## Regimen: Capecitabine with Radiotherapy for Pancreatic Cancer

ICD10 codes pre-fixed with C25.

### Indication
Locally advanced non-metastatic cancer of the pancreas in patients with good performance status and who have not progressed on first-line chemotherapy
Funding must be agreed locally prior to use.

### Regimen details

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monday to Friday for 5½ weeks (Mon, Tues, Weds in week 6) concurrent with radiotherapy</td>
<td>Capecitabine</td>
<td>830mg/m²²</td>
<td>PO</td>
<td>BD</td>
</tr>
</tbody>
</table>

### Administration
Capecitabine should be swallowed whole with water not later than 30 minutes after a meal.
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.

### Frequency
Capecitabine is taken Monday to Friday twice a day 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.

### Extravasation
Capecitabine is an oral anticancer medicine so there is no extravasation risk

### Premedication
Ondansetron (or 5HT3 antagonist of choice) 8mg po once daily, one hour prior to radiotherapy
Metoclopramide 10-20mg po TDS PRN

### Emetogenicity
Capecitabine has mild emetogenic potential, radiotherapy is highly emetogenic– refer to local protocol

### Additional recommended supportive medication
Proton Pump Inhibitor (of local choice) for 12 weeks from the start of this regimen
Loperamide 4mg initially then 2mg after each loose stool for diarrhoea.

### Pre-treatment evaluation
- FBC Baseline – results valid for 14 days
- U+E Baseline – results valid for 14 days
- LFT Baseline – results valid for 14 days
- CA19-9 Baseline - results valid for 14 days
- Clinical Examination including Weight

### Regular investigations
- FBC Results valid for 72 hrs
- U+E Results valid for 72 hrs
- LFT Results valid for 72 hrs

### Standard limits for administration to go ahead – if blood results not within range, authorisation to administer
- Neutrophil count >1.0 x 10⁹/L
- Platelet count >100 x 10⁹/L
- Creatinine clearance GFR must be greater than 50 mls/min
- Bilirubin <35micromol/L
must be given by prescriber/consultant
### Dose modifications

#### Haematological toxicity

<table>
<thead>
<tr>
<th>Neutrophil x 10^9/l</th>
<th>Platelet x 10^9/l</th>
<th>Capecitabine arm</th>
<th>RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1.0</td>
<td>&gt;100</td>
<td>100% dose</td>
<td>Continue</td>
</tr>
<tr>
<td>≥1.0</td>
<td>75 - 100</td>
<td>75% dose</td>
<td>Continue</td>
</tr>
<tr>
<td>&lt;0.5</td>
<td>&lt;75</td>
<td>Omit dose for the week. Subsequent dose at 75%</td>
<td>Stop RT if neutrophil &lt;0.5 or platelets &lt;50; repeat FBC in 3 days. Restart RT alone if neutrophil &gt;0.5 and platelets &gt;50. Restart chemotherapy when neutrophil &gt;1 and platelets &gt;75.</td>
</tr>
</tbody>
</table>

#### Renal impairment

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Capecitabine Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;50</td>
<td>100% dose</td>
</tr>
<tr>
<td>30-50</td>
<td>75% dose</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Omit</td>
</tr>
</tbody>
</table>

#### Hepatic impairment

| Bilirubin > 3 x ULN or ALT/AST > 2.5 ULN | Omit Capecitabine until liver function recovers |

#### NCI Common toxicity criteria

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Grade</th>
<th>Capecitabine</th>
<th>RT</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/ Vomiting</td>
<td>Grade 1 / 2</td>
<td>Full dose</td>
<td>Continue</td>
<td>Maximize anti-emetics</td>
</tr>
<tr>
<td></td>
<td>Grade 2</td>
<td>Withhold until G1. Restart at 75% dose</td>
<td>Withhold until G1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade 3</td>
<td>Withhold until G1. Restart at 75% dose</td>
<td>Withhold until G1</td>
<td>Maximize anti-emetics</td>
</tr>
<tr>
<td></td>
<td>Grade 3</td>
<td>Stop CRT</td>
<td>Stop CRT</td>
<td>Stop CRT</td>
</tr>
<tr>
<td></td>
<td>Grade 4</td>
<td>Stop CRT</td>
<td>Stop CRT</td>
<td>Stop CRT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Grade</th>
<th>Capecitabine</th>
<th>RT</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea</td>
<td>Grade 1 / 2</td>
<td>Full dose</td>
<td>Continue</td>
<td>Maximize anti-diarrhoeal</td>
</tr>
<tr>
<td></td>
<td>Grade 2</td>
<td>Withhold until G1. Restart at 75% dose</td>
<td>Withhold until G1</td>
<td>Maximize anti-diarrhoeal</td>
</tr>
<tr>
<td></td>
<td>Grade 3</td>
<td>Withhold until G1. Restart at 75% dose</td>
<td>Withhold until G1</td>
<td>Maximize anti-diarrhoeal</td>
</tr>
<tr>
<td></td>
<td>Grade 3</td>
<td>Stop CRT</td>
<td>Stop CRT</td>
<td>Stop CRT</td>
</tr>
<tr>
<td></td>
<td>Grade 4</td>
<td>Stop CRT</td>
<td>Stop CRT</td>
<td>Stop CRT</td>
</tr>
</tbody>
</table>
### Other NCI toxicities

<table>
<thead>
<tr>
<th>Toxicity NCI Grade</th>
<th>Action</th>
<th>Dose adjustment for next cycle (% of starting dose)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Maintain dose level</td>
<td>Maintain dose level</td>
<td></td>
</tr>
<tr>
<td>Grade 2 1(^{st}) appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>2(^{nd}) appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>3(^{rd}) appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>4(^{th}) appearance</td>
<td>Discontinue treatment permanently</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Grade 3 1(^{st}) appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>2(^{nd}) appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>3(^{rd}) appearance</td>
<td>Discontinue treatment permanently</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Grade 4 1(^{st}) appearance</td>
<td>Discontinue permanently or if deemed to be in the patient’s best interest to continue, interrupt until resolved to grade 0-1.</td>
<td>50%</td>
<td></td>
</tr>
</tbody>
</table>

### Adverse effects

#### Rare or serious side effects
- Gastro-intestinal haemorrhage
- Gastro-intestinal perforation
- Subacute intestinal obstruction
- Chronic Renal damage
- Second malignancy

#### Frequently occurring side effects
- Nausea and vomiting
- Diarrhoea
- Acute gastritis
- Fatigue
- Palmar-plantar erythrodysthesia
- Paraesthesia
- Bilirubin increased
- Lymphopenia
- Neutropenia
- Thrombocytopenia
- Anaemia

### Other

#### Significant drug interactions

**Coumarin derivative anticoagulants** e.g. warfarin
- Monitor INR or PT regularly. Increased risk of bleeding. It is suggested participants change to low molecular weight heparin for duration of treatment

**Phenytoin**
- Increased plasma phenytoin levels. Monitor levels regularly

**Folinic acid**
- Folinic acid has a pharmacodynamic effect on capecitabine, reducing maximum tolerated dose and hence increasing potential side effect toxicity profile

**Antacids**
- Aluminium hydroxide and magnesium hydroxide containing antacids have been shown to produce a slight increase in plasma concentration of capecitabine and one metabolite (5DFCR)

**Cytochrome P-450 drugs** e.g. angiotensin II blockers – losartan,
valsartan; oral hypoglycaemics – glipizide, rosiglitazone, tolbutamide; NSAID – celecoxib, diclofenac, ibuprofen and indomethacin

**Tamoxifen**

Tamoxifen in combination with gemcitabine or capecitabine may result in increased adverse events

**Comments**

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

**Cumulative Doses**

**References**

- 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.

**Document** Chemotherapy Protocol Template
**Number** ASWCS13 GI029
**Approval date** 14/01/2013
**Written by** Georgina Holmes, Pharmacist, UHBristol NHSFT
**Checked by** Steve Falk, Consultant Clinical Oncologist, UHBristol NHSFT
**Authorised by** Jeremy Braybrooke, Chair ASWCS Drugs and Therapeutics Committee
**Review date** 14/01/2015
**Version number** 0.1.a

*Only valid on day of printing*