BC Cancer Protocol Summary for Consolidation and Salvage Therapy for Nonseminoma Using Etoposide, CISplatin, Ifosfamide, Mesna

Protocol Code	*GUVIP2*
Tumour Group	*Genitourinary*
Contact Physician	*Dr. Christian Kollmannsberger* *Dr. Bernie Eigl*

ELIGIBILITY

Gonadal and Extragonadal Germ Cell Tumors

1. High Risk Presentation (international consensus prognostic [Cambridge] classification: see GUBEP protocol for definition)
   - GUVIP2 may be used as an alternative to GUBEP for contraindications to bleomycin/mediastinal GCT.
2. Evidence of resistance to induction:
   a) Persistent markers
   b) Viable pathology
   c) Relapse post chemo

TESTS

- Repeat abnormal tests every 3 weeks (scans optional)
- Prior to each cycle: CBC and diff, platelets, creatinine, electrolytes panel, magnesium, bilirubin, albumin, hematuria, AFP, beta hCG tumour marker, mental status, random glucose.
- Urine dipstick pre-treatment and once daily during chemotherapy. If positive, notify MD - see supportive care protocol – SCMESNA
- Daily weight, input/output, vital signs every 8 hrs while admitted.
- Repeat CBC, diff, platelets and creatinine on day 5.
- CBC, differential, platelets days 10 and 14

PREMEDICATIONS:

- Antiemetic protocol for highly emetogenic chemotherapy protocols (see SCNAUSEA).
- hydrocortisone and diphenhydrAMINE for history of hypersensitivity to etoposide or etoposide phosphate (ETOPOPHOS)

Activated: N/A Revised: 1 Mar 2023 (Etoposide phosphate added, premedications, dose modifications, precautions and references updated)

TREATMENT:

Cycle length three weeks

Hour	Agents	Days				
		1	2	3	4	5
0 to 1.0	etoposide 75 mg/m² IV in 250 to 500 mL NS over 1 hour (use non-DEHP equipment with 0.2 micron in-line filter)	x	x	x	x	x
1.0 to 1.5	CISplatin 20 mg/m² IV in 100 mL NS over 30 min	x	x	x	x	x
1.5 to 1.75	mesna 300 mg/m² IV in 100 mL D5W over 15 min	x	x	x	x	
2 to 3	ifosfamide 1500 mg/m² IV in 500 mL D5 ½ NS over 1 hour	x	x	x	x	
7	mesna 300 mg/m² IV in 100 mL D5W over 15 min	x	x	x	x	
11	mesna 300 mg/m² IV in 100 mL D5W over 15 min	x	x	x	x	
	OR Mesna 720 mg/m² PO in carbonated beverage at Hour 5 and 9 (ie, 2 and 6 hours after the Ifosfamide)	x	x	x	x	

Hydration at discretion of the oncologist.

SUPPORT MEDICATION:

furosemide 20 mg IV for urine output less than 500 mL over 4 hours

Optional: cotrimoxazole DS 1 PO BID x 10 days to start on Day 10.
OR If allergic, use ciprofloxacin 500 mg PO BID x 10 days to start on day 10.
OR filgrastim (G-CSF) support to avoid dose reductions or delays.

DOSE MODIFICATIONS

Serum creatinine greater than 200 micromol/L:	prehydrate reduce ifosfamide by 25%
Serum creatinine greater than 300 micromol/L:	reduce CISplatin by 25% reduce ifosfamide by 33%
Neutropenic fever:	reduce etoposide or etoposide phosphate (ETOPOPHOS) by 25%

- Delay one week if ANC less than 0.5 x 10^9/L or platelets less than 50 x 10^9/L.
- Filgrastim (G-CSF) may be used for febrile neutropenia. Refer to Pharmacare Guidelines.

Hypersensitivity: etoposide only:

When etoposide cannot be used due to severe hypersensitivity reaction to etoposide, it can be replaced by etoposide phosphate (ETOPOPHOS) as shown, below. Approval from the Health Canada Special Access Program must be obtained for each patient.

Hour	Agent	Days				
		1	2	3	4	5
0 to 1.0	etoposide phosphate (ETOPOPHOS) 75 mg/m²/day IV in 500 mL NS over 1 hour	x	x	x	x	x

PRECAUTIONS

1. **Bleomycin**: may cause severe and life threatening pulmonary toxicity. Limiting the total dose to 270 units should decrease the risk but clinical assessment before each cycle must include a careful survey of respiratory symptoms, chest auscultation, and chest radiograph for pulmonary toxicity. Pulmonary function tests should be repeated in suspect cases. Febrile reaction can be prevented by hydrocortisone premedication. Oxygen may precipitate or aggravate bleomycin pulmonary toxicity. The FI O_2 must not exceed 30-40% unless absolutely necessary. The anesthesiologist must be aware of the bleomycin history before any surgery: an alert bracelet is recommended.
1. **Hypersensitivity**: Monitor infusion of etoposide for the first 15 minutes for signs of hypotension. Hypersensitivity reactions have also been reported for CISplatin. Refer to BC Cancer Hypersensitivity Guidelines. Etoposide phosphate (ETOPOPHOS): Allergic reactions may be less common and severe than etoposide because etoposide phosphate does not contain polysorbate 80. Etoposide phosphate has been safely administered in patients with previous hypersensitivity although rare cross-sensitivity has been reported.
2. **Extravasation**: Etoposide and etoposide phosphate (ETOPOPHOS) cause irritation if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Avoid aminoglycosides.
4. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics.

Contact Dr. Christian Kollmannsberger, Dr. Bernie Eigl or tumour group delegate at (604) 877-2730 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Loehrer PJ, Lauer R, Roth BJ, et al. Salvage therapy in recurrent germ cell cancer: ifosfamide and cisplatin plus either vinblastine or etoposide. Ann Int Med 1988;109:540-6.
2. Siderov J, Prasad P, De Boer R, et al. Safe administration of etoposide phosphate after hypersensitivity reaction to intravenous etoposide. Br J Cancer. 2002 Jan 7;86(1):12-3.
3. Collier K, Schink C, Young AM, et al. Successful treatment with etoposide phosphate in patients with previous etoposide hypersensitivity. J Oncol Pharm Pract. 2008 Mar;14(1):51-5.