CEMIPLIMAB (Libtayo) CARBOPLATIN PACLITAXEL

INDICATION (ICD10) C34

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (CEM2)

1. Cemiplimab with platinum-based chemotherapy for untreated metastatic or advanced non-small-cell lung cancer not suitable for definitive chemoradiation and would be a candidate for pembrolizumab with platinum-based chemotherapy. Stage IIIB or IIIC or IV NSCLC or disease that has recurred more than 6 months after potentially curative treatment with local management of NSCLC with surgery/chemoradiotherapy/radiotherapy. EGFR, ROS1 and ALK negative and PD-L1 positive in 1% or more of the tumour cells. The mandatory interval between the last date of administration of any prior adjuvant/neoadjuvant/maintenance immunotherapy and the date of first relapse is at least 6 months. Has no symptomatically active brain metastases or leptomeningeal metastases. PS 0 or 1. (TA1165)

REGIMEN

Cycles 1 to 4

Day 1 CEMIPLMAB 350mg in 100ml sodium chloride 0.9% IV infusion over 30 minutes
Premedication 30 minutes prior to infusion:
Dexamethasone 20 mg IV bolus
Chlorphenamine 10 mg IV bolus
PACLITAXEL 200mg/m^2 in #ml sodium chloride 0.9% infusion over 3 hours
CARBOPLATIN AUC 5 or 6 in #ml glucose 5% infusion over 30 minutes
Dose calculated by EDTA GFR or calculated CrCl + 25 x AUC.
(Maximum dose when using CrCl 125+25 x AUC)

Cycles 5 to 35

Day 1 CEMIPLIMAB 350mg in 100ml sodium chloride 0.9% IV infusion over 30 minutes

diluent volume for dose prescribed as per national standardised product specification

Cemiplimab infusion related reactions initiate symptomatic management and for grade 1 or 2 interrupt or slow rate of infusion, for grade 3 or 4 permanently discontinue.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Combination every 21 days for 4 cycles
Cemiplimab monotherapy every 21 days up to maximum 2 years cycles

ANTI-EMETICS

Moderate risk day 1 cycles 1 to 4
Low emetic risk day 1 cycles 5 to 35

CONCURRENT MEDICATION REQUIRED

Carboplatin	Anaphylaxis treatment should be prescribed if the patient has had an anaphylactic episode previously. Dexamethasone 20mg IV bolus Chlorphenamine 10mg IV bolus Carboplatin should be given at a slower rate e.g. 2-4 hours.
Cemiplimab	None
Paclitaxel	Ensure premedication given before paclitaxel

EXTRAVASATION AND TYPE OF LINE / FILTERS

Carboplatin - irritant
Paclitaxel – vesicant
Cemiplimab – neutral (treat symptomatically, non-vesicant, non-irritant but extravasation has occurred)

Paclitaxel via polyethylene lined or DEHP free administration set with ≤0.22micron filter
Cemiplimab – Use non pyrogenic, low protein binding 0.2 to 5micron in-line or add-on filter.

Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E (including Mg^{++}) and LFTs, every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
GFR assessed using EDTA result or calculated creatinine clearance at the Consultant's discretion.
Thyroid function baseline, then every cycle
Random cortisol baseline, then every cycle
Random glucose every cycle
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Carboplatin	Ototoxicity – monitor Neurotoxicity - monitor
Cemiplimab	Immune related toxicities - pneumonitis, colitis or hepatitis, severe cutaneous adverse reactions etc
Paclitaxel	(2% risk of severe hypersensitivity) Reactions range from mild hypotension (light-headedness) to full cardiac collapse (anaphylactic shock). Discontinue infusion and resuscitate appropriate to reaction. If reaction is mild and settles promptly (i.e. within 5-10 minutes), cautiously restart at a slower rate under close supervision. If further reactions occur stop treatment.

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Paclitaxel	DOACs to be used with caution, need dose modifications or to be avoided eg apixaban Clopidogrel interacts with paclitaxel Paclitaxel is catalysed, by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. inhibitors (e.g. erythromycin, fluoxetine, gemfibrozil) use with caution. inducors (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, efavirenz, nevirapine) use with caution.

DOSE MODIFICATIONS

Non-haematological

Cemiplimab

Immune-related adverse reactions - refer to TV immune-oncology agent immune related adverse event clinical guideline.

Paclitaxel

If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration

If grade ≥2 neuropathy, consider paclitaxel dose reduction

If grade >3 peripheral neuropathy is >grade 3 omit further paclitaxel

Hepatic impairment

Carboplatin

No need for dose adjustment is expected

Cemiplimab

No dose adjustment is recommended for patients with mild or moderate hepatic impairment.
Cemiplimab has not been studied in patients with severe hepatic impairment.

Paclitaxel

In the absence of Gilbert's syndrome:

Transaminase <10xULN and bilirubin ≤1.25xULN	no dose reduction
Transaminase <10xULN and bilirubin 1.26-2xULN	give 77% of original dose
Transaminase <10xULN and bilirubin 2·01-5xULN	give 51% of original dose
Transaminase ≥10xULN or bilirubin >5xULN	contraindicated

Renal impairment

Carboplatin

GFR / calculated CrCl ≤20ml/min or ≤30ml/min with pre-existing severe renal impairment	contraindicated

Cemiplimab

No dose adjustment of cemiplimab is recommended for patients with renal impairment.
Cemiplimab has not been studied in patients CrCl <21ml/min.

Paclitaxel

No need for dose adjustment is expected

REFERENCES

1. SPC