Nab-paclitaxel (Abraxane), Carboplatin, Trastuzumab and Pertuzumab

Indication

Neoadjuvant treatment of locally advanced, inflammatory or early breast cancer at high risk of recurrence in patients with HER2 positive disease (**interim COVID 19 funding arrangements**)

Regimen details

Trastuzumab 6mg/kg (first dose 8mg/kg) in 250ml 0.9% sodium chloride over 30 minutes (first dose over 90 minutes)
Pertuzumab 420mg (first dose 840mg) in 250ml 0.9% sodium chloride over 30 minutes (first dose over 60 minutes)
Nab-paclitaxel (Abraxane) 200mg/m^2 over 30 minutes
Carboplatin AUC6 in 500ml 5% glucose over 60 minutes

Cycle frequency

Repeat every 3 weeks

Number of cycles

6 cycles, followed by further 12 cycles of trastuzumab or trastuzumab/pertuzumab combination or 14 cycles of trastuzumab emtansine (Kadcyla)

Administration

Pertuzumab and trastuzumab may be administered in any order but both should be given before chemotherapy. An observation period of 30-60 minutes is recommended after pertuzumab before other drugs are administered

Administer Abraxane via a 15µm filter, do not use 0.2µm in-line filters

Infusion Reactions:

Mild – Stop infusion. Give 10 mg IV chlorphenamine and 100 mg IV Hydrocortisone. Re start infusion slowly after 30 minutes. If further problems discontinue infusion and seek senior advice

Severe – Stop infusion. Give 100 mg Hydrocortisone and 10 mg chlorphenamine stat. Get HELP. May need further resuscitation. Patient to be admitted.

Pre-medication

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

Emetogenicity

Moderate

Additional supportive medication

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

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
MUGA or echocardiogram	

Investigations –pre subsequent cycles

FBC/U&Es/LFTs/Bone every 3 weeks during chemotherapy, then every 3 months when on trastuzumab single agent
LVEF assessment on MUGA or ECHO every 3 cycles during combination treatment.
Investigations and consultations prior to each cycle:
FBC U&Es and LFTs.
Magnesium once a month, random glucose or BM once a month
Consultation every three weeks
The U&Es and LFTs need to be checked the day before so that results are available pre-chemotherapy

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 (calculated)	≥ 60 mL/min
Bilirubin	≤ 1.5 x ULN
AST	< 1.5 x ULN

Dose modifications

Reduce Abraxane and carboplatin doses by 20% following febrile neutropenia or prolonged delay due to neutropenia/thrombocytopenia

Reduce Abraxane dose by 20% if bilirubin 1.5-5x ULN and AST <10x ULN
Discontinue Abraxane if bilirubin >5x ULN or AST >10x ULN

Withhold Abraxane and carboplatin in the event of grade 3 sensory neuropathy and restart with 20% dose reduction when resolved

Discontinue Abraxane if CrCl <30ml/min

Recalculate carboplatin dose if serum creatinine alters by >20%

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 is greater than 6 weeks then a loading dose of 840mg should be administered.
If the interval between subsequent doses of trastuzumab is greater than 4 weeks then a loading dose of 8mg/kg should be administered

Adverse effects –

for full details consult product literature/ reference texts

Hair loss, prolonged neutropenia, allergic reactions, diarrhoea, neuropathy, nausea, vomiting, fatigue, anaemia, thrombocytopaenia, mucositis

Additional comments

Carboplatin dose is calculated using calculated creatinine clearance
Dose = (CrCl + 25) x AUC

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

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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