LONDON CANCER ALLIANCE West and South

Breast Pathway Group – KADCYLA Trastuzumab Emtansine in Advanced Breast Cancer

Indication:

HER2 positive locally advanced / unresectable or metastatic (stage IV) breast cancer

National Cancer Drug Fund criteria:

- Progression of HER2 positive locally advanced or metastatic breast cancer
- Progression during or after the most recent treatment for advanced stage disease or within 6 months of completing treatment for early stage disease
- PS 0 or 1
- Previous treatment with a taxane
- Previous treatment with trastuzumab
- Left ventricular ejection fraction of 50% or more

Ensure funding has been approved prior to starting treatment.

Regimen details: Kadycla (Trastuzumab Emtansine) 3.6mg/kg IV Day 1

Administration:

In 250ml Sodium Chloride 0.9% IV over 90 minutes
Administer via 0.22 micron PVC-free in-line filter
If the initial dose was well tolerated, the next dose may be administered over 30 minutes

Patients should be observed during the infusion and for at least 90 minutes after the first infusion, and for 30 minutes after subsequent infusions for signs and symptoms of administration-related reactions.
Administration-related reactions/hypersensitivity reactions such as chills and/or fever, dyspnoea, hypotension, wheezing, bronchospasm, tachycardia, reduced oxygen saturation, respiratory

Version: 1.0 Supersedes: all other versions	Approved by LCA Breast Pathway Chemotherapy Lead: Mark Harries
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Lisa Yuen	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson
Second check by: Laura Cameron	Date prepared: February 2014 Review Date: July 2016

	distress, rash, nausea, vomiting, headache are known to occur. Availability of resuscitation equipment must be ensured as a standard precaution.
Frequency:	Day 1, every 21 days, until disease progression or unacceptable toxicity
Pre-medication:	Not routinely required
Anti- emetics:	Low emetogenicity Follow Local Anti-emetic Policy
Supportive medication:	Paracetamol / Chlorphenamine / Hydrocortisone can be given for administration-related reactions such as chills / fever
Extravasation:	Non-vesicant
Regular investigations:	Prior to Cycle 1: FBC — Day 1 (within 14 days) LFTs — Day 1 (within 14 days) U&Es — Day 1 (within 14 days) LVEF (MUGA/ ECHO) — Baseline, at 4 and 8 months then 4 to 6 monthly thereafter (see cardiac monitoring) Prior to Day 1 (all cycles): FBC — Day 1 (within 72 hours) LFTs — Day 1 (within 72 hours) U&Es — Day 1 (within 72 hours)
Toxicities:	Administration-related reactions (see above), thrombocytopenia, anaemia, hypokalaemia, cardiotoxicity, pulmonary events, diarrhoea, rash, hepatotoxicity**,** musculoskeletal pain, fatigue, peripheral neuropathy.

DOSE MODIFICATIONS

Haematological Toxicity

Prior to cycle 1

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Dose
≥ 1.5	&	≥ 100	100% dose

Prior to subsequent cycles (cycle 2 onwards)

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Dose
≥ 1.5	&	≥ 75	100% dose
		> 25 - < 75	Delay until platelet count recovered to ≥ 75 x 10^9/L. No dose modification required
< 1.5	& / or	< 25	Delay until platelet count recovered to ≥ 75 x 10^9/L and dose reduce to 3mg/kg. If platelet count < 25 x 10^9/L for the second time, do not administer until platelet count recovered to ≥ 75 x 10^9/L and dose reduce to 2.4mg/kg. If platelet count < 25 x 10^9/L for the third time, discontinue treatment.

The dose should not be re-escalated after a dose reduction has been made

Non-haematological Toxicities

Renal Impairment

No information. Monitor patients with severe renal impairment carefully.

Hepatic Impairment

Bilirubin		AST / ALT	Dose
< 1.5 x ULN	**& / or**	< 5 x ULN	No dose modification required
> 1.5 - ≤ 3 x ULN		< 5 x ULN	Do not administer until bilirubin recovers to < 1.5 x ULN. No dose modification required.
> 3 to ≤ 10 x ULN		> 5 to ≤ 20 x ULN	Do not administer until bilirubin recovers to < 1.5 x ULN and dose reduce to 3mg/kg. Do not administer until AST / ALT recovers to < 5 x ULN and dose reduce to 3mg/kg. For 2nd occurrence: withhold treatment until recovers to below these levels then dose reduce to 2.4mg/kg. For 3rd occurrence: Discontinue treatment
> 10 x ULN		> 20 x ULN	Discontinue treatment

Dose modifications for other toxicities

Cardiac monitoring

LVEF < 40%	LVEF > 45%	LVEF 40% to ≤ 45% and decrease is < 10% points from baseline	LVEF 40% to ≤ 45% and decrease is ≥ 10% points from baseline	Symptomatic CHF
Do not administer Repeat LVEF assessment within 3 weeks. If LVEF < 40% is confirmed, discontinue	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	Discontinue

Peripheral Neuropathy

Discontinue in patients experiencing grade 3 or 4 peripheral neuropathy until resolution to ≤ grade 2. Dose reduction may be considered – discuss with the consultant.

Pulmonary events

Cases of pulmonary interstitial lung disease including pneumonitis have been reported. Signs and symptoms include dyspnoea, cough, fatigue and pulmonary infiltrates. Patients with pulmonary interstitial lung or pneumonitis should not be treated.

Location of regimen delivery: Outpatient setting
Availability of resuscitation equipment must be ensured as a standard precaution.

Drug interactions: No formal drug interaction studies have been performed.

References:

Roche Products Limited, 2013. Summary of product characteristics: Kadcyla 100mg and 160mg powder for concentrate for solution for infusion. Available via www.medicines.org.uk
Verma S *et al*. N Eng J med 2012; 367: 1783-1791

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