SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti-Cancer Therapy Protocol

Atezolizumab, Carboplatin and Etoposide (Oral and IV regimens) Small Cell Lung Cancer (SCLC)

PROTOCOL REF: MPHAACEFLU
(Version No: 2.1)

Approved for use in

First-line treatment of extensive stage small cell lung cancer (SCLC) and fulfills the following criteria:

- Previous treatment with concurrent chemoradiotherapy for limited stage SCLC is PERMITTED provided therapy was completed at least 6 months prior to the diagnosis of recurrent and extensive stage disease.
- ECOG performance status (PS) 0 to 1.

BLUETEQ REGISTRATION REQUIRED

Exclusions

- History of pneumonitis, organ transplantation, autoimmune disorders, HIV infection, myocarditis, active hepatitis B or C infection
- Active infection requiring systemic treatment
- Less than 4 weeks from major surgery
- History of clinically severe autoimmune disease (can proceed with immunotherapy if well controlled autoimmune disease at the discretion of the clinical team, this needs to be documented on Meditech).
- Patient with active CNS disease (symptomatic despite steroid treatment) or carcinomatosis meningitis

Dosage

SUBCUTANEOUS ADMINISTRATION OF ATEZOLIZUMAB IS THE PREFERRED ROUTE UNLESS PATIENT INTOLERANT

Cycles 1 to 4

Drug	Dose	Route	Frequency
Atezolizumab	**1875mg (flat dose)**	SC	Day 1 only Every 3 weeks
OR			
Atezolizumab	**1200mg (flat dose)**	IV infusion	Day 1 only Every 3 weeks
Carboplatin	**AUC 5**	IV infusion	Day 1 only Every 3 weeks
Etoposide phosphate OR Etoposide	**100mg/m^2**	IV infusion	
Etoposide*	**200mg/m^2**	PO in 2 divided doses	Days 2 & 3 Every 3 weeks
OR			
Etoposide* (as standard etoposide or etoposide phosphate)	**100mg/m^2**	IV Infusion	Days 2 & 3 Every 3 weeks

Followed by maintenance immunotherapy

Cycle 5 onwards

SUBCUTANEOUS ADMINISTRATION OF ATEZOLIZUMAB IS THE PREFERRED ROUTE UNLESS PATIENT INTOLERANT

Drug	Dosage	Route	Frequency	Duration of Treatment
Atezolizumab	1875mg** (Flat dose)	Subcutaneous Injection	3 weekly	Disease progression or unacceptable toxicity
OR				
Atezolizumab	1680mg (Flat dose)	IV Infusion	4 weekly	Disease progression or unacceptable toxicity
OR				
Atezolizumab	1200mg** (Flat dose)	IV Infusion	3 weekly	Disease progression or unacceptable toxicity

Where risk factors (e.g. pre-existing autoimmune disease) for toxicity are present and patient **requires IV treatment due to intolerance or side-effects with subcutaneous route, the 3 weekly dosing is recommended.*

Routine prophylaxis against infusion related reactions is not required. However, monitor during the infusion and treatment given if necessary (antihistamines, steroids etc.). For **grade 1-2 injection site reactions** the following pre-medication to subsequent cycles and administered ahead of **SUBCUTANEOUS DOSE**:

- Paracetamol PO 1g
- Chlorphenamine PO 4mg

Please refer to the CCC Hypersensitivity; Management Prevention Policy.

Etoposide

Etoposide is available as two formulations standard etoposide or etoposide phosphate. There has been a longstanding supply problem with etoposide phosphate therefore the formulation currently in use at CCC is standard etoposide. However, the following protocol outlines administration for both formulations in case etoposide phosphate becomes available in the future as this has better stability.

Days 2 and 3 can be given orally but oral absorption is variable in comparison to the IV route (100 mg oral dose would be comparable to a 75 mg intravenous dose; a 400 mg oral dose would be comparable to a 200 mg intravenous dose).

Carboplatin

Meditech calculates creatinine clearance/GFR using the Wright formula (application for using

Wright formula is available on the Remote Citrix Web Portal). Please refer to 'Carboplatin Dosing Calculator' SOP outlining process for checking carboplatin dose ahead of each cycle of treatment.

Creatinine clearance should be capped at 125mL/min for carboplatin

Calvert formula for Carboplatin dosage-:

Carboplatin dose in mg = AUC x (GFR or CrCl + 25)

As with all platinum based chemotherapy, patients may experience allergic reaction during administration. Please refer to the CCC Hypersensitivity; Management Prevention Policy.

For severe reactions, discuss with Consultant before continuing with treatment. It should be strongly noted that patients who have severe reactions should not be re-challenged.

Counselling Points

Women of childbearing potential should use effective contraception throughout treatment and for at least 5 months following the last dose of atezolizumab.

Oral etoposide is available as 50mg or 100mg soft capsules. Unless there is a supply shortage of 50mg strength capsules, dose will be rounded to the nearest 50mg capsule and supplied in this strength. To be swallowed whole on an empty stomach (one hour before or 2 hours after food).

Please contact the triage line if any of the following symptoms occur:

- Easy bruising or bleeding.
- Uncontrolled nausea, vomiting or constipation.
- Severe jaw pain or headache.
- Redness, swelling, pain or sores where the needle was place or along the arm.
- Redness, swelling, pain or sores on your lips, tongue, mouth or throat.
- Skin rash or itching.
- Ringing in your ears or hearing problems.
- Numbness or tingling in feet or hands or painful leg cramps.
- Signs of anaemia such as unusual tiredness, shortness of breath or weakness.
- New or worsening cough, chest pain or shortness of breath
- Diarrhoea or severe abdominal pain (with or without blood/mucous)
- Jaundice, severe nausea or vomiting, or easy bruising or bleeding
- Persistent or unusual headache, extreme weakness, dizziness or fainting, or vision changes
- Monitor for signs of infection / sepsis

- Subcutaneous injection ONLY: monitor for injection site reaction- pain, swelling and rash.

Emetogenic risk:

Cycles 1 to 4: Moderately emetogenic.
Cycle 5 onwards: Mildly emetogenic.

Supportive Treatments:

Cycles 1 to 4

Dexamethasone orally 4mg twice daily for 3 days

Metoclopramide 10mg orally up to 3 times a day as required. Administration for a maximum of 5 consecutive days.

Aprepitant 125mg orally 1 hour before treatment on day 1 then 80mg once a day 1 hour before treatment on days 2 and 3 (2nd line anti-emetic).

Filgrastim to be supplied as secondary prophylaxis- subcutaneous injection daily for 7 days starting on day 5, dose as follows:

- Weight < 70kg- Filgrastim 300 micrograms daily SC.
- Weight ≥ 70kg- Filgrastim 480 micrograms daily SC.

Interactions

Please consult SmPC for full information on interactions.

Aminoglycosides e.g. gentamicin, vancomycin and diuretics

Increased risk of nephrotoxicity and ototoxicity with carboplatin. Renal function should be well monitored and audiometric tests carried out as indicated.

Phenytoin- Carboplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.

Co-administration of antiepileptic drugs and etoposide can lead to decreased seizure control

Warfarin

The effects of warfarin may be increased. Monitor INR closely.

No formal pharmacokinetic drug interaction studies have been conducted with atezolizumab. **Since atezolizumab is cleared from the circulation through catabolism, no metabolic drug-drug interactions are expected.**

Extravasation risk

Atezolizumab is a monoclonal antibody: Neutral.

Carboplatin: Irritant

Etoposide (as standard etoposide or etoposide phosphate): Irritant

Refer to the CCC policy for 'Prevention and Management of Extravasation Injuries'

Dosing in renal and hepatic impairment:

Renal	Atezolizumab	GFR ≥ 30ml/min- proceed with treatment GFR < 30ml/min- limited data use with caution
	Carboplatin	Patients with creatinine clearance values of less than 60 mL/min are at greater risk to develop myelosuppression. Carboplatin is eliminated primarily in the urine and is nephrotoxic. If there is any significant renal toxicity discuss with consultant before proceeding. Ahead of each cycle of treatment calculate creatinine (CrCl) clearance using the Wright formula (refer to 'Administration' Section) Carboplatin is contraindicated if CrCl ≤ 20 ml/min. Do not give carboplatin and discuss with clinical team.
	Etoposide	GFR > 50 ml/min: no dose adjustment is needed

		GFR 10-50 ml/min: 75% of the original dose, increase if tolerated Haemodialysis: not dialysed, consider 75% of the original dose

Hepatic	Atezolizumab	Administered with caution in patients with: Moderate (total bilirubin > 1.5 -3 × ULN and any AST) or Severe (total bilirubin > 3 × ULN and any AST*) hepatic impairment. * Within normal limits or high Refer to 'Dose Modification and Toxicity' section if LFTs become deranged AFTER starting treatment with immunotherapy
	Carboplatin	No need for dose adjustment is required.
	Etoposide	Bilirubin < 50 micromol/L and normal albumin and normal renal function: no need for dose adjustment is expected Bilirubin ≥ 50 micromol/L or decreased albumin levels: consider 50% of the dose, increase if tolerated

Administration

Cycles 1 to 4 every 21 days

<u>Oral etoposide on days 2 and 3</u>

Day	Drug	Dose	Route	Diluent and rate
1	Dexamethasone	8mg	PO	30 minutes before chemotherapy
	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Atezolizumab	1875mg (Flat dose)	SC	Over 7 minutes
	SUBCUTANEOUS ROUTE IS THE PREFERRED ROUTE UNLESS PATIENT INTOLERANT			

	The injection site should be alternated between the left and right thigh only. New injections should be given at least 2.5 cm from the old site and never into areas where the skin is red, bruised, tender, or hard. During the treatment course with atezolizumab SC formulation other medicinal products for subcutaneous administration should preferably be injected at different sites.			
	OR			
	Atezolizumab	1200mg (Flat dose)	IV	250mL Sodium Chloride 0.9%. Infused over 60 minutes for cycle 1 if well tolerated cycle 2 onwards can be administered over 30 minutes via a non-pyrogenic line with a 0.2 micron filter.
	Carboplatin	**AUC 5**	IV	In 500mL glucose 5% over 30 to 60 minutes
	Etoposide phosphate	**100mg/m^2**	IV	In 100mL sodium chloride 0.9% infusion over 15 minutes
2	**Etoposide capsules**	**200mg/m^2**	PO	in 2 divided doses
3	**Etoposide capsules**	**200mg/m^2**	PO	in 2 divided doses

OR

Day	Drug	Dose	Route	Diluent and rate
1	Dexamethasone	8mg	PO	30 minutes before chemotherapy
	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Atezolizumab	1875mg (flat dose)	SC	Over 7 minutes
	SUBCUTANEOUS ROUTE IS THE PREFERRED ROUTE UNLESS PATIENT INTOLERANT The injection site should be alternated between the left and right thigh only. New injections should be given at least 2.5 cm from the old site and never into areas where the skin is red, bruised, tender, or hard. During the treatment course with			

	atezolizumab SC formulation other medicinal products for subcutaneous administration should preferably be injected at different sites.			
	OR			
	Atezolizumab	1200mg (flat dose)	IV	250mL Sodium Chloride 0.9%. Infused over 60 minutes for cycle 1 if well tolerated cycle 2 onwards can be administered over 30 minutes via a non-pyrogenic line with a 0.2 micron filter.
	Carboplatin	**AUC 5**	IV	In 500mL glucose 5% over 30 to 60 minutes
	Etoposide	**100mg/m^2**	IV	In 250mL to 1000ml sodium chloride 0.9% infusion over 60 minutes
2	**Etoposide capsules**	**200mg/m^2**	PO	in 2 divided doses
3	**Etoposide capsules**	**200mg/m^2**	PO	in 2 divided doses

ALTERNATIVELY

Cycles 1 to 4 every 21 days

<u>IV etoposide on days 2 and 3</u>

Day	Drug	Dose	Route	Diluent and rate
1	Dexamethasone	8mg	PO	30 minutes before chemotherapy
	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Atezolizumab	1875mg (flat dose)	SC	Over 7 minutes

	SUBCUTANEOUS ROUTE IS THE PREFERRED ROUTE UNLESS PATIENT INTOLERANT The injection site should be alternated between the left and right thigh only. New injections should be given at least 2.5 cm from the old site and never into areas where the skin is red, bruised, tender, or hard. During the treatment course with atezolizumab SC formulation other medicinal products for subcutaneous administration should preferably be injected at different sites.			
	OR			
	Atezolizumab	1200mg (flat dose)	IV	250mL Sodium Chloride 0.9%. Infused over 60 minutes for cycle 1 if well tolerated cycle 2 onwards can be administered over 30 minutes via a non-pyrogenic line with a 0.2 micron filter.
	Carboplatin	**AUC 5**	IV	In 500mL glucose 5% over 30 to 60 minutes
	Etoposide phosphate	**100mg/m^2**	IV	In 100mL sodium chloride 0.9% infusion over 15 minutes
2	**Etoposide phosphate**	**100mg/m^2**	IV	In 100mL sodium chloride 0.9% infusion over 15 minutes
3	**Etoposide phosphate**	**100mg/m^2**	IV	In 100mL sodium chloride 0.9% infusion over 15 minutes

OR

Day	Drug	Dose	Route	Diluent and rate
1	Dexamethasone	8mg	PO	30 minutes before chemotherapy
	Ondansetron	16mg	PO	30 minutes before chemotherapy
	Atezolizumab	1875mg (flat dose)	SC	Over 7 minutes

	SUBCUTANEOUS ROUTE IS THE PREFERRED ROUTE UNLESS PATIENT INTOLERANT The injection site should be alternated between the left and right thigh only. New injections should be given at least 2.5 cm from the old site and never into areas where the skin is red, bruised, tender, or hard. During the treatment course with atezolizumab SC formulation other medicinal products for subcutaneous administration should preferably be injected at different sites.			
	OR			
	Atezolizumab	1200mg (flat dose)	IV	250mL Sodium Chloride 0.9%. Infused over 60 minutes for cycle 1 if well tolerated cycle 2 onwards can be administered over 30 minutes via a non-pyrogenic line with a 0.2 micron filter.
	Carboplatin	**AUC 5**	IV	In 500mL glucose 5% over 30 to 60 minutes
	Etoposide	**100mg/m^2**	IV	In 250mL to 1000ml sodium chloride 0.9% infusion over 60 minutes
2	**Etoposide**	**100mg/m^2**	IV	In 250mL to 1000ml sodium chloride 0.9% infusion over 60 minutes
3	**Etoposide**	**100mg/m^2**	IV	In 250mL to 1000ml sodium chloride 0.9% infusion over 60 minutes

Cycle 5 onwards

Day	Drug	Dose	Route	Frequency	Diluent and rate
1	**Atezolizumab**	**1875mg** (flat dose)	**SC**	3 weekly	Administer over 7 minutes
SUBCUTANEOUS ROUTE IS THE PREFERRED ROUTE UNLESS PATIENT INTOLERANT The injection site should be alternated between the left and right thigh only. New injections should be given at least 2.5 cm from the old site and never into areas where					

the skin is red, bruised, tender, or hard. During the treatment course with atezolizumab SC formulation other medicinal products for subcutaneous administration should preferably be injected at different sites.					
OR					
1	Sodium chloride 0.9%	250mL	IV	Prior to each Atezolizumab infusion.	Flush
	Atezolizumab	**1680mg** (flat dose)	**IV**	4 weekly	250mL sodium chloride 0.9%. Infused over 60 minutes for cycle 1 if well tolerated cycle 2 onwards can be administered over 30 minutes in a non-pyrogenic line with a 0.2 micron filter
OR					
1	Sodium chloride 0.9%	250mL	IV	Prior to each Atezolizumab infusion.	Flush
	Atezolizumab	**1200mg*** (flat dose)	**IV**	3 weekly	250mL sodium chloride 0.9%. Infused over 60 minutes for cycle 1 if well tolerated cycle 2 onwards can be administered over 30 minutes in a non-pyrogenic line with a 0.2 micron filter

Until progression or unacceptable toxicity.

Where risk factors (e.g. pre-existing autoimmune disease) for toxicity are present and patient **requires IV treatment due to intolerance or side-effects with subcutaneous route, the 3 weekly dosing is recommended.*

Routine prophylaxis against infusion related reactions is not required. However, monitor during the infusion and treatment given if necessary (antihistamines, steroids etc.). For **grade 1-2 injection site reactions** the following pre-medication to subsequent cycles and administered ahead of **SUBCUTANEOUS DOSE**:

- Paracetamol PO 1g
- Chlorphenamine PO 4mg

Please refer to the CCC Hypersensitivity; Management Prevention Policy.

Main Toxicities

For full details on assessment and management of immune-related toxicities refer to CCC Immuno-Oncology toxicity specific guidance for adverse event management.

Atezolizumab	
Immune-Mediated Pneumonitis Pneumonitis occurred in 3% of melanoma patients (including G3 in 0.2%).	Monitor patients for signs and symptoms and evaluate with radiographic imaging and administer corticosteroids for toxicities of grade 2 or above.
Immune-Mediated Colitis	Monitor patients for signs and symptoms and administer corticosteroids for grade 2 or greater.

Other Immune-Mediated Toxicities: Hepatitis Hypophysitis Nephritis Hyperthyroidism or Hypothyroidism Less frequently: Exfoliative dermatitis, uveitis, arthritis, myositis, pancreatitis, haemolytic anaemia, Guillain-Barré syndrome	Monitor LFTs, biochemistry, cortisol, TFTs and blood glucose, consider corticosteroids for grade 2 or greater.
Other non-immune adverse events: Fatigue, anaemia Cough, dyspnoea Nausea, decreased appetite Pruritis, rash Constipation, diarrhoea Arthralgia	Symptomatic management for grade 1 with close monitoring
Laboratory abnormalities: Hyponatraemia, hypocalcaemia, hyperglycaemia, hypertriglyceridaemia	Monitor at each cycle and rule out immune-medicated reaction
Injection site reaction	
Injection site pain, erythema, and rash	Symptomatic management for grade 1 with close monitoring. Pre-medication to be added to subsequent cycles.

Carboplatin and Etoposide	
Gastrointestinal	Nausea, vomiting, diarrhoea, abdominal pain,anorexia constipation, mucositis (including stomatitis and oesophagitis)

General disorders	Decreases in serum electrolytes (sodium, magnesium, potassium and calcium) Renal function impairment Hyperuricaemia: Serum levels of uric acid can be decreased by allopurinol. Malaise, urticaria. flu-like syndrome, rash, pruritus, alopecia
Haematological	Neutropenia, anaemia, thrombocytopenia Myelosuppression may be more severe and prolonged in patients with impaired renal function, extensive prior treatment, poor performance status and age above 65.
Vascular	Etoposide can cause hypertension, transient systolic hypotension following rapid intravenous administration.
Hepatobiliary	Abnormalities of liver function tests (usually mild to moderate).The alkaline phosphatase (ALP) level is increased more frequently than transaminases or total bilirubin. The majority of these abnormalities regress spontaneously during treatment.
Hypersensitivity reactions	Skin rash, urticaria, erythematous rash, and fever with no apparent cause or pruritus Risk of hypersensitivity and anaphylaxis may increase with previous exposure to platinum therapy
Nervous system	Paraesthesia and decreased deep tendon reflexes.
Ototoxicity	Carboplatin- tinnitus and hearing loss

Investigations and treatment plan

If suspicion of endocrinopathies: request TSH, T4, T3, ACTH, cortisol, LH, FSH, testosterone (men) and prolactin (women)

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed Consent	x				
Clinical Assessment	x		x		Then every 12 weeks or as clinically indicated
SACT Assessment (to include PS and toxicities)	x	x	x	x	Every cycle
Immunotherapy bloods as per Meditech order set: FBC, U&E/renal profile, Magnesium, LFTs (ALT, AST and Bilirubin), TFTs, cortisol, blood glucose, LDH, CRP	x	x	x	x	Every cycle
Lipid profile (cholesterol)	x				At baseline then if clinically indicated

Fatigue profile as per Meditech order set: B12, folate, Iron profile, vitamin D, Zinc, Testosterone (men only), ESR	x				At baseline then if clinically indicated
Full set of observations (*BP, heart rate, temperature, respiratory rate and O_2 sats*)		x			At baseline then if clinically indicated
Creatinine Clearance (Cockcroft and Gault)*	x	x	x	x	<u>Cycles 1 to 6 (with chemotherapy)</u> Every cycle <u>Atezolizumab ONLY (no chemotherapy)</u> With every cycle only if baseline CrCL <40ml/min or creatinine increases above 1.5x upper limit of normal or baseline
CT scan	x			x	First response assessment CT scan to be done after 2-3 cycles then every 12 weeks or as clinically indicated
Trop-T, CK, pro-BNP	x				At baseline (refer to 'Pre-assessment Baseline Cardiac
ECG	x				

					Pathway' guidance) and thereafter as clinically indicated (ECG to be reviewed by ANP or ECG clinic or clinical team)
Weight recorded	x	x	x	x	Every cycle
Height recorded	x				

Pregnancy test if applicable.

* Please refer to:

- 'Dosage' section for full details on carboplatin dosing.
- 'Carboplatin Dosing Calculator' SOP outlining process for checking carboplatin dose ahead of each cycle of treatment.

Dose Modifications and Toxicity Management

- Dose modifications due to toxicity are ONLY permitted on chemotherapy agents (carboplatin and etoposide).
- Only dosing delay or discontinuation due to toxicity are permitted for atezolizumab based on individual safety and tolerability.
- Guidelines for permanent discontinuation or withholding of atezolizumab doses are contained in 'Treatment Threshold' section below.
- Detailed guidelines for the management of immune-related adverse reactions are provided in the CCC Immuno-Oncology toxicity specific guidance for adverse event management.

Haematological Toxicity

Treatment Threshold

Atezolizumab, Carboplatin and Etoposide (Cycles 1 to 4)

Administer treatment on day 1 if:

SACT	Platelets	Neutrophils	Serum Creatinine	Bil	AST/ ALT	TSH and Free T4
atezolizumab	≥ 100 x 10^9/L **(Must be within normal range prior to cycle 1*)**	≥ 1.0 x 10^9/L	≤1.5 x ULN or baseline	<3 x ULN	<3 x ULN	Within range or no change from base line
carboplatin/ etoposide			**Refer to 'Dosing in renal and hepatic impairment' section for recommended dose modifications for carboplatin and etoposide based on individual renal and hepatic function**			

ULN = upper limit of normal

*****If platelets or ANC still below required levels for treatment at week 2, delay treatment again and patient will need assessment and chemotherapy dose reduction

Atezolizumab ONLY (Cycle 5 onwards)

Administer treatment on day 1 if:

Platelets	Neutrophils	Serum Creatinine	Bilirubin	AST/ALT	TSH and Free T4
≥ 75 x 10^9/L	≥ 1.0 x 10^9/L	≤ 1.5 ULN or baseline	<3 x ULN	<3 x ULN	Within range or no change from base line

Non Haematological Toxicity

Infusion related reactions	These can occur with carboplatin and rarely with etoposide. Hypotension can occur if etoposide is administered too quickly – slower the infusion and give subsequent infusions at the slower rate Hypertension and flushing can also occur – stop infusion, monitor; blood pressure usually reverts to normal after a few hours

Detailed guidelines are provided in the CCC clinical network immunotherapy acute oncology guidelines. Systemic high-dose corticosteroid with or without additional immunosuppressive therapy may be required for management of severe immune-related adverse reactions.

Toxicity Grade	Action
Grade 1 Mild	Continue treatment increase monitoring and provide symptomatic treatment.
Grade 2 Moderate	Withhold treatment until resolved to ≤ grade 1. Refer to Immuno-Oncology toxicity specific guidance for adverse event management.
Grade 3 and Grade 4 Severe	Withhold treatment. Treatment will be permanently discontinued for any unresolving grade 3-4, severe or life-threatening adverse reaction at the treating clinician's discretion. Refer to Immuno-Oncology toxicity specific guidance for adverse event management.

References

1. Liu, Stephen V., et al. "Updated overall survival and PD-L1 subgroup analysis of patients with extensive-stage small-cell lung cancer treated with atezolizumab, carboplatin, and etoposide (IMpower133)." Journal of Clinical Oncology 39.6 (2021): 619.
2. SmPC for Carboplatin 10 mg/ml Intravenous Infusion, Hospira – accessed via electronic medicines compendium at https://www.medicines.org.uk/emc (Last updated June 2020)

3. SmPC for ETOPOPHOS 100mg Powder for Solution for Injection, Neon Healthcare Ltd – accessed via electronic medicines compendium at https://www.medicines.org.uk/emc (Last updated February 2022)
4. SmPC for Etoposide 20 mg/ml Concentrate for Solution for Infusion, Accord Helathcare Ltd – accessed via electronic medicines compendium at https://www.medicines.org.uk/emc (Last updated April 2019)
5. SmPC for Tecentriq 1,200 mg concentrate for solution for infusion, Roche products Limited- accessed via www.medicines.org.uk/emc/medicine (Last updated 1st September 2023).
6. SmPC for VEPESID 100 mg soft capsule, soft, Neon Healthcare Ltd – accessed via electronic medicines compendium at https://www.medicines.org.uk/emc (Last updated january 2021)
7. Supplement to: Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; 20: e201–08.
8. NICE TA638: Atezolizumab with carboplatin and etoposide for untreated extensive-stage small-cell lung cancer. Published: 01 July 2020

Circulation/Dissemination

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Version History

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June 2020	2.0	Tara Callagy Lung SRG Pharmacist	New regimen protocol
September 2023	2.1	Hala Ghoz Lung SRG Pharmacist	Routine protocol update