Indication	The treatment of locally advanced, stage III unresectable non-small cell lung cancer (NSCLC) in adults whose tumours express PD-L1 on ≥ 1% of tumour cells and whose disease has not progressed following platinum-based combination chemotherapy given concurrently with definitive radical radiotherapy. The patient has not received prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody (excluding treatment received as part of Astra Zenecas EAMS for durvalumab).
Treatment Intent	Adjuvant
Frequency and number of cycles	**Schedule 1** Every 2 weeks or alternatively **Schedule 2** Every 4 weeks Until disease progression or unacceptable toxicity, or a maximum of 12 months total active treatment (i.e. a maximum of 26 x 2-weekly cycle or 13 x 4 weekly cycles). The first dose of durvalumab will commence within 42 days of the last active treatment date of the concurrent chemoradiotherapy treatment program. A formal medical review as to whether treatment with durvalumab should continue or not will be scheduled to occur at least by the end of the first 3 cycles 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. • 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. • **Infusion-related reactions:** 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. • 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. • **Renal impairment:** No dose adjustment is necessary in mild or moderate renal impairment. No data in severe impairment (<30ml/min). • **Hepatic impairment.** No dose adjustment is necessary. • **Dose modification**: *Patients with a body weight </=30 kg must receive weight-based dosing, either as 10mg/kg given every 2 weeks or as a dose of 20 mg/kg every 4 weeks. • **Adverse reactions** Dose escalation or reduction is not appropriate. Dosing delay or discontinuation may be required based on individual safety and tolerability. • **Immune-related reactions:** Most common reactions are pneumonitis, colitis, nephritis, hepatitis, hyperthyroidism, hypothyroidism, hypophysitis / hypopituitarism, diabetes,

	immune-related rash. See table 1 for *Recommended treatment modifications and management recommendations for immune related reactions*. • For suspected immune-mediated adverse reactions, consider increasing dose of corticosteroids and/or using additional systemic immunosuppressants if there is worsening or no improvement. Upon improvement to </= Grade 1, corticosteroid taper should be initiated and continued over at least 1 month. 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. • 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):** No interaction studies have been performed.
References	SPC accessed online 25.09.2023 KMCC protocol LUN-035 V4

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**	**Corticosteroid treatment unless otherwise specified**
Immune-mediated pneumonitis/interstitial lung disease	Grade 2	Withhold dose	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
	Grade 3 or 4	Permanently discontinue	1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Immune-mediated hepatitis	Grade 2 with ALT or AST > 3-5 x ULN and/or total bilirubin > 1.5-3 x ULN	Withhold dose	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
	Grade 3 with AST or ALT > 5-≤ 8 x ULN or total bilirubin > 3-≤ 5x ULN		
	Grade 3 with AST or ALT > 8 x ULN or total bilirubin > 5 x ULN	Permanently discontinue	
	Concurrent ALT or AST > 3 x ULN and total bilirubin > 2 x ULN with no other cause		
Immune-mediated colitis or diarrhoea	Grade 2 or 3	Withhold dose	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
	Grade 4	Permanently discontinue	
Immune-mediated hyperthyroidism, thyroiditis	Grade 2-4	Withhold dose until clinically stable	Symptomatic treatment, see section 4.8
Immune-mediated hypothyroidism	Grade 2-4	No changes	Initiate thyroid hormone replacement as clinically indicated
Immune-mediated adrenal insufficiency or hypophysitis/hypopituitarism	Grade 2-4	Withhold dose until clinically stable	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement as clinically indicated
Immune-mediated type 1 diabetes mellitus	Grade 2-4	No changes	Initiate treatment with insulin as clinically indicated
Immune-mediated nephritis	Grade 2 with serum creatinine > 1.5-3 x (ULN or baseline)	Withhold dose	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
	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	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
	Grade 3		
	Grade 4	Permanently discontinue	
Immune-mediated myocarditis	Grade 2	Withhold dose[b]	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
	Grade 3 or 4, or any Grade with positive biopsy	Permanently discontinue	
	Grade 2 or 3	Withhold dose[c]	

Immune-mediated myositis/polymyositis	Grade 4	Permanently discontinue	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Immune-mediated myasthenia gravis	Grade 2-4	Permanently discontinue	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Immune-mediated Myelitis transverse	Any Grade	Permanently discontinue	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Immune-mediated meningitis	Grade 2	Withhold dose	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
	Grade 3 or 4	Permanently discontinue	
Immune-mediated encephalitis	Grade 2-4	Permanently discontinue	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Immune-mediated Guillain-Barré syndrome	Grade 2-4	Permanently discontinue	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Other immune-mediated adverse reactions	Grade 2 or 3	Withhold dose	Initiate 1 to 2 mg/kg/day prednisone or equivalent followed by taper
	Grade 4	Permanently discontinue	

a Common Terminology Criteria for Adverse Events, version 4.03.

b If no improvement within 2 to 3 days despite corticosteroids, promptly start additional immunosuppressive therapy. Upon resolution (Grade 0), corticosteroid taper should be initiated and continued over at least 1 month, after which durvalumab can be resumed based on clinical judgment.

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

Schedule 1 Repeat every 2 weeks

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Metoclopramide	20mg	PO		stat
	DURVALUMAB	**10mg/kg**	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	
Day 1	Metoclopramide	10mg	PO	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.	

Schedule 2 Repeat every 4 weeks

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Metoclopramide	20mg	PO		stat
	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.
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 consecutive days.	