Systemic Anti-Cancer Treatment Protocol

Nivolumab
Squamous Head and Neck Cancer

PROTOCOL REF: MPHANIVHN
(Version No: 1.2)

This protocol has been temporarily amended due to COVID-19 pandemic.

Approved for use in:

Nivolumab as monotherapy is indicated for the treatment of **squamous** cell cancer of the head and neck progressing on or after platinum-based chemotherapy when the following conditions are met:

- Patient has recurrent or metastatic head and neck cancer that is not amenable to local therapy with curative intent (surgery and/or radiation therapy with or without chemotherapy)
- Patient's disease has progressed or recurred during or within 6 months of the last dose of previously received platinum-based chemotherapy.
- ECOG performance status 0 or 1 and would otherwise be potentially fit for docetaxel-based or methotrexate-based 2nd line chemotherapy
- No previous treatment with anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-cytotoxic T-lymphocyte-associated-antigen-4 (CTLA-4) antibody.
- Confirm that every effort has been made for the patient to have PD-L1 testing to determine the TPS and state TPS score.
    - Or state if TPS cannot be quantified
    - Or state if PD-L1 testing was not possible as the pathologist has documented that there was insufficient tissue.
- The patient does not have symptomatically active brain metastases or leptomeningeal metastases.

Blueteq registration required

Dosage:

Drug	Dosage	Route	Frequency
Nivolumab	240mg	IV infusion	2 weekly until disease progression or unacceptable toxicity* or to maximum of 2 years
Nivolumab	480mg**	IV infusion	4 weekly until disease progression or unacceptable toxicity* or to maximum of 2 years

- *Atypical responses (i.e. an initial transient increase in tumour size or small new lesions within the first few months followed by tumour shrinkage) have been observed. It is recommended to continue treatment for clinically stable patients with initial evidence of disease progression until further disease progression is confirmed.
- ** Nivolumab 480mg every 4 weeks is an unlicensed dose that is permitted during the COVID-19 pandemic. Patients previously receiving 240mg must have a consultation with the treating clinician and clear documentation in the notes that the patient agrees to the switch to 480mg due to its unlicensed status.
- 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 network immunotherapy acute oncology guidelines.

Extravasation risk:

None

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	Nivolumab	240mg	IV infusion	100mL sodium chloride 0.9%. Infused over 30 minutes in a non-pyrogenic line with a 0.2 micron filter

Day	Drug	Dose	Route	Diluent and rate
1	Nivolumab	480mg	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		X	X	X				Every cycle
FBC, U&E, LFTs and LDH *Local hospital/GP surgery 48 hours before due dose*	X		X		X	X	X				Every Cycle
TFTs *Local hospital/GP surgery 48 hours before due dose*	X				X		X				Every 6 weeks
Blood glucose	X										Repeat if clinically indicated
Lipid profile (cholesterol)	X				X		X				Every 6 weeks
CT scan	X										Every 12 weeks or as clinically indicated
Blood pressure	X	X	X		X	X	X				Every cycle
ECOG PS	X	X	X		X	X	X				Every cycle
Weight recorded	X	X	X		X	X	X				Every cycle

Home treatment if eligible

Imaging with review by oncology team 1 week later

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*	<5 x ULN	<5 x ULN	Within range or no change from base line

* 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
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 4 weeks.

Nivolumab will be permanently discontinued for any unresolving grade 3-4, severe or life-threatening adverse reaction at the treating clinician's discretion.

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

Opdivo® SPC available at: **https://www.medicines.org.uk/emc/medicine/30476** date of last revision of text 17 May 2018

NICE FAD Sept 2017

SSC1872 Nivolumab SPC update 12 June 2018