Systemic Anti Cancer Treatment Protocol

Raltitrexed & Oxaliplatin (TOMOX)

PROTOCOL REF: MPHATOMOXGA
(Version No: 1.0)

Approved for use in:

Patients with advanced colorectal cancer who are intolerant to 5-fluorouracil or capecitabine, or for whom these drugs are not suitable (for example, patients who develop cardiotoxicity). Oxaliplatin can be omitted from this regimen for patients unlikely to tolerate, or unable to tolerate oxaliplatin.

Dosage:

Drug	Dosage	Route	Frequency
Raltitrexed	3mg/m^2	IV	Every 21 days
Oxaliplatin	100mg/m^2	IV	Every 21 days

Supportive treatments:

Antiemetic risk - moderate

Domperidone 10mg oral tablets, up to 3 times a day or as required

Dexamethasone 4mg twice a day for three days

Loperamide 4mg initially, then 2mg after each loose stool (maximum 16mg in 24hrs)

Extravasation risk:

Oxaliplatin is IRRITANT and raltitrexed is a non-vesicant. Follow Trust/Network guidance.

Administration:

Day	Drug	Dosage	Route	Diluent and rate
1	Dexamethasone 30 mins before chemotherapy	8mg	Oral	
1	Ondansetron 30 mins before chemotherapy	16mg	Oral	
1	Raltitrexed	3mg/m^2	IV	100mL Sodium Chloride 0.9% over 15 minutes
1	Oxaliplatin	100mg/m^2	IV	500mL Glucose 5% infusion over 2 hours

Caution in patients with pre-existing neurotoxicity

Be aware of infusion related allergic reactions. For severe reactions, discuss with Consultant before continuing with treatment.

Main Toxicities:

Oxaliplatin

Infusion reactions, neurotoxicity, myelosuppression, mucositis, diarrhoea, nausea and vomiting.

Raltitrexed

Myelosuppression, anaemia, nausea and vomiting, abdominal discomfort, diarrhoea, loss of appetite, constipation, stomatitis, mouth ulcers, fatigue, dry skin or skin rashes, hepatic impairment, conjunctivitis / sore eyes.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing	Last cycle
Clinical Assessment	X		X		X	Alternate cycles	
SACT Assessment	X	X	X	X	X	Every cycle	Check has OPD appointment
FBC	X	X	X	X	X	Every cycle	X
U&E & LFT	X	X	X	X	X	Every cycle	X
Creatinine Clearance	X	X	X	X	X	Every cycle	X
CT scan	X					Inform consultant team if not booked	Check has date for CT
Informed Consent	X					Verbal each cycle	
Weight recorded	X	X	X	X	X	Every cycle	X

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if all apply:-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

Delay 1 week on day 1 if any apply:-

ANC $\leq$ 0.9 x 10^9/L	Platelets $\leq$ 99 x 10^9/L

If platelets or ANC (Absolute Neutrophil Count) are still below required levels for a second week, delay treatment again and patient will need assessment and chemotherapy dose reduction.

Non-haematological toxicity

Renal

Calculate Creatinine Clearance (CrCl) using Cockcroft and Gault before each cycle.

CrCl (mL/min)	Raltitrexed	Oxaliplatin
≥ 65	Full dose	Full dose
55 – 64.9	75% and reduce frequency to 4 weekly	Full dose every 4 weeks
30 – 54.9	50% and reduce frequency to 4 weekly	Full dose every 4 weeks
25 – 29.9	50% and reduce frequency to 4 weekly	Omit
<25	Omit	Omit

Cockcroft and Gault formula

Male patient $\frac{1.23 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

Female patients $\frac{1.04 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

Hepatic

Liver function	Oxaliplatin dose
Bilirubin > 3 x ULN	50%

No raltitrexed dosage adjustment is recommended for patients with mild to moderate hepatic impairment. Raltitrexed has not been studied in patients with severe hepatic impairment and its use in such patients should be discussed with a consultant. Note that significantly impaired hepatic function might be a sign of disease progression and require cessation or change of treatment.

Always discuss deteriorating organ function with consultant

Oxaliplatin

Neurotoxicity – see notes below for specific cases

Neurotoxicity	Oxaliplatin dose
Grade 1 any duration or grade 2 < 7days but resolving before next cycle	No dose reduction
Grade 2 persisting for 7 days or Grade 3 resolved by next cycle	Reduce by 20%
Grade 3 persisting to next cycle or any grade 4	Stop oxaliplatin

Acute cold related dysaesthesia (CRD)

Transient paraesthesia of hands and feet as well as laryngopharyngeal dysaesthesia (unpleasant sensations in throat) is common. Onset is during or within hours of infusion

	and it resolves in minutes or days. Symptoms are exacerbated by cold – advise patients on suitable precautions eg avoid cold drinks. Should not require dose reduction, but if troublesome then infusion duration can be increased to 6 hours. Whilst the recommended increase in duration of infusion is to 6 hours – where the oncologist and the treating team agree, this can be reduced to 4 hours dependent on the severity of the reaction and the tolerability of the infusion over this time.
Laryngopharyngeal dysaesthesia	Stop infusion, provide symptomatic treatment. Resume at slower infusion rate. Give subsequent infusions over 6 hours (see note below)
Cumulative dose related sensory neuropathy	Usually occurs after a cumulative dose of 800mg/m^2. It can occur after treatment is completed, is usually reversible taking about 3-5 months to recover
Allergic reactions during infusion	Stop the infusion and call for help. Follow trust hypersensitivity policy. Treat with IV corticosteroid and antihistamine. Consultant to advise on further treatment.

References:

National Institute for Health and Care Excellence. Colorectal cancer: diagnosis and management [CG131] (2011, accessed 1 November 2018)

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