

BCCA Protocol Summary for Therapy of Non-Dysgerminomatous Ovarian Germ Cell Cancer Using Bleomycin, Etoposide, and Cisplatin

Protocol Code

GOBEP

Tumour Group

Gynecology

Contact Physician

Dr. Ken Swenerton

ELIGIBILITY:

- non-dysgerminomatous ovarian germ cell cancer
- as an adjuvant, or for patients with low, intermediate or high risk 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 hCG less than 5000 unit/L or LDH less than 1.5 x N.

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
- hCG greater than 5000 unit/L but less than 50,000 unit/L
- LDH greater than 1.5 x N but less than 10 x N

High Risk:

Mediastinal primary OR non-pulmonary visceral mets OR AFP greater than 10,000 mcg/L OR hCG greater than 50,000 unit/L OR LDH greater than 10 x N.

EXCLUSIONS:

- Inadequate renal function (measured GFR less than 40 mL/min)
- Inadequate hematologic function
- Chronic pulmonary disease considered a risk factor for bleomycin toxicity.
- Recent thoracic irradiation (bleomycin risk)

TESTS:

- Baseline: CBC and differential, liver enzymes (including LDH), creatinine, electrolytes, magnesium, calcium, AFP, HCG, CEA, pulmonary function tests
- consider baseline audiogram for pre-treatment hearing impairment
- Before each cycle: CBC and differential, creatinine, LDH, AFP, HCG, magnesium
- Day 5 (not required on day 5 of first cycle): repeat CBC if ANC on day 1 was less than $1 \times 10^9/L$; repeat creatinine
- Repeat creatinine on day 5 if creatinine on day 1 greater than the upper limit of normal
- Day 8 or 9 and day 15 or 16 (if patient receiving bleomycin): repeat creatinine
- Day 12 (optional): nadir CBC and differential

ANTIEMETICS:

- Antiemetic protocol for highly emetogenic chemotherapy protocols (see SCNAUSEA)

HYDRATION:

- Before chemotherapy: 1000 mL NS with 20 mEq potassium chloride and 2 g magnesium sulfate IV over 1 hour.
- After chemotherapy: 500 mL NS IV over 0.5 to 1 hour.

TREATMENT:

Drug	Dose	BCCA Administration Guideline
Etoposide	100 mg/m ² /day x 5 days (days 1 to 5)	IV in 500 mL NS (non-PVC bag) over 45 minutes (use non-PVC tubing)
cisplatin	20 mg/m ² /day x 5 days (days 1-5)	in 100 mL NS over 30 minutes
hydrocortisone	100 mg pre-bleomycin	IV in 50 to 100 mL NS over 10 to 15 minutes
bleomycin	30 units on day 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 $1 \times 10^9/L$ 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.

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 BCCA Hypersensitivity Guidelines.
3. **Extravasation:** Etoposide causes irritation if extravasated. Refer to BCCA Extravasation Guidelines.
4. **Neutropenia:** 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. Ken Swenerton or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: 28 Apr 1989 (as GUBEP)

Date last revised: 01 June 2011 (Infusion section revised)

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).