Docetaxel + Cyclophosphamide (TC 6)
Adjuvant Breast Cancer

**Background:** For high risk adjuvant breast patients (node positive, ER positive, HER 2 negative) with operable tumours. FEC-T is the standard chemotherapy for these patients but in patients where an anthracycline is contraindicated, Docetaxel and cyclophosphamide is an acceptable alternative.

**Patient Group:**

Adjuvant chemotherapy for patients with operable tumour, Node positive, ER positive, and HER 2 negative and **anthracyclines are contraindicated** where standard practice would be an anthracycline based regime (eg. FEC-T).

PS 0-2

**Pre-treatment Assessment:**
Weight, FBC, U&E, LFTs and Creatinine clearance

**Treatment Threshold**
- WBC $\geq 3.0 \times 10^9$/L
- ANC $\geq 1.0 \times 10^9$/L
- Platelets $\geq 100 \times 10^9$/L
- CrCl $> 50$ mL/min

**Regimen Details:**

**Day 1**
- Cyclophosphamide 600mg/m² I.V bolus over 3-5 minutes
- Docetaxel 75mg/m² 250-500ml sodium chloride infusion over 60 minutes

Repeated every 21 days for 6 cycles
Administration: Patients should be observed closely for hypersensitivity reactions especially during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of docetaxel, thus facilities for the treatment of hypotension and bronchospasm should be available. If hypersensitivity reactions occur, minor symptoms such as flushing or localized cutaneous reactions do not require interruption of therapy. However, severe reactions, such as severe hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of docetaxel and appropriate therapy. Patients who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel.

Pre-Meds: Dexamethasone 8mg PO BD for 3 days starting the day before chemotherapy. Ondansetron 8-16mg IV 30 minutes prior to chemotherapy.

Anti-emetics: Highly emetic

Additional Medication: Ciprofloxacin 500mg BD 7/7 starting day 5 of cycle.

Monitoring and Assessment:
Clinical Assessment
FBC – prior to each cycle
U&E, LFT creatinine clearance (calculated) – prior to each cycle

Dose Modifications:

*Haematological toxicity*

Neutrophils < 1.0 x 10^9/L defer dose
Platelets < 100 x 10^9/L defer dose

Febrile neutropenia: First occasion – 100% dose with GCSF support.

If febrile neutropenia, neutrophil < 500cells/mm² for more than one week, or if a second occurrence of febrile neutropenia then give Docetaxel 60mg/m² and Cyclophosphamide at 75% dose plus GCSF support.

*Non Haematological Toxicity (Excluding Alopecia)*
CHEMOTHERAPY PROTOCOL

For toxicities of up to grade 2 - delay treatment by one or more weeks until recovery to grade 0 or 1.

For severe or cumulative cutaneous reactions or severe peripheral neuropathy during docetaxel therapy, the dose of docetaxel should be reduced from 75 to 60mg/m². (Cyclophosphamide dose should remain at 100%).

For other grade 3 or 4 non-haematological toxicities docetaxel should be reduced from 75 to 60mg/m² and cyclophosphamide dose reduced by 25%. If the patient continues to experience these reactions the treatment should be discontinued

**Renal Impairment**

<table>
<thead>
<tr>
<th>Clearance (mL/min)</th>
<th>Cyclophosphamide (% of previous)</th>
<th>Docetaxel (% of previous)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-50</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>10-20</td>
<td>75%</td>
<td>100%</td>
</tr>
<tr>
<td>&lt;10</td>
<td>50% or OMIT</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Hepatic Impairment**

Cyclophosphamide –Clinical decision (refer to SPC)

Docetaxel at 100mg/m² as single agent, patients who have both elevations of transaminase (ALT and/or AST) greater than 1.5 times the upper limit of the normal range (ULN) and alkaline phosphatase greater than 2.5 times the ULN, the recommended dose of docetaxel is 75 mg/m². For those patients with serum bilirubin > ULN and/or ALT and AST > 3.5 times the ULN associated with alkaline phosphatase > 6 times the ULN, no dose-reduction can be recommended and docetaxel should not be used unless strictly indicated.

**Pharmaceutical Care:**

- If a dose greater than 185mg of docetaxel (192 mg if not withdrawing equivalent amount of infusion fluid) is required, use a larger volume of the infusion vehicle so that a concentration of 0.74mg/ml docetaxel is not exceeded.

**CONTROLLED DOCUMENT- ONLY VALID ON DATE OF PRINTING**
CHEMOTHERAPY PROTOCOL

- Clinically significant interactions which induce, inhibit or are metabolised by cytochrome P450-3A, include: ciclosporine, terfenadine, ketoconazole, erythromycin and troleandomycin.

Most Common Toxicities:
- Myelosuppression ± infection / bleeding
- Nausea and vomiting
- Hypersensitivity (May be severe)
- Diarrhoea
- Stomatitis
- Fatigue
- Alopecia
- Sensory neuropathy
- Skin reaction (May be severe)
- Oedema
- Nail disorder
- Myalgia and Arthralgia
- Motor neuropathy
- ↑ LFTs
- Anorexia
- Dizziness
- Eye disorders

References:


3. Jones SE, Mavin MA, Holmes FA et al Phase III trial comparing doxorubicin plus cyclophosphamide with docetaxel plus cyclophosphamide as adjuvant therapy for operable breast cancer. JCO 2006; 24: 53817