PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Durvalumab
Adjuvant Treatment
Non-Small Cell Lung Cancer (NSCLC)

PROTOCOL REF: MPHADURVLU
(Version No.: 1.2)

Approved for use in:

Patients with locally advanced, unresectable NSCLC which is either stage IIIA, IIIB or IIIC at the time of commencing concurrent chemoradiotherapy who meet the following conditions:

- PS 0 or 1
- Patients must have recently completed treatment with 2 or more cycles of platinum-based combination chemotherapy given concurrently with definitive radical radiotherapy which must have been at a dose of 54-66Gy (or a biologically equivalent dose of 54-66Gy).
    - Note: durvalumab is **not approved by NICE for use after sequential chemotherapy and radiotherapy.**
- Patients must be re-staged after completion of chemoradiotherapy and NOT have any evidence of disease progression or metastatic spread.
- Patients must not have received prior treatment with immunotherapy for NSCLC
- First treatment with durvalumab must commence within 42 days of the last active treatment date of the concurrent chemoradiotherapy treatment program.
- PD-L1 testing must be completed with an approved and validated test to determine the PD-L1 Tumour Proportion Score (TPS) prior to treatment and the result must either demonstrates a PD-L1 score of ≥1%. If the PD-L1 TPS

cannot be ascertained despite a clear intent and a reasonable attempt to do so durvalumab may still be given. Note: durvalumab is **not approved for use if the PD-L1 result is <1% or negative.**

******Blueteq registration is required******

Exclusions

History of pneumonitis, organ transplantation, autoimmune disorders, HIV infection, active hepatitis B or C infection

Active infection requiring systemic treatment

Less than 4 weeks from major surgery

History of clinically severe autoimmune disease

Dosage:

Drug	Dosage	Route	Frequency	Duration
Durvalumab	10mg/kg*	IV infusion	2 weekly*	Until disease progression or unacceptable toxicity **up to a maximum of 12 months (26 2-weekly or 13 4 weekly cycles) whichever is longer**
Durvalumab	1500mg	IV infusion	4 weekly	

Where risk factors for toxicity are present e.g. pre-existing autoimmune disease or previous toxicity, the 2-weekly regime may be used.

Extravasation risk:

Monoclonal antibody – considered to be neutral.

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

Dosing in renal and hepatic impairment (Prior to start of treatment ONLY/Baseline):

Renal	Durvalumab	CrCl ≥ 30ml/min proceed with treatment CrCl < 30ml/min- not studied, proceed with caution.

Hepatic	Durvalumab	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

Patient Counselling Points

Women of childbearing potential should use effective contraception throughout treatment and for at least 3 months following the last dose of durvalumab.

Contact the triage team for the following:

- 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

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	Durvalumab	10mg/kg (2 weekly) *or 1500mg (4 weekly)*	IV infusion	250-500mL Sodium Chloride 0.9% over 60 minutes through a 0.2 micron filter

Until disease progression or unacceptable toxicity up to a **maximum of 12 months (26 x 2-weekly or 13 x 4-weekly cycles)** whichever is longer.

Where risk factors for toxicity are present e.g. pre-existing autoimmune disease or previous toxicity, the 3 weekly regime may be used.

Routine prophylaxis against infusion related reactions is not required. However, monitor during the infusion and treatment given if necessary (antihistamines, steroids etc.). 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.

Immune-Mediated Pneumonitis Pneumonitis occurred in 3% of melanoma patients (including G3 in 0.2%).	Refer to Immuno-Oncology toxicity specific guidance for adverse event management
Immune-Mediated Colitis Colitis occurred in 1% of patients (including G3 in 0.5%).	Refer to Immuno-Oncology toxicity specific guidance for adverse event management
Other Immune-Mediated Toxicities: Hypophysitis Nephritis Hyperthyroidism or Hypothyroidism Less frequently: Exfoliative dermatitis, uveitis, arthritis, myositis, pancreatitis, haemolytic anaemia	Monitor LFTs, biochemistry, cortisol and TFTs regularly Refer to Immuno-Oncology toxicity specific guidance for adverse event management
Other non-immune adverse events: Fatigue, anaemia Cough, dyspnoea Nausea, decreased appetite Pruritis, rash Constipation, diarrhoea Arthralgia	Refer to Immuno-Oncology toxicity specific guidance for adverse event management
Laboratory abnormalities: Hyponatraemia, hypocalcaemia, hyperglycaemia, hypertriglyceridaemia	Refer to Immuno-Oncology toxicity specific guidance for adverse event management

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	Home treatment if eligible	Prior to cycle 3	Cycle 3	Ongoing
Informed Consent	x						
Clinical Assessment	x				x*		Every 12 weeks thereafter or as clinically indicated
SACT Assessment (to include PS and toxicities)	x	x	x			x	Every cycle
OTR/ Go-ahead	x		x			x	Every cycle
Immunotherapy bloods as per Meditech order set: FBC, U&E/renal profile, Magnesium, LFTs (AST, ALT and bilirubin), TFTs, cortisol, blood glucose, LDH, CRP	x	x	x			x	Every cycle
Lipid profile (cholesterol)	x					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, hear rate, temperature, respiratory rate and O_2 sats*)	x	x	x		x	x	Every cycle
Creatinine Clearance (Cockcroft and Gault)	x						Every cycle only if baseline CrCL <40ml/min or creatinine increases above 1.5x upper limit of normal or baseline
CT scan**	x						Every 12 weeks/if clinically indicated
Trop-T, CK, pro-BNP	x						At baseline for all Renal and Melanoma and thereafter as clinically indicated (ECG to be reviewed by clinical team)
ECG	x						

Weight recorded	x	x	x			x	Every cycle
Height recorded	x						

*Formal medical review (can be virtual) to assess the tolerability of treatment and whether treatment should continue (as per NHS England criteria).

**CT Scan only required every 6 months in adjuvant setting.

Pregnancy test if applicable

Dose Modifications and Toxicity Management:

- Dosing delay or discontinuation may be required based on individual safety and tolerability.
- Guidelines for permanent discontinuation or withholding of doses are contained in dose modifications.
- Detailed guidelines for the management of immune-related adverse reactions are provided in the CCC Immuno-Oncology toxicity specific guidance for adverse event management.

Treatment Threshold

Administer treatment on day 1 if:

Platelets	Neutrophils	Serum Creatinine	Bilirubin	AST/ALT	Alkaline Phosphatase	TSH and Free T4
≥ 75 x 10^9/L	≥ 1.0 x 10^9/L	≥ 1.5 x ULN or baseline	<3 x ULN	<5 x ULN	<5 x ULN	Within range or no change from base line

ULN = upper limit of normal

Platelets must be within normal range prior to Cycle 1.

Toxicity management:

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:

IMFINZI 50 mg/mL concentrate for solution for infusion, Summary of Product Characteristics AstraZeneca UK Limited. Available from www.medicines.org.uk/emc/medicine. Last updated 19th October 2021.

NICE TA 578: Durvalumab for treating locally advanced unresectable non-small-cell lung cancer after platinum-based chemoradiation. Published: 01 May 2019.

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.

Circulation/Dissemination

Date added into Q-Pulse	14th December 2021
Date document posted on the Intranet	

Version History

Date	Version	Author name and designation	Summary of main changes
		Tara Callagy **Lung SRG Pharmacist**	New Regimen Protocol Version 1.0
		Tara Callagy **Lung SRG Pharmacist**	**Interim COVID19 amendment added** **Version 1.1**
		Hala Ghoz **Protocols Pharmacist**	**Aligned with standard IO protocol** **Updated with flat 4 weekly dosing** **Version 1.2**