Breast Pathway Group - Epirubicin weekly in Advanced Breast Cancer

Indication: First line palliative therapy in advanced breast cancer who have not been previously treated with anthracycline and are not fit for combination chemotherapy with AC, EC, FEC or 3-weekly epirubicin

Regimen details: Epirubicin *20 - 30 mg/m² IV Day 1
*Consider Epirubicin 20mg/m² in patients > 60 years

Administration: IV bolus injection via a fast-running Sodium Chloride 0.9% infusion

Frequency: Day 1, every 7 days, for 18 cycles
OR
Day 1 and day 8, every 21 days for 6 cycles

Pre-medications: 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 each cycle
FBC Weekly (within 48 hours)
LFTs Weekly (within 48 hours)
U&Es Weekly (within 48 hours)
CT scan Every 9 weeks
MUGA scan / ECHO See Comments
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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

<table>
<thead>
<tr>
<th>Neutrophils (x 10^9/L)</th>
<th>Platelets (x 10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.5 &amp; ≥ 100</td>
<td>100% dose</td>
<td></td>
</tr>
<tr>
<td>&lt; 1.5 or &lt; 100</td>
<td>Delay for 1 week.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Repeat FBC, if recovered resume at 100% dose. Consider dose reduction for &gt;1 delay.</td>
<td></td>
</tr>
</tbody>
</table>

- 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

<table>
<thead>
<tr>
<th>Bilirubin (µmol/L)</th>
<th>Epirubicin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 – 51</td>
<td>Give 50%</td>
</tr>
<tr>
<td>51 – 85</td>
<td>Give 25%</td>
</tr>
<tr>
<td>&gt; 85</td>
<td>Omit</td>
</tr>
</tbody>
</table>

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 delivery:

Version: 1.0 Supersedes: all other versions Approved by LCA Breast Pathway Chemotherapy Lead: Mark Harries November 2014

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

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Comments: Maximum cumulative dose of epirubicin = 950mg/m²
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 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:
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