CapOx - Oxaliplatin and Capecitabine

Indication
First line treatment of locally advanced or metastatic gastric/gastroesophageal cancer.

ICD-10 codes
Codes prefixed with C15 and C16.

Regimen details

Day	Drug	Dose	Route
1	Oxaliplatin	130mg/m^2	IV infusion
1-21	Capecitabine	625mg/m^2 BD	PO

All patients must have documented DPYD status and capecitabine doses adjusted accordingly prior to commencing treatment as per local practice.

Cycle frequency
21 days

Number of cycles
Maximum of 8 cycles.

Administration
Oxaliplatin is administered in 250-500mL glucose 5% over 2 hours. If patients experience laryngo-pharyngeal dyaesthesia (see below), subsequent infusions should be should be given over 4-6 hours.

Oxaliplatin is not compatible with sodium chloride 0.9%. Lines must not be piggybacked or flushed with sodium chloride 0.9% immediately after the infusion.

Patients should be observed closely for platinum hypersensitivity reactions, particularly during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of oxaliplatin. Facilities for the treatment of hypotension and bronchospasm must be available.
If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy: the infusion may be temporarily interrupted and when symptoms improve re-started at a slower infusion rate. Chlorphenamine 10mg IV may be administered.
Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of oxaliplatin and appropriate therapy.

Oxaliplatin may cause transient paraesthesia of hands and feet and laryngopharyngeal dysaesthesia (unpleasant sensations in the throat). Onset is during or within hours of infusion and resolves within minutes to a few days. Symptoms are exacerbated by cold, so patients should be advised on precautions to be taken. This does not require treatment discontinuation or dose reduction but subsequent infusions should be given over 4 - 6 hours.

Capecitabine is available as 150mg and 500mg tablets.
Tablets should be taken after food, within 30 minutes of a meal, and swallowed whole with a glass of water.

Capecitabine should be banded as per national dose banding: https://www.england.nhs.uk/publication/national-dose-banding-table-capecitabine/

Pre-medication

Patients who have previously experienced Grade 1 or 2 platinum hypersensitivity should receive the following premedication:

- 45 minutes prior to Oxaliplatin: Dexamethasone 20mg IV
- 30 minutes prior to Oxaliplatin: Chlorphenamine 10mg IV and consider H2 antagonist as per local practice

Patients who develop peripheral neuropathy may be considered for calcium gluconate 1g and magnesium sulphate 1g given together in 250mL 5% glucose IV over 20 minutes pre- and post-oxaliplatin infusion. Caution is required in giving this treatment to patients with known hypercalcemia or those receiving therapy with digoxin or thiazide diuretics.

Emetogenicity

This regimen has a moderate emetogenic potential

Additional supportive medication

Mouthwashes as per local policy.
Loperamide if required.

Extravasation

Oxaliplatin is an exfoliant (Group 4).

Investigations – pre first cycle

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

DPYD status must be available prior to starting Capecitabine treatment as per local practice.

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days
Magnesium	7 days
Calcium	7 days

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	≥ 75 x 10^9/L
Bilirubin	< 1.5 x ULN
Creatinine Clearance (CrCl)	> 50mL/min

Dose modifications

- **Haematological toxicity**

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)	**Dose**
≥ 1.0	and	≥ 75	100%
0.5 - < 1.0	or	50-74	Withhold treatment. Delay until count recovery Resume with Oxaliplatin 100mg/m^2, Capecitabine 100% dose

- **Renal impairment**

CrCl (mL/min)	**Oxaliplatin dose**	**Capecitabine dose**
> 50	100%	100%
30-49	75%	75%
< 30	omit	contraindicated

- **Hepatic impairment**

Capecitabine and oxaliplatin:
Lack of information available. In patients with mild to moderate hepatic dysfunction due to liver metastases (bilirubin < 3 x ULN and/or AST/ALT < 5 x ULN) no dose reduction is usually necessary – discuss with consultant

Oxaliplatin:
Little information available. Probably no dose reduction necessary, consultant decision.

- **Other toxicities**

Capecitabine:
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.

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		

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

Oxaliplatin:
Neurological toxicity:
If neurological symptoms occur, use the following oxaliplatin dose adjustments:

Toxicity grade	**Oxaliplatin dose**
1	100%
2 (persisting until next cycle)	100mg/m^2
3 (>7 days but resolved before next cycle)	100mg/m^2
3 (persisting until next cycle) or 4	Discontinue

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

- **Serious side effects**

Myelosuppression
Infertility
Allergic reactions
Neurotoxicity
Cardiomyopathy
Nephrotoxicity
Severe toxicity due to DPD deficiency

- **Frequently occurring side effects**

Laryngopharyngeal dysaesthesia
Nausea and vomiting
Diarrhoea
Stomatitis and mucositis
Palmar-plantar erythema
Alopecia
Fatigue

- **Other side effects**

Dysguesia
Headache
Dizziness

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

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

Oxaliplatin:
Avoid nephrotoxic agents as these may increase toxicity of oxaliplatin.

Capecitabine:
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.

Phenytoin and fosphenytoin – toxicity has occurred during concomitant capecitabine therapy – monitor levels regularly.

Sorivudine and its analogues – co-administration causes increased toxicity which may be fatal.

Allopurinol – A decrease in capecitabine activity has been shown when taken in combination of allopurinol. Avoid if possible.

Antacids – the use of antacids with capecitabine can decrease absorption – avoid.

Additional comments

Dose related peripheral sensory neuropathy can occur with oxaliplatin. It usually occurs after a cumulative dose of 800mg/m2. It can occur after treatment with oxaliplatin is completed, and is usually reversible, taking approximately 3 – 5 months to recovery.

References

- Summary of Product Characteristics Oxaliplatin (Sanofi) accessed 15 January 2020 via www.medicines.org.uk
- Summary of Product Characteristics Capecitabine (Roche) accessed 15 January 2020 via www.medicines.org.uk
- NICE Clinical Guideline (NG83) Oesophago-gastric cancer: assessment and management in adults. Accessed 15 January 2020 via www.nice.org.uk
- Hall P et al. Optimizing chemotherapy for frail and elderly patients with advanced gastroesophageal cancer (aGOAC): The GO2 Phase III trial. J Clin Oncol 2019. 37, 15 (suppl) 4006.

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