

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

Indication: Palliative treatment of Metastatic unresectable and stage IV Merkel Cell carcinoma
Eligible for patients able to tolerate and comply with oral dosage forms

Regimen details:

| | | | |
|-------------|-----------------------------|--------|-----------------|
| Carboplatin | AUC 5 (see comments) | IV | Day 1 |
| Etoposide | 100 - 120 mg/m ² | IV | Day 1 |
| Etoposide | 200mg/m ² | Orally | Day 2 and Day 3 |

(Reduced doses or single agent Carboplatin to be considered in elderly patients, or in patients with poor PS)

Daily dose of etoposide capsules can be divided in two if necessary (i.e. 100mg/m² BD orally Day 2 and 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)
Monitor Etoposide infusion for the first 15 minutes for signs of hypotension
Etoposide Oral: Capsules to be swallowed whole on an empty stomach half an hour before or 2 hours after a meal.
Available as 50mg and 100mg capsules.

Aluminium-containing equipment should not be used during preparation and administration of Carboplatin

Frequency: Day 1 to Day 3, every 21 days, for 4 cycles

Pre-medication: Not routinely required

Anti- emetics: Day 1 Moderate emetogenicity

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| 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 |
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Days 2 and 3 Low emetogenicity

Supportive medication: Not applicable

Extravasation: Non-vesicant

Regular investigations: Prior to Cycle 1:
 FBC Day 1 (within 14 days)
 LFTs Day 1 (within 14 days)
 U&Es Day 1 (within 14 days)
 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, myelosuppression- risk of sepsis and thrombocytopenia, constipation and/or diarrhoea, hypotension, moderate alopecia, peripheral neuropathy (low), neurotoxicity (ototoxicity-low) , 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

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| 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

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

Location of regimen: Day-case setting. Oral etoposide to be supplied to the patient for self-administration

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: www.medicines.org.uk

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