BC Cancer Protocol Summary for Induction Treatment of Locally Advanced Nasopharyngeal Cancer with CISplatin and Gemcitabine

Protocol Code: *HNNLAPG*

Tumour Group: *Head and Neck*

Contact Physician: *Dr. Cheryl Ho*

ELIGIBILITY:
- Locally advanced nasopharyngeal cancer (T3-4, N1-3, M0)
- Disease infiltrating or abutting neurologic structures rendering radiation to radical doses technically difficult
- Suitable for radical radiation
- Adequate hematologic, hepatic and renal function.
- Age greater than or equal to 18 years.
- ECOG performance status 0, 1 or 2.
- Protocol **NOT** to be delivered with concurrent radiotherapy.
- To be followed by HNNLAPRT.

EXCLUSIONS:
- Contraindications to CISplatin (eg. nephropathy, neuropathy, intolerance to fluid load)

TESTS:
- Baseline: CBC & Diff, creatinine, ALT, alkaline phosphatase, albumin, total bilirubin
- If clinically indicated for patients judged to be at risk for hepatitis B baseline: (required, but results do not have to be available to proceed with treatment): HBsAg, HBsAb and HBcoreAb
- Before each treatment:
  - Day 1 – CBC & Diff, creatinine, ALT, total bilirubin.
  - Day 8 – CBC & Diff
- If clinically indicated: HBV viral load

PREMEDICATIONS:
Antiemetic protocol for high moderate emetogenic chemotherapy protocols (see protocol SCNAUSEA).

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
(Administer gemcitabine first)		
gemcitabine	1000 mg/m²/day on Days 1 and 8 (total dose per cycle = 2000 mg/m²)*	IV in 250 mL NS over 30 min
CISplatin	80 mg/m²/day on Day 1	Prehydrate with 1000 mL NS over 1 hour, then CISplatin IV in 500 mL NS with 20 mEq potassium chloride, 1 g magnesium sulfate, 30 g mannitol over 1 hour

*Patients that started treatment on gemcitabine 1250mg/m2/day prior to January 1, 2025 may continue on the same dose for the duration of their treatment

- Repeat every 21 days x 2 to 3 cycles

Warning: The information contained in these documents are a statement of consensus of BC Cancer Agency professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is at your own risk and is subject to BC Cancer Agency's terms of use available at www.bccancer.bc.ca/legal.htm

DOSE MODIFICATIONS:

1. **Hematology**:

For gemcitabine day 1 of each cycle

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
greater than or equal to 1.0	and	greater than or equal to 100	100%
0.5 to less than 1.0	or	75 to less than 100	75%
less than 0.5	or	less than 75	**Delay***
***Platinum also delayed**			

For gemcitabine day 8 of each cycle

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose**
greater than or equal to 1.0	and	greater than or equal to 100	100%
0.5 to less than 1.0	or	75 to less than 100	75%
less than 0.5	or	less than 75	**Omit**
****Dose adjustment only for the day of treatment the CBC is drawn**			

2. **Renal Dysfunction**:

Calculated Cr Clearance (mL/min)	CISplatin dose	gemcitabine dose
greater than or equal to 60	100%	100%
45 to 59	80% CISplatin (same prehydration as 80 mg/m^2 dose)	100%
less than 45	Delay CISplatin with additional IV	75%
less than 30	Omit	Omit

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3. **Other Toxicities**: for gemcitabine only

Grade	Stomatitis	Diarrhea	Dose
1	Painless ulcers, erythema or mild soreness	Increase of 2 to 3 stools/day	100%
2	Painful erythema, edema, or ulcers but can eat	Increase of 4 to 6 stools, or nocturnal stools	Omit until toxicity resolved then resume at 100%
3	Painful erythema, edema, or ulcers and cannot eat	Increase of 7 to 9 stools/day or incontinence, malabsorption	Omit until toxicity resolved then resume at 75%
4	Mucosal necrosis, requires parenteral support	Increase of greater than or equal to 10 stools/day or grossly bloody diarrhea requiring parenteral IV support	Omit until toxicity resolved then resume at 50%

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
2. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare) with gemcitabine. Use caution with pre-existing renal dysfunction.
3. **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.
4. **Hepatitis B Reactivation:** All head and neck cancer patients should be screened for hepatitis B reactivation risk. Patients with a positive result may require antiviral prophylaxis during treatment and for several months after treatment completion, in addition to close monitoring. Management should be reviewed with an appropriate specialist.

Call Dr. Cheryl Ho or tumour group delegate at (604) 930-2098 or 1-800-523-2885 with any problems or questions regarding this treatment program.

References:

1. Yau TK, Lee AW, Wong DH, Yeung RM, et al. Induction chemotherapy with cisplatin and gemcitabine followed by accelerated radiotherapy and concurrent cisplatin in patients with stage IV(A-B) nasopharyngeal carcinoma. Head Neck 2006;28(10):880-7.
2. Zhang Y, Chen L, Hu G et al. Gemcitabine and Cisplatin Induction Chemotherapy in Nasopharyngeal Carcinoma. N Engl J Med. 2019 Sep 19;381(12):1124-1135.

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