate after 2000 mL, notify physician.
Post-CISplatin:	D5W-1/2NS with potassium chloride 20 mEq/L plus magnesium sulphate 2 g/L IV at 200 mL/h for 12 h. Measure every 3 h in\output while on IV. If output less than 300 mL during a 3 h period, increase IV to 300 mL/h for 3 h. If urine output still less than 300 mL in a subsequent 3 h period, give **furosemide** 20 mg IV x 1. If output still not adequate, notify physician. May discontinue IV and discharge after post hydration if urine output adequate and patient not vomiting.

Radiation:

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

DOSE MODIFICATIONS:

1. Hematological:

ANC (x 10^9/L)		Platelets (x 10^9/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 less than 100	75%
less than 1.0	or	less than 75	Delay one week

2. **Renal dysfunction:**

Calculated Creatinine clearance (mL/min)	Dose
Greater than or equal to 60	100%
45 to less than 60	80% CISplatin
Less than 45	Hold CISplatin or delay with additional fluids

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%
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%	Consider 75% if hyperalimentation instituted, otherwise discontinue (at physician's discretion)

4. **Neuropathy**: Dose modification or discontinuation of CISplatin may be required (see BC Cancer Cancer Drug Manual).

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Neurotoxicity:** CISplatin may have to be discontinued if functionally important neuropathy develops.
3. **Ototoxicity:** CISplatin is ototoxic and its use must be cautioned in individuals with existing hearing loss.

4. **Mutagen:** CISplatin is mutagenic. Women of childbearing age must practice an appropriate form of contraception while being treated.

RADIATION TREATMENT

For locally advanced head and neck cancer, radiation will be delivered using IMRT technique. Total dose to the planning target volume (PTV) of gross disease will be 70Gy in 35 (once daily) fractions over 7 weeks. Total dose to the planning volume of at risk or subclinical disease (1)will be 56 Gy in 35#. For suspicious disease, e.g. suspicious but not clinically positive nodes, there is the option of treating this planning volume to an intermediate dose of 63 Gy in 35#. For post operative adjuvant radiotherapy of high risk patients (2,3), the planning target volume of post operative at risk regions will be treated to 66Gy in 33 fractions.

For dose heterogeneity, PTV should be covered by 95% of the prescription dose. No more than 1% of any PTV will receive less than 93% of the prescription dose. No volume will receive greater than 115% of the high dose PTV and the mean dose of high dose PTV to be ≤ 105%.

Treatment interruption compensation will be determined at the discretion of the treating radiation oncologist.

Critical organs-at-risk must be contoured on every CT slice in which they appear inside or within 1cm to planning volumes. They are spinal cord, brainstem, optic nerves and optic chiasm. Other structures to be contoured may include, but not limited to, parotid glands, submandibular glands, auditory apparatus, and brachial plexus.

Critical organ at risk dose limits to be considered:

Region of interest	Criterion	Dose limit
Brainstem	Maximum point dose	54 Gy
	Maximum does to 0.1cc	50 Gy
Brainstem + 5mm expansion	Maximum dose to 0.1cc	60 Gy
Spinal cord	Maximum point dose	48 Gy
	Maximum does to 0.1cc	45Gy
Spinal cord + 5mm expansion	Maximum does to 0.1cc	52 Gy
Optic structures	Maximum point dose	45 Gy

Call Dr. Cheryl Ho or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

REFERENCES:

1. Forastiere AA, et al. Phase III trial to preserve the larynx: induction chemotherapy and radiotherapy versus concomitant chemoradiotherapy versus radiotherapy alone, Intergroup Trial R91-11. Proc Am Soc Clin Oncol 2001;20:abstr 4.
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3. Blanchard P, et al. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC):a comprehensive analysis by tumour site. Radiother Oncol 2011;100:33-40.

4. Cooper JS, et al. Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. N Engl J Med 2004;350(19):1937-44.
5. Bernier J, et al. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. N Engl J Med 2004;350:1945-52.
6. Ang K, et al. A phase III trial (RTOG0129) of two radiation-cisplatin regimens for head and neck carcinomas (HNC): impact of radiation and cisplatin intensity on outcome. J Clin Oncol 2010;28(15suppl):abstr 5507.
7. Gregoire V, et. al. Proposal for the delineation of the nodal CTV in the node-positive and post-operative neck. Radiother Oncol 2006;79:15-20.

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 > 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%	-----