Chemotherapy Protocol

BREAST CANCER

KADCYLA

(trastuzumab emtansine)

Kadcyla (trastuzumab emtansine) is NOT the same drug as Herceptin (trastuzumab). There is considerable risk of confusion between the two products during the prescription, preparation, and administration processes.

Confusion can lead to overdose, undertreating and / or toxicity.

Healthcare professions should use the full INN name, trastuzumab emtansine, and invented name Kadcyla when prescribing, preparing, and administering Kadcyla (trastuzumab emtansine)

This protocol may require funding

Regimen

- Breast Cancer – Kadcyla (trastuzumab emtansine)

Indication

- Kadcyla (trastuzumab emtansine) is indicated, as a single agent, for the treatment of adult patients with HER2-positive, unresectable, locally advanced or metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either

  - received prior therapy for locally advanced or metastatic disease or
  - developed disease recurrence during or within six months of completing adjuvant therapy.

- WHO PS 0, 1

- LVEF of more than 50%

- Must only be used in patients whose tumours have HER2 over-expression at a 3+ level as determined by immunohistochemistry (HER2 +++ by IHC or FISH)

Toxicity

Drug	Adverse Effect
Kadcyla (trastuzumab emtansine)	Peripheral neuropathy, interstitial lung disease, left ventricular dysfunction, thrombocytopenia, hypersensitivity

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- Prior to the first cycle

  - HER2 test
  - Cardiac assessment (history, physical examination, ECG, echocardiogram with or without MUGA

- Prior to all cycles

  - FBC, U&Es and creatinine, LFTs

- Monitor LVEF every three months

Dose Modifications

The dose modifications listed are for a limited number of toxicities. Dose adjustments may be necessary for other toxicities as well.

The Kadycla (trastuzumab emtansine) dose should not be re-escalated after a dose reduction is made.

Please discuss all dose reductions / delays with the relevant consultant before prescribing if appropriate. The approach may be different depending on the clinical circumstances. The following applies;

Dose reduction schedule (Starting dose is 3.6 mg/kg)	Dose to be administered
First dose reduction	3 mg/kg
Second dose reduction	2.4 mg/kg
Requirement for further dose reduction	Discontinue treatment

Haematology

Prior to prescribing on day one of cycle one the following criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1.5x10^9$/L
Platelets	equal to or more than $100x10^9$/L

Consider blood transfusion if patient symptomatic of anaemia or haemoglobin of less than 8g/dL

Grade 3 (Platelets 25,000 to 50,000/mm3)	Grade 4 (Platelets less than 25,000/mm3)
Do not administer until the platelet count recovers to grade 1 or below (platelets more than or equal to 75,000/mm3). No dose modification is required.	Do not administer until the platelet count recovers to grade 1 or below (platelets more than or equal to 75,000/mm3), and then dose reduce by one dose level

Hepatic Impairment

Transaminases (AST / ALT)		
Grade 2 (2.5 to 5xULN)	**Grade 3 (5 to 20xULN)**	**Grade 4 (more than 20xULN)**
No dose modification is required.	Do not administer until AST/ALT recovers to grade 2 or below, and then reduce by one dose level.	Permanently discontinue

Bilirubin		
Grade 2 (1.5 to 3×ULN)	**Grade 3 (3 to 10×ULN)**	**Grade 4 (more than 10×ULN)**
Do not administer until the total bilirubin recovers to grade 1 or below (more than ULN to 1.5xULN). No dose modification is required.	Do not administer until total bilirubin recovers to grade 1 or below (ULN to 1.5xULN), and then reduce by one dose level	Discontinue

Renal Impairment

Drug	Dose (% of original dose)
Kadcyla (trastuzumab emtansine)	No dose adjustment needed in patients with mild or moderate renal impairment. Insufficient data in patients with severe renal impairment hence monitored patient carefully.

Others

Cardiac

LVEF less than 40%	LVEF more than 45%	LVEF 40% to 45% and decrease is less than 10% points from baseline	LVEF 40% to 45% and decrease is more than or equal to 10% points from baseline	Symptomatic CHF
Do not administer Repeat LVEF assessment within 3 weeks. If LVEF is less than 40% is confirmed, discontinue treatment	Continue treatment	Continue treatment. Repeat LVEF assessment within 3 weeks.	Do not administer. Repeat LVEF assessment within 3 weeks. If the LVEF has not recovered to within 10% points from baseline, discontinue treatment	Discontinue

Peripheral neuropathy

Treatment should be temporarily discontinued in patient experiencing NCI-CTC grade 3 or 4 peripheral neuropathy until resolution to NCI-CTC grade 2 or below. At retreatment a dose reduction may be considered according to the dose reduction schedule.

Regimen

21 day cycle until disease progression or toxicity occurs (six cycles will be set in Aria)

Drug	Dose	Days	Administration
Kadcyla (trastuzumab emtansine)	3.6mg/kg	1	Sodium chloride 0.9% 250ml over 90 minutes for the first infusion, if this is well tolerated subsequent infusions may be given over 30 minutes

Dose Information

- Kadcyla (trastuzumab emtansine) will be dose banded according to the agreed bands

Administration Information

Extravasation

- Mild irritant

Others

- The reconstituted solution should be diluted in polyvinyl chloride (PVC) or latex-free PVC-free polyolefin infusion bags.
- The use of 0.22 micron in-line polyethersulfone (PES) filter is required for the infusion.
- The infusion should be slowed for mild infusion related reactions. It should be stopped for those that are life threatening or severe.
- Administer the first infusion over 90 minutes. Patients should be observed during the infusion and for at least 90 minutes following the initial dose for fever, chills, or other infusion related reactions. For subsequent infusions administer over 30 minutes, if the prior infusions were well tolerated. Patients should be observed during the infusion and for at least 30 minutes after infusion.

Additional Therapy

- Antiemetics

  As take home medication;

  - metoclopramide 10mg three times a day oral when required

- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed

Coding

- Procurement – 71.5
- Delivery – 72.2, 72.3

References
1,Verma S, Miles D, Gianni L et al. Trastuzumab emtansine for HER2 positive advanced breast cancer. N Engl J Med 2012; 367 (19): 1783-1791.

REGIMEN SUMMARY

Kadcyla (trastuzumab emtansine)

Day One

1. Kadcyla (trastuzumab emtansine) 3.6mg/kg in 250ml sodium chloride 0.9% over 90 minutes

Take Home Medicines

3. Metoclopramide 10mg three times a day when required oral

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	April 2014	None	Dr Deborah Wright Pharmacist	Dr Jennifer Bradbury Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospitals NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.