EC – DOCETAXEL$_{100}$ (6 cycle regimen)

For adjuvant treatment of early stage node-positive breast cancer (NICE Approved Nov 2006)
and high risk node-negative breast cancer

Drugs / Dosage:	Epirubicin	90mg/m^2	IV	Day 1 } every 3 weeks for 3 cycles
	Cyclophosphamide	600mg/m^2	IV	Day 1 }
	followed by (3 weeks after Cycle 3 of EC):			
	Docetaxel	100mg/m^2	IV	Day 1, every 3 weeks for 3 cycles

Administration: Epirubicin via fast running infusion of 0.9% sodium chloride
Cyclophosphamide may be given as bolus injections
Docetaxel doses ≤ 185mg, in 250ml sodium chloride 0.9% over 1 hour
Docetaxel doses > 185mg, in 500ml sodium chloride 0.9% over 1 hour

Main Toxicities: **EC:**
myelosuppression; alopecia; mucositis; cardiomyopathy;
haemorrhagic cystitis; ovarian failure/infertility
Docetaxel:
hypersensitivity reactions (infusion-related and ↑ risk with 1st/2nd treatment);
myelosuppression; alopecia; fluid retention; stomatitis;
skin reactions & nail changes; peripheral neurotoxicity;
diarrhoea; myalgia / arthralgia; ovarian failure / infertility

Anti-emetics: EC: highly emetogenic Docetaxel: moderately emetogenic

Other Drugs: **EC:** Primary G-CSF prophylaxis s/c once daily for 5 days, starting on Day 3.
With the third cycle of EC, remember to prescribe the dexamethasone pre-med for the first cycle of docetaxel

Docetaxel: Primary G-CSF prophylaxis s/c once daily for 5 days, starting on Day 3.
Dexamethasone 8mg po bd for 3 days, starting the morning of the day prior to docetaxel chemotherapy (to prevent hypersensitivity reactions and fluid retention)
If the patient has not taken the oral pre-med for any reason, intravenous dexamethasone is not recommended and can only be substituted if prescribed by a Consultant.

Extravasation: epirubicin is a vesicant

Regular Investigations:	FBC	Day 1 of each cycle
	U&Es & LFTs	Day 1 of each cycle
	Echo/MUGA	baseline pre chemotherapy, see Comments plus for all HER2+ve patients, post-anthracycline LVEF result required before trastuzumab starts

Comments: Offer scalp cooling

Ciprofloxacin prophylaxis 250mg bd for 7 days, starting on Day 5 may be prescribed, according to Consultant preference, in patients with additional risk factors for neutropenic sepsis.

Reason for Update: New protocol, adapted from FEC-T, but with 5FU removed and EC dosing reviewed; option for weekly paclitaxel removed	Approved by Consultant: Dr R Laing
Version: 1	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: All versions of FEC-T	Date: 6.1.16
Prepared by: S Taylor	Checked by: C Tucker

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. MUGA scan should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative anthracycline dose approaches maximum.

For HER2 +ve patients, trastuzumab (Herceptin) may commence with the first cycle of docetaxel (1st dose of s/c herceptin may be given on the same day as Cycle 1 docetaxel; loading dose for IV Herceptin to be given on the day before Cycle 1 of docetaxel)

***For patients with severe hypersensitivity reactions to docetaxel**, paclitaxel substitution may be attempted according to the following:*

Drug / Dosage:	***Paclitaxel***	*175mg/m^2 IV every 2 weeks*	
Frequency:	*2 weekly cycle:*	*if replacing 3 doses of docetaxel, give 4 cycles of paclitaxel;*	
		if replacing 2 doses of docetaxel, give 3 doses of paclitaxel	
Anti-emetics:	*mildly emetogenic*		
Administration and Other Drugs:	*Primary G-CSF prophylaxis s/c once daily for 5 days, starting on Day 3*		
	Pre-medication:		
	Dexamethasone	*16mg*	*IV 60 mins prior to paclitaxel administration*
	Chlorphenamine	*10mg*	*IV 30–60 mins prior to paclitaxel administration*
	Ranitidine	*50mg*	*IV 30–60 mins prior to paclitaxel administration*
	Paclitaxel in 500ml 0.9% sodium chloride over 3 hours via non–PVC administration set with a 0.2 micron in-line filter		
Regular Investigations:	*FBC*	*every 2 weeks*	
	U&Es & LFTs	*every 2 weeks*	

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 due to neutropenia or episode of febrile neutropenia occurs despite the use of G-CSF, consider a longer course of G-CSF. The doses of epirubicin or docetaxel should 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 1.1 x 10^9/l - 1.4 x 10^9/l and Platelets > 100 x 10^9/l	**EC**: Contact the Consultant (preferably) or SpR for his decision on whether to delay treatment as below, or to proceed. **Docetaxel**: Delay for 1 week as below
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

If ALT/AST > 1.5 x ULN **and** ALP > 2.5 x ULN, give docetaxel 75mg/m^2
If Bilirubin > 22 µmol/l **or** ALT/AST > 3.5 x ULN **with** ALP > 6 x ULN, docetaxel should not be administered without Consultant approval.

For 2-weekly paclitaxel, if bilirubin < 1.25 x ULN and ALT < 10 x ULN, proceed with full dose. Otherwise, consider a dose reduction.
Paclitaxel not recommended in severe hepatic impairment.

Other Docetaxel-Related Toxicities:

If Grade 2 neuropathy, reduce docetaxel dose by 25%. If symptoms return, stop docetaxel.
If Grade 3 or 4 neuropathy, discontinue treatment.
If Grade 3 or 4 cutaneous reactions, once patient recovered, reduce dose by 25%. If symptoms return, stop docetaxel.

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

For 2-weekly paclitaxel, if a Grade 2 or worse peripheral neuropathy develops, reduce the dose to 135mg/m^2 in all subsequent cycles.
If progressive neuropathy is observed after this dose reduction, then treatment with paclitaxel should be discontinued.

References:

Martin, M et al; NEJM (2005); 352 (22): 2302 – 2313
Roche, H et al; JCO (2006); 24 (36) (PACS 01 trial)
Citron, M et al; JCO 2003; 21 (8): 1431 – 1439 (2-weekly paclitaxel substitution)
Del Maestro, L et al; Lancet 2015; 385: 1863 – 1872 (no benefit for 5FU)