Protocol Contains CHECKPOINT INHIBITOR IMMUNOTHERAPY	
Indication	For the treatment of metastatic or locally advanced stage IIIB or IIIC or IV non-small cell lung cancer (NSCLC) which: • is PD-L1 positive in 1% or more of the tumour cells • has no EGFR, ALK or ROS1 aberrations • is not suitable for definitive chemoradiation and would otherwise be a candidate for pembrolizumab with platinum-based chemotherapy. NB patients should have had no prior treatment with an anti PD-1, anti-PD-L1, anti-PD-L2, anti-CD137 or anti-cytotoxic T-lymphocyte-associated antigen-4 (CTL-4) antibody unless the patient completed or discontinued checkpoint inhibitor immunotherapy as part of adjuvant/neoadjuvant/maintenance therapy without disease progression on treatment and at least 6 months elapsed between the date of last immunotherapy treatment and the date of first diagnosis of relapse with recurrent or metastatic disease.
Treatment Intent	Palliative
Frequency and number of cycles	**Combination therapy**: Cemiplimab with carboplatin & paclitaxel repeated every 21 days for a maximum of **4 cycles,** Followed by, in the absence of disease progression, **Cemiplimab Monotherapy:** repeated every 21 days until disease progression or unacceptable toxicity or patient choice or for a maximum of 2 years (total of 36 cycles of cemiplimab), whichever occurs first.

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.
	• **Pre-treatment cardiac assessment:**
	  ○ **ECG** baseline, then every 6 weeks or as clinically indicated.
	  ○ Check **BNP**, and **Troponin T** prior to treatment.
	• **EDTA/DTPA** should be used to measure GFR prior to cycle 1, must be >/= 30ml/min. C+G to estimate CrCl may be used before CYCLE 1 if there is a delay in obtaining EDTA/DTPA result.
	• Discuss with consultant if creatinine clearance drops by 25%.
	• **Haematological monitoring and parameters:**
	• Monitor **FBC, U&Es, LFTs** and **glucose** at each cycle.
	• If neuts <1.5 and/or PLT <100 defer treatment by one week and consider dose reduction of paclitaxel and carboplatin on subsequent cycles. Do not reduce cemiplimab.
	• **Thyroid function** must be assessed at baseline then every 6 weeks or as clinically indicated. To avoid delays, use previous results for prescribing purposes.
	• **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 24 hours of the last steroid dose**.**
	• **Hepatic impairment:**
	  ○ **Cemiplimab:** (prior to treatment, for immune related hepatitis see below). No dose adjustment in mild or moderate impairment. Insufficient data in severe impairment for dosing recommendations.
	  ○ **Carboplatin:** no dose adjustment necessary.
	  ○ **Paclitaxel:** If bilirubin < 1.25 x ULN and transaminase < 10 x ULN, dose at full dose. Otherwise consider dose reduction, not recommended in severe hepatic impairment.

- **Renal impairment:**
  - **Cemiplimab**: No dose adjustment recommended. There are limited data for CrCL<30ml/min.
  - **Carboplatin:** stop if CrCl<30ml/min.
  - **Paclitaxel:** no dose reduction necessary.
- **Infusion-related reactions:** If the infusion related reaction can be attributed to a particular agent, treat as follows:
  - **Cemiplimab:** in the event of any grade 1 or 2 infusion related reaction interrupt or slow the rate of infusion and manage symptomatically (including with corticosteroids); premedication with antipyretic, corticosteroids and antihistamines should be considered for subsequent infusions. For any grade 3 or 4 infusion related reaction permanently discontinue cemiplimab.
  - **Paclitaxel:** Patients developing hypersensitivity reactions may be re-challenged with full dose Paclitaxel following prophylactic medication (e.g. famotidine 40mg po given 4 hours prior to treatment plus hydrocortisone 100mg iv and chlorphenamine 10mg iv 30 minutes prior to treatment), then give paclitaxel over 3-6 hours (i.e. starting at over 6 hours and gradually increase rate if possible).
  - **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 re-challenged at a later date with additional prophylaxis. In the event of further reaction (grade 1-3), stop infusion and consider desensitisation regimen.
  - Severe (grade 3): Do not restart infusion. Consider re-challenge with carboplatin desensitisation regimen.
  - Anaphylaxis (grade 4): Follow anaphylaxis protocol. Discontinue permanently and consider alternative treatment.
- **Management of adverse reactions and dose adjustments:**
  - **Cemiplimab:** Dose reductions are not recommended. Dosing delay or discontinuation may be required based on individual safety and tolerability.
  - Immune-related reactions can involve any organ system, including, but not limited to meningitis, paraneoplastic encephalomyelitis, arthritis, Guillain-Barre syndrome, encephalitis, chronic inflammatory demyelinating polyradiculoneuropathy, central nervous system inflammation, autoimmune myocarditis, and immune thrombocytopenic purpura, myalgia, Sjogren's syndrome, vasculitis, myasthenia gravis. Also see table below for management of selected immune related adverse reactions.
  - Patients should be monitored for evidence of severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).
  - If corticosteroids are used to treat an immune related reaction they should be tapered over at least 1 month. Treatment should not be resumed while the patient is receiving immunosuppressive doses of corticosteroids (>10mg/day of prednisolone or equivalent) or other immunosuppressive therapy. Prophylactic antibiotics should be used to prevent opportunistic infections in patients receiving immunosuppressive therapy.
  - For guidance on managing immune related reactions see table 1 below and guidelines available on KMCC website : https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/immunotherapy/
  - Cemiplimab should be used with caution in immunosuppressed patients.
  - **Paclitaxel:** Dose reduce by 20% in the event of grade >/= 2 neuropathy and consider delay until recovery to </= grade 1. Consider omitting Paclitaxel in event of recurrent grade >/=3 neuropathy OR recurrent or persistent >/=grade 2 neuropathy following a dose reduction.
  - For adverse events (other than immune-related adverse events, nausea and vomiting and alopecia, and those stated above), dose reduction of paclitaxel and/or carboplatin should be considered if grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2. Delay until resolution of toxicity to </= grade 1.

	• **Common drug interactions (for comprehensive list refer to BNF/SPC):**
	  ○ **Cemiplimab:** No drug to drug studies have been performed, monitor poly pharmacy patients closely.
	  ○ The use of systemic corticosteroids or immunosuppressants before starting cemiplimab, except for physiological doses of systemic corticosteroid (≤ 10 mg/day prednisone or equivalent), should be avoided. However, systemic corticosteroids or other immunosuppressants can be used after starting cemiplimab to treat immune mediated adverse reactions.
	  ○ **Carboplatin:** Caution with other nephrotoxic drugs.
	  ○ **Paclitaxel:** Caution should be exercised when administering paclitaxel concomitantly with medicines known to inhibit either CYP2C8 or CYP3A4 (e.g. ketoconazole, erythromycin, fluoxetine, clopidogrel, cimetidine, ritonavir and nelfinavir); toxicity may be increased. CYP2C8 or CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, efavirenz, nevirapine) may reduce efficacy.
	• **Pregnancy and contraception:**
	  ○ Cemiplimab: Women of childbearing potential should use effective contraception during treatment with cemiplimab and for at least 4 months after the last dose of cemiplimab.
	  ○ Carboplatin/Paclitaxel: 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:** Fatigue has been reported following administration of cemiplimab, if effected patients should avoid driving or using machinery.
	• Cemiplimab contains polysorbate 80, which may cause allergic reactions.
	• The patient should be provided with the **Libtayo®** patient card, this should be carried during and after the last dose of treatment and patients must be advised to contact the oncology team or the 24 hour hot-line immediately they experience any side effect, as some side effects worsen rapidly. Prompt management of side effects can ensure that the patient continues with treatment.

References	SPC accessed online 08.06.2026 CDF list accessed online 05.06.2026

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

Table 1: Recommended treatment modifications of cemiplimab

Adverse reaction	Severity	Dose modification	Additional intervention
Immune-mediated adverse reactions			
Pneumonitis	Grade 2	Withhold	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume if pneumonitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day prednisone or equivalent	
	Grade 3 or 4 or recurrent Grade 2	Permanently discontinue	Initial dose of 2 to 4 mg/kg/day prednisone or equivalent followed by a taper
Colitis	Grade 2 or 3	Withhold	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume if colitis or diarrhoea improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day prednisone or equivalent	
	Grade 4 or recurrent Grade 3	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Hepatitis	Grade 2 with AST or ALT > 3 and ≤ 5 × ULN or total bilirubin > 1.5 and ≤ 3 × ULN	Withhold	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume if hepatitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day prednisone or equivalent or returns to baseline AST or ALT after completion of corticosteroid taper	
	Grade ≥ 3 with AST or ALT > 5 × ULN or total bilirubin > 3 × ULN	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Hypothyroidism	Grade 3 or 4	Withhold	Initiate thyroid hormone replacement as clinically indicated
		Resume when hypothyroidism returns to Grade 0 to 1 or is otherwise clinically stable	
Hyperthyroidism	Grade 3 or 4	Withhold	Initiate symptomatic management
		Resume when hyperthyroidism returns to Grade 0 to 1 or is otherwise clinically stable	
Thyroiditis	Grade 3 to 4	Withhold	Initiate symptomatic management
		Resume when thyroiditis returns to Grade 0 to 1 or is otherwise clinically stable	
Hypophysitis	Grade 2 to 4	Withhold	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement as clinically indicated
		Resume if hypophysitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day prednisone or equivalent or is otherwise clinically stable	
Adrenal insufficiency	Grade 2 to 4	Withhold	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement as clinically indicated
		Resume if adrenal insufficiency improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent or is otherwise clinically stable	
Type 1 diabetes mellitus	Grade 3 or 4 (hyperglycaemia)	Withhold	Initiate treatment with anti-hyperglycaemics as clinically indicated
		Resume when diabetes mellitus returns to Grade 0 to 1 or is otherwise clinically stable	
Skin adverse reactions	Grade 2 lasting longer than 1 week, Grade 3 or suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)	Withhold	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume if skin reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day prednisone or equivalent	
	Grade 4 or confirmed SJS or TEN	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Immune-mediated skin reaction or other	Grade 2	Withhold	Initiate management immediately, including initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper

immune-mediated adverse reactions in patients with prior treatment with idelalisib		Resume if skin reaction or other immune-mediated adverse reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day prednisone or equivalent	
	Grade 3 or 4 (excluding endocrinopathies) or recurrent Grade 2	Permanently discontinue	Initiate management immediately, including initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Nephritis with renal dysfunction	Grade 2 creatinine increased	Withhold	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume if nephritis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day prednisone or equivalent	
	Grade 3 or 4 creatinine increased	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Other immune-mediated adverse reactions (including but not limited to paraneoplastic encephalomyelitis, meningitis, myositis, solid organ transplant rejection, graft-vs-host disease, Guillain-Barre syndrome, central nervous system inflammation, chronic inflammatory demyelinating polyradiculoneuropathy, encephalitis, myasthenia gravis, neuropathy peripheral, myocarditis, pericarditis, immune thrombocytopaenia, vasculitis, arthralgia, arthritis, muscular weakness, myalgia, polymyalgia rheumatica, Sjogren's syndrome, pruritus, keratitis, immune-mediated gastritis, stomatitis and haemophagocytic lymphohistiocytosis)	Grade 2 or 3 based on type of reaction	Withhold	Initiate symptomatic management including initial dose of 1 to 2 mg/kg/day prednisone or equivalent as clinically indicated followed by a taper
		Resume if other immune-mediated adverse reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day prednisone or equivalent	
	– Grade 3 based on type of reaction or Grade 4 (excluding endocrinopathies) – Grade 3 or 4 neurologic toxicity – Grade 3 or 4 myocarditis or pericarditis – Confirmed haemophagocytic lymphohistiocytosis – Recurrent Grade 3 immune-mediated adverse reaction – Persistent Grade 2 or 3 immune-mediated adverse reactions lasting 12 weeks or longer (excluding endocrinopathies) – Inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent as clinically indicated followed by a taper
Infusion-related reactions			
Infusion-related reaction	Grade 1 or 2	Interrupt or slow rate of infusion	Initiate symptomatic management
	Grade 3 or 4	Permanently discontinue	

Combination therapy: Cycle 1 to 4
Repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Metoclopramide	20mg	PO		stat
	CEMIPLIMAB	**350mg**	IV	30 mins	In 50ml Sodium chloride 0.9% via in-line 0.22 microns filter.
	Give pre-meds 30 minutes prior to paclitaxel				
	Dexamethasone	16mg*	IV	bolus	
	Chlorphenamine	10mg	IV	bolus	
	Ondansetron	< 75yrs 16mg >/=75yrs 8mg	IV	15 min	In 50ml sodium chloride 0.9% 30 minutes prior to paclitaxel
	PACLITAXEL	**175mg/m²**	IV	Over 3 hours	In 500ml Sodium Chloride 0.9% (if dose <150mg in 250ml 0.9% sodium chloride) Use non-PVC bag and non-PVC administration set via in-line 0.22 microns filter. Flush with sodium chloride 0.9%
	CARBOPLATIN	**(AUC 5)** **Dose = AUC X (GFR + 25)** **(max 700mg)**	IV	30min	500ml glucose 5%
	***From 3rd infusion dexamethasone maybe reduced to 12mg IV**				
TTO	Drug	Dose	Route	Directions	
Day 1	Dexamethasone	6mg	PO	OD for 3 days starting on day 2.	
	Metoclopramide	10mg	PO	Take 10mg THREE times a day for 3 days then take 10mg up to THREE times a day when required (Maxi-mum of 30mg per day). Do not take for more than 5 days continuously.	

Monotherapy: cycle 5 to 36 repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Metoclopramide	20mg	PO		stat
	CEMIPLIMAB	**350mg**	IV	30 mins	In 50ml Sodium chloride 0.9% via in-line 0.22 microns filter.