

BC Cancer Protocol Summary for Treatment of Advanced Squamous Cell Carcinoma of the Head and Neck Cancer using Fluorouracil and Platinum

Protocol Code: HNAVFUP
Tumour Group: Head and Neck
Contact Physician: Dr. Cheryl Ho

ELIGIBILITY:

- Locoregionally recurrent/metastatic head and neck cancer (squamous cell, sinonasal undifferentiated carcinoma) with ECOG status 0-2
- normal hepatic and renal function
- adequate marrow function
- Intravascular device (e.g. PORT-A-CATH or PICC line) is highly recommended
- If there is a contraindication to CISplatin (e.g. deafness, intolerance to fluid overload, neuropathy), consideration should be given to using CARBOplatin.

TESTS:

- Baseline: CBC & diff, platelets, creatinine, sodium, potassium, serum calcium, serum magnesium, serum albumin, ALT, bilirubin
- Before each treatment: CBC & diff, creatinine
- If indicated: bilirubin

PREMEDICATION:

- For CISplatin use antiemetic protocol for highly emetogenic chemotherapy (see SCNAUSEA)
- For CARBOplatin use antiemetic protocol for moderately emetogenic chemotherapy (see SCNAUSEA)

TREATMENT:

Drug	Dose	BC Cancer Administration Guidelines
CISplatin	25 mg/m ² Daily for 3 to 4 days	IV in 100 to 250 mL NS over 30 min (use 250 mL NS if greater than 60 mg)
fluorouracil	1,000 mg/m ² /day for 4 days (total dose = 4,000 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: 1,000 mg/m²/day in 1,000 mL D5W by continuous infusion daily over 24 h for 4 days

- The cycle is repeated every 4 weeks.

Alternatively, CARBOplatin may be used instead of CISplatin:

DRUG	DOSE	BC Cancer Administration Guidelines
CARBOplatin	AUC 5 or 6 DAY 1 only Dose = AUC [†] x (GFR* + 25)	IV in 100 to 250 mL NS over 30 minutes.

[†] determined at discretion of the attending medical oncologist.

*GFR preferably from nuclear renogram, if not possible use:

$$\text{GFR} = \frac{N \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}} \quad N = 1.04 \text{ (women) or } 1.23 \text{ (men)}$$

The estimated GFR should be capped at 125 mL/min when it is used to calculate the initial CARBOplatin dose. When a nuclear renogram is available, this clearance would take precedence.

DURATION OF THERAPY:

Treatment may continue for a total of 6 cycles or to patient tolerance.

DOSE MODIFICATIONS:

1. Hematological

- Modify fluorouracil ONLY:

ANC (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Dose (fluorouracil only)
1.0 to 1.5	or	75 to 100	750 mg/m ² /d x 4 days
less than 1.0	or	less than 75	375 mg/m ² /d x 4 days

2. Renal Toxicity

- Modify CISplatin dose according to renal function

Creatinine clearance (mL/min)	Dose (CISplatin only)
greater than or equal to 60	100%
45 to 59	50%
less than 45	Hold CISplatin or delay with additional fluids or go to CARBOplatin option.

Calculation of the creatinine clearance rate (estimated using standard formula) should be done every cycle because patients who have lost weight may have normal serum creatinine, but have abnormal estimated creatinine clearance. If estimated creatinine clearance changes to less than 60 mL/min, dose reduction should be considered.

$$\text{Creatinine clearance} = \frac{N^* \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine micromol/L}}$$

* for males N = 1.23, for females N = 1.04

3. Neurotoxicity:

- Tinnitus, mild high frequency hearing loss, and delayed peripheral neuropathy may occur secondary to CISplatin. The latter are generally reversible with time. If clinically significant hearing loss or functionally significant peripheral neuropathy occurs, discontinue CISplatin only.
- CNS toxicity due to fluorouracil is infrequent, but would necessitate cessation of treatment

4. GI Toxicity:

Symptom	Grade	Description	Dose
Nausea and Vomiting	4	greater than 10 episodes in 24 h or needs parenteral support, dehydration	If not controlled by antiemetics, give 75% dose CISplatin, change to CARBOplatin, or stop treatment

G.I. tract toxicity consisting of stomatitis or diarrhea and cramps suggestive of drug toxicity and is indication to stop therapy.

PRECAUTIONS:

1. **Nausea and vomiting** are common and patients should be treated with ondansetron and dexamethasone before and at least every 12 hours regularly during this treatment; netupitant-palonosetron may be substituted for ondansetron (see premedication section).
2. **Renal toxicity** may occur with a salt and water losing nephropathy. Patients should be encouraged to maintain good oral hydration.
3. **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.

4. **Possible drug interactions with fluorouracil and warfarin, phenytoin and fosphenytoin** have been reported and may occur at any time. Close monitoring is recommended (eg, for warfarin, monitor INR weekly during fluorouracil therapy and for 1 month after stopping fluorouracil).

Contact 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. Jacobs, C. et al. Phase III Randomized study comparin cisplatin and fluorouracil as single agents and in combination for advanced squamous cell carcinoma of the head and neck. J Clin Oncol 1992;10(2):257-63.
2. Forastiere, A. et al. Phase III randomized comparison of cisplatin plus fluorouracil and carboplatin plus fluorouracil versus methotrexate in advanced squamous-cell carcinoma of the head and neck: A Southwest Oncology Group Study. J Clin Oncol 1992;10(8):1245-51.