SERPLULIMAB (Hetronifly) CARBOPLATIN ETOPOSIDE

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/) (SER1)

1. Serplulimab in combination with carboplatin and etoposide for the first-line treatment of adult patients with extensive-stage small cell lung cancer, has a histologically or cytologically determined diagnosis of small cell lung cancer (SCLC) and has extensive stage disease. (Previous treatment with concurrent chemoradiotherapy with / without maintenance durvalumab 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.) Has no symptomatically active brain metastases or leptomeningeal metastases. PS 0 or 1.

REGIMEN

Cycles 1 to 4 (serplulimab before chemotherapy)

Day 1	SERPLULIMAB	4.5mg/kg in #ml sodium chloride 0.9% IV infusion
	CARBOPLATIN	AUC 5 in #ml glucose 5% IV infusion over 30 minutes Dose calculated by EDTA GFR or calculated (CrCl + 25) x AUC. Maximum dose when using CrCl 125+25 x AUC
	ETOPOSIDE	100mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes
Day 2	ETOPOSIDE	100mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes
Day 3	ETOPOSIDE	100mg/m^2 in #ml sodium chloride 0.9% IV infusion over 60 minutes

Cycle 5 onwards

Day 1	SERPLULIMAB	4.5mg/kg in #ml sodium chloride 0.9% IV infusion

diluent volume for dose prescribed as per national standardised product specification

The serplulimab initial infusion rate should be set up to 100ml/hour. If the first infusion is well tolerated, all subsequent infusions may be shortened to 30 minutes.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Combination every 21 days for up to 4 cycles
Serplulimab monotherapy from cycle 5 every 21 days until disease progression

ANTI-EMETICS

Moderate emetic risk day 1 cycles 1 to 4
Low emetic risk days 2 and 3 cycles 1 to 4, day 1 cycle 5 onwards

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.
GCSF	GCSF starting at least 24 hours after chemotherapy

EXTRAVASATION AND TYPE OF LINE / FILTERS

Carboplatin – irritant
Etoposide – irritant
Serplulimab - neutral

Serplulimab - use low-protein binding 0.2 to 5.0µm in-line or add-on filter.

Peripheral or central line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Ideally EDTA GFR should be used
Creatinine clearance (GFR) calculated, at the Consultants discretion
Serum creatinine - each cycle,
Thyroid function baseline, then every cycle
Random cortisol baseline, then every cycle (or as specified in Trust guideline)
Random glucose every cycle
HbA1C baseline
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Carboplatin	Ototoxicity - monitor Neurotoxicity – monitor.
Serplulimab	Immune related toxicities - pneumonitis, colitis or hepatitis etc

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

Carboplatin	Aminoglycosides increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests as required. Carboplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.

DOSE MODIFICATIONS

Haematological

Carboplatin and Etoposide
Neutrophil <0.5x10^9/L for more than 5 days, or low neutrophils with fever or infection, or platelets <25x10^9/L subsequent doses should be reduced.

Non-haematological

Carboplatin and Etoposide
Any grade 3 or 4 toxicity subsequent doses should be reduced.

Serplulimab
Monitored for clinical signs and symptoms of infusion-related reactions.
Grade 1 infusion-related reactions may continue administration under close monitoring.
The rate of infusion should be reduced, or treatment should be interrupted in patients with grade 2 infusion-related reactions. Antipyretic and antihistamines may be considered. Treatment with serplulimab may be resumed under close monitoring when grade 2 infusion-related reactions are controlled.
For grade ≥3 infusion-related reactions, infusion should be stopped immediately, treatment should be permanently discontinued, and appropriate treatment should be given.

Hepatic impairment
Carboplatin
No need for dose adjustment is expected

Etoposide

Bilirubin ≥50micromol/L or decreased albumin	give 50% dose

Serplulimab
No dose adjustment is needed for patients with mild (bilirubin ≤ULN and AST >ULN or bilirubin >1 to 1.5×ULN and any AST) hepatic impairment.
There are insufficient data in patients with moderate (bilirubin >1.5 to 3×ULN and any AST) hepatic impairments and no data are available in severe (bilirubin >3×ULN and any AST) hepatic impairments. No dose recommendation can be made for patients with moderate or severe hepatic impairment.

Renal impairment
Carboplatin

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

Etoposide

CrCl >50ml/min	give 100% dose
CrCl 15-50ml/min	give 75% dose
CrCl <15ml/min	Further dose reduction

Serplulimab
No dose adjustment is needed for patients with mild (CrCl 60-89ml/min) or moderate (CrCl 30-59ml/min) renal impairment.
There are insufficient data and no dose recommendation can be made in patients with severe (CrCl 15-29ml/min) renal impairment.

REFERENCES
1. CDF list