Pertuzumab/Trastuzumab (subcutaneous) and nab-paclitaxel (Abraxane)

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-***using Abraxane as per NICE interim COVID19 guidance***

Regimen details

Pertuzumab/trastuzumab 1200mg/600mg subcutaneous injection with cycle 1 (subsequent doses 600mg/600mg)
Nab-paclitaxel (Abraxane) 260mg/m^2 over 30 minutes

Cycle frequency

Every 3 weeks

Number of cycles

6 cycles, then pertuzumab/trastuzumab to be given until disease progression or intolerance

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

Nab-paclitaxel (Abraxane) is given intravenously over 30 minutes. Filters of less than 15µm must not be used

Pre-medication

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

Emetogenicity

Low

Additional supportive medication

None

Extravasation

Abraxane is a vesicant

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

Criteria
Life expectancy greater than 6/12
WHO performance status ≥2
Baseline LVEF ≥50%

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	≥ 60 mL/min
Bilirubin	≤ 1.5x ULN
AST	≤ 10x ULN

Dose modifications

1. Reduce Abraxane dose by 20% following febrile neutropenia or prolonged delay due to neutropenia/thrombocytopenia
2. Reduce Abraxane dose by 20% if bilirubin 1.5-5x ULN and AST <10x ULN
3. Discontinue Abraxane if bilirubin >5x ULN or AST >10x ULN
4. Withhold Abraxane in the event of grade 3 sensory neuropathy and restart with 20% dose reduction when resolved
5. Discontinue Abraxane if CrCl <30ml/min

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

The metabolism of paclitaxel is catalysed, in part, by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. Therefore, in the absence of a PK drug-drug interaction study, caution should be exercised when administering paclitaxel concomitantly with medicines known to inhibit either CYP2C8 or CYP3A4 (e.g. ketoconazole and other imidazole antifungals, erythromycin, fluoxetine, gemfibrozil, clopidogrel, cimetidine, ritonavir, saquinavir, indinavir, and nelfinavir) because toxicity of paclitaxel may be increased due to higher paclitaxel exposure. Administering paclitaxel concomitantly with medicines known to induce either CYP2C8 or CYP3A4 (e.g. rifampicin, carbamazepine, phenytoin, efavirenz, nevirapine) is not recommended because efficacy may be compromised because of lower paclitaxel exposures

Additional comments

References

Abraxane SPC – https://www.medicines.org.uk/emc/product/6438
Phesgo SPC - https://www.medicines.org.uk/emc/product/11988

THIS PROTOCOL HAS BEEN DIRECTED BY DR NEVILLE-WEBBE, CONSULTANT ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

Date: January 2021
Review: January 2023
VERSION: 1