BC Cancer Protocol Summary for Therapy for Low Risk Gestational Trophoblastic Cancer using Methotrexate

Protocol Code	*GOTDLRM*
Tumour Group	*Gynecology*
Contact Physician	*Dr. Jenny Ko*

ELIGIBILITY:

Patients must have:

- **Low 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 0 to 4, or beta hCG ≤10,000 (if missing items so cannot calculate risk score) are considered low 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*

- And poor response to DACTINomycin (GOTDLRA):
  - Rising hCG (>10% change) following 2 cycles of treatment
  - hCG level plateau (<10% decrease) for 3 cycles of treatment
- **<u>Contact BC Cancer for recommendations if more than one year post normal pregnancy and not currently pregnant</u>**

EXCLUSIONS:

- Moderate and high risk GTN (prognostic score greater than 4). These patients should be treated on the BC Cancer moderate risk protocol GOTDMR (risk score of 5 or 6) and high risk protocol GOTDEMACO (risk score ≥7), respectively.
- Patients with poor initial hCG response to GOTDLRA, a rapid rising hCG after 1 cycle, or hCG increase to greater than 300 should be treated with GOTDEMACO.

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 & differential, beta hCG tumour marker, creatinine, sodium, potassium, bilirubin, ALT, alk phos, LDH, GGT, pelvic ultrasound, chest X-ray, CT brain (if post normal pregnancy, liver mets, or CNS symptoms), CT abdo/pelvis (if post normal pregnancy or if post molar pregnancy with positive chest X-ray)
- **Before each cycle:** CBC & differential, beta hCG tumour marker, creatinine, bilirubin, ALT. Optional: albumin, chest X-ray

PREMEDICATIONS:

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

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
methotrexate	Standard regimen: 50 mg on Days 1, 3, 5 and 7 OR Alternative regimen (if treatment must be interrupted by weekends)†: 50 mg on Days 1, 3, 5 and 8	IM*
leucovorin	Standard regimen: 15 mg on Days 2, 4, 6 and 8 OR Alternative regimen (if treatment must be interrupted by weekends): 15 mg on Days 2, 4, 6 and 9	PO, 30 hours after each methotrexate dose

† If treatment is given on Day 8 (alternative regimen), it is recommended that treatments on Days 1, 3 and 5 are given late in the afternoon, and Day 8 treatment given in early morning.

* IM route is preferred. Alternatively, may give IV if IM is not possible:

Drug	Dose	BC Cancer Administration Guideline
methotrexate	0.4 mg/kg/day on Days 1 to 5‡ (maximum 25 mg/day)	IV push

‡ Note: dosing schedule is different and leucovorin is not required.

Repeat every 14 days. Treat until beta hCG tumour marker less than 5 mIU/mL, and then additional 3 cycles (e.g. if beta hCG tumour marker is normal at the start of cycle 3, give 6 cycles total).

DOSE MODIFICATIONS:

1. Hematological

ANC (x10^9/L)		Platelets (x10^9/L)	Dose
greater than or equal to 1.0	and	greater than or equal to 100	100%
less than 1.0	or	less than 100	Delay

If further dose reduction is required, use 70% of starting dose

2. Renal dysfunction:

Creatinine clearance (mL/min)	Dose
greater than 30	100%
15 to 30	50 %
Less than 15	Avoid

3. Hepatic dysfunction:

Bilirubin (micromol/L)		ALT	Dose
greater than 2 x ULN	or	greater than 3 x ULN	75%

ULN = upper limit of normal

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 until recovery

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.

Call Dr. Jenny Ko or tumour group delegate at (604) 851-4710 or 1-877-547-3777 with any problems or questions regarding this treatment program.

References:

1. Sita-Lumsden A, Short D, Lindsay I, et al. Treatment outcomes for 618 women with gestational trophoblastic tumours following a molar pregnancy at the Charing Cross Hospital, 2000-2009. Br J Cancer 2012;107:1810-1814.
2. Braga A, de Souza Hartung Araujo C, Mora PAR, et al. Comparison of treatment for low-risk GTN with standard 8-day MTX/FA regimen versus modified MTX/FA regimen without chemotherapy on the weekend. Gynecol Oncol 2020;156(3):598-605.
3. Kanno T, Matsui H, Akizawa Y, Usui H, Shozu M. Treatment results of the second-line chemotherapy regimen for patients with low-risk gestational trophoblastic neoplasia treated with 5-day methotrexate and 5-day etoposide. J Gynecol Oncol 2018;29(6):e89.
4. Lawrie TA, Alazzam M, Tidy J, Hancock BW, Osborne R. First-line chemotherapy in low-risk gestational trophoblastic neoplasia. Cochrane Database Syst Rev. 2016 Jun 9;2016(6):CD007102.