Pertuzumab/Trastuzumab (subcutaneous) and paclitaxel – palliative regimen

Indication

Metastatic breast or locally recurrent unresectable breast cancer in patients whose tumours are HER2 positive (IHC 3+ or ISH positive) and who have not received previous anti-HER2 therapy or chemotherapy for their metastatic disease

Regimen details

Day 1:
Pertuzumab/trastuzumab 1200mg/600mg subcutaneous injection with cycle 1 (subsequent doses 600mg/600mg)

Days 1,8,15:
Paclitaxel 80mg/m^2 in 0.9% sodium chloride over 1 hour, given weekly

Cycle frequency

Every 3 weeks

Number of cycles

Paclitaxel – maximum of 6 cycles
Pertuzumab/trastuzumab continued until disease progression

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

Paclitaxel is given intravenously over 1 hour in 100-250ml 0.9% sodium chloride via a 0.2µm inline filter

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 paclitaxel or carboplatin. Facilities for the treatment of hypotension and bronchospasm and anaphylaxis must be available.

If hypersensitivity reactions occur, consult "Protocol for the management of hypersensitivity to carboplatin and taxane-based chemotherapy" document

Pre-medication

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

Pre-medicate 30 mins pre chemo with:
Chlorphenamine 10mg I.V. bolus
Famotidine 20mg oral (or alternative H_2 antagonist)

Week 1:
Dexamethasone 20mg 100mls NaCl 0.9%

For subsequent weeks reduce dexamethasone dose as below.

If patient experiences any hypersensitivity reaction do not reduce the dose further but continue on the same dose.

If severe reaction consider increasing pre-med dose back to 20mg. See hypersensitivity protocol

Week 2	dexamethasone 8mg
Week 3	dexamethasone 4mg
Week 4 and subsequent	no dexamethasone required

Emetogenicity

Low

Additional supportive medication

None routinely prescribed

Extravasation

Paclitaxel is a vesicant

Investigations – pre first cycle

Standard network pre-SACT tests

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/LFT – every week during paclitaxel treatment, every 3 months thereafter unless clinically indicated
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 6 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	≥ 1.0 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Creatinine clearance	≥ 30 mL/min
Bilirubin	≤ 1.5x ULN
AST/ALT	≤ 5x ULN

Dose modifications

Haematological toxicity
If neutrophils < 1.0 x 10^9 /L and/or platelets < 100 x 10^9 /L delay for 1 week then resume at 100% dose (omit paclitaxel dose if day 8 or 15).
If delayed/omitted for > 1 week discuss with consultant. In the case of febrile neutropenia reduce paclitaxel to 60mg/m2 for all future doses

Hepatic impairment
Paclitaxel is not recommended in severe hepatic impairment. If bilirubin < 1.5 x ULN and AST/ALT < 5 x ULN proceed with 100% dose. For more severe hepatic impairment, treatment may only proceed on consultant's decision, at a reduced dose with weekly monitoring of LFTs

Renal impairment

Discuss with consultant if creatinine clearance <30ml/min

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

Paclitaxel is a CYP 2C8/9 and CYP 3A4 substrate. Drug levels may be increased by inhibitors of these enzymes and decreased by inducers of these enzymes.

References

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

THIS PROTOCOL HAS BEEN DIRECTED BY DR DESAI, CONSULTANT ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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