Systemic Anti Cancer Treatment Protocol

Kadcyla
(Trastuzumab Emtansine)

PROTOCOL REF: MPHAKADBR
(Version No: 1.0)

Approved for use in:

Single agent treatment for patients with HER2 positive metastatic breast cancer who have previously received a taxane and trastuzumab

Requires blueteq registration

Due to risk of error with different dosing schedule to trastuzumab, this conjugate product will be referred to by its brand name **Kadcyla** throughout all documentation.

Dosage:

Drug	Dose	Route	Frequency
Kadcyla	3.6mg/kg	IV	Every 21 days

Supportive Treatments:

Dexamethasone tablets, 4mg twice daily for 3 days. If no nausea/vomiting then consider reducing and stopping after the first two cycles.

Domperidone 10mg tablets, to be taken three times a day as required

Extravasation risk:

Non-vesicant: no specific antidote

Administration:

Day	Medicine	Dose	Route	Diluent and rate
1	**Ondansetron**	**16mg**	**PO**	30mins before chemotherapy
	Dexamethasone	**12mg**	**PO**	30mins before chemotherapy
	KADCYLA	**3.6mg/kg**	**IV**	250mL sodium chloride 0.9%. 1st dose to be given over 90mins, if tolerated subsequent doses to be given over 30mins Give via 0.22 micron filter

Main Toxicities:

Haematological	Neutropenia, anaemia, thrombocytopenia,
Cardiac and Vascular disorders	LVEF reduction Hypokalaemia
Gastrointestinal	Nausea, vomiting, diarrhoea, constipation, mucositis
Nervous system	Peripheral neuropathy
Hepatobiliary	Elevation of liver transaminases, alkaline phosphatase and bilirubin.
General disorders and administration site conditions	Infusion related reactions Fatigue, pneumonitis, dyspneoa Infertility and early menopause

Investigations and Treatment Plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Comments
Medical Assessment	X		X		X		X	Then every 12 weeks
Nursing Assessment	X	X	X	X	X	X	X	Every cycle
ECHO	X				X			12 weekly initially then as clinically indicated
FBC	X		X	X	X	X	X	Every cycle
U&E & LFT	X		X	X	X	X	X	Every cycle
Informed Consent	X							
CT scan	X							Every 8 to 12 weeks as clinically indicated
PS recorded	X	X	X	X	X	X	X	Every cycle
Toxicities documented		X	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

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

Haematological Toxicity:

Proceed on day 1 if-

Plt ≥ 75 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Delay 1 week on day 1 if-

Plt ≤ 74 x 10^9/L	ANC ≤ 0.9 x 10^9/L

Platelet count	Dose to be administered
25 to 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 by one level

Consider dose reduction to next dose level if neutropenia persists for more than 7 days or 2 subsequent deferrals

Non-haematological toxicity

Renal impairment:

No dose adjustment is required for patients with CrCl above 30mL/min

Limited information on patients with severe renal impairment therefore should be used with caution

Hepatic impairment:

Liver functions tests	Management
ALT / AST below 5 x ULN	No 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 and ≤20 x ULN Or Bilirubin >3 and < 10 x ULN	Withhold treatment until ALT/AST 2.5 to 5 x ULN and bilirubin 1 to 1.5 x ULN then dose reduce by one level
ALT / AST > 20 x ULN Or Bilirubin >10 x ULN	Discontinue Kadcyla

Neuropathy:

For grade 3 or 4 peripheral neuropathy, withhold treatment until recovered to grade 2.

When restarting consider dose reduction by one level.

LVEF

As all patients will have previously received trastuzumab, repeat ECHO monitoring 12 weekly for the first 12 months, then if stable only repeat if clinically appropriate

Cardiac function	Management
LVEF >45%	No dose modification required
LVEF 40 to 45%	If decrease is < 10 ejection fraction 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%	With hold treatment and repeat LVEF in 3 weeks' time if LVEF remains < 40% discontinue treatment
Symptomatic congestive heart failure	Discontinue Kadcyla

References:

Kadcyla 100 mg & 160 mg Powder for Concentrate for Solution. Summary of Product Characteristics. Roche Products www.medicines.org.uk/emc/medicine last updated 11/02/2014.

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