Indication	First line treatment for RAS wild-type metastatic colorectal cancer NB: or as 2nd line treatment if treated with 1st line pembrolizumab (or 1st line nivolumab; previously available as an Interim COVID option) for MSI-H/dMMR disease.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 14 days. Continue until disease progression or unmanageable toxicity or patient choice. Assess every 12 weeks. NB cetuximab is unlicensed for 2-weekly administration.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • ECG cycle 1 • Monitor FBC, LFTs and U&Es prior to treatment and every 2 weeks thereafter, in particular Mg^{2+}, K^{+} and Ca^{2+} • Neuts <1.5 and PLT<100 delay one week. • Before starting treatment GFR (C+G) should be >/= 50ml/min • **DPD testing** must be undertaken in all patients before starting treatment; the result must be checked before treatment is started. • **Renal Impairment:** o Capecitabine is contraindicated if CrCl <30ml/min. o Oxaliplatin: Consider dose adjustment in severe renal impairment. o Cetuximab: no data available in patients with impaired function. • **Hepatic Impairment:** o Capecitabine: No dose adjustments in hepatic impairment (insufficient data of capecitabine to make a dose recommendation). o Cetuximab: no dose reduction required. o Oxaliplatin: no dose reduction required. • **Cardiotoxicity:** caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris. • **Dose interruption and reduction**: • Oxaliplatin: See **Table 1** for oxaliplatin induced neuropathy guidance. • Capecitabine: o Interrupt capecitabine in the event of >/= grade 2 non-haematological toxicity (with the exception of side effects such as alopecia, alteration in taste etc, considered to be not serious) until resolution of toxicity to grade 0-1. o Dose reduction should be considered if grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2 (except N&V and alopecia). Delay until resolution of toxicity to </= grade 1. • **Adverse reactions:** • **Cetuximab infusion rate and infusion related reactions (IRRs):**

	• Cetuximab can cause severe infusion related reactions, pre-meds must be given 30-60 minutes prior to the infusion and patients must be monitored every 30 minutes during the infusion and for a 1-hour period after. If the patient experiences a mild or moderate infusion-related reaction, the infusion rate may be decreased. It is recommended to maintain this lower infusion rate in all subsequent infusions. For severe reactions discontinue treatment. • **Skin reactions:** Capecitabine can induce severe skin reactions such as Stevens-Johnson syndrome and Toxic Epidermal Necrolysis. Patients should be informed of the possibility of such reactions and informed to seek urgent medical advice should any symptoms of a severe skin reaction occur. Treatment should be permanently discontinued in affected patients. For full guidance on cetuximab induced rashes see KMCC document "Guidelines for Cetuximab Induced Rashes" **www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/sact-pathways-guidelines-for-the-management-of-sact-induced-adverse-reactions-and-nursing/** • **Interstitial lung disease (ILD):** Patients should report any new or worsening respiratory symptoms. Cetuximab should be permanently discontinued in patients with confirmed ILD. • **Ocular toxicities:** Cetuximab should be used with caution in patients with a history of keratitis ulcerative keratitis or severe dry eye. If a diagnosis of ulcerative keratitis is confirmed, treatment with cetuximab should be interrupted or discontinued. If keratitis is diagnosed, the benefits and risks of continuing treatment should be carefully considered. • **Common drug/food interactions (for comprehensive list refer to BNF/SPC):** ○ Capecitabine must not be given with concurrent sorivudine or derivatives (e.g. brivudine), see SPC. ○ Monitor PT and INR regularly in patients taking coumarin-derivative anticoagulants. ○ Monitor phenytoin levels with concomitant use. ○ Caution with folinic acid or folic acid – potential for increased toxicity. ○ Avoid concomitant allopurinol. • **Driving:** Capecitabine/Oxaliplatin may cause dizziness, fatigue and nausea. Patients should be aware this may affect their ability to drive or operate machinery. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.
References	ARIA regimen COL-032 SPC accessed online 10.05.2022 KMCC proforma COL-005 V6 KMCC proforma COL-027 V5

NB For funding information, refer to the refer to CDF and NICE Drugs Funding List

Repeat every 14 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Chlorphenamine	10mg	IV	stat	To be administered 30-60 minutes prior to cetuximab.
	Dexamethasone	8mg	PO		
	CETUXIMAB	**500mg/m²**	IV	1st dose 2hrs 2nd dose onwards – over 90mins (or 60mins if tolerated)	To be given undiluted or diluted in 0.9% sodium chloride to a total volume of 250ml. Flush line with sodium chloride 0.9% IV post cetuximab infusion.
	Give cytotoxic chemo at least 1 hour after MAb				
	Ondansetron	<75yrs 16mg ≥75yrs 8mg	IV	15min	Sodium chloride 0.9% 50ml
	FLUSH WITH 5 % GLUCOSE BEFORE AND AFTER ADMINISTRATION OF OXALIPLATIN				
	OXALIPLATIN	**85mg/m²**	IV	2- 6 hrs	250-500ml 5% glucose (to give a concentration between 0.2 mg/ml and 0.70 mg/ml).

TTO	Drug	Dose	Route	Directions
Day 1	**CAPECITABINE**	**1600mg/m²/day** In 2 divided doses	PO	BD Take the first dose in the evening of **Day 1** and the last dose in the morning of **Day 10**, followed by a 5-day rest period. Take within 30 minutes after food, and approximately every 12 hours. Available as 500mg and 150mg tablets.
	Dexamethasone	6mg	PO	OM for 3 days.
	Metoclopramide	10mg	PO	10mg three times a day for 3 days then 10mg up to 3 times a day as required. Do not take for more than 5 days continuously.
	If required prescribe doxycycline 100mg OD at onset of rash.			

Guidance on the assessment and management of oxaliplatin induced neuropathy

Introduction

- Use the neuropathy assessment tool on KOMS at each pre-chemo review.
- Symptoms of sensory or functional neuropathy may include tingling or numbness which may persist to the next pre-chemotherapy assessment.
- This guidance is for patients receiving treatment outside the context of a clinical trial. For patients being treated within a clinical trial setting, follow trial protocol (using assessment below as far as possible).
- Do not assess oxaliplatin induced neuropathy using CTC toxicity criteria.
- Dysaesthesia in the jaw is an unpleasant sensation and/or pain in the jaw.
- Laryngopharyngeal spasm is a sensation of difficulty in swallowing / breathing.

Assessment and action

Normal occurrence / Caution	Symptoms	Action at nurse assessment	Consultant review required / Action by consultant
Normal occurrence with oxaliplatin	Dysaesthesia (tingling in hands and feet) occurring with and up to 72 hours after infusion	No action required.	
	Dysaesthesia in the jaw (during infusion) and cold induced laryngopharyngeal spasm up to 48 hrs after infusion.	Advise patients to avoid cold drinks / cold weather. Consider administering next oxaliplatin infusion over 6 hours (SmPC).	
First caution / warning sign	Tingling persisting beyond 72 hours or painful cold-induced neuropathy	d/w consultant or clinicians authorised to prescribe chemotherapy Close monitoring at each subsequent cycle. Ask the following specific questions at each nursing assessment: 1. Is the dysaesthesia (during the infusion) and / or cold induced laryngopharyngeal spasm more severe? 2. Has the tingling continued for longer than during the previous cycle and / or is tingling still present when next cycle is due?	1. If yes, consultant review required. For consideration of DR at next cycle or omission of oxaliplatin. 2. If yes, consultant review required, for consideration of DR at next cycle or omission of oxaliplatin
Serious caution	Numbness in hands or feet Severe excitability channel neuropathy during infusion (very rare) seen as severe pain and numbness on infusion Painful neuropathy	Must be reviewed by a consultant Must be reviewed by a consultant Must be reviewed by a consultant	Consider DR or omission of oxaliplatin. Repeat consultant review before next cycle Consider DR or omission of oxaliplatin. Repeat consultant review before next cycle Consider Duloxetine. Starting at 30mg-60mg OD where available on Trust formulary. Alternatively, d/w pain management specialist.
Other cautions	A cumulative dose of 700-800mg/m^2 oxaliplatin has been reached	Must be reviewed by a consultant	
	All patients restarting oxaliplatin based chemotherapy after a break in treatment (this may be due to an intervention such as rectal cancer patients having surgery)	Must be reviewed by a consultant to assess for delayed onset neuropathy	

Notes

- Neurology referral should be considered in severe cases.
- Initial dose reductions should be at a 25% level. If there is no improvement or worsening symptoms, based on an assessment of risk and benefit, consider further dose reduction. Once reduced, doses should not be re-escalated.