Systemic Anti Cancer Treatment Protocol

Nivolumab
Adjuvant Treatment of Melanoma

PROTOCOL REF: MPHANIADSK
(Version No: 1.0)

Approved for use in:

Nivolumab, as monotherapy, for the adjuvant treatment of newly diagnosed and completely resected stage III or completely resected stage IV malignant melanoma.

*** Blueteq registration is required ***

Dosage:

Drug	Dosage	Route	Frequency
Nivolumab	3mg/kg	IV infusion	2 weekly for a maximum of 12 months (or a maximum of 26 cycles when given 2-weekly).

- Dose escalation or reduction is not recommended. 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 network immunotherapy acute oncology guidelines.

Extravasation risk:

None

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	Nivolumab	3mg/kg	IV infusion	100mL sodium chloride 0.9%. Infused over 60 minutes in a non-pyrogenic line with a 0.2 micron filter

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

Main Toxicities:

Nivolumab	
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 G2 or greater.
Immune-Mediated Colitis Colitis occurred in 1% of patients (including G3 in 0.5%).	Monitor patients for signs and symptoms and administer corticosteroids for G2 or greater.
Other Immune-Mediated Toxicities: Hepatitis Hypophysitis Nephritis Hyperthyroidism or Hypothyroidism Less frequently: Exfoliative dermatitis, uveitis, arthritis, myositis, pancreatitis, haemolytic anaemia	Monitor LFTs, biochemistry and TFTs As above, consider corticosteroids for G2 or greater
Other non-immune adverse events: Fatigue, anaemia Cough, dyspnoea Nausea, decreased appetite Pruritis, rash Constipation, diarrhoea Arthralgia	Symptomatic management for G1/G2 Monitor diarrhoea – as this may be the first sign of colitis
Laboratory abnormalities: Hyponatraemia, hypocalcaemia, hyperglycaemia, hypertriglyceridaemia	Monitor at each cycle

Investigations:

	Pre	C1	C2		C3	C4	C5	C6		C7	Ongoing
		Week 1	Week 3		Week 5	Week 7	Week 9	Week 11		Week 13	
Oncology Team Assessment	X						X				Every 12 weeks thereafter or as clinically indicated
Informed Consent	X										
Pre-Assessment	X										
Nursing Pre-Treatment Assessment Including toxicity assessment *Home treatments- 24-48 hours before due dose*		X	X	**Home treatment if eligible**	X	X	X	X	**Imaging with review by oncology team 1 week later**	X	Every cycle
FBC, U&E, LFTs and LDH *Local hospital/GP surgery 72 hours before due dose*	X		X		X	X	X	X		X	Every Cycle
TFTs *Local hospital/GP surgery 48 hours before due dose*	X		X		X	X	X	X		X	Every Cycle
Blood glucose	X		X		X	X	X	X		X	Every Cycle
Lipid profile (cholesterol)											Only if clinically indicated
CT scan	X										Every 6 months
Blood pressure & full observations set	X	X	X		X	X	X	X		X	Every cycle
ECOG PS	X	X	X		X	X	X	X		X	Every cycle
Weight recorded	X	X	X		X	X	X	X		X	Every cycle

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

Dose Modifications and Toxicity Management:

Haematological toxicity

- Dose escalation or reduction is not recommended. 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 is provided in the clinical network immunotherapy acute oncology guidelines.

Proceed on day 1 if:-

Platelets	Neutrophils	Creatinine Clearance	Bilirubin	AST/ALT	Alkaline Phosphatase	TSH and Free T4
≥ 75 x 10^9/L	≥ 1.0 x 10^9/L	≥30 mL/min	<3 x ULN[a]	<5 x ULN	<5 x ULN	Within range or no change from base line

[a] ULN = upper limit of normal

The dose should be omitted if appropriate. Inform consultant if there has been an increase in liver function test from previous results.

Toxicity management:

Systemic high-dose corticosteroid with or without additional immunosuppressive therapy may be required for management of severe immune-related adverse reactions.

Non-haematological toxicity

Toxicity Grade	Action
Grade 1 Mild	No action. Provide symptomatic treatment
Grade 2 Moderate	Withhold Nivolumab until resolved to <grade 1. Consider systemic corticosteroids in addition to appropriate symptomatic treatment. Once recovered the dosing interval in subsequent cycles will be increased by one week (e.g. to 4 weeks)
Grade 3 and Grade 4 Severe	Withhold Nivolumab. Discontinue if unable to reduce corticosteroid dose to < 10 mg per day prednisolone equivalent within 12 weeks of toxicity. Systemic corticosteroids (1 to 2 mg/kg prednisolone or equivalent per day) are indicated in addition to appropriate symptomatic treatment. Steroid taper should be considered once symptoms improve to Grade 1 or less and tapered over at least 4 weeks

Following each dose delay due to toxicity, the dosing interval should increase by an additional week. For example, if a patient has stopped drug twice due to a drug-related toxicity, the dosing interval should be every 5 weeks.

Nivolumab will be permanently discontinued for any Grade 3-4, severe or life-threatening adverse reaction.

Patient Counselling Points

Contact the triage team for the following:

New or worsening cough, chest pain or shortness of breath

Diarrhoea or severe abdominal pain

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

References:

https://www.medicines.org.uk/emc/medicine/30476

NICE: Nivolumab for adjuvant treatment of resected stage III and IV melanoma [ID1316]

Blueteq CDF Form: (NIV7_ver1.0)