Provincial Melanoma Treatment Guidelines
(Approved at the Provincial Melanoma Guideline Meeting on September 7, 2012)

Clinical practice guidelines have been developed after multi-disciplinary consensus based on best available literature. As the name suggests, these are to be used as a guide only. These guidelines do not replace Physician judgment which is based on multiple factors including, but not limited to, the clinical and social scenario, comorbidities, performance status, age, available resources and funding considerations. SCA disclaims all liability for the use of guidelines except as expressly permitted by SCA. No portion of these guidelines may be copied, displayed for redistribution to third parties for commercial purposes or any non-permitted use without the prior written permission from SCA.

Benefits and risk of the proposed should be discussed with patient.

Participating in clinical trials is encouraged when available. Involvement of a multidisciplinary team is strongly recommended.

Screening:

None

Diagnosis:

Suspected pigmented lesions should be removed with biopsy with a margin of 1 to 3 mm for suspected melanoma however shave biopsy is not recommended.

Once melanoma is confirmed, the patient should be referred to the specialist team for further surgery with wide local excision with or without Sentinel Lymph Node(SLN) biopsy.

Work Up:

1. Biopsy.
2. History and Physical examination, Labs.
3. CT scans, PET scan and MRI in selected cases after discussing with the melanoma team.

Pathology:

Minimum dataset required are:

1. Ulceration.
2. Thickness.
3. Mitotic rate.
4. Histological subtype.
5. Margin of excision.
6. Pathological staging.

7. Growth phase.
8. Regression.
9. Tumour infiltrating lymphocytes.
10. Lymphovascular invasion/Perineural invasion.
11. Microsatellites.

It is recommended that if there is a positive confirmation of cancer, the patient should be referred to a dermatologist, oncologist or specialist surgeon.

In Situ Melanoma:

Wide local excision is recommended with at least a margin of 0.5cm, a bigger margin maybe necessary for large melanoma in situ

Stage 1A:

No routine imaging is required unless clinically indicated.

Surgery to the primary site with adequate clinical margins of at least 1 cm if anatomically and functionally feasible. (See Appendix A)

No routine role for SLN Biopsy apart from selected patients with high risk features.

No role for adjuvant treatment.

Stage 1B/II:

No routine imaging is required unless clinically indicated.

Surgery to the primary site with adequate margins of at least 1 to 2cm if anatomically and functionally feasible and depending upon the thickness. ie 2 cms should be considered for melanomas 4mm thick (See Appendix A)

Discuss and consider SLN biopsy at the time of wider excision.

Discuss and consider adjuvant high dose interferon for fit and well-motivated Stage IIC patients with T4 lesions.

Stage III, SLN positive:

Imaging is recommended: CT scans, PET scan and MRI as deemed appropriate.

Complete lymph node dissection.

Surgery to the primary site with adequate margins of at least 1 to 2cm if anatomically and functionally feasible and depending upon the thickness. ie 2 cms should be considered for melanomas 4mm thick (See Appendix A)

Adjuvant Radiotherapy to the nodal area if multiple lymph nodes are involved or there is ECE (refer to adjuvant radiotherapy section).

Discuss and consider adjuvant high dose interferon for fit and well-motivated patients .

At this time, the sequencing of adjuvant interferon and adjuvant radiotherapy is unclear.

Stage III, Clinically Positive Lymph nodes:

Imaging is recommended: CT scans, PET scan and MRI as deemed appropriate.

FNA biopsy or excision biopsy of lymph node.

Anatomically complete lymph node dissection of the involved basin.

Surgery to the primary site with adequate margins of atleast 1 to 2cm if anatomically and functionally feasible and depending upon the thickness. (See Appendix A)

Adjuvant Radiotherapy to the nodal area if multiple lymph nodes are involved or there is ECE (refer to adjuvant radiotherapy section).

Discuss and consider adjuvant high dose interferon for fit and well-motivated patients.

At present the sequencing of adjuvant interferon and adjuvant radiotherapy is unclear.

Stage III Intransit:

Imaging is recommended: CT scans, PET scan and MRI as deemed appropriate.

FNA or biopsy is recommended of satellite lesions.

Complete surgical excision if feasible. If, surgical excision is not feasible, consider palliative radiation, Isolated limb perfusion in centres with the expertise or intralesional interleukin as per protocol and by a trained oncologist.

Discuss and consider adjuvant high dose interferon for fit and well-motivated patients.

Stage IV:

Imaging is recommended: CT scans, PET scan and MRI as deemed appropriate.

FNA or biopsy is recommended.

Resection of limited metastatic disease if feasible. If limited metastatic disease is completely resected, patient can be observed.

Radiation for brain metastases.

For unresectable disease, consider systemic treatment if applicable.

Braf testing to be done in all Stage IV cases suitable for systemic therapy C KIT testing for mucosal or acral melanoma).

Occult Primary:

Patients presenting with isolated nodal disease without primary site should be treated as Stage III disease with nodal dissection with or without adjuvant radiotherapy and chemotherapy.

Patients presenting with Stage IV disease without a primary site should be referred to the dermatologist to rule out melanoma primary.

Follow Up:

Semi-Annual skin exam by a Dermatologist.

Educate patient about monthly skin examination.

History and Physical examination and skin nodal examinations every 3 to 4 months for the first 3 years and then every 6months for up to 5 yrs. After 5 yrs, annual examination and as clinically indicated.

There is no role for routine imaging or blood tests unless the patient becomes symptomatic or an abnormality is picked up on examination.

In selected high risk cases CT surveillance can be considered on case by case basis.

Radiotherapy:

Adjuvant Radiotherapy to Primary site:

Adjuvant radiotherapy to the primary site can be considered to reduce local recurrence in the following conditions:

1. Melanomas with desmoplastic or neurotropic features.
2. Melanomas, > 4mm deep, especially if ulcerated or with satellite nodules.
3. Melanomas of Head and Neck mucosal origin.
4. Where it is not possible to get negative surgical margins or close margins.
5. Identification of intransit or satellite lesions on wide local excision.
6. Re-excision after local recurrence.

The sequencing of adjuvant immunotherapy and adjuvant RT is unclear.

Suggested radiation doses are:

1. 48Gy in 20 fractions,
2. 30Gy in 5 fractions over 2.5 weeks
3. 24Gy in 3 fractions over 3 weeks (RTOG 0721 Protocol only)

For involved margins:

1. 50.4 Gy in 21 fractions OR
2. 36Gy in 6 fractions with 2 fractions delivered weekly.

Adjuvant Radiotherapy to nodal site:

Adjuvant radiotherapy to the nodal areas can be considered to reduce local recurrence in the following situations:

1. Extracapsular extension.
2. $\geq$ 3 inguinal nodes involved.
3. Lymph nodes $\geq$ 3cms (cervical) or 4cms inguinal.
4. $\geq$ 2 cervical or axillary lymph node.
5. Recurrent nodal disease.
6. Patients with positive SLN and complete nodal dissection is not planned.

The sequencing of adjuvant immunotherapy and adjuvant RT is unclear.

Suggested radiation doses are:

1. 48Gy in 20 fractions.

2. 30Gy in 5 over 2.5 week.
3. 24Gy in 3 fractions over 3 weeks (RTOG 0721 Protocol only).

For involved margins:

4. 50.4Gy in 21 fractions OR
5. 36Gy in 6 fractions with 2 fractions delivered weekly.

Definitive Radiotherapy:

Radiotherapy alone is rarely used as the primary treatment in malignant melanoma.

This can be considered if the patient is not suitable or refuses surgery. The aim of the radiotherapy is local control of the disease.

Radical radiation can also be considered for Superficial Lentigo maligna and Lentigo Maligna melanoma.

Suggested radiation doses are:

1. 50Gy in 20 fractions.
2. 36Gy in 6 fractions with 2 fractions delivered weekly.

Palliative Radiotherapy:

Palliative radiotherapy to the metastatic sites to reduce symptoms can be considered.

Suggested radiation doses are:

1. 20Gy in 5 Fractions,
2. 40Gy in 15 Fractions.
3. 30Gy in 10 Fractions.
4. 8Gy in 1 Fraction.
5. 24Gy in 3 Fractions over 3 weeks.

Stereotactic radiation for brain metastasis may be considered depending upon clinical situation.

Chemotherapy:

Adjuvant Therapy:

High dose Interferon Alfa 2b.

Induction Phase 20 million units/m2 IV daily days 1 to 5 for 4 weeks.

Maintenance Phase 10 million units/m2 s/c 3 times a week for 48 weeks.

Palliative Therapy:

50 percent of melanoma patients have Braf mutation. Braf testing should be considered in fits patients suitable for treatment.

If Braf mutation is positive, Vemurafenib 960mg Bid PO.

If Braf mutation is negative, consider Ipilimumab 3mg/kg IV every 3 weeks for upto 4 cycles. At present Health Canada approval is for second line treatment.

The sequencing of Vemurafenib and Ipilimumab is unclear at present.

High dose Interlukein with or without chemotherapy can be considered in fit young patients with low volume disease and in centres equipped with administering this regime.

Other options with limited responses include:

1. Dacarbazine 1000mg/m2 IV 3 weekly.
2. Temozolomide 200mg/m2 PO Days1to5 every 28 days especially in patients with brain metastasis.
3. Carboplatin AUC 6 IV 3 weekly.
4. Carboplatin and Taxol.

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Useful Resources:

British Columbia Cancer Agency Guidelines:
http://www.bccancer.bc.ca/HPI/CancerManagementGuidelines/default.htm

Cancer Care Ontario Guidelines:
https://www.cancercare.on.ca/toolbox/qualityguidelines/diseasesite/melanoma-ebs/

National Comprehensive Cancer Network Guidelines:
http://www.nccn.org/professionals/physician_gls/f_guidelines.asp

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