LONDON CANCER ALLIANCE
West and South

Breast Pathway Group - Epirubicin (3 weekly) in Advanced Breast Cancer

Indication:	First line palliative therapy in advanced breast cancer patients who have not been previously treated with anthracycline and are not fit for combination chemotherapy with AC, EC or FEC
Regimen details:	Epirubicin *75 mg/m^2 (*) IV Day 1 * Consultant may consider Epirubicin 60 – 90 mg/m^2, depending on patient status e.g. Epirubicin 60mg/m^2 if patient > 60 years
Administration:	IV bolus injection via a fast-running Sodium Chloride 0.9% infusion
Frequency:	Day 1, every 21 days, for 6 cycles
Pre-medication:	Not routinely required
Anti- emetics:	Moderate emetogenicity Follow Local Anti-emetic Policy
Supportive medication:	Mouthcare as per local policy
Extravasation:	Vesicant Epirubicin 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) MUGA scan/ECHO See Comments

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Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Graeme Hood	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson
Second check by: Lisa Yuen	Date prepared: November 2014 Review Date: November 2016

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)
CT scan	Every 3 cycles

Toxicities: Myelosuppression, cardiotoxicity, mucositis, stomatitis, nausea, vomiting, diarrhoea, alopecia,urine discoloration, potential risk of infertility / early menopause, fatigue, skin sensitivity to sun exposure

DOSE MODIFICATIONS

Haematological Toxicity

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 resume at 100% dose. Consider dose reduction for >1 delay.

- Dose reduction and / or delay is more appropriate in the advanced setting
- If during the preceding cycle, the patient has experienced neutrophils <0.5 x 10^9/L or has febrile neutropenia diagnosed, GCSF should be considered
- If platelets persistently < 100 x 10^9/L on Day 1 despite dose delay – see Consultant advice and consider dose reduction by 25%

Non-haematological Toxicities

Renal Impairment

Consider dose reduction in severe renal impairment (GFR < 10ml/min) or serum creatinine > 3.0 – 6.0 x ULN. Discuss with the Consultant and consider dose reduction.

Hepatic Impairment

Bilirubin (µmol/L)	Epirubicin Dose
24 – 51	Give 50%
51 – 85	Give 25%
> 85	Omit

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Dose modifications for other toxicities as appropriate

Mucositis may appear 5-10 days after the start of treatment, and usually involves stomatitis with areas of painful erosions, mainly along the side of the tongue and the sublingual mucosa. For grade III Painful erythema or ulcers requiring IV rehydration resolving to Grade I or less painless ulcers or mild soreness: give Epirubicin 80% dose and recommend regular mouth care

Location of regimen delivery:	Outpatient setting
Comments:	Maximum cumulative dose epirubicin = 950mg/m^2 A baseline MUGA scan should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, obese, smoker, elderly, previous exposure to anthracyclines, previous thoracic radiotherapy. MUGA scan should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative anthracycline dose approaches maximum.
Drug interactions:	Use of Epirubicin with cardioactive compounds (e.g. calcium channel blockers) requires careful monitoring throughout treatment. Avoid commencing epirubicin based therapy for up to 25 weeks after stopping trastuzumab therapy Cimetidine and Ciclosporin: can increase Epirubicin serum level Verapamil: possibly increases Epirubicin bone marrow depressant effects Cimetidine and Ciclosporin: can increase epirubicin serum levels Clozapine: increased risk of agranulocytosis, avoid concomitant use Digoxin tablets: reduced absorption (resolved by giving the liquid formulation of digoxin) Phenytoin: reduced absorption of the antiepileptic Verapamil: possibly increases epirubicin bone marrow depressant effects Avoid live vaccines

References:

Hospira UK Ltd, 2013. Summary of Product Characteristics: Epirubicin. Available at www.medicines.org.uk [Accessed 15/11/13]
Bastholt L et al. JCO (1996) vol 14, 1146 – 1155
UCLH- Dosage Adjustment for Cytotoxics in Renal Impairment. Jan 2009
UCLH- Dosage Adjustment for Cytotoxics in Hepatic Impairment. Jan 2009
LCA Breast Cancer Clinical Guidelines October 2013

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