Systemic Anti Cancer Therapy Protocol

Enhertu (Trastuzumab Deruxtecan) HER2 Positive Advanced Breast Cancer

PROTOCOL REF: MPHAENTDBR
(Version No: 1.0)

Approved for use in:

- HER2 positive unresectable locally advanced or metastatic breast cancer after 2 or more anti-HER2 therapies
- ECOG PS = 0 or 1
- LVEF of at least 50% on commencing treatment
- Refer to blueteq form for full inclusion criteria.

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

********************Blueteq Form Required*******************

Dosage:

Drug	Dose	Route	Frequency
Enhertu	**5.4mg/kg**	IV infusion	Every 21 days

Treatment continues until disease progression or unacceptable toxicity

Administration:

Counsel patients to report cough, dyspnoea, fever and/or any new or worsening respiratory symptoms immediately – need to be reviewed for signs of interstitial lung disease

Appropriate contraceptive measures are required

Emetogenic risk:

Moderately emetogenic.

Supportive treatments:

Dexamethasone 4mg orally twice daily for 3 days

Metoclopramide 10mg three times a day when required

Extravasation risk:

No information currently available, consider non-vesicant.

Refer to the CCC policy for the '**Prevention and Management of Extravasation Injuries'.**

Dosing in renal and hepatic impairment:

Renal	No adjustment in mild to moderate renal impairment required. No data if CrCl is less than 30mL/min

Hepatic	Treatment can continue if bilirubin is less than 3 times upper limit of normal (ULN) and AST/ALT are less than 5 x ULN

Interactions:

No clinically relevant interactions currently known

Treatment schedule:

Day	Medicine	Dose	Route	Diluent and rate
1	**Ondansetron**	**16mg**	**PO**	30mins before chemotherapy
	Dexamethasone	**12mg**	**PO**	30mins before chemotherapy
	ENHERTU	**5.4mg/kg**	**IV**	100mL glucose 5%. 1st dose to be given over 90mins, if tolerated subsequent doses to be given over 30mins Give via 0.22 micron filter

Main toxicities:

Patients presenting with cough and/or increasing shortness of breath: defer treatment and ensure urgent medical review, for CT scan and/or ECHO depending on clinical picture

Haematological	Neutropenia, anaemia, thrombocytopenia,
Cardiac and Vascular disorders	LVEF reduction Hypokalaemia
Gastrointestinal	Nausea, vomiting, diarrhoea, constipation, decreased appetite, abdominal pain
Respiratory system	**Interstitial lung disease / pneumonitis** **Dyspnoea, cough**
Hepatobiliary	Elevation of liver transaminases, alkaline phosphatase and bilirubin.
General disorders and administration site conditions	Infusion related reactions Fatigue, headache, alopecia, dry eyes Epistaxis Rash

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Ongoing
Informed Consent	X						
Clinical Assessment	X			X			As clinically indicated
SACT Assessment (to include PS and toxicities)	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	Every cycle
U&E & LFTs & Magnesium	X	X	X	X	X	X	Every Cycle
CrCl (Cockcroft and Gault)	X	X	X	X	X	X	Every cycle
CT scan	X						As clinically indicated
ECHO*	X						If clinically indicated
Full set of observations**	X						If clinically indicated

Weight recorded	X	X	X	X	X	X	Every cycle
Blood glucose	X						Repeat if clinically indicated
Height	X						

***ECHO: whilst LVEF monitoring is recommended the patients commencing enhertu will have had previous HER2 targeted treatment and a new baseline ECHO is not mandated, although it is recommended if time allows.**

****Patients presenting with cough and/or increasing shortness of breath: defer treatment and ensure urgent medical review, for CT scan and/or ECHO depending on clinical picture (refer to 'Main Toxicities' Section**

Dose Modifications and Toxicity Management:

	Dose level
Recommended starting dose	5.4mg/kg
First dose reduction	4.4mg/kg
Second dose reduction	3.2mg/kg
Third dose reduction	discontinue

Haematological toxicity (if required):

Proceed on day 1 if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 100 x 10^9/L

Delay 1 week on day 1 if-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 99 x 10^9/L

For 2 consecutive deferrals due to neutropenia or an episode of neutropenic sepsis: **reduce dose by one level**.

Non- Haematological toxicity:

For any grade 3 toxicity, delay for one week and review within 7 days to ensure recovering to baseline levels

Interstitial lung disease

CTC grading

Grade 1	Asymptomatic, clinical or diagnostic observations only
Grade 2	Symptomatic, limiting instrumental activities of daily living
Grade 3	Severe symptoms, limiting self-care activities of daily living; oxygen indicated
Grade 4	Life-threatening respiratory compromise

Patients should monitor for cough, dyspnoea, fever and/or new or worsening respiratory symptoms.

Signs and symptoms of ILD/pneumonitis should be investigated with CT scan. Asymptomatic ILD (grade 1) consider prednisolone 0.5mg/kg. **Withhold enhertu until recovered to grade 0.**

If resolves within 28 days then can continue with current dose. If longer than 28 days to resolve then reduce dose by one level

Grade 2 or above (i.e. symptomatic): Promptly initiate prednisolone 1mg/kg for at least 14 days or until complete resolution of clinical and chest CT findings. Gradually taper the dose over next 4 weeks.

Discontinue enhertu

LVEF

Enhertu should be discontinued if LVEF falls below 40% or there is a 20% drop from baseline

Infusion related reactions

Grade 1 and 2: Stop infusion and provide supportive treatments (as per CCC policy). When resolved, infusion can be resumed at half the rate if clinically appropriate.

Add prophylactic chlorphenamine IV 10mg and hydrocortisone IV 100mg to subsequent cycles

LFTs

AST or ALT	Bilirubin	Action
Grade 2 (< 5 x ULN)	Grade 1 or no change from baseline	continue
Grade 3 (5 to 20 x ULN)	Grade 2 (increased to between 1.5 and 3 x ULN)	Hold treatment and repeat in 7 days. If resolved to baseline within 7 days continue on current dose
	Grade 3 (3 to 10 x ULN)	Hold treatment and repeat in 7 days. If resolved to less than 1.5 x ULN then resume at dose reduction
Grade 4	Grade 4	Discontinue

References:

1. SmPC Enhertu 100 mg powder for concentrate for solution for infusion (Daiichi Sankyo UK Limited) accessed via https://www.medicines.org.uk/emc (last updated 2nd March 2021).
2. NICE FAD April 2020
3. DESTINY-BREAST01 trial Modi et al, NEJM 2020382:610-621