DURVALUMAB (Imfinzi) 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/) (DUR4)

1. Durvalumab in combination with etoposide plus carboplatin for the first-line treatment of adult patients with extensive-stage small cell lung cancer (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). Has no symptomatically active brain metastases or leptomeningeal metastases PS 0 or 1. (TA1041)

REGIMEN

Cycles 1 to 4

Day 1	DURVALUMAB	1500mg in 250ml sodium chloride 0.9% IV infusion over 60 minutes
	CARBOPLATIN	AUC 5 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)
	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

Cycles 5 onwards

Day 1	DURVALUMAB	1500mg in 250ml sodium chloride 0.9% IV infusion over 60 minutes

diluent volume for dose prescribed as per national standardised product specification

NB Etoposide - days 2 and 3 can be given orally ETOPOSIDE 200mg/m^2/day but is not recommended as oral absorption is variable (it may cause reduced efficacy or severe toxicity in patients), the intravenous route is preferred. However for logistical reasons the oral route may be necessary.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Combination treatment every 21 days for 4 cycles.
A formal medical review as to how durvalumab plus chemotherapy is being tolerated and whether treatment with durvalumab plus chemotherapy should be completed or not will be scheduled to occur at least by the end of the first 6 weeks of treatment
Durvalumab every 28 days cycle 5 until disease progression
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ANTI-EMETICS

Moderate risk day 1 cycles 1 to 4
Minimal risk day 1 cycles 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	Consider GCSF starting at least 24 hours after chemotherapy

EXTRAVASATION AND TYPE OF LINE / FILTERS

Carboplatin - irritant
Durvalumab – neutral
Etoposide - irritant

Durvalumab – Use low protein binding 0.2 or 0.22micron in-line or add-on filter
Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs, every cycle
Mg^{++} baseline and then as clinically indicated
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 1 to 2 cycles
Random cortisol baseline, then every 1 to 2 cycles
Random glucose every cycle
Baseline weight and every cycle cycles 1 to 4, then every 3rd cycle cycles 5 to 16

MAIN TOXICITES AND ADVERSE REACTIONS

Carboplatin	Ototoxicity – monitor Neurotoxicity - monitor
Durvalumab	Immune related toxicities

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

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

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

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

Hepatic impairment

Durvalumab
No dose adjustment is needed for patients with hepatic impairment.

Etoposide

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

Renal impairment

Carboplatin

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

Durvalumab

No dose adjustment is required in mild or moderate renal impairment. There is insufficient data from patients with severe renal impairment (CrCl <30ml/min) for dosing recommendations.

Etoposide

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

REFERENCES

1. CDF