Protocol Contains CHECKPOINT INHIBITOR IMMUNOTHERAPY	
Indication	Durvalumab in combination with FLOT as neoadjuvant and adjuvant treatment, followed by adjuvant durvalumab monotherapy for the treatment of resectable gastric or gastro-oesophageal junction adenocarcinoma. NB patients should have had no prior chemotherapy or immunotherapy (including anti–CTLA-4, anti–PD-1, anti–PD-L1, or anti–PD-L2 antibodies) for the treatment of gastric or gastro-oesophageal junction cancer. NB Patients who have received durvalumab in this indication via the company sponsored early access programme are permitted to move to NHS commissioned supply, only if they meet all other criteria.
Treatment Intent	Neo-adjuvant followed by adjuvant.
Frequency and number of cycles	**Neo-adjuvant combination therapy:** Durvalumab in combination with FLOT. Repeat every 28 days, for up to 2 cycles prior to surgery followed by **Adjuvant combination therapy:** Durvalumab in combination with FLOT. Repeat every 28 days for up to 2 cycles followed by **Adjuvant monotherapy:** Durvalumab every 28 days, to continue until disease progression or unacceptable toxicity or patient choice to stop treatment or up to a maximum of 10 cycles, whichever occurs sooner (total adjuvant therapy must not exceed 12 cycles of durvalumab).

Monitoring Parameters	• **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.
	• **DPD testing:** DPD testing must be undertaken in all patients before starting treatment; the result must be checked before treatment is started.
	• **Thyroid function** must be assessed at baseline then every 8 weeks or as indicated based on clinical evaluation.
	• **Cortisol monitoring** should be undertaken in line with ESMO immunotherapy toxicity guidance available on KMCC website (see link below). Cortisol level should not be taken within 24hours of the last steroid dose.
	• **Pre-treatment cardiac assessment:**
	  ○ **ECG** baseline and as clinically indicated.
	  ○ Check **BNP**, and **Troponin T** prior to treatment.
	• **Cardiotoxicity:** caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris.
	• **Ensure dexamethasone pre-medication is prescribed and given to the patient at new patient chat**
	• Monitor **FBC, U&Es, LFTS**, on day 1 and day 15 of adjuvant and neo-adjuvant combination therapy (cycle 1 to 4) and then at each cycle from cycle 5 onwards.
	• Monitor **blood pressure and random blood glucose (BM) at** each cycle.
	• **Haematological parameters:**
	  ○ **Combination therapy:** If neuts >/=1.5 and PLT >/=100 continue with treatment. If neuts <1.5 or PLT <100 delay one week.
	  ○ **Durvalumab monotherapy**: if PLT <75 or neuts <1.0 d/w consultant.
	• **Hepatic impairment:**
	  ○ **Durvalumab:** No dose adjustment is necessary.
	  ○ **Docetaxel** is not recommended in severe hepatic impairment. A dose reduction of docetaxel may be made dependent on PS and liver function.

	○ **Oxaliplatin:** No dose adjustment recommended. ○ **Fluorouracil:** In moderate hepatic impairment consider reducing the dose by 30% and for severe impairment by 50%. If the bilirubin is >85umol/L and / or AST >180 fluorouracil is contra-indicated. • **Renal impairment:** ○ **Durvalumab:** No dose adjustment is necessary in mild or moderate renal impairment. No data in severe impairment (<30ml/min). ○ **Docetaxel:** no need for dose reduction. ○ **Oxaliplatin:** If CrCl <30ml/min consider 50% of original dose. ○ **Fluorouracil:** consider dose reduction in severe renal impairment. • **Infusion-related reactions:** ○ Durvalumab: In the event of grade 3 to 4 infusion-related reactions, discontinue durvalumab and administer appropriate treatment. In the event of a mild or moderate reaction, interrupt or slow the rate of the infusion. Pre-medication for prophylaxis of subsequent infusion reactions should be considered. • **Management of adverse reactions and dose adjustments:** ○ **Oxaliplatin:** Reference should be made to 'Guidance on the Assessment and Management of Oxaliplatin Induced Neuropathy' available at: www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/sact-pathways-guidelines-for-the-management-of-sact-induced-adverse-reactions-and-nursing/ ○ Dose reduction should be considered if any other 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 ○ **Docetaxel hypersensitivity:** Patients who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel. ○ **Durvalumab Immune-related reactions:** Most common reactions are pneumonitis, colitis, nephritis, hepatitis, hyperthyroidism, hypothyroidism, hypophysitis / hypopituitarism, diabetes, immune-related rash. See table 1 for SPC Recommended treatment modifications and management recommendations for immune related reactions. ○ Treatment with corticosteroids or endocrine therapy should be initiated as appropriate. For events requiring corticosteroid therapy, and upon improvement to </= Grade 1, corticosteroid taper should be initiated and continued over at least 1 month. Consider increasing dose of corticosteroids and/or using additional systemic immunosuppressants if there is worsening or no improvement. After withholding treatment, durvalumab can be resumed within 12 weeks if the adverse reactions improved to </= Grade 1 and the corticosteroid dose has been reduced to </=10 mg prednisone or equivalent per day. ○ Permanently discontinue for recurrent Grade 3 (severe) immune-mediated adverse reactions and for any Grade 4 (life-threatening) immune-mediated adverse reactions, except for endocrinopathies that are controlled with replacement hormones. ○ For guidance on managing immune-related adverse reactions, refer to SPC and guidelines available on KMCC website https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/immunotherapy/ ○ **Durvalumab non-immune-mediated adverse reactions**, withhold treatment for Grade 2 and 3 adverse reactions until </= Grade 1 or baseline. ○ Discontinue in the event of Grade 4 adverse reactions (with the exception of Grade 4 laboratory abnormalities, about which the decision to discontinue should be based on accompanying clinical signs/symptoms and clinical judgment).

	○ Patients must be advised to contact the oncology team if they experience any side effect, as some side effects worsen rapidly. Prompt management of side effects can ensure that the patient continues with treatment. ○ **Durvalumab dose adjustments:** Dose escalation or reduction of durvalumab is not appropriate. Dosing delay or discontinuation may be required based on individual safety and tolerability. ○ *Patients with a body weight of 30 kg or less must receive weight-based dosing of durvalumab at 20 mg/kg. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** ○ **Durvalumab** - No interaction studies have been performed. ○ The use of systemic corticosteroids or immunosuppressants before starting durvalumab should be avoided unless as part of this SACT protocol. Systemic corticosteroids or other immunosuppressants can be used after starting durvalumab to treat immune-related adverse reactions. ○ **Oxaliplatin:** Caution is advised when oxaliplatin treatment is co-administered with other medicinal products known to cause QT interval prolongation. In case of combination with such medicinal products, the QT interval should be closely monitored. ○ Caution is advised when oxaliplatin treatment is administered concomitantly with other medicinal products known to be associated with rhabdomyolysis. ○ **Docetaxel:** Concomitant use with medicines which induce, inhibit or are metabolised by cytochrome P450-3A (e.g. ciclosporin, ketoconazole and erythromycin) may affect levels of docetaxel use with caution. ○ Avoid concomitant use with strong CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, clarithromycin and ritonavir), if treatment cannot be avoided consider dose reduction of docetaxel and monitor patient closely for signs of toxicity. ○ **5FU:** 5FU 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. • **Pregnancy and contraception:** ○ **Durvalumab:** Women of childbearing potential should use effective contraception during treatment and for at least 3 months after the last dose of durvalumab. ○ **Oxaliplatin and docetaxel:** Women of childbearing potential should use effective contraception and not consider pregnancy during treatment and men should be advised to use effective contraception and not to conceive children during treatment, please refer to the brand specific SPC for further guidance. • **Driving and machinery:** Patients should be advised that whilst receiving FLOT treatment it may affect their ability to drive and use machines.
References	KMCC protocol UGI-058 V3 SPC accessed online 20.05.2026 CDF list V1.399 accessed online 22.05.2026

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

Table 1 SPC Recommended treatment modifications and management recommendations for immune related reactions

Adverse reactions	**Severity** [a]	**Treatment modification**
Immune-mediated pneumonitis/ interstitial lung disease	Grade 2	Withhold dose
	Grade 3 or 4	Permanently discontinue
Immune-mediated hepatitis	ALT or AST > 3 - ≤ 5 x ULN or total bilirubin > 1.5 - ≤ 3 x ULN	Withhold dose
	ALT or AST > 5 - ≤ 10 x ULN	Withhold dose
	Concurrent ALT or AST > 3 x ULN and total bilirubin > 2 x ULN[b]	Permanently discontinue
	ALT or AST > 10 x ULN or total bilirubin > 3 x ULN	
Immune-mediated colitis or diarrhoea	Grade 2	Withhold dose
	Grade 3 for monotherapy	Withhold dose
	Grade 4	Permanently discontinue
Immune-mediated hyperthyroidism, thyroiditis	Grade 2-4	Withhold dose until clinically stable
Immune-mediated hypothyroidism	Grade 2-4	No changes
Immune-mediated adrenal insufficiency or hypophysitis/hypopituitarism	Grade 2-4	Withhold dose until clinically stable
Immune-mediated type 1 diabetes mellitus	Grade 2-4	No changes
Immune-mediated nephritis	Grade 2 with serum creatinine > 1.5 - 3 x (ULN or baseline)	Withhold dose
	Grade 3 with serum creatinine > 3 x baseline or > 3-6 x ULN; Grade 4 with serum creatinine > 6 x ULN	Permanently discontinue
Immune-mediated rash or dermatitis (including pemphigoid)	Grade 2 for > 1 week	Withhold dose
	Grade 3	
	Grade 4	Permanently discontinue
Immune-mediated myocarditis	Grade 2-4	Permanently discontinue
Immune-mediated myositis/ polymyositis/rhabdomyolysis	Grade 2 or 3	Withhold dose[f]
	Grade 4	Permanently discontinue
Infusion-related reactions	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue
Infection	Grade 3 or 4	Withhold dose until clinically stable
Immune-mediated myasthenia gravis	Grade 2-4	Permanently discontinue
Immune-mediated Myelitis transverse	Any Grade	Permanently discontinue
Immune-mediated meningitis	Grade 2	Withhold dose
	Grade 3 or 4	Permanently discontinue
Immune-mediated encephalitis	Grade 2-4	Permanently discontinue

Immune-mediated Guillain-Barré syndrome	Grade 2-4	Permanently discontinue
Other immune-mediated adverse reactions[g]	Grade 2 or 3	Withhold dose
	Grade 4	Permanently discontinue

a Common Terminology Criteria for Adverse Events, version 4.03. ALT: alanine aminotransferase; AST: aspartate aminotransferase; ULN: upper limit of normal; BLV: baseline value.

b For patients with alternative cause follow the recommendations for AST or ALT increases without concurrent bilirubin elevations.

[f] Permanently discontinue IMFINZI if adverse reaction does not resolve to ≤ Grade 1 within 30 days or if there are signs of respiratory insufficiency.

[g] Includes immune thrombocytopenia, pancreatitis, immune-mediated arthritis, uveitis, cystitis noninfective, and polymyalgia rheumatica.

NEO-ADJUVANT: Cycle 1 and 2 repeat every 28 days

Day	Drug	Dose	Route	Infusion Duration	Administration Details	
1	Metoclopramide	20mg	PO		stat	
	DURVALUMAB	**1500mg *(see notes)**	IV	60 minutes	In 100ml sodium chloride 0.9% (final concentration 1-15 mg/mL) via in-line low-protein binding 0.22micron filter.	
	*Patients with a body weight of 30 kg or less must receive weight-based dosing of durvalumab at 20 mg/kg.					
	Ondansetron	<75yrs 16mg ≥75yrs 8mg	IV	15 min	NaCl 0.9% 50ml	
	Ensure dexamethasone pre-med taken before administration of docetaxel					
	DOCETAXEL	**50mg/m²**	IV	1 hr	Sodium Chloride 0.9% 250ml	
	Flush with 5% glucose before and after oxaliplatin administration					
	OXALIPLATIN	**85mg/m²**	IV	2 - 6hrs	250-500ml 5% glucose (to give a concentration between 0.2 mg/ml and 0.70 mg/ml)	**Can be run concurrently**
	CALCIUM FOLINATE (calcium leucovorin)	**200mg/m²**	IV	2 hrs	Glucose 5% 250ml	
	5-FLUOROURACIL	**2600mg/m²**	IV	**24 hr pump**	continuous infusion	
15	Ondansetron	<75yrs 16mg ≥75yrs 8mg	IV	15 min	NaCl 0.9% 50ml	
	Ensure dexamethasone pre-med taken before administration of docetaxel					
	DOCETAXEL	**50mg/m²**	IV	1 hr	Sodium Chloride 0.9% 250ml	
	Flush with 5% glucose before and after oxaliplatin administration					
	OXALIPLATIN	**85mg/m²**	IV	2 - 6hrs	250-500ml 5% glucose (to give a concentration between 0.2 mg/ml and 0.70 mg/ml)	**Can be run concurrently**
	CALCIUM FOLINATE (calcium leucovorin)	**200mg/m²**	IV	2 hrs	Glucose 5% 250ml	
	5-FLUOROURACIL	**2600mg/m²**	IV	**24 hr pump**	continuous infusion	

TTOs Cycle 1 and 2

TTO	Drug	Dose	Route	Directions
Day 1 and 15	Dexamethasone	8mg	PO	BD for 3 days starting one day prior to next cycle of Chemotherapy.
	Metoclopramide	10mg	PO	3 times a day for 3 days, then 10mg up to 3 times a day as required. Max 30mg per day including pre-chemotherapy dose. Do not take for more than 5 days continuously.
	Filgrastim	300 micrograms **or consider dose of 480 micrograms if patient > 80kg**	SUB CUT	OD starting on day 4 and day 18 for 5 days

ADJUVANT: Cycle 3 and 4 repeat every 28 days.

Day	Drug	Dose	Route	Infusion Duration	Administration Details	
1	Metoclopramide	20mg	PO		stat	
	DURVALUMAB	**1500mg *(see notes)**	IV	60 minutes	In 100ml sodium chloride 0.9% (final concentration 1-15 mg/mL) via in-line low-protein binding 0.22micron filter.	
	*Patients with a body weight of 30 kg or less must receive weight-based dosing of durvalumab at 20 mg/kg.					
	Ondansetron	<75yrs 16mg ≥75yrs 8mg	IV	15 min	NaCl 0.9% 50ml	
	Ensure dexamethasone pre-med taken before administration of docetaxel					
	DOCETAXEL	**50mg/m²**	IV	1 hr	Sodium Chloride 0.9% 250ml	
	Flush with 5% glucose before and after oxaliplatin administration					
	OXALIPLATIN	**85mg/m²**	IV	2 - 6hrs	250-500ml 5% glucose (to give a concentration between 0.2 mg/ml and 0.70 mg/ml)	**Can be run concurrently**
	CALCIUM FOLINATE (calcium leucovorin)	**200mg/m²**	IV	2 hrs	Glucose 5% 250ml	
	5-FLUOROURACIL	**2600mg/m²**	IV	**24 hr pump**	continuous infusion	
15	Ondansetron	<75yrs 16mg ≥75yrs 8mg	IV	15 min	NaCl 0.9% 50ml	
	Ensure dexamethasone pre-med taken before administration of docetaxel					
	DOCETAXEL	**50mg/m²**	IV	1 hr	Sodium Chloride 0.9% 250ml	
	Flush with 5% glucose before and after oxaliplatin administration					
	OXALIPLATIN	**85mg/m²**	IV	2 - 6hrs	250-500ml 5% glucose (to give a concentration between 0.2 mg/ml and 0.70 mg/ml)	**Can be run concurrently**
	CALCIUM FOLINATE (calcium leucovorin)	**200mg/m²**	IV	2 hrs	Glucose 5% 250ml	
	5-FLUOROURACIL	**2600mg/m²**	IV	**24 hr pump**	continuous infusion	

TTOS cycle 3 and 4.

TTO	Drug	Dose	Route	Directions
Day 1 and 15	Dexamethasone	8mg	PO	BD for 3 days starting one day prior to next cycle of Chemotherapy. Do not dispense on cycle 4 day 15.
	Metoclopramide	10mg	PO	3 times a day for 3 days, then 10mg up to 3 times a day as required. Max 30mg per day including pre-chemotherapy dose. Do not take for more than 5 days continuously.
	Filgrastim	300 micrograms **or consider dose of 480 micrograms if patient > 80kg**	SUB CUT	OD starting on day 4 and day 18 for 5 days

ADJUVANT monotherapy: Cycle 5 to 14 repeat every 28 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Metoclopramide	20mg	PO		stat
	DURVALUMAB	**1500mg *(see notes)**	IV	60 minutes	In 100ml sodium chloride 0.9% (final concentration 1-15 mg/mL) via in-line low-protein binding 0.22micron filter.
	*Patients with a body weight of 30 kg or less must receive weight-based dosing of durvalumab at 20 mg/kg.				
TTO	Drug	Dose	Route	Directions	
Day 1	Metoclopramide	10mg	PO	10mg up to 3 times a day as required (max. 30mg per day including 20mg pre-chemo dose) Do not take for more than 5 days continuously.	