BC Cancer Protocol Summary for Treatment of Newly Diagnosed Nasal, Extranodal Natural Killer (NK) or T-cell lymphoma, using Concurrent Radiation and weekly CISplatin followed by Etoposide, Ifosfamide, CISplatin and Dexamethasone

Protocol Code	*LYVIPDRT*
Tumour Group	*Lymphoma*
Contact Physician	*Dr. Kerry Savage*

ELIGIBILITY:
- Newly diagnosed nasal, extranodal NK/T-Cell lymphoma (ENKTL), stage IE to IIE
- Bilirubin less than or equal to 2 x ULN
- ALT less than or equal to 3 X ULN
- ECOG 0-2

EXCLUSIONS:
- Prior or concomitant malignant tumours
- ENKTL with non-nasal sites
- Other subtypes of non-Hodgkin's lymphoma

TESTS:
- Baseline: CBC & diff, platelets, creatinine, sodium, potassium, calcium, albumin, magnesium, bilirubin, ALT, LDH, Hepatitis B serology (HBsAg, anti-HBsAg, anti-HBcore Ab), if not previously done
- Cycle 1 day 1, 8, 15, 22: CBC & diff, platelets, creatinine
- Cycle 2, 3, 4 day 1: CBC & diff, platelets, creatinine
- Cycle 2, 3, 4 days 1 to 3: urine dipstick for blood

PREHYDRATION:
1000 mL NS with potassium chloride 20 mEq and magnesium sulphate 2 g IV over 1 hour prior to CISplatin

ANTIEMETICS:
Antiemetic protocol for highly emetogenic chemotherapy (see SCNAUSEA protocol)

ANTIVIRAL:
If HBsAg or HBcoreAb positive, start lamiVUDine 100 mg PO daily for the duration of chemotherapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive.

TREATMENT:

<u>Cycle 1</u>: Weekly CISplatin with Radiation Therapy

Since CISplatin is a radio-sensitizing agent, it is to be administered on a day when radiation therapy is delivered. If radiation therapy is cancelled, do not give CISplatin that day: postpone until radiation therapy resumes.

Drug	Dose	BC Cancer Administration Guideline
CISplatin	30 mg/m^2	IV in 500 mL NS over 1 hour*

* Concomitant with RT:

Repeat weekly x 4

<u>Cycle 2, 3, 4</u>: etoposide, Ifosfamide, CISplatin, dexamethasone (VIPD)

Drug	Dose	BC Cancer Administration Guideline
etoposide	100 mg/m^2/day x 3 days (days 1 to 3)	IV in 250 to 1000 mL NS over 45 minutes to 1 hour and 30 minutes (use non-DEHP equipment with 0.2 micron in-line filter)
ifosfamide	1200 mg/m^{2}day x 3 days (days 1 to 3)	IV in 500 D51/2NS over 1 hour
mesna	240 mg/m^2 day x 3 days (days 1 to 3)	IV in 100 mL D5W over 15 min
CISplatin	33 mg/m^2 day x 3 days(days 1 to 3)	IV in 500 mL NS with potassium chloride 20 mEq and magnesium sulphate 1 g and mannitol 30 g over 1 hour
dexamethasone	40 mg on days 1 to 4	PO

- Repeat after 21 days for 3 cycles i.e., 2, 3, 4

DOSE MODIFICATIONS:

1. **Hematological:**

Cycle 1 Day 1, 8, 15, 22

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
greater than or equal to 0.8	and	greater than or equal to 80	100%
less than 0.8	or	less than 80	*50% dose reduction*

Table 1. CYCLE 2 to 4, Day 1

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
greater than or equal to 1.5	and	greater than or equal to 75	100% all drugs
less than 1.5	or	less than 75	delay 1 week and repeat CBC

Table 2. Cycles 2 to 4, Day 1

ANC less than 1.5 x10^9/L and/or platelets less than 75 x 10^9/L ***after a one week delay***

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
greater than or equal to 1	or	greater than or equal to 50	100 % CISplatin 75 % ifosfamide, mesna, etoposide
less than 1	or	less than 50	delay 1 week and repeat CBC

Table 3. Cycles 2 to 6, Day 1

ANC less than 1.5 x10^9/L and/or platelets less than 75 x 10^9/L ***after a two week delay***

ANC (x 10^9/L)		Platelets (x 10^9/L)	Dose
greater than or equal to 1	or	greater than or equal to 50	100 % CISplatin 75 % ifosfamide, mesna, etoposide
less than 1	or	less than 50	*discontinue*

2. Renal dysfunction:

Table 1. Cycle 1 to 4

Creatinine Clearance (mL/min)	Dose
Greater than or equal to 40 mL/min	100 %
less than 40 mL/min	delay 1 week and repeat CrCl

Table 2. Cycles 1 to 4

CrCl less than 40 mL/min ***after a one week delay***

Creatinine Clearance (mL/min)	Dose
Greater than or equal to 40 mL/min	100 %
less than 40 mL/min	delay 1 week and repeat CrCl

Table 3. Cycles 1 to 4

CrCl less than 40 mL/min ***after a two week delay***

Creatinine Clearance (mL/min)	Dose
Greater than or equal to 40 mL/min	100 %
less than 40 mL/min	discontinue CISplatin

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
2. **Extravasation**: Etoposide causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Etoposide hypersensitivity**: Monitor infusion of etoposide for the first 15 minutes for signs of hypotension. Refer to BC Cancer SCDRUGRX protocol.
4. **Urotoxicity:** Ifosfamide can cause hemorrhagic cystitis, hematuria and nephrotoxicity. Administration with MESNA and ample hydration is required (also see SCMESNA protocol). Avoid concurrent nephrotoxic drugs.
5. **Venous access**: Ensure good venous access prior to starting ifosfamide so that mesna can be given at completion of ifosfamide.

6. **CNS toxicity:** Ifosfamide can cause encephalopathy (manifest as confusion, lethargy, seizures or coma). Avoid CNS depressant medications. If drowsiness develops while receiving ifosfamide, discontinue all sedating medications and continue ifosfamide. If patient is confused, not arousable or comatose, discontinue ifosfamide. If ifosfamide is the cause of CNS depression, then it should not be given again. If the CNS changes are not due to ifosfamide, then ifosfamide can be re-instituted providing the previous medications contributing to CNS toxicity are not given again with it. If a seizure occurs on ifosfamide, then that cycle should be discontinued. Further cycles may be given if the patient is on anticonvulsants.
7. **Hepatitis B Reactivation:** All lymphoma patients should be tested for both HBsAg and HBcoreAb. If either test is positive, such patients should be treated with lamiVUDine during chemotherapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA at least every two months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with an appropriate specialist with experience managing hepatitis and consideration given to halting chemotherapy.

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

References:

1. Kim, Seok Jun, et al. Phase II Trial of Concurrent Radiation and Weekly Cisplatin Followed by VIPD Chemotherapy in Newly Diagnosed, Stage IE to IIE, Nasal, Extranodal NK/T-Cell Lymphoma: Consortium for Improving Survival of Lymphoma Study. J Clin Oncol 2009;27:6027-6032