BC Cancer Protocol Summary for Treatment of Metastatic Adrenocortical Cancer with Etoposide, DOXOrubicin, CISplatin and Mitotane

Protocol Code:	*GUEDPM*
Tumour Group:	*Genitourinary*
Contact Physician:	*Dr. Kim Chi*

ELIGIBILITY:

- Treatment of metastatic adrenocortical cancer or selected patients with high risk disease post-resection. Because of the rarity of these cancers, discussion at the GU Conference is recommended.
- ECOG performance status 0-2.

TESTS:

- Baseline: CBC & diff, platelet, sodium, potassium, creatinine, calcium, magnesium, random glucose, phosphate, ALT, GGT, alk phos, bilirubin, albumin, 24 hour urinary cortisol or serum cortisol.
- Before each cycle: CBC & diff, platelet, sodium, potassium, creatinine, calcium, magnesium, ALT, alk phos, bilirubin, random glucose.
- DHEAS **or** 24 hour urinary cortisol or serum cortisol, if appropriate for patients with functioning tumours, to be measured after on stable tolerated dose for four weeks, then every 3-4 months along with other tumour measures and imaging.

PREMEDICATIONS:

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

TREATMENT:

Drug	Dose	BC Cancer Administration Guidelines
DOXOrubicin	40 mg/m² on **Day 1**	IV push
etoposide	100 mg/m²/day on **Days 1, 2 and 3**	IV in 250 to 1000 mL NS over 45 min to 1 hour 30 min (use non-DEHP equipment with 0.2 micron in-line filter)
CISplatin	40 mg/m²/day on **Days 1 and 2**	IV in 100 to 250 mL* NS over 30 minutes
***If CISplatin dose less than or equal to 60 mg use 100 mL NS, if CISplatin dose greater than 60 mg use 250 mL NS**		

Repeat every 28 days for 4-6 cycles

Drug	Dose	BC Cancer Administration Guidelines
mitotane	Starting dose is 2 grams daily in 4 divided doses; then escalate by 1 gram per day once every 1 to 2 weeks to maximum tolerated dose. Usual dose limiting toxicity is anorexia and nausea.	PO
cortisone acetate	25 mg every morning and 12.5 mg every evening. Omit if patient has increased levels of serum cortisol.	PO
fludrocortisone acetate	0.1 mg every morning. Omit if patient has increased levels of serum cortisol.	PO

- Continue treatment as long as there is a clinical benefit and no excessive toxicity

DOSE MODIFICATIONS:

1. **Hematological: for etoposide and DOXOrubicin**

ANC (X 10^9/L)		Platelets (x 10^9/L)	Dose (all drugs)
greater than or equal to 1.5	and	greater than or equal to 100	100%
1 to 1.49	or	75 to 99	75%
less than 1	or	less than 75	**Delay**

2. **Hepatic dysfunction:** for etoposide

Bilirubin (micromol/L)	Dose	
less than 25	100%	100 mg/m^2/day x 3 days
25 to 50	50%	50 mg/m^2/day x 3 days
51 to 85	25%	25 mg/m^2/day x 3 days
greater than 85	**Delay**	

Dose modification required for DOXOrubicin. Refer to BC Cancer Drug Manual.

3. **sRenal dysfunction:** for CISplatin

Serum Creatinine (micromol/L)	Dose	
less than 135	100%	40 mg/m^2/day x 2 days
135 to 185	60%	24 mg/m^2/day x 2 days
greater than 185	**Delay**	

PRECAUTIONS:

1. **Hypoadrenalism**: Mitotane will cause potentially permanent **hypoadrenalism**. Patients must take cortisone acetate and fludrocortisone acetate as above and continue them even after mitotane is discontinued. In the event of physiologic stress, glucocorticoid supplementation should be given. Occasional patients will require lifelong replacement even after mitotane is stopped, so it should not be discontinued without evaluation for adequate adrenal function. Patients with functioning tumours produce excessive cortisol. Replacement with gluco- and mineralocorticoid should not be started until cortisol levels have been documented to fall to normal or below.

2. **Cardiac Toxicity**: DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction. Cardiac assessment recommended if lifelong dose of 450 mg/m^2 to be exceeded. Refer to BC Cancer Drug Manual.
3. **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.
4. **Extravasation**: DOXOrubicin causes pain and tissue necrosis if extravasated. Etoposide causes irritation if extravasated. Refer to BC Cancer Extravasation Guidelines.
5. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BC Cancer Febrile Neutropenia Guidelines.
6. **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Strongly encourage oral hydration. If oral hydration is not possible (e.g. excessive nausea), IV hydration is indicated. Avoid nephrotoxic drugs such as aminoglycoside antibiotics.

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

References:

1. Fassnacht, M, Terzolo M, Allolio, B, et al. Combination chemotherapy in advanced adrenocortical carcinoma. N Engl J Med 2012;366:2189-97.