BC Cancer Protocol Summary for Palliative Therapy for Unresectable, Platinum-refractory, Recurrent or Metastatic Squamous Cell Cancer of the Head and Neck Using 4-Weekly Nivolumab

Protocol Code	*UHNAVNIV4*
Tumour Group	*Head and Neck*
Contact Physician	*Dr. Cheryl Ho*

ELIGIBILITY:

- Histologically confirmed recurrent or metastatic SCCHN (oral cavity, oropharynx, pharynx, larynx, primary unknown), stage III/IV and not amenable to local therapy with curative intent (surgery or radiation therapy with or without chemotherapy)
- Patients have received at least 1 prior line of platinum chemotherapy in the neoadjuvant, adjuvant, concurrent, or metastatic setting
- ECOG 0-2
- Adequate hepatic and renal function
- Patients may be PDL1 positive or negative
- Patients may be p16 positive or negative
- Access to a treatment centre with expertise to manage immune-mediated adverse reactions of nivolumab
- A BC Cancer “Compassionate Access Program” (CAP) approval
- CAP approval is not required to switch between UHNAVNIV and UHNAVNIV4

EXCLUSIONS:

- Recurrent or metastatic cancers of the salivary gland, nasopharyngeal carcinoma, or non-squamous histologies
- Active central nervous system metastases (should be asymptomatic and/or stable)
- Active autoimmune disease, active hepatitis B, C or HIV (HCV antibody or negative HCV RNA permitted)
- Use with caution in patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)

TESTS:

- Baseline: CBC/differential, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, random glucose, TSH
- Before each treatment: CBC/differential, creatinine, alkaline phosphatase, ALT, total bilirubin, LDH, sodium, potassium, glucose, TSH
- If clinically indicated: chest x-ray, free T3 and free T4, morning serum cortisol, lipase, serum ACTH levels, FSH, LH, testosterone, estradiol
- Weekly telephone assessment for signs and symptoms of side effects while on treatment (optional but recommended)

PREMEDICATIONS:

- Antiemetic protocol for low emetogenic chemotherapy protocols (see SCNAUSEA). Antiemetics are not usually required.

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
nivolumab	6 mg/kg (maximum 480 mg)	IV in 50 to 100 mL NS over 30 minutes using a 0.2 micron in-line filter

Repeat **every 4 weeks** until disease progression or unacceptable toxicity.

DOSE MODIFICATIONS:

No specific dose modifications. Toxicity managed by treatment delay and other measures (see SCIMMUNE protocol for management of immune-mediated adverse reactions to checkpoint inhibitors immunotherapy).

PRECAUTIONS:

- **Serious immune-mediated reactions**: these can be severe to fatal and usually occur during the treatment course. They may include enterocolitis, intestinal perforation or hemorrhage, hepatitis, dermatitis, neuropathy, endocrinopathy, as well as toxicities in other organ systems. Early diagnosis and appropriate management are essential to minimize life-threatening complications (**see SCIMMUNE protocol for management of immune-mediated adverse reactions to checkpoint inhibitors immunotherapy**).
- **Infusion-related reactions:** isolated cases of severe reaction have been reported. In case of a severe reaction (Grade 3 or 4), nivolumab infusion should be permanently discontinued and appropriate medical therapy administered. Patients with mild or moderate infusion reaction may receive nivolumab with close monitoring. Premedications with acetaminophen and antihistamine may be considered if there is a history of reaction.

Call Dr. Cheryl Ho or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

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3. Ferris L, Blumenschein G, Fayette J, et.al. Further evaluations of nivolumab (nivo) versus investigators choice (IC) chemotherapy for recurrent or metastatic (R/M) squamous cell carcinoma of the head and neck (HNSCC): CheckMate 141. J Clin Oncol Asco Meeting Abstracts 34:6009, May 2016.

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5. Bristol-Myers Squibb Canada. OPDIVO® product monograph. Montreal, Quebec; 26 August 2016.
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7. Waterhouse D, Horn L, Reynolds C, et al. Safety profile of nivolumab administered as 30-min infusion: analysis o f data from CheckMate 153. Cancer Chemother Pharmacol 2018;81:679-86.
8. Zhao X, Suryawanshi S, Hruska M, et al. Assessment of nivolumab benefit-risk profile of a 240-mg flat dose relati ve to a 3-mg/kg dosing regimen in patients with advanced tumors. Ann Oncol 2017;28(8):2002-8.
9. Zhao X, Ivaturi V, Gopalakrishnan M, et al. Abstract CT101: A model-based exposure-response (ER) assessmen t of a nivolumab (NIVO) 4-weekly (Q4W) dosing schedule across multiple tumor types. Cancer Res 2017;77(13 s uppl):DOI: 10.1158/1538-7445.AM2017-CT101.