Trastuzumab emtansine (Kadcyla)

Indication

Treatment of HER2 positive unresectable locally advanced or metastatic breast cancer for patients who have previously received a taxane and trastuzumab, separately or in combination
Patients should have received prior therapy for locally advanced or metastatic disease OR have relapsed within 6 months of completing adjuvant therapy.

Adjuvant treatment of HER2-positive early breast cancer in adults who have residual invasive disease in the breast or lymph nodes after neoadjuvant taxane-based and HER2-targeted therapy

Warning:
Kadcyla (trastuzumab emtansine) is a very different product to Herceptin (trastuzumab). These products should not be used interchangeably

Regimen details

Trastuzumab emtansine (Kadcyla) 3.6 mg/kg in 250ml 0.9% sodium chloride as an intravenous infusion using 0.22µm in-line filter

Cycle frequency

Every 3 weeks

Number of cycles

Metastatic disease: until disease progression or unacceptable toxicity

Adjuvant treatment: total of 14 cycles unless disease progression or unacceptable toxicity

Administration

Kadcyla is administered in 250mL sodium chloride 0.9% non-PVC infusion bag with a 0.22 micron in-line filter. The first dose is administered over 90 minutes and patients should be observed for infusion related reactions (fever, chills or other infusion related reactions) for 90 minutes following completion of the infusion. The infusion site should be closely monitored for possible subcutaneous infiltration during administration.
If the previous infusion was well tolerated, subsequent doses may be administered over 30 minutes. Patients should be observed for at least 30 minutes following completion of the infusion.
In the event of infusion related reactions, the infusion rate should be slowed or discontinued in severe or life threatening cases

Pre-medication

Nil

Emetogenicity

Mild

Additional supportive medication

Non required routinely

Extravasation

Neutral

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
Echocardiogram	Baseline

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST)
Echocardiogram every 6 months (metastatic disease); every 3-4 months during adjuvant treatment

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
Platelet count	≥ 75 x 10^9/L (if 50-74, contact consultant, see under Dose Modifications below)
Creatinine clearance	≥ 30 mL/min
Bilirubin	≤ 1.5 x ULN
AST	< 5 x ULN

Dose modifications

First dose reduction is to 3mg/kg, second dose reduction to 2.4mg/kg

THROMBOCYTOPENIA:
If platelets drop to <50 then defer until count >75
If platelets 50-74 treatment may continue at consultant discretion if platelets have never been below 50
If platelets drop to <25 then defer until count >75 and then resume with dose reduction
Consider dose reduction if patient requires 2 delays due to thrombocytopenia

LIVER FUNCTION:
If ALT or AST increase to >5ULN then withhold drug until recovers to <5x ULN and reduce subsequent doses, unless >20 ULN in which case discontinue drug permanently
If bilirubin 1.5-3x ULN then withhold drug until bilirubin recovers to <1.5x ULN
If bilirubin 3-10x ULN then withhold drug until bilirubin recovers to <1.5x ULN and reduce dose
If bilirubin >10xULN then discontinue treatment

NEUROPATHY:
Delay for grade 3 or 4 peripheral neuropathy until recovered to grade 2 or better then reduce subsequent doses

LVEF:
If LVEF >45% continue drug
If LVEF <40% withhold drug and repeat LVEF within 3 weeks, if remains <40% discontinue drug
If LVEF 40-45% and less than 10 point reduction from baseline continue drug but repeat LVEF within 3 weeks
If LVEF 40-45% and more than 10 point reduction from baseline withhold drug repeat LVEF within 3 weeks
If not recovered to within 10 points of baseline discontinue drug
Discontinue if patient experiences symptomatic heart failure

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Cardiotoxicity
Haemorrhage
Hepatobiliary disorders
Neurotoxicity
ILD, Pneumonitis

- **Frequently occurring side effects**

Myelosuppression
Raised transaminases
Infusion related reactions
Hypokalaemia
Stomatitis
Diarrhoea
Musculoskeletal pain
Dyspnoea
Fatigue
Peripheral neuropathy

- **Other side effects**

Insomnia
Headaches, dizziness
Rash
Arthralgia, Myalgia

Significant drug interactions

– for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

CYP24A inhibitors: (ketoconazole, itraconazole, clarithromycin, atazanivir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, and voriconazole): avoid concomitant administration – increased risk of toxicity.

Additional comments

References

Kadcyla SPC: https://www.medicines.org.uk/emc/product/5252/smpc

SWCN protocol: http://www.swscn.org.uk/wp/wp-content/uploads/2020/09/Kadcylav2.pdf

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THIS PROTOCOL HAS BEEN DIRECTED BY DR YOUNG, DESIGNATED LEAD CLINICIAN FOR

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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