# TRASTUZUMAB EMTANSINE (KADCYLA) IV

Single agent treatment for patients with HER2+ve metastatic breast cancer who have previously received a taxane and trastuzumab.
Patients should either have received prior therapy for metastatic disease, or relapsed within 6 months of completing trastuzumab for early stage disease.

Blueteq registration is required before treatment may start

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| Drug/Dosage: | Trastuzumab EMTANSINE (Kadcyla) | 3.6mg/kg | IV | Day 1 |

Administration: Paracetamol 1000mg po 30 minutes before the 1st dose only.
All doses in 250ml sodium chloride 0.9% and infused via a giving set with a 0.2 micron in-line filter.

**1st dose:** infuse over 90 minutes, then observe for infusion-related reactions for a further 90 minutes after infusion ends.

**Subsequent doses:** infuse over 30 minutes if prior infusions were well tolerated. Then observe for infusion-related reactions for 30 minutes after the infusion ends.

Patients should be observed for 90 minutes after the end of the first infusion and for 30 minutes post-infusion for subsequent doses.
If a decision is made to allow the patient to leave in advance of these times, they must be counselled about the possibility of delayed infusion-related symptoms and instructed to contact the hospital in the event of these occurring.

The infusion rate should be slowed or interrupted in the event of any infusion-related symptoms, and discontinued in patients with life-threatening reactions.

If the patient misses a dose, administer the next dose (i.e. the missed dose) as soon as possible. The interval between consecutive doses should not be less than three weeks.

Frequency: every 3 weeks - administer until disease progression

Main Toxicities: thrombocytopenia; myelosuppression; increased transaminases; infusion-related reactions; hypokalaemia; musculoskeletal pain; cardiotoxicity; dyspnoea; pneumonitis

Anti-emetics: mildly emetogenic

Extravasation: non-vesicant – no specific antidote

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| Regular Investigations: | FBC | Day 1 |
| | U&Es and LFTs | Day 1 |
| | CA 15-3 | Day 1, only if elevated prior to treatment |
| | Echo*/MUGA scan | baseline (must be ≥ 50%); at 4 and 8 months, then every 6 months thereafter<br>Patients who develop asymptomatic cardiac dysfunction will require more frequent monitoring e.g. every 6–8 weeks. |
| | Blood pressure** | baseline, at 4 and 8 months, then every 6 months |

* An echocardiogram is the preferred test, but whichever test is used initially for an individual, should ideally be used throughout

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| Reason for Update: need for PVC-free giving set removed; hepatic section updated | Approved by Consultant: Dr A Neal |
| Version: 3 | Approved by Lead Chemotherapy Nurse: P Deery |
| Supersedes: Version 2 | Date: 23.1.17 |
| Prepared by: S Taylor | Checked by: C Tucker |

** If blood pressure ≥ 140/90 mmHg, a diagnosis of hypertension needs to be confirmed by asking patient to visit GP for ambulatory or home blood pressure monitoring.
Patients with a confirmed diagnosis of hypertension should be treated with an ACE inhibitor which is also licensed for the treatment of heart failure e.g. ramipril.

Dose Modifications: Doses should not be re-escalated after a dose reduction is made.

| Dose reduction schedule | Dose to be administered |
|---|---|
| 1st dose reduction | 3 mg/kg |
| 2nd dose reduction | 2.4 mg/kg |
| Requirement for further dose reduction | Discontinue treatment |

Haematological Toxicity:

| Platelet Count | Management |
|---|---|
| 25 – 49 x $10^9$/l | Withhold until platelets ≥75 x $10^9$/l. No dose reduction required. |
| < 25 x $10^9$/l | Withhold until platelets ≥75 x $10^9$/l, then dose reduce trastuzumab emtansine by one level. |

Hepato-toxicity:

| LFTs | Management |
|---|---|
| ALT / AST 2.5 - 5 x ULN | No delay or dose modification required |
| Bilirubin > 1.5 to ≤ 3 x ULN | Withhold treatment until bilirubin ≤ 1.5 x ULN. No dose modification is required. |
| ALT / AST > 5 - 20 x ULN or Bilirubin > 3 - 10 x ULN | Withhold treatment until ALT/AST 2.5 – 5 x ULN and bilirubin 1 – 1.5 x ULN, then dose reduce trastuzumab emtansine by one level |
| ALT / AST > 20 x ULN or Bilirubin > 10 x ULN | Discontinue trastuzumab emtansine (Kadcyla) |

Cardiotoxicity:

| Cardiac Function | Management |
|---|---|
| LVEF > 45% | Continue with trastuzumab emtansine (Kadcyla) |
| LVEF 40 – 45% | If decrease is < 10 ejection fraction (EF) points from baseline, continue treatment and repeat LVEF in 3 weeks. If decrease is ≥ 10 EF points from baseline, withhold treatment and repeat LVEF in 3 weeks' time. If LVEF has not recovered to < 10 EF points from baseline, discontinue treatment. |
| LVEF < 40% | Withhold treatment and repeat LVEF in 3 weeks' time. If LVEF remains < 40%, discontinue treatment. |
| Symptomatic congestive heart failure | Discontinue trastuzumab emtansine (Kadcyla) |

Neuropathy: For Grade 3 or 4 peripheral neuropathy, withhold treatment until recovered to ≤ Grade 2. When re-starting, consider a dose reduction by one level.

Renal Impairment: No dose adjustment is required for patients with CrCl ≥ 30ml/min. There is limited data in patients with CrCl < 30ml/min, and so no dose recommendations can be made.

Hepatic Impairment: No starting dose adjustment in mild or moderate hepatic impairment. Trastuzumab emtansine has not been studied in patients with severe hepatic impairment.