Protocol Contains CHECKPOINT INHIBITOR IMMUNOTHERAPY	
Indication	Durvalumab, in combination with carboplatin and etoposide, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer. NB: Previous treatment with concurrent chemoradiotherapy for limited stage SCLC is allowed as long as therapy was completed at least 6 months prior to the diagnosis of recurrent and extensive stage disease. The patient has had no prior treatment with anti-PD-L1/PD-1 therapy for small cell lung cancer, unless this was received for this indication via a company early access program.
Treatment Intent	Palliative
Frequency and number of cycles	**Induction phase:** repeat every 21 days for 4 cycles **Maintenance phase:** repeat every 28 days until disease progression, unacceptable toxicity or patient's choice. A formal medical review as to whether treatment with durvalumab in combination with etoposide plus carboplatin should continue or not will be scheduled to occur at least by the end of the first 6 weeks of treatment.

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.
	• Monitor FBC, U&Es, LFTs, blood pressure and random blood glucose (BM) at each cycle.
	• DPTA / EDTA or estimated CrCl (C&G) prior to cycle 1 must be >/= 30ml/min.
	• **Haematological parameters:**
	• **Induction phase Cycles 1 – 4 (in combination with chemotherapy):**
	  ○ If neuts >/=1.5 and PLT >/=100 continue with treatment.
	  ○ If neuts 1.0-1.4 and PLT >/=100 d/w consultant.
	  ○ If neuts <1.0 and/or PLT <100 delay treatment.
	• **Maintenance phase Cycle 5 onwards**: If PLT <75 or neuts <1.0 d/w consultant.
	• 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.
	• **Renal impairment:**
	  ○ **Durvalumab:** No dose adjustment is necessary in mild or moderate renal impairment. No data in severe impairment (<30ml/min).
	  ○ **Carboplatin:** If CrCl falls by >25% repeat / do EDTA to dose carboplatin. Discontinue carboplatin if CrCl <30ml/min.
	  ○ **Etoposide**: If CrCl </= 50ml/min consider dose reduction.
	• **Hepatic impairment.**
	  ○ **Durvalumab:** No dose adjustment is necessary.
	  ○ **Etoposide:** Clinical decision. As a guide, if bilirubin 26-51 or AST 60-180 consider reducing dose by 50%.
	• **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. • **Carboplatin:** ○ Mild/moderate reactions (grade 1-2): If symptoms resolve after treatment with hydrocortisone and chlorphenamine, the infusion may be restarted at 50% rate for 30 mins, then, if no further reaction, increase to 100% rate. ○ If symptoms do not resolve after treatment with hydrocortisone and chlorphenamine, do not restart the infusion. At consultant's discretion, patients may be rechallenged at a later date with additional prophylaxis. In the event of further reaction (grade 1-3), stop infusion and consider alternative treatment. ○ Severe (grade 3): Do not restart infusion. Consider alternative treatment. ○ Anaphylaxis (grade 4): Follow anaphylaxis protocol. Discontinue permanently and consider alternative treatment. • The use of systemic corticosteroids or immunosuppressants before starting durvalumab should be avoided. Systemic corticosteroids or other immunosuppressants can be used after starting durvalumab to treat immune-related adverse reactions. Dexamethasone is permitted as an anti-emetic as prescribed within protocol. • **Dose modification:** ○ **Carboplatin and etoposide:** d/w consultant if chemotherapy is delayed due to haematological toxicity. 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 ○ **Durvalumab:** *Patients with a body weight </=30 kg must receive weight-based dosing of 20mg/kg. Dose escalation or reduction is not appropriate. Dosing delay or discontinuation may be required based on individual safety and tolerability. • **Adverse reactions** • **Durvalumab - Immune-related reactions:** Most common reactions are pneumonitis, colitis, nephritis, hepatitis, hyperthyroidism, hypothyroidism, hypophysitis / hypopituitarism, diabetes, immune-related rash. • For suspected immune-mediated adverse reactions, based on the severity of the adverse reaction, treatment should be withheld or permanently discontinued (See table 1 for *Recommended treatment modifications and management recommendations for immune related reactions*). • Treatment with corticosteroids or endocrine therapy should be initiated. 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/ • 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. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** o **Durvalumab:** No interaction studies have been performed. o **Etoposide:** Ciclosporin (high doses) increases etoposide plasma levels/toxicity use with caution. o **Carboplatin:** Carboplatin: Caution with other nephrotoxic drugs. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.
References	KMCC protocol LUN-035 SPC accessed online 24.01.2025 CDF list V1.343 accessed online 24.01.2025 CDF list V1.344 accessed online 27.01.2024

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

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

Adverse reactions	Severity[a]	Treatment modification
Immune-mediated pneumonitis/interstitial lung disease	Grade 2	Withhold
	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
	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
	Grade 3	Withhold
	Grade 4	Permanently discontinue
Intestinal perforation[d]	Any grade	Permanently discontinue
Immune-mediated hyperthyroidism, thyroiditis	Grade 2 - 4	Withhold until clinically stable
Immune-mediated hypothyroidism	Grade 2 - 4	No changes
Immune-mediated adrenal insufficiency or hypophysitis/hypopituitarism	Grade 2 - 4	Withhold 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
	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
	Grade 3	
	Grade 4	Permanently discontinue
Immune-mediated myocarditis	Grade 2-4	Permanently discontinue
Immune-mediated myositis/polymyositis/rhabdomyolysis	Grade 2 or 3	Withhold[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
	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
Pure red cell aplasia (PRCA)[h]	Any grade	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.

[d] Adverse drug reaction is only associated with IMFINZI in combination with tremelimumab.

[f] Permanently discontinue 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 and cystitis noninfective.

[h] Adverse drug reaction is only associated when olaparib maintenance treatment is used in combination with IMFINZI, following treatment with IMFINZI in combination with platinum-based chemotherapy.

Induction
Repeat every 21 days for 4 cycles

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Dexamethasone	8mg	PO		
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 min	Sodium chloride 0.9% 50ml
	DURVALUMAB	**1500mg *(see notes above)**	IV	60 minutes	In 100ml sodium chloride 0.9% (final concentration 1-15 mg/mL) via in-line low-protein binding 0.22micron filter.
	CARBOPLATIN	**AUC 5 Dose = AUC X (GFR + 25) (max 700mg)**	IV	30 minutes	In glucose 5% 500ml
	ETOPOSIDE	**100mg/m²**	IV	I hour	In Sodium Chloride 0.9% 500-1000ml (doses >200mg in 1000ml Sodium chloride 0.9%)
TTO	Drug	Dose	Route	Directions	
Day 1	**ETOPOSIDE**	**200mg/m² (max 400mg)** (round to the nearest 50 mg)	PO	OD on day **TWO** and **THREE** only. Take an hour before food or on an empty stomach.	
	Dexamethasone	6mg	PO	OM for 3 days with or after food	
	Metoclopramide	10mg	PO	TDS for 3 days, then 10mg up to 3 times a day when required. Do not take for more than 5 days continuously.	
	Ondansetron	8mg	PO	BD for 3 days.	
	Filgrastim	300micrograms or consider dose of 480 micrograms if patient > 80kg	S/C	Daily from Day 3 to Day 7	

Maintenance Phase
Cycle 5 onwards: Repeat every 28 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Metoclopramide	20mg	PO		stat
	DURVALUMAB	**1500mg**	IV	60 minutes	In 100ml sodium chloride 0.9% (final concentration 1-15 mg/mL) via in-line low-protein binding 0.22micron filter.
TTO	Drug	Dose	Route	Directions	
Day1	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 consecutive days.	