BC Cancer Protocol Summary for Therapy for Moderate Risk Gestational Trophoblastic Cancer using DACTINomycin and Methotrexate

Protocol Code	*GOTDMR*
Tumour Group	*Gynecology*
Contact Physician	*Dr. Anna Tinker*

ELIGIBILITY:

- **Moderate Risk Gestational Trophoblastic Neoplasm (GTN)** as determined using the modified World Health Organization (WHO) Prognostic Scoring System as adapted by the International Federation of Gynecology and Obstetrics (FIGO).
    - Patients with a Risk Score of 5 or 6 are considered moderate risk
    - The risk score is calculated as follows:

Risk Factor	**SCORE**			
	0	**1**	**2**	**4**
Age (years)	<40	>40		
Antecedent pregnancy	Mole	Abortion	Term	
Interval (months)*	<4	4-6	7-12	>12
Pre-treatment serum beta hCG (mIU/mL)**	$<10^3$	10^3-10^4	10^4-10^5	$>10^5$
Sites of metastases	Lung	Spleen and kidney	GI tract	Brain and liver
Number of metastases	-	1-4	5-8	>8
Largest tumour size (including uterus) (cm)		3-4	5	
Prior failed chemotherapy	-	-	Single drug	≥2 drugs

** interval (in months) between end of antecedent pregnancy and start of chemotherapy*
*** use the immediate pre-treatment beta hCG - not the peak hCG during pregnancy or prior to uterine evacuation*

- **<u>Contact BC Cancer for recommendations if more than one year post normal pregnancy and not currently pregnant</u>**

EXCLUSIONS:

- High risk GTN (prognostic score greater than or equal to seven). These patients should be treated on the BC Cancer high risk protocol GOTDEMACO.
- Low risk GTN (prognostic score 0 to 4; or beta hCG ≤10,000 if missing risk score values). These patients should be treated on the BC Cancer low risk protocol GOTDLRA.

TESTS:

- If the GTN was not confirmed histopathologically (e.g. only products of conception were identified at the time of the dilation and curettage) then a pelvic ultrasound within 5-7 days of treatment initiation is required to rule out a previously undetected viable intra-uterine pregnancy.
- **Baseline:** CBC & diff, beta hCG tumour marker, sodium, potassium, creatinine, bilirubin, ALT, alkaline phosphatase, LDH, GGT, chest X-ray, CT of brain (if post normal pregnancy, liver metastasis, or CNS symptoms), CT abdomen/pelvis (if post normal pregnancy or if post molar pregnancy with positive chest X-ray)
- **Before each treatment:** CBC & diff, beta hCG tumour marker, sodium, potassium, creatinine, bilirubin, ALT, alkaline phosphatase, LDH, GGT, albumin
- Check urine pH at least q8h during pre- and post-hydration
- If admission creatinine greater than 100 micromol/L, perform methotrexate level 48 h after start of methotrexate infusion and q AM thereafter; if level greater than 1 x 10^{-7} at 48 h, continue leucovorin until methotrexate levels (repeat q 24h) are less than 1 x 10^{-7}. If creatinine greater than 150 micromol/L, contact BC Cancer.

PREMEDICATIONS:

Antiemetic protocol for moderately emetogenic chemotherapy (see protocol SCNAUSEA).

PREHYDRATION:

- 1000 mL D5W-1/2NS with 20 mEq Potassium chloride and 100 mEq Sodium bicarbonate/L at 200 mL/h IV. When urine output at least 100 mL/h and urine pH greater than 7, start chemotherapy.

TREATMENT:

Drug	**Dose**	**BC Cancer Administration Guideline**
DACTINomycin	0.6 mg/m^2 on days 1 and 2	IV push
methotrexate	100 mg/m^2 on day 1 (***after*** DACTINomycin)	IV push, *or* IV in 100 mL NS over 30 minutes
	300 mg/m^2 on day 1 (***after*** 100 mg/m^2 methotrexate dose)	IV in 500 mL NS over 4 hours
leucovorin	15 mg every 6 hours x 9 doses *(PO route preferred if possible)*	PO or IV Start 24 hours after start of methotrexate infusion

Repeat every 14 days. Treat until beta hCG tumour marker less than 5 mIU/mL, and then additional 2 cycles (e.g. if beta hCG tumour marker is normal at the start of cycle 3, give 4 cycles total)

POST-HYDRATION:

- 1000 mL D5W-1/2NS with 20 mEq Potassium chloride and 100 mEq Sodium bicarbonate/L at 200 mL/h IV for 20 hours after the end of the methotrexate infusion.

DOSE MODIFICATIONS:

1. **Hematological**
   on treatment day:

ANC (x10^9/L)	Platelets (x10^9/L)	DACTINomycin Dose	Methotrexate Dose
greater than 1.0	greater than 100	100%	100%
0.7 to 1.0	75 to 100	80%	100%
less than 0.7	less than 75	Hold until next cycle, then 66%	100%

2. **Renal dysfunction:** Dose modification of methotrexate may be required.

BC Cancer Drug Manual© suggested dose modifications:

Creatinine clearance (mL/min)	Methotrexate dose
61 to 80	75%
51 to 60	70%
10 to 50	30 to 50%
less than 10	avoid

Calculated creatinine clearance = $\frac{1.04 \times (140 - \text{Age}) \times \text{weight (kg)}}{\text{Serum Creatinine in micromol/L}}$

3. **Hepatic dysfunction**:

Bilirubin (micromol/L)	DACTINomycin Dose	Methotrexate Dose
greater than 2 x ULN	60%	75%

If bilirubin less than 2 x ULN:

ALT	DACTINomycin Dose	Methotrexate Dose
greater than 3 x ULN	100%	75%
greater than 5 x ULN	60%	Hold

If bilirubin and/or ALT continue to rise despite dose reduction, contact tumour group designate for recommendations

4. **Third space fluids** (ascites, pleural effusions, very large ovarian cysts): Hold methotrexate until recovery.
5. **Stomatitis:** decrease DACTINomycin to 0.5 mg/m^2

PRECAUTIONS:

1. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Filgrastim (G-CSF) may be needed to maintain white count.
2. **Extravasation**: DACTINomycin causes pain and tissue necrosis if extravasated. Refer to BC Cancer Extravasation Guidelines.
3. **Renal Toxicity**: Nephrotoxicity is possible with high (greater than 1 g/m^2) doses of methotrexate. The risk of renal failure can be minimised by brisk diuresis and alkalinization of the urine with sodium bicarbonate to maintain pH greater than 7.0. Refer to "TESTS" section of this protocol and to BC Cancer Drug Manual. Encourage oral hydration.

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.