LONDON CANCER ALLIANCE
West and South

Skin Pathway Group – CVD (Cisplatin, Vinblastine, Dacarbazine) in Melanoma

Indication:	Advanced, unresectable melanoma			
Regimen details:	Vinblastine	2.5mg/m^2	IV	Day 1 to Day 3 (inclusive)
	Dacarbazine	250 mg/m^2	IV	Day 1 to Day 3 (inclusive)
	Cisplatin	30mg/m^2	IV	Day 1 to Day 3 (inclusive)

Administration: Suggested hydration schedule (for days 1 to 3):

Furosemide 40mg PO
Vinblastine in 50 ml Sodium Chloride 0.9% over 5-10 minutes
Dacarbazine in 500ml Sodium Chloride 0.9% over 60 min (see notes)
Cisplatin in 1 litre Sodium Chloride 0.9% IV over 60 min
1 litre Sodium Chloride 0.9% + 20 mmol KCl + 1g MgSO4 IV over 60 minutes

Then **either** 500ml Sodium Chloride 0.9% IV over 60 minutes **or** 500ml drinking water

Aluminium containing equipment should not be used during preparation and administration of cisplatin.

Anaphylactic-like reactions to cisplatin have been reported. Facial oedema, bronchoconstriction, tachycardia, and hypotension may occur within minutes of administration. Adrenaline, corticosteroids, and antihistamines have been effectively employed to alleviate symptoms.

Dacarbazine infusion rate can be decreased and volume can be increased to avoid venous pain during infusion.
Dacarbazine is light-sensitive. It is likely that pain during the infusion may be caused by degradation products on exposure to light. Use light protective giving set or cover the line with aluminium foil,

Version: 1.0 Supersedes: all other versions	Approved by LCA Skin Pathway Chemotherapy Lead: Mark Harries
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Ravi Shaunak	Approved by LCA Medicines & Chemotherapy Steering Group Chair:
Second check by: Sanna Eestila	Date prepared: January 2015 Review Date: January 2017

	protect the infusion bag from light. Solution turns pink on exposure to light.
Frequency:	3 weekly cycle, maximum 6 cycles
Pre-medication:	Not routinely required
Anti- emetics:	Very High emetogenicity Follow Local Anti-emetic Policy
Supportive medication:	Not routinely required
Extravasation:	Vesicant Vinblastine and Dacarbazine should be administered with appropriate precautions to prevent extravasation. If there is any possibility that extravasation has occurred, contact a senior member of the medical team and follow local protocol for dealing with cytotoxic extravasation Cisplatin is not a vesicant
Regular investigation:	Prior to Cycle 1: FBC Day 1 (within 14 days) LFTs Day 1 (within 14 days) U&Es Day 1 (within 14 days) Audiometric testing if clinically indicated Prior to Day 1 (cycle 2 onwards): FBC Day 1 (within 72 hours) LFTs Day 1 (within 72 hours) U&Es Day 1 (within 72 hours)
Toxicities:	Total alopecia, thrombocytopenia, GI symptoms, anorexia, mucositis, cardiovascular, hypotension, infertility, ototoxicity, neurotoxicity, CNS symptoms with Dacarbazine, hepato-toxicity (dacarbazine)

DOSE MODIFICATIONS

Haematological Toxicity

Neutrophils (x 10^9/L)		Platelets x (x 10^9/L)	Dose
≥ 1.0	**&**	≥ 100	Give 100 % dose
< 1.0	**or**	< 100	Delay for 1 week. Repeat FBC, if recovered to above these levels, give 100% dose.

If low counts persists after delay of 1 week, reduce all doses by 25%. Maintain 25% dose reduction for subsequent cycles.

Non-haematological Toxicities

Renal Impairment

Creatinine Clearance (ml/min)	Cisplatin Dose	Dacarbazine Dose
> 60	100%	100%
45-59	75%	80%
30-45	Omit cisplatin, consider carboplatin	75%
<30	Omit cisplatin, consider carboplatin	70%

Cisplatin-induced nephrotoxicity is dose-related and cumulative. It manifests early by elevations in blood urea, creatinine, and wasting of potassium and magnesium. Renal toxicity may be irreversible and is more prolonged and severe with repeated courses

Hepatic Impairment

Cisplatin — No dose adjustment is necessary in liver impairment

Dacarbazine — Activated and metabolised by the liver, can be hepatotoxic- consider dose reductions

Bilirubin (micromol/L)		AST / ALT (units/L)	Vinblastine Dose
26-51	**or**	60-180	50% dose
>51	**&**	within reference range	50% dose
>51	**&**	> 180	Omit

Location of regimen: delivery — Day case setting

Version: 1.0 Supersedes: all other versions	Approved by LCA Skin Pathway Chemotherapy Lead: Mark Harries
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Ravi Shaunak	Approved by LCA Medicines & Chemotherapy Steering Group Chair:
Second check by: Sanna Eestila	Date prepared: January 2015 Review Date: January 2017

Drug interactions:

Anti-epileptics: Cisplatin and Dacarbazine - reduced absorption of phenytoin
Nephrotoxic drugs: additive nephrotoxic effect with Cisplatin
Erythromycin : Vinblastine toxicity may be increased
Dacarbazine is metabolised by cytochrome P450, therefore the co-administration of other drugs which are metabolised by the same hepatic enzymes can present a theoretical interaction

References:

www.medicines.org.uk,
Summerhayes M et al. Practical Chemotherapy a multidisciplinary guide 2003 Radcliffe Medical Press.
Eton et al. (2002) Journal of Clinical Oncology 20;8:2045-2052.
Bajetta et al. (2006) Annals of Oncology 17:571-577.

Version: 1.0 Supersedes: all other versions	Approved by LCA Skin Pathway Chemotherapy Lead: Mark Harries
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Ravi Shaunak	Approved by LCA Medicines & Chemotherapy Steering Group Chair:
Second check by: Sanna Eestila	Date prepared: January 2015 Review Date: January 2017