

BC Cancer Protocol Summary for Therapy of Ovarian Germ Cell Cancer using Bleomycin, Etoposide, and CISplatin

Protocol Code

GOBEP

Tumour Group

Gynecology

Contact Physician

Dr. Anna Tinker

ELIGIBILITY:

Patients must have:

- Ovarian germ cell cancer, any histology
- Indication for adjuvant treatment, or
- Low, intermediate or high risk prognosis according to the international consensus prognostic classification (based upon the more frequent experience with analogous testicular tumours).

Adjuvant Criteria:

Retroperitoneal lymph node dissection pathology demonstrating involvement estimated to be associated with greater than 50% risk of subsequent relapse: 5 or more nodes involved, any involved node greater than or equal to 2 centimeters in diameter, or involved lymph node with extracapsular extension.

Low Risk:

Ovary/retroperitoneal primary AND no non-pulmonary visceral metastases AND AFP less than 1000 mcg/L or serum beta hCG less than 5000 unit/L or LDH less than 1.5 times normal.

Intermediate Risk:

Ovary/retroperitoneal primary AND no non-pulmonary visceral mets AND Intermediate Markers:

AFP greater than 1000 mcg/L but less than 10,000 mcg/L
Serum beta hCG greater than 5000 unit/L but less than 50,000 unit/L
LDH greater than 1.5 times normal but less than 10 times normal.

High Risk:

Mediastinal primary OR non-pulmonary visceral mets OR AFP greater than 10,000 mcg/L OR serum beta hCG greater than 50,000 unit/L OR LDH greater than 10 times normal.

Note:

- Primary prophylaxis with G-CSF is not mandatory, but may be considered if patient has one or more of the following risk factors:
 - Prior chemotherapy or radiation therapy
 - Persistent neutropenia
 - Recent surgery and/or open wounds
 - Liver dysfunction
 - Renal dysfunction
 - Older than 65 years of age and receiving full chemotherapy dose intensity

EXCLUSIONS:

Patients must not have:

- Stage IA, grade 1 immature teratoma and stage IA pure dysgerminoma
- Inadequate renal function (measured GFR less than 40 mL/minute)
- Inadequate hematologic function
- Chronic pulmonary disease considered a risk factor for bleomycin toxicity
- Recent thoracic irradiation (bleomycin risk)

TESTS:

- Baseline: CBC & Diff, total bilirubin, ALT, alkaline phosphatase, LDH, , creatinine, sodium, potassium, magnesium, calcium, AFP, beta hCG tumour marker, CEA,
- Baseline if clinically indicated: GGT, pulmonary function tests
- consider baseline audiogram for pre-treatment hearing impairment
- Before each cycle: CBC & Diff, creatinine, LDH, AFP, beta hCG tumour marker, magnesium
- Day 5 (not required on Day 5 of first cycle): repeat CBC & Diff if ANC on Day 1 was less than $1.0 \times 10^9/L$
- Repeat creatinine on Day 5 if creatinine on Day 1 was greater than the upper limit of normal
- Day 9 and Day 16 (if patient receiving bleomycin): repeat creatinine
- Day 12 (optional): nadir CBC & Diff

ANTIEMETICS:

- Antiemetic protocol for highly emetogenic chemotherapy protocols. [Extended antiemetic prophylaxis may be considered for patients receiving a 5-day cisplatin regimen](#) (see [SCNAUSEA](#)).

HYDRATION:

- Before CISplatin on Days 1 to 5: 1000 mL NS with 20 mmol potassium chloride and 2 g magnesium sulfate IV over 60 minutes.
- After chemotherapy on Days 1 to 5: 500 mL NS IV over 30 to 60 minutes.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
CISplatin	20 mg/m ² /day x 5 days (Days 1 to 5)	IV in 100 mL NS over 30 minutes
etoposide	100 mg/m ² /day x 5 days (Days 1 to 5)	IV in 250 to 1000 mL NS (non-DEHP bag) over 45 to 90 minutes (use non-DEHP tubing with 0.2 micron in-line filter)
hydrocortisone	100 mg pre-bleomycin	IV in 50 to 100 mL NS over 10 to 15 minutes
bleomycin	30 units on Days 2, 9 and 16, to maximum dose (see Duration, below)	IV in 50 mL NS over 10 minutes

- Repeat every 21 days, regardless of ANC
- Give treatments on 5 consecutive days
- Duration (by Risk Category):
 - Adjuvant: 2 cycles of GOBEP (total bleomycin 180 units) may be substituted for 3 cycles of GOEP
 - Low risk metastatic: 3 cycles of GOBEP (total bleomycin 270 units) may be substituted for 4 cycles of GOEP
 - Intermediate risk metastatic: 3 cycles of GOBEP plus 1 cycle of GOEP (total bleomycin 270 units)
 - High risk metastatic: 4 cycles of GOBEP (total bleomycin 360 units)

DOSE MODIFICATIONS:

- No dose reduction or delay is permitted for counts, except omit Day 5 etoposide if ANC less than $1.0 \times 10^9/L$ on Day 5.
- This program is given with curative intent and any delay or dose reduction may have serious implications. In the event of elevated creatinine (e.g. greater than 200 micromol/L), neutropenic fever or low platelets, phone consultation with a contact physician is recommended.
- **Filgrastim is indicated in patients receiving their second or subsequent cycle of GOBEP who have had an episode of neutropenic fever or who have not recovered their neutrophil count by Day 5.**

PRECAUTIONS:

1. **Bleomycin** may cause severe and life-threatening pulmonary toxicity. Limiting the total dose 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 O₂ 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.

2. **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.
3. **Extravasation:** Etoposide causes irritation if extravasated. Refer to BC Cancer Extravasation Guidelines.
4. **Febrile Neutropenia:** Risk of febrile neutropenia is 10 to 20%. If a patient has additional risk factors outlined in Eligibility Note above, risk of febrile neutropenia may be considered to be greater than 20%; consider prophylactic filgrastim per discretion of the treating physician. Febrile neutropenia can result in serious patient harm, treatment delays, and hospitalization. Fever or other evidence of infection must be assessed promptly and treated aggressively. Avoid aminoglycoside antibiotics.
5. **Renal Toxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics.

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

References:

1. International germ cell consensus collaborative group. International germ cell consensus classification: a prognostic factor-based staging system for metastatic germ cell cancers. *J Clin Oncol* 15:564-603, 1997
2. Einhorn LH, Williams SD, Loehrer PJ, et al. Evaluation of optimal duration of chemotherapy in favorable-prognosis disseminated germ cell tumors: a Southeastern Cancer Study Group protocol. *J Clin Oncol* 1989;7:387-91.
3. Williams SD, Birch R, Einhorn LH, et al. Treatment of disseminated germ-cell tumors with cisplatin, bleomycin, and either vinblastine or etoposide. *N Engl J Med* 1987;316:1435-40.
4. de Wit R, Roberts JT, Wilkinson P, et al. Final analysis demonstrating the equivalence of 3 BEP vs 4 cycles and the 5 day schedule vs 3 days per cycle in good prognosis germ cell cancer. An EORTC/MRC phase III study. *Proc Am Soc Clin Oncol* 2000;19a:326a (abstract 1281).