Pertuzumab/Trastuzumab (subcutaneous) and docetaxel – (neo)adjuvant regimen

Indication

Neoadjuvant or adjuvant treatment of locally advanced, inflammatory or early breast cancer at high risk of recurrence in patients with HER2 positive disease (to be used following 3 cycles of EC100)

Regimen details

Pertuzumab/trastuzumab 1200mg/600mg subcutaneous injection with cycle 1 (subsequent doses 600mg/600mg)
Docetaxel 75mg/m^2 in 250-500ml 0.9% sodium chloride over 1 hour

(Docetaxel dose can be escalated to 100 mg/m2 at clinician's discretion if initial dose is well tolerated)

Cycle frequency

Every 3 weeks

Number of cycles

3 cycles followed by further 15 cycles of trastuzumab or pertuzumab/trastuzumab combination (or 14 cycles of trastuzumab emtansine (Kadcyla), in the event of pathological residual disease post neoadjuvant chemotherapy)

Administration

The first dose of pertuzumab/trastuzumab should be given subcutaneously over 8 minutes and the patient observed for a period of 30 minutes before any subsequent administration of chemotherapy
If tolerated, subsequent doses of pertuzumab/trastuzumab should be given subcutaneously over 5 minutes and the patient observed for 15 minutes before any subsequent administration of chemotherapy

Docetaxel is given intravenously over 1 hour

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of docetaxel and therefore facilities for the treatment of hypotension and bronchospasm must be available. If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve restarted at a slower infusion rate. Severe reactions, such as 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-medication

Paracetamol 1g 30-60 minutes before pertuzumab/trastuzumab, and regularly for 24 hours after treatment

Pre-medicate with 8mg Dexamethasone twice daily orally for 3 days starting 24 hours before docetaxel

Emetogenicity

Low

Additional supportive medication

Patients should receive GCSF support x 5 days (filgrastim 5 mcg/kg SC on days 3-7) with each cycle

Extravasation

Docetaxel is an exfoliant

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Bone profile	14 days
MUGA scan/echocardiogram to assess LVF	Baseline

Cautions
Cardiac dysfunction (see below)
Uncontrolled hypertension or angina
Known allergies to animal proteins
Raised levels of liver enzymes (see below)

Investigations –pre subsequent cycles

1. FBC/U&Es/LFTs
2. The liver function test may be retrospectively looked at (i.e. after the chemotherapy treatment) unless they are known to be abnormal then they need to be repeated the day before so that the results are available pre-chemotherapy
3. LVEF assessment by MUGA or ECHO every 4 months

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	≥ 1.5 x 10^9/L (contact consultant if 1.2-1.5)
Platelet count	≥ 100 x 10^9/L
Creatinine clearance	≥ 20 mL/min
Bilirubin	≤ 1.5 x ULN
AST	≤ 1.5 x ULN

Dose modifications

If febrile neutropenia or neutrophils < 0.5 x 10^9/L for more than 1 week consider reducing doses of all drugs to 80% (except trastuzumab and pertuzumab) for future cycles

Hepatic impairment

AST/ALT (x ULN)		Alkaline phosphatase (x ULN)	Docetaxel dose
≤ 1.5	And	< 2.5	100%
>1.5	Or	≥ 2.5- 6	75%
> 3.5	Or	≥ 6	Discuss with consultant

If bilirubin > 1.0 x ULN – contact consultant

Other toxicity

Toxicity	Definition	Docetaxel dose
Peripheral neuropathy	Grade 2	75%
	Grade 3 or 4	Discuss with consultant
Diarrhoea*	Grade 3 or 4	1st occurrence – 75%
		2nd occurrence – 60%
Stomatitis	Grade 3 or 4	1st occurrence – 75%
		2nd occurrence – 60%

*Consider interrupting pertuzumab treatment in the event of severe diarrhoea

Left ventricular dysfunction

Pertuzumab and trastuzumab should be withheld for at least 3 weeks for any of the following:
- Signs and symptoms suggestive of congestive heart failure (Pertuzumab should be discontinued if symptomatic heart failure is confirmed)
- A drop in left ventricular ejection fraction (LVEF) to less than 40%
- A LVEF of 40%-45% associated with a fall of ≥ 10% points below pre-treatment values.

Pertuzumab and trastuzumab may be resumed if the LVEF has recovered to > 45% or 40-45% associated with <10% points below pre-treatment value.
If after a repeat assessment within approximately 3 weeks, the LVEF has not improved, or has declined further, discontinuation of Pertuzumab and trastuzumab should be strongly considered, unless the benefits for the individual patient are deemed to outweigh the risks

Dose Delays

If the interval between subsequent doses of pertuzumab/trastuzumab is greater than 6 weeks then a loading dose of 1200mg/600mg should be administered

Adverse effects –

for full details consult product literature/ reference texts

Hypersensitivity, myelosuppression, neuropathy, sepsis, pneumonitis, cardiotoxicity, nausea, vomiting, diarrhoea, injection site reactions

Significant drug interactions

– for full details consult product literature/ reference texts

CYP3A4 Enzyme inducers/inhibitors: in vitro studies suggest that CYP3A inhibitors (such as ketoconazole, ritonavir, clarithromycin and erythromycin) may raise docetaxel levels, whereas CYP3A inducers (such as rifampicin and barbiturates) may reduce docetaxel levels

References

Phesgo SPC - https://www.medicines.org.uk/emc/product/11988
Docetaxel SPC - https://www.medicines.org.uk/emc/product/7206/

THIS PROTOCOL HAS BEEN DIRECTED BY DR EATON, CONSULTANT ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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