Capecitabine – Breast cancer

Indication
Metastatic or locally advanced breast cancer

Adjuvant treatment for triple negative breast cancer in patients who have not achieved pathological complete response to neo-adjuvant chemotherapy

Regimen details
Capecitabine 1250mg/m^2 orally twice daily for 2 weeks

Cycle frequency
Every 21 days

Number of cycles
For metastatic or locally advanced breast cancer, treatment is given until disease progression or unacceptable toxicity

For adjuvant treatment, give 8 cycles

Administration
Tablets should be swallowed with water within 30 minutes of a meal
For patients with swallowing difficulties, the tablets may be dispersed in water (do not crush)

Patients should be informed of the need to interrupt treatment immediately if they develop moderate or severe side-effects particularly diarrhoea (not controlled by loperamide), palmar plantar erythrodyaesthesia, chest pain or infection.
Any unused tablets to be returned at the next appointment

Cycle must finish 14 days after starting irrespective of how many delays or tablets not taken

Pre-medication
None required

Emetogenicity
Minimal

Additional supportive medication
Supply metoclopramide and loperamide with first cycle

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
DPYD	Baseline

Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced fluorouracil metabolism (this can present as severe diarrhoea and/or severe stomatitis early in the first cycle). Patients require DPYD testing prior to administration. Dose adjustments should be made in accordance with local DPD policy

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST)

LFTs may be looked at retrospectively **unless** they are known to be abnormal, then they need to be checked the day before so that the results are available pre-chemotherapy

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	≥ 1.5 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Hb	≥ 95 g/L
Creatinine clearance	≥ 50 mL/min
Bilirubin	≤ 3 x ULN
AST	< 2.5 x ULN

Dose modifications

Renal impairment

CrCl (ml/min)	Capecitabine dose
>50	100%
30-50	75% (closely monitored)
<30	Contraindicated

Dose modifications should be made as per the following table:

Toxicity grade	1st occurrence	2nd occurrence	3rd occurrence	4th occurrence
0-1	100%	100%	100%	100%
2	Delay then 100%	Delay then 75%	Delay then 50%	Discontinue
3	Delay then 75%	Delay then 50%	Discontinue	
4	Delay then 50%	Discontinue		

Once dose has been reduced it should not be increased at a later time

Patients presenting with diarrhoea must be carefully monitored until the symptoms have disappeared as a rapid deterioration can occur

Adverse effects –

for full details consult product literature/ reference texts

Palmar Plantar Erythrodysaesthesia (PPE or hand/foot syndrome)
Diarrhoea
Abdominal pain
Nausea & vomiting
Pyrexia
Fatigue
Asthenia
Anorexia
Myelosuppression
Hyperbilirubinaemia
Stomatitis
Cardiotoxicity (occasionally patients may experience coronary artery spasm)

Significant drug interactions

– for full details consult product literature/ reference texts

Brivudine can lead to increased capecitabine toxicity. There must be a 4 week waiting period between end of treatment with brivudine and start of capecitabine therapy. Treatment with brivudine can be started 24 hours after the last dose of capecitabine.

Cytochrome P-450 2C9 substrates
Exercise care when capecitabine is co-administered with 2C9 substrates. Capecitabine increases the effects of warfarin (monitor INR and adjust dose), and phenytoin (monitor concentration)

Allopurinol
Avoid concomitant treatment with capecitabine and allopurinol

Folinic/folic acid
Toxicity of capecitabine may be enhanced by folinic acid (and possibly folic acid)

Additional comments

References

Adjuvant Capecitabine for Breast Cancer after Preoperative Chemotherapy N Engl J Med 2017; 376:2147-2159

Capecitabine SPC - https://www.medicines.org.uk/emc/product/9939/smpc

THIS PROTOCOL HAS BEEN DIRECTED BY DR BEZECNY, CONSULTANT ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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