LONDON CANCER ALLIANCE West and South

Skin Pathway Group – Carboplatin Etoposide (IV) in Merkel Cell Carcinoma

Indication:	Adjuvant and palliative treatment of high risk, unresectable or stage IV disease			
Regimen details:	Carboplatin	AUC 5 (see comments)	IV	Day 1
	Etoposide	100 - 120 mg/m^2	IV	Day 1 to Day 3
Administration:	Carboplatin in 500ml Glucose 5% IV over 60 minutes Etoposide in Sodium Chloride 0.9% IV over 60 min (See comments for volume) Aluminium-containing equipment should not be used during preparation and administration of Carboplatin Monitor Etoposide infusion for the first 15 minutes for signs of hypotension.			
Frequency:	Day 1 to Day 3, every 21 days, for 4 cycles			
Pre-medication:	Not routinely required			
Anti- emetics:	Day 1	Moderate emetogenicity		
	Days 2 and 3	Low emetogenicity		
	Follow Local Anti-emetic Policy			
Supportive medication:	Not applicable			
Extravasation:	Non-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)		

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

EDTA
Baseline Imaging

Prior to Cycle 2 onwards:

FBC	Day 1 (within 72 hours)
LFTs	Day 1 (within 72 hours)
U&Es	Day 1 (within 72 hours)

Toxicities: Nausea and vomiting, myelosupression - risk of sepsis and thrombocytopenia, constipation and/or diarrhoea, hypotension, moderate alopecia, peripheral neuropathy, neurotoxicity (ototoxicity) , nephrotoxicity, stomatitis, dysgeusia, fatigue, ovarian failure/infertility

Anaphylactic reactions have been reported following Etoposide administration.

Adequate contraceptive methods should be used during therapy

DOSE MODIFICATIONS

Haematological Toxicity

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Carboplatin Dose	Etoposide Dose
≥ 1.5	**&**	≥100	100%	100%
< 1.5	**or**	< 100	Delay*	Delay*

*Delay therapy for 1 week.
Reduce doses for subsequent cycles if febrile neutropenia occurs.

Non-haematological Toxicities

Renal Impairment Carboplatin Contra-indicated if GFR < 20ml/min

Creatinine Clearance (ml/min)	Etoposide Dose
> 50	100% dose
15 – 50	75% dose
<15	50% dose
Subsequent doses based on clinical response	

Hepatic Impairment Carboplatin No dose modifications for hepatic impairment

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Bilirubin (micromol/L)		AST (units/L)	Etoposide Dose
26-51	**or**	60-180	50% dose
>51	**or**	>180	Clinical decision

Location of regimen delivery: Day case setting

Comments: Etoposide infusion should have maximum concentration of 0.2 - 0.4 mg/ml. (PVC free)

Carboplatin dose should be calculated using the Calvert formula:
Dose = Target AUC x (25 + GFR)
GFR should be calculated using the Cockcroft & Gault equation in all patients; if the calculated GFR < 60 or >120ml/min measure EDTA clearance or creatinine clearance before prescribing. EDTA calculation will lead to higher doses than Cockroft & Gault equation, so dose adjustment may be required. Monitor trends in serum creatinine between treatments: if >25% from baseline value re-calculate GFR using the Cockcroft & Gault equation.

Drug interactions: Aminoglycoside antibiotics-increased risk of ototoxicity (with Carboplatin)
Cyclosporin (high doses) increase Etoposide plasma levels/ toxicity.
Glucosamine- possible reduced Etoposide effectiveness
Grapefruit juice- reduced Etoposide plasma levels
Monitor INR levels carefully if on concomitant warfarin
Nephrotoxic drugs (with Carboplatin)
Phenytoin, carbamazepine – Carboplatin decreases efficiency
St John's Wort- possible reduced Etoposide effectiveness

References:
M.Poulsen et al.(2003) Journal of Clinical Oncology 21(23):4371-4376

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