Nivolumab

Indication

- Advanced renal cell carcinoma after prior therapy
- Palliative treatment for metastatic melanoma
- Adjuvant treatment for completely resected melanoma
- Squamous Cell Cancer of the Head and Neck (SCCHN) progressing on or after platinum-based therapy
- Unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma after prior fluoropyrimidine- and platinum-based combination chemotherapy
- Non-small cell lung cancer (NSCLC) after prior chemotherapy
- Relapsed or refractory classical Hodgkin's lymphoma
- Adjuvant monotherapy for patients with completely resected oesophageal or gastro-oesophageal carcinoma who have residual pathological disease at surgery following prior neoadjuvant chemoradiotherapy
- Adjuvant treatment for resected high-risk invasive urothelial cancer
- **Compassionate use** for pre-treated metastatic/recurrent squamous cell anal cancer
- **Compassionate use** for pre-treated squamous cell vulval cancer
- In combination with platinum-based chemotherapy for the neoadjuvant treatment of NSCLC

ICD-10 codes

Dependant on tumour site

Regimen details

Day	Drug	Dose	Route
1	Nivolumab	240mg, 360mg or 480mg	IV infusion

Cycle frequency

Single agent treatment given every 2 weeks (240mg) or 4 weeks (480mg)

In combination with platinum-based chemotherapy for neoadjuvant treatment of NSCLC:

- 360mg every 3 weeks

Number of cycles

Metastatic melanoma, head and neck cancer, oesophageal cancer and renal cell carcinoma

Until unacceptable toxicity, disease progression or consultant discretion (sustained complete response).

Other metastatic indications

Until unacceptable toxicity, disease progression or consultant discretion (sustained complete response). Treatment should stop at 2 years.

Adjuvant treatment

Adjuvant treatment should continue for 12 months (13x 4 weekly cycles) or until disease progression, withdrawal of consent, or unacceptable toxicity.

In combination with chemotherapy for the neoadjuvant treatment of NSCLC
Give 3 cycles only

Switching regimens:
When switching from 2-weekly regimen to 4-weekly regimen, give first 480mg dose two weeks after the last 240mg dose
When switching from 4-weekly regimen to 2-weekly regimen, give first 240mg dose four weeks after the last 480mg dose

Administration

Nivolumab 240mg in 50ml sodium chloride 0.9% over 30 minutes
Nivolumab 360mg in 100ml sodium chloride 0.9% over 30 minutes
Nivolumab 480mg in 100ml sodium chloride 0.9% over 30 minutes
Patients should be monitored every 30 minutes during the infusion (blood pressure, pulse and temperature) and for infusion related reactions. For mild to moderate reactions, decrease the infusion rate and closely monitor. Premedication with paracetamol and chlorphenamine should be used for further doses. For severe infusion related reactions discontinue treatment.

Pre-medication

Nil

Emetogenicity

This regimen has low emetogenic potential

Additional supportive medication

Antiemetics as per local policy, if required.

Extravasation

Neutral (Group 1)

Investigations – pre first cycle

See network pre-SACT bloods list

PD-L1 tumour expression if required for some indications, please refer to indications list above.

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	48 hours
U+E (including creatinine)	48 hours
LFT inc AST	48 hours
LDH (melanoma only)	48 hours
Thyroid function	Every 6 weeks unless otherwise clinically indicated
Glucose	48 hours
Calcium	As clinically indicated
Cortisol/Trop/CK/BNP	At consultant discretion

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	**Limit**
Neutrophil count	≥ 1.0 x 10^9/L
Platelets	≥ 75 x 10^9/L
Creatinine Clearance (CrCl)	≥ 30mL/min
Serum Creatinine	≤1.5 X ULN
Bilirubin	Serum total bilirubin ≤1.5 X ULN or direct bilirubin

	≤ULN for patient with total bilirubin level >1.5 ULN
ALT/AST	≤2.5 X ULN or ≤5 X ULN with liver metastases
Alkaline Phosphatase	< 5 x ULN

Dose modifications

Do not amend the dose of nivolumab

Consider immunotherapy driven toxicity as a potential reason for all changing laboratory results and discuss with a consultant if any concerns.

Treatment of toxicities

Immunotherapy toxicities should be aggressively managed as can cause permanent and life threatening complications.
Refer to UKONS and ESMO guidance for treatment of immune related toxicities.
Available at:
https://www.lancashireandsouthcumbria.icb.nhs.uk/our-work/canceralliance/information-professionals/clinical-reference-groups/acute-oncology-crg-metastatic-spinal-cord-compression-mscc-crg

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Pneumonitis
Colitis
Hepatitis
Nephritis
Endocrinopathies Pancreatitis

- **Frequently occurring side effects**

Myelosuppression
Reduced appetite
Headache Dizziness
Dry eyes
Cough
Diarrhoea
Nausea Rash
Fatigue
Hyperglycaemia
Hypocalcaemia

- **Other side effects**

Arthralgia

Significant drug interactions – for full details consult product literature/ reference texts

Corticosteroids: use of systemic corticosteroids at baseline, before starting nivolumab, should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of nivolumab. However, systemic corticosteroids or other immunosuppressants can be used after starting nivolumab to treat immune-related adverse reactions.

Additional comments

Women of child bearing potential should use effective contraception during treatment and for at least 4 months after the last dose.

References

- http://www.swscn.org.uk/guidance-protocols/cancer-protocols/ accessed 9 Jul 2020
- Summary of Product Characteristics Nivolumab via www.medicines.org.uk

THIS PROTOCOL HAS BEEN DIRECTED BY PROFESSOR BOARD, DESIGNATED LEAD CLINICIAN FOR MELANOMA

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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