

Lung Pathway Group – Docetaxel & Carboplatin in Non-Small Cell Lung Cancer (NSCLC)

Indication:	First line palliative therapy for previously untreated Stage IIIB or IV NSCLC patients			
Regimen details:	Docetaxel	75 mg/m ²	IV	Day 1
	Carboplatin	AUC 5 (EDTA)	IV	Day 1
Administration:	Docetaxel in 250ml or 500ml Sodium Chloride 0.9% depending on final concentration IV over 1 hour Carboplatin in 500ml Glucose 5% IV over 30 to 60 minutes			
	Aluminium containing equipment should not be used during preparation and administration of carboplatin			
	Hypersensitivity reactions may occur, such as flushing, rash with or without pruritus, chest tightness, back pain, dyspnoea and fever or chills, usually during the first and second infusions and within a few minutes following the start of the infusion; the infusion should be slowed down or interrupted and the necessary supportive medication should be administered. Severe reactions such as hypotension and/or bronchospasm or generalised rash/erythema requires immediate discontinuation. Availability of resuscitation equipment must be ensured as a standard precaution.			
Frequency:	Day 1, every 21 days, for 4 to 6 cycles			
Pre-medication:	Oral dexamethasone 8mg BD for 3 days, starting the day before docetaxel administration to reduce the incidence and severity of fluid retention and hypersensitivity reactions. If the patient has not taken the oral premedication, clinicians may prescribe dexamethasone IV 20mg, chlorphenamine IV 10mg and ranitidine IV 50mg to be administered 1 hour prior to chemotherapy.			

Version: 1.0 Supersedes: all other versions	Approved by LCA Lung Pathway Chemotherapy Lead: Dr Rohit Lal	
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl	
Prepared by: Lisa Yuen	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson	
Second check by: Laura Cameron	Date prepared: November 2014	Review Date: November 2016
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(note: there is no data available to support the use of IV steroids in this setting, responsibility remains with the prescribing clinician).

Paracetamol / Chlorphenamine / Hydrocortisone can be given for administration-related reactions such as chills / fever.

Anti- emetics: Moderate emetogenicity
Follow Local Anti-emetic Policy

Supportive medication: Mouthcare as per local policy

Extravasation: Docetaxel - Vesicant
Carboplatin – non-vesicant
Docetaxel 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

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	See Comments
CT scan	Baseline

Comments:

Carboplatin dose should be calculated using the Calvert formula: $\text{Dose} = \text{Target AUC} \times (25 + \text{GFR})$. GFR should be calculated using EDTA clearance before prescribing. (If EDTA not available prior to cycle 1, initiate treatment using the Cockcroft & Gault formula to calculate GFR, and ensure EDTA prior to cycle 2).

Monitor trends in serum creatinine between treatments, if >25% from baseline value re-calculate GFR using the Cockcroft & Gault formula or EDTA.

Prior to Day 1 (all cycles)	
FBC	Day 1 (within 72 hours)
LFTs	Day 1 (within 72 hours)
U&Es	Day 1 (within 72 hours)
Imaging	After 3 cycles

Toxicities: Myelosuppression, anaemia, nausea, vomiting, diarrhoea, stomatitis, asthenia, peripheral neuropathy, hypersensitivity reactions, fluid retention, cutaneous reactions, alopecia, nail disorder, cystoid macular oedema, arthralgia, myalgia, ovarian failure, infertility.

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DOSE MODIFICATIONS**Haematological Toxicity**

Neutrophils (x 10 ⁹ /L)		Platelets (x 10 ⁹ /L)	Dose
≥ 1.5	&	≥ 100	100%
< 1.5	or	< 100	Delay for 1 week. Repeat FBC, if recovered to above this levels, resume at 100% dose. Consider dose reduction for >1 delay.

Reduce docetaxel dose to 60 mg/m² and carboplatin by 1 x AUC if:

Neutrophils < 0.5 x 10⁹/L for more than 1 week,

Or febrile neutropenia diagnosed,

Or platelets < 25 x 10⁹/L

Do not escalate for subsequent cycles.

Non-haematological Toxicities**Renal Impairment**

Creatinine Clearance (ml/min)	Carboplatin Dose
≥ 20	Give 100% dose
< 20	Contraindicated

Docetaxel: No dose adjustment required

Hepatic Impairment

Carboplatin: Dosage adjustment not required

ALP		AST / ALT		Bilirubin	Docetaxel Dose
≤ 2.5 X ULN	&	≤ 1.5 x ULN			100% dose
2.5 – 6 x ULN	&	1.6 – 3.5 x ULN			75% dose
> 6 ULN	&	> 3.5 x ULN	& / or	> 22µmol/L	Not recommended. Docetaxel should be administered with Consultant approval

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Dose modifications for other toxicities

NCI CTCAE Grade	Cutaneous Reactions	Docetaxel Dose
1	Erythema without associated symptoms	100% dose
2	Localised erythema of the palms of the hands and soles of the feet with oedema followed by desquamation	Consider dose reduction to 75% dose
3	Severe, generalised eruptions followed by desquamation	Delay until recovery to \leq Grade 2, reduce to 75% dose For 2 nd occurrence, discontinue docetaxel
4	Generalised exfoliative, ulcerative or bullous dermatitis	Discontinue docetaxel permanently

NCI CTCAE Grade	Sensory Neuropathy	Docetaxel Dose
1	Paraesthesia (including tingling), but not interfering with function	100% dose
2	Paraesthesia interfering with function, but not interfering with activities of daily living	Consider dose reduction to 75% dose
3	Paraesthesia interfering with activities of daily living	Delay until recovery to \leq Grade 2, reduce to 75% dose For 2 nd occurrence, discontinue docetaxel
4	Disabling	Discontinue docetaxel permanently

Location of regimen delivery:

Day case setting
Availability of resuscitation equipment must be ensured as a standard precaution.

Drug interactions:

Docetaxel
Concomitant administration of substrates, inducers or inhibitors of cytochrome P450-3A e.g. ciclosporin, terfenadine, ketoconazole, erythromycin etc may alter the pharmacokinetics of docetaxel presenting a potential interaction.

Carboplatin
Clozapine - increased risk of agranulocytosis, avoid concomitant use
Diuretics - increased risk of nephrotoxicity and ototoxicity
Nephrotoxic drugs - increased nephrotoxicity, not recommended
Phenytoin - reduced absorption of the antiepileptic

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