PRINCESS MARGARET CANCER CENTRE
CLINICAL PRACTICE GUIDELINES

HEAD AND NECK

MUCOSAL MELANOMA
1. Introduction
   - Sinonasal mucosal melanoma is a rare tumor accounting for <1% of melanomas
   - Affects both genders equally; peak incidence is in the 7th decade
   - Involve nasal cavity most frequently, followed by paranasal sinus, oral cavity and less commonly other mucosal sites in the upper aerodigestive tract
   - Usually (70-80% present with localized disease), 20-30% develop nodal metastases; and 40-70% will develop distant metastases to lung, liver, bone, brain

2. Prevention
   - Although exposure to tobacco and possibly other agents (e.g. formaldehyde) have been suggested as possible etiologic factors, there is no definite causatory link; reduction in exposure to tobacco is however important in prevention of other head and neck malignancies (SCC)

3. Screening and Early Detection
   - There is currently no role for screening or evidence for early detection in improving outcomes
   - Oral melanosis as a precursor lesion for mucosal melanoma is controversial, and the need for excision or follow-up of these lesions is not established

4. Diagnosis / Initial Assessment
   All patients should be assessed prior to treatment intervention, by the multidisciplinary Head & Neck Team.

**History and Physical evaluation:**
   - Record height, weight and ECOG performance status
   - History and Physical examination including mucosal survey for synchronous primaries
     - Record
     - smoking
       - Non-smoker / Current / ex-smoker
       - pack years
     - alcohol history in standard drinks/week;
       - None / Light <10 drink/wk / Mod 10-20 / Heavy >20
     - Record exposure to other potential carcinogens e.g. formaldehyde
   - Record stage (current edition TNM)
     - Note that for mucosal melanoma only T3 and T4 category exist
   - Specify location of primary including dimensions and involvement of anatomic subsites
   - Documentation of specific nodal level(s) involved
     - Size and extent of nodal involvement (e.g. fixed/mobile)
Investigations (Baseline):

- Panendoscopy or examination under anaesthesia if deemed necessary
- Biopsy
  - UHN pathology review;
  - molecular diagnostic testing including BRAF mutation, c-kit status
- CT scan Head and Neck
- MRI Head and Neck (T1 + gadolinium, T2 sequences), if indicated
- CT thorax / abdomen / pelvis
- Consider PET scan
- Bloodwork: CBC, creatinine, electrolytes, liver function, glucose, coagulation studies (APTT, INR)
- Pregnancy test where indicated
- Other staging investigations as clinically indicated (bone scan etc)

5. Pathology

- Neoplastic cells are derived from melanocytes in the mucosa of the upper aerodigestive tract
- Tumors are composed of epithelioid, spindled, rhabdoid or plasmacytid cells
  - Mitoses frequent; vascular / perineural invasion in ~40%
  - S100, vimentin positive; variable expression of HMB-45
- Pathology reporting (for surgical specimens) should follow a standard format for mucosal malignant melanoma, and include the following SYNOPTIC DATA, as per the College of American Pathologists 2011 cancer protocols (see www.cap.org):
  - Specimen:
  - Procedure:
  - Specimen Size:
    - Greatest dimension:
    - Additional dimension(s):
  - Specimen Laterality:
  - Tumor Site:
  - Tumor Focality:
  - Tumor Size:
    - Greatest dimension:
    - Additional dimension(s):
  - Histologic Type
    - Histologic Grade:
  - Margin status for invasive carcinoma
    - Margin(s):
  - Margin status for carcinoma in situ
    - Margin(s):
  - Lymph-Vascular Invasion:
  - Perineural Invasion:
o Lymph Nodes, Extranodal Extension:
  o TNM Descriptors [note unique staging for mucosal melanoma] :
    ▪ Primary Tumor (pT):
    ▪ Regional Lymph Nodes (pN):
      • Number of regional lymph nodes examined:
      • Number of regional lymph nodes involved:
    ▪ Distant Metastasis (pM):
  • Consideration should be given to molecular diagnostic testing (relevant to potential systemic therapy), including:
    o BRAF mutation
    o c-kit status

6. Management

**Overall Management Approach**

- These guidelines apply to patients with melanoma arising in the mucosa of the head and neck region
- Primary surgical resection is the standard approach, with post-operative radiotherapy to the primary site +/- neck (regional nodes)
- There is no standard role for chemotherapy, and chemotherapy is not recommended pre, during or post radiation therapy, as a routine. However, referral to medical oncology is warranted for consideration of other therapies and clinical trials (e.g. BRAF inhibitors), which should not be combined with radiation therapy, unless on a clinical study
- All patients should be assessed for inclusion on available current trial protocols and, if eligible and appropriate, offered inclusion on trial

**Standard Treatment (off clinical trial)**

**Post-operative Radiotherapy**

* Dose fractionation schedules
  - 60-66Gy in 2 Gy per fraction

* Treatment volumes
  - Inclusion of the entire mucosal region of origin (e.g. entire nasal fossa, or sinus of origin)
  - Inclusion of the neck (ipsilateral or bilateral) may be indicated

**Definitive Radiotherapy**

* Dose fractionation schedules
  - 70Gy in 2 Gy per fraction for radical intent
• 50Gy in 20 fractions, or 60Gy in 25 fractions for radical-palliation

 Patients not suitable for radical treatment
• Refer to separate guideline: Palliative Management of Patients with H&N malignancy (SECTION 12)

6.1 Surgery
• Primary site
  o Combined modality therapy with surgery and adjuvant radiotherapy
  o Paranasal sinuses: as per “Nasal cavity / paranasal sinus” guideline
  o Oral cavity: resection and reconstruction per section “Oral cavity” guideline
• Neck
  o N0: no neck dissection
  o N+: perform selective neck dissection dictated by location of neck disease

6.2 Chemotherapy
• There is no standard role for chemotherapy, and chemotherapy is not recommended pre, during, or post radiation therapy, as a routine.
• However, referral to medical oncology is warranted for consideration of other therapies and clinical trials (e.g. of BRAF inhibitors), which should not be combined with radiation therapy, unless on a clinical study.
• Patients not suitable for curative therapies, may be suitable for palliative systemic therapy; the optimal agents are being defined and patients should be considered for available clinical trials

6.3 Radiation Therapy

Pre-Treatment Assessment
• Dental assessment
• Nutritional assessment and consultation (pre-treatment, or during first weeks of treatment)
• Audiology
  o Pts receiving platinum-type chemoRx
  o Pts receiving high-dose adjacent to auditory apparatus
• Medical Oncology assessment (for consideration of future Rx)
• Ophthalmology consult as indicated
• Written consent to be obtained prior to simulation
• Pre-radiotherapy review: patients are reviewed by the radiation oncologist in the week prior to commencing treatment for assessment and to review the treatment plan

**TREATMENT**

• CLINICAL CARE DURING RADIOTHERAPY:
  o Pts shall be reviewed by the RO at least weekly during RT
  o ASSESSMENT:
    ▪ acute toxicities (RTOG criteria) documented in MOSAIQ
    ▪ Weight and nutritional review (weekly nutritional review for pts with G-tube, or as clinically indicated)
    ▪ Bloodwork prior to each cycle of chemotherapy, or as clinically indicated
  o Management of acute toxicities: refer to Nursing / Supportive Care guideline

6.4 Oncology Nursing Practice

Refer to *Head and Neck Nursing Care*

7. **Supportive Care**

7.1 **Patient Education**

Refer to *general patient education practices*

7.2 **Dental Care**

Refer to *dental care for Head and Neck Cancers*

7.3 **Symptom Management**

Refer to *general symptom management care guidelines*

7.4 **Clinical Nutrition**

Refer to *general clinical nutrition care guidelines*
7.5  Palliative Care

Refer to *palliative management of Head and Neck Cancers*

7.6  Speech Pathology

Refer to *speech language pathology for Head and Neck Cancers*

8.  Follow-up Care

- Setting: Assessment in multidisciplinary clinic
- Schedule:
  - 2-6 weeks post radiotherapy
  - Q3 months or more frequent for two years
  - Q4 months or more frequent for third year
  - Q6 months or more frequent for years 4-5
  - Annually for years 6-10

- Investigations and assessment (follow-up):
  - Fibre-optic nasendoscopy
  - Imaging
    - CT head and neck at 10-12 weeks post-treatment
    - MRI Head and Neck if indicated
  - Pharyngeal function (speech/swallow), if indicated
  - Dental assessment where applicable
  - Audiometry or ophthalmology where applicable

**ASSESSMENT and MANAGEMENT of PERSISTENT / RECURRENT DISEASE (SALVAGE)**

- Biopsy / histological confirmation
- Record site of failure (local, regional, distant)
- Date of failure/recurrence
- Determine site of recurrence relative to the initial target volume
- RE-STAGE
  - CT Head, neck, thorax
  - Other imaging as clinically indicated
- salvage options:
  - RE-IRRADIATION: refer to guideline for re-treatment of pts with H&N malignancy for re-irradiation
    - RT volumes
    - Fractionation
    - Use of concurrent Rx