Capecitabine and temozolomide

Indication
Metastatic/Non-resectable Neuroendocrine carcinoma/Tumour

Regimen details
Capecitabine 750mg/m^2 orally twice daily on Days 1- 14 (2 weeks)
Temozolomide 200mg/m^2 orally once daily on Days 10-14 (5 Days)

Cycle frequency
Every 28 days

Number of cycles
Until disease progression

Administration
Capecitabine should be taken after food
Temozolomide should be taken on an empty stomach
If vomiting occurs after a dose is taken, patients should not take an additional dose

Pre-medication
N/A

Emetogenicity
Low emetogenicity on days 1-14, high on 10-14

Additional supportive medication
Ondansetron 8mg BD on days 10-14 (i.e. with temozolomide)
Metoclopramide prn

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
DPD mutation analysis	

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 DPD 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)

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	≥ 75 x 10^9/L
Creatinine clearance	≥ 50 mL/min
Bilirubin	≤ 3 x ULN
AST	< 2.5 x ULN

Dose modifications

For haematological toxicity

At the start of each cycle

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Capecitabine and temozolomide doses			
			1st occurrence	2nd occurrence	3rd occurrence	4th occurrence
≥1.5	And	≥75	100%	100%	100%	100%
1-1.49	Or	50-74	Delay until recovery then 100%	Delay until recovery then 75%	Delay until recovery then 50%	Discontinue
0.5-0.99	Or	25-49	Delay until recovery then 75%	Delay until recovery then 50%	Discontinue	Discontinue
<0.5	Or	<25	Discontinue or delay until recovery then 50%	Discontinue	Discontinue	Discontinue

Renal Impairment

Capecitabine

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

Hepatic Impairment

Capecitabine

AST / ALT (x ULN)		Bilirubin (x ULN)	Capecitabine dose
≤ 2.5	and	≤ 3	100%
> 2.5	or	> 3	Consultant decision

Temozolomide – Caution in patients with severe hepatic impairment – discuss with consultant if bilirubin > 3 x ULN and/or AST/ALT > 2.5 x ULN

Other toxicities

Reduce capecitabine by 25% in the event of palmar plantar erythrodysesthesia, diarrhoea or stomatitis.

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Cardiotoxicity
Myelosuppression
Diarrhoea
Myopathy
Thrombus/embolism
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
Constipation
Anorexia, weight loss
Seizure, headache

- **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 fluorouracil.
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.
Sodium valproate - may decrease clearance of temozolomide

Additional comments

Temozolomide is contraindicated in patients hypersensitive to dacarbazine (DTIC)

References

South West Clinical Network protocol – accessed 29/07/20

THIS PROTOCOL HAS BEEN DIRECTED BY DR LAU, CONSULTANT ONCOLOGIST

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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