LONDON CANCER ALLIANCE
West and South

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

Indication:	First line treatment option in advanced or metastatic NSCLC Induction therapy prior to definitive irradiation in stage IIIA / IIIB			
Regimen details:	Gemcitabine	1250 mg/m^2	IV	Days 1 and 8
	Carboplatin	AUC 5 (EDTA)	IV	Day 1

Administration:

Day 1

Gemcitabine in 250 - 500ml Sodium Chloride 0.9% IV over 30 minutes
Carboplatin in 500ml Glucose 5% IV over 60 minutes.

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

Day 8

Gemcitabine in 250 - 500ml Sodium Chloride 0.9% IV over 30 minutes

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 and 8, every 21 days for 4 to 6 cycles.

Pre-medication: Not routinely required

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

Anti- emetics:	Day 1: High emetogenicity Day 8: Low emetogenicity Follow local anti-emetic policy
Supportive medication:	Mouthcare as per local policy Paracetamol / Chlorphenamine / Hydrocortisone can be given for administration-related reactions such as chills / fever.
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)
CT scan	Baseline
EDTA	See comments

Comments:
Carboplatin dose should be calculated using the Calvert formula: Dose = Target AUC x (25 + 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 8 (all cycles):

FBC	Day 8 (within 48 hours)

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, skin rash, alopecia (mild), mucositis, diarrhoea, neurotoxicity (including ototoxicity), nephrotoxicity, ovarian failure/infertility, nausea/vomiting.

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DOSE MODIFICATIONS

Haematological Toxicity

Prior to day 1

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Dose
≥ 1.5	**&**	≥ 100	100% dose
< 1.5	**&/or**	< 100	Delay for 1 week. Repeat FBC, if recovered above these levels give 100% dose.

If neutrophils < 0.5 x 10^9/L for more than 5 days or < 0.1 x 10^9/L for more than 3 days,
or platelets < 25 x 10^9/L ,
or febrile neutropenia is diagnosed,
or toxicity related delay is > 1 week
- gemcitabine dose should be reduced to 75% from previous dose (do not escalate for subsequent cycles).

Prior day 8

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Gemcitabine Dose
> 1.0	**&**	> 100	Give 100% dose
0.5 – 0.9	**or**	75 - 99	Give 75% dose Dose can be re-escalated in subsequent cycles, providing the FBC has returned to normal limits.
< 0.5	**or**	< 75	Omit Re-assess on day 1 of the next cycle

Non-haematological Toxicities

Renal Impairment

Creatinine Clearance (ml/min)	Gemcitabine Dose	Carboplatin Dose
≥ 30	Give 100% dose	Give 100% dose
< 30	Use with caution, no specific dosing recommendations available	Give 100% dose
< 20		Contraindicated

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Hepatic Impairment

Carboplatin No dose modifications required

Gemcitabine

Use gemcitabine with caution in the presence of hepatic dysfunction.

In clinical trials, gemcitabine was associated with transient elevations of serum transaminases in approximately 70% of patients. However, there is no evidence that longer duration of gemcitabine exposure or greater total cumulative gemcitabine dose increases hepatic toxicity. Administration of gemcitabine in patients with concurrent liver metastases or a pre-existing medical history of hepatitis, alcoholism, or liver cirrhosis may lead to exacerbation of the underlying hepatic insufficiency.

Bilirubin (µmol/L)		**ALT or ALP**	**Gemcitabine Dose**
> 27 and ≤ 30			Give 800mg/m^2
> 30	**or**	> 3 x ULN (or > 5 x ULN if liver metastases present)	Withhold and seek consultant advice – high risk of sepsis

Dose modifications for other toxicities

Neurotoxicity

Neurotoxicity	**Gemcitabine Dose**	**Carboplatin Dose**
Grade 2	Give 100% dose	Give 50% dose
Grade 3 or 4	Discontinue	Discontinue

Other toxicities

Grade	**Stomatitis**	**Diarrhoea**	**Dose Reductions**
1	Painless ulcers, erythema or mild soreness	Increase of 2-3 stools/day or mild increase in loose watery colostomy output	Give 100% doses
2	Painful erythema, edema, or ulcers but can eat	Increase of 4-6 stools, or nocturnal stools or mild increase in loose watery colostomy output	Omit until resolved, then resume at 100% doses For 2nd occurrence, resume at 75% doses
3	Painful erythema, edema, or ulcers and cannot eat	Increase of 7-9 stools/day or incontinence, malabsorption, or severe increase in loose watery colostomy output	Omit until resolved, then resume at 75% doses
4	Mucosal necrosis, requires parenteral support	Increase of 10 or more stools/day or grossly bloody diarrhoea, or grossly bloody colostomy output	Omit until resolved, then resume at 50% doses (except for mucositis – give

		or loose watery colostomy output requiring parenteral support, dehydration	75% doses)

Doses reduced for toxicity should not be re-escalated

Location of regimen: Day case setting

Comments:

Haemolytic anaemia – Gemcitabine
Gemcitabine should be discontinued at the first signs of any evidence of micro-angiopathic haemolytic anaemia, such as rapidly falling haemoglobin with concomitant thrombocytopenia, elevation of serum bilirubin, serum creatinine, blood urea nitrogen, or LDH, which may indicate development of haemolytic uraemic syndrome. Renal failure may not be reversible, even with discontinuation of therapy, and dialysis may be required

Women of childbearing potential must use effective contraception during treatment.
Sexually mature males are advised not to father a child during the treatment, and up to 6 months thereafter. If appropriate, male patients should be advised to seek counselling on sperm storage before starting treatment.

Drug interactions:

Gemcitabine is radiosensitiser
Warfarin - increased risk of bleeding (Gemcitabine)
Phenytoin – Carboplatin decreases efficiency
Nephrotoxic drugs (with Carboplatin)

References:

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