

<b>Indication</b>	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.
<b>Treatment Intent</b>	Palliative
<b>Frequency and number of cycles</b>	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.
<b>Monitoring Parameters pre-treatment</b>	<ul style="list-style-type: none"> <li>• <b>Virology screening:</b> 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.</li> <li>• ECG cycle 1</li> <li>• Monitor FBC, LFTs and U&amp;Es prior to treatment and every 2 weeks thereafter, in particular Mg<sup>2+</sup>, K<sup>+</sup> and Ca<sup>2+</sup></li> <li>• Neuts &lt;1.5 and PLT&lt;100 delay one week.</li> <li>• Before starting treatment GFR (C+G) should be &gt;= 50ml/min</li> <li>• <b>DPD testing</b> must be undertaken in all patients before starting treatment; the result must be checked before treatment is started.</li> <li>• <b>Renal Impairment:</b> <ul style="list-style-type: none"> <li>○ Capecitabine is contraindicated if CrCl &lt;30ml/min.</li> <li>○ Oxaliplatin: Consider dose adjustment in severe renal impairment.</li> <li>○ Cetuximab: no data available in patients with impaired function.</li> </ul> </li> <li>• <b>Hepatic Impairment:</b> <ul style="list-style-type: none"> <li>○ Capecitabine: No dose adjustments in hepatic impairment (insufficient data of capecitabine to make a dose recommendation).</li> <li>○ Cetuximab: no dose reduction required.</li> <li>○ Oxaliplatin: no dose reduction required.</li> </ul> </li> <li>• <b>Cardiotoxicity:</b> caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris.</li> <li>• <b>Dose interruption and reduction:</b></li> <li>• Oxaliplatin: For guidance on oxaliplatin induced neuropathy see KMCC document "Guidance on the assessment and Management of Oxaliplatin induced Neuropathy" see KMCC website <a href="https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/guidelines-for-the-management-of-sact-induced-adverse-reactions/">https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/guidelines-for-the-management-of-sact-induced-adverse-reactions/</a> .</li> <li>• Capecitabine: <ul style="list-style-type: none"> <li>○ Interrupt capecitabine in the event of &gt;= 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.</li> <li>○ Dose reduction should be considered if grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2 (except N&amp;V and alopecia). Delay until resolution of toxicity to &lt;= grade 1.</li> </ul> </li> </ul>

Protocol No	COL-032	Kent and Medway SACT Protocol Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere.	
Version	V2	Written by	M.Archer
Supersedes version	V1	Checked by	C.Waters V2 B.Willis V1 KMCC website link changes only to V2
Date	25.04.2024	Authorising consultant (usually NOG Chair)	M.Hill V1

	<ul style="list-style-type: none"> <li>• <b>Adverse reactions:</b></li> <li>• <b>Cetuximab infusion rate and infusion related reactions (IRRs):</b></li> <li>• 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.</li> <li>• <b>Skin reactions:</b> 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" <a href="https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/guidelines-for-the-management-of-sact-induced-adverse-reactions/">https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/guidelines-for-the-management-of-sact-induced-adverse-reactions/</a></li> <li>• <b>Interstitial lung disease (ILD):</b> Patients should report any new or worsening respiratory symptoms. Cetuximab should be permanently discontinued in patients with confirmed ILD.</li> <li>• <b>Ocular toxicities:</b> 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.</li> <li>• <b>Common drug/food interactions (for comprehensive list refer to BNF/SPC):</b> <ul style="list-style-type: none"> <li>○ Capecitabine must not be given with concurrent sorivudine or derivatives (e.g. brivudine), see SPC.</li> <li>○ Monitor PT and INR regularly in patients taking coumarin-derivative anticoagulants.</li> <li>○ Monitor phenytoin levels with concomitant use.</li> <li>○ Caution with folic acid or folic acid – potential for increased toxicity.</li> <li>○ Avoid concomitant allopurinol.</li> </ul> </li> <li>• <b>Driving:</b> Capecitabine/Oxaliplatin may cause dizziness, fatigue and nausea. Patients should be aware this may affect their ability to drive or operate machinery.</li> <li>• For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.</li> </ul>
<b>References</b>	COL-032 V1

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

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## 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			
	<b>CETUXIMAB</b>	<b>500mg/m<sup>2</sup></b>	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.	
	<b>Give cytotoxic chemo at least 1 hour after MAb</b>					
	Ondansetron	<75yrs 16mg ≥75yrs 8mg	IV	15min	Sodium chloride 0.9% 50ml	
	<b>FLUSH WITH 5 % GLUCOSE BEFORE AND AFTER ADMINISTRATION OF OXALIPLATIN</b>					
	<b>OXALIPLATIN</b>	<b>85mg/m<sup>2</sup></b>	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	<b>CAPECITABINE</b>	<b>1600mg/m<sup>2</sup>/day</b>  In 2 divided doses	PO	BD Take the first dose in the evening of <b>Day 1</b> and the last dose in the morning of <b>Day 10</b> , 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.					

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