ACCELERATED EC - ACCELERATED PACLITAXEL

For adjuvant or neo-adjuvant treatment of triple negative early stage breast cancer, for high risk and fit patients

Drugs / Dosage:

Epirubicin	90mg/m^2	IV	Day 1	every **2 weeks** for up to 4 cycles*
Cyclophosphamide	600mg/m^2	IV	Day 1	every **2 weeks** for up to 4 cycles*

followed by (2 weeks after last cycle of EC):

Paclitaxel	175mg/m^2	IV	Day 1	every **2 weeks** for up to 4 cycles

* In the neo-adjuvant setting, the decision may be taken to proceed to paclitaxel after 3 cycles of EC.

Administration:

Epirubicin via fast running infusion of 0.9% sodium chloride
Cyclophosphamide may be given as bolus injections
Paclitaxel to be infused over 3 hours in 500ml 0.9% sodium chloride
Administer with PVC-free giving set with a 0.2 micron in-line filter

Main Toxicities:

myelosuppression; alopecia; diarrhoea; mucositis;
cardiotoxicity (epirubicin); haemorrhagic cystitis (cyclophosphamide);
hypersensitivity reactions to paclitaxel (infusion-related and ↑ risk with 1st/2nd treatment);
myalgia/arthralgia (paclitaxel); peripheral neuropathy (paclitaxel); ovarian failure / infertility

Anti-emetics:

EC: highly emetogenic Paclitaxel: mildly emetogenic

Other Drugs:

Accelerated EC:
Primary G-CSF prophylaxis s/c once daily for **7** days, starting on Day 3

Accelerated Paclitaxel:
Primary G-CSF prophylaxis s/c once daily for 5 days, starting on Day 3
Pre-medication for paclitaxel:

Dexamethasone	16mg	IV 60 minutes prior to paclitaxel administration
Chlorphenamine	10mg	IV 30–60 minutes prior to paclitaxel administration
Ranitidine	50mg	IV 30–60 minutes prior to paclitaxel administration

Extravasation:

epirubicin and paclitaxel are vesicants

Regular Investigations:

FBC	Day 1 of each cycle
U&Es & LFTs	Day 1 of each cycle
Echo/MUGA	baseline pre chemotherapy, see Comments

Comments:

Counsel patients that although cold capping could be offered with EC cycles, it is not likely to work for paclitaxel.

Maximum cumulative dose of epirubicin = 950mg/m^2
A baseline echo/MUGA 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. Echo/MUGA should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative anthracycline dose approaches maximum.

Reason for Update: N/A – new protocol	Approved by Consultant: Dr R Laing
Version: 1	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes:	Date: 3.12.15
Prepared by: S Taylor	Checked by: C Tucker

Dose Modifications

Haematological Toxicity:

In (neo-)adjuvant treatment, dose reduction and/or delays can compromise outcome.
Primary G-CSF prophylaxis is standard with all cycles.
If any delay, or episode of febrile neutropenia occurs despite the use of G-CSF, the doses of epirubicin or paclitaxel may be reduced by 25%. If in doubt, contact the relevant Consultant.

Neutrophils ≥ 1.5 x 10^9/l and Platelets ≥ 100 x 10^9/l	Proceed with chemotherapy.
Neutrophils 1.0 x 10^9/l - 1.4 x 10^9/l and Platelets ≥ 100 x 10^9/l	Contact the Consultant (preferably) or SpR for the decision on whether to delay treatment as below, or to proceed.
Neutrophils < 1.0 x 10^9/l or Platelets < 100 x 10^9/l	Delay for 1 week. Repeat FBC - if within normal parameters, resume treatment, as discussed above.

Renal Impairment:

CrCl (ml/min)	Cyclophosphamide Dose
10 – 20	Give 75%
< 10	Give 50%

Hepatic Impairment:

Bilirubin (µmol/l)	Epirubicin Dose
24 – 51	Give 50% dose
52 – 85	Give 25% dose
> 85	Omit

For paclitaxel, if bilirubin < 1.25 x ULN and ALT < 10 x ULN, proceed with full dose. Otherwise, consider a dose reduction.
Paclitaxel is not recommended in severe hepatic impairment.

Other Paclitaxel-Related Toxicities:

If a Grade 2 or worse peripheral neuropathy develops, paclitaxel should be reduced to 135mg/m^2 for all subsequent cycles
If progressive neuropathy is observed after this dose reduction, then treatment with paclitaxel should be discontinued

Myalgia and arthralgia often co-exist while on taxanes, usually Grade 1 or Grade 2. Management consists of reassuring patients that it is self-limiting. Consider use of NSAIDs, although not always effective.

References:

Del Maestro, L et al; Lancet 2015; 385: 1863 - 1872