Capecitabine and radiotherapy (pancreas)

Indication

Locally advanced non-metastatic cancer of the pancreas in patients with good performance status (WHO 0-1) and who have not progressed on first-line chemotherapy.

ICD-10 codes

Codes with a prefix C25

Regimen details

Day	Drug	Dose	Route
Monday to Friday for 5 ½ weeks (Monday, Tuesday and Wednesday only in week 6) – concurrent with radiotherapy	Capecitabine	830mg/m^2 BD	PO

Cycle frequency

Capecitabine is taken Monday to Friday BD for 5½ weeks (Monday, Tuesday and Wednesday in the final half week) concurrently with radiotherapy. It is not taken on weekends or any other days when radiotherapy is not given.

Number of cycles

As above

Administration

Capecitabine is available as 150mg and 500mg tablets.
Tablets should be taken after food.
The first dose of capecitabine should ideally be taken at least 1 to 2 hours before the first fraction of radiotherapy with subsequent doses taken in the morning after breakfast and in the evening after the evening meal including on the last day of treatment.
The calculated dose should be rounded to the nearest whole tablet size.

Pre-medication

$5HT_3$ antagonist 1 hour prior to radiotherapy.

Emetogenicity

This regimen has moderate-low emetic potential

Additional supportive medication

H_2 antagonist or proton pump inhibitor for 12 weeks from the start of this regimen.
Loperamide if required.
Topical emollients to prevent PPE.
Additional antiemetics if required.

Extravasation

N/A

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
CA19-9	14 days

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	weekly
U+E (including creatinine)	weekly
LFTs	weekly

Standard limits for administration to go ahead

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

Investigation	**Limit**
Neutrophils	≥ 1.0 x 10^9/L
Platelets	> 100 x 10^9/L
Creatinine clearance (CrCl)	> 50 mL/min
Bilirubin	≤ 3 x ULN
AST/ALT	≤ 2.5 x ULN

Dose modifications

- **Haematological toxicity**

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)	**Capecitabine dose**	**Radiotherapy**
≥ 1.0	and	> 100	100%	Continue
≥ 1.0	and	75-100	75%	Continue
< 1.0	or	<75	Omit for 1 week. Restart at 75% dose	Stop if neutrophils <0.5 or platelets <50. Repeat FBC in 3 days. Restart radiotherapy alone if neutrophils > 0.5 and platelets > 50. Restart capecitabine when neutrophils >1.0 and platelets > 75.

- **Renal impairment**

CrCl (mL/min)	**Capecitabine dose**
>50	100%
30-50	75% (with close monitoring)
<30	Omit

- **Hepatic impairment**

AST +/or ALT (x ULN)		**Bilirubin (x ULN)**	**Capecitabine dose**
≤ 2.5	and	≤ 3	100%
> 2.5	or	> 3	Omit until liver function recovers

- **Other toxicities**

Other toxicities should be managed by symptomatic treatment and/or dose modification (i.e. by treatment interruption or undertaking a dose reduction).
Once the dose has been reduced, it should not be increased at a later time.

For those toxicities considered unlikely to become serious or life-threatening (e.g. alopecia, altered taste or nail changes) treatment can be continued at the same dose without reduction or interruption.

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 such as, painful walking or infection.

Diarrhoea:

Toxicity grade	Capecitabine dose	Radiotherapy	Comments
1-2	100%	Continue	Maximise antidiarrhoeal treatment
2 (with full antidiarrhoeal treatment)	Withhold until ≤ grade 1. Restart at 75% dose.	Withhold until ≤ grade 1.	Maximise antidiarrhoeal treatment
3 (1st occurrence)	Withhold until ≤ grade 1. Restart at 75% dose.	Withhold until ≤ grade 1.	Maximise antidiarrhoeal treatment
3 (2nd occurrence)	Discontinue	Discontinue	
4	Discontinue	Discontinue	

Nausea and vomiting:

Toxicity grade	Capecitabine dose	Radiotherapy	Comments
1-2	100%	Continue	Maximise antiemetic treatment
2 (with full antiemetic treatment)	Withhold until ≤ grade 1. Restart at 75% dose.	Withhold until ≤ grade 1.	Maximise antiemetic treatment
3 (1st occurrence)	Withhold until ≤ grade 1. Restart at 75% dose.	Withhold until ≤ grade 1.	Maximise antiemetic treatment
3 (2nd occurrence)	Discontinue	Discontinue	
4	Discontinue	Discontinue	

Other toxicities:

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		

Any delays should be until the toxicity has resolved to grade 0-1.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Cardiotoxicity
Myelosuppression
Diarrhoea
Gastrointestinal haemorrhage
Severe toxicity due to DPD deficiency (see comments below)

- **Frequently occurring side effects**

Nausea and vomiting
Stomatitis/Mucositis
Myelosuppression
PPE
Fatigue
Skin reactions

Nail changes
Taste disturbance

- **Other side effects**

Myalgia
Fluid retention
Alopecia
Rash
Deranged liver function

Significant drug interactions – for full details consult product literature/ reference texts

Folinates: Avoid concomitant use of folinic and folic acid – enhanced toxicity of capecitabine.

Co-trimoxazole/trimethoprim: Avoid if possible – enhances antifolate effect. If essential, monitor FBC regularly.

Warfarin/coumarin anticoagulants: Avoid use due to elevations in INR. Switch to low molecular weight heparin during treatment.

Sorivudine, Allopurinol, Phenytoin: close monitoring is necessary if prescribed with any of these agents.

Antacids: Aluminium hydroxide and magnesium hydroxide containing antacids have been shown to produce a slight increase in plasma concentration of capecitabine.

Additional comments

This regimen is contraindicated if known or suspected dihydropyrimidine dehydrogenase (DPD) deficiency.

Radiotherapy is given as 50.4Gy given as 28 fractions (1.8Gy/fraction) on Mondays to Fridays for 5½ weeks.

References

- Summary of Product Characteristics Caepcitabine - Xeloda®(Roche) accessed 11 June 2014 available at http://www.medicines.org.uk
- NCRI Upper GI Clinical Studies Group, 2009. Multi-centre randomised phase II study of induction chemotherapy followed by gemcitabine or capecitabine based chemoradiotherapy for locally advanced non-metastatic pancreatic cancer.

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Date: 11 December 2014