

# REFERRAL AND FOLLOW-UP SURVEILLANCE OF CUTANEOUS MELANOMA

Effective Date: February 2013

The recommendations contained in this guideline are a consensus of the Alberta Cutaneous Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

## **BACKGROUND**

Early recognition of malignant melanoma presents the best opportunity for cure and accordingly patients with lesions suspicious of melanoma should be referred urgently to a specialist with an interest in pigmented lesions.

The purpose of surveillance of patients who have been diagnosed with malignant melanoma is to: <sup>1-3</sup>

- Monitor the success of the primary treatment of the melanoma
- Detect local, regional or disseminated recurrences early so that early treatment can be undertaken
- Examine for a second primary malignant melanoma
- Provide patient education
- Provide reassurance and emotional support for the patient

Routine follow-up of malignant melanoma patients is the investigation of asymptomatic people with appropriate evaluation and intervention where necessary. A structured follow-up program assumes that early detection of any recurrence of melanoma will be more amenable to surgery. Although there are no randomized controlled trials, there is data to suggest that earlier detection of distant disease may influence survival. Patient education on what to watch for is important because many recurrences are found by patients.

The most important part of follow-up is a careful history and physical examination, including evaluation of the patient's general well being, history of weight loss, and specific symptoms such as cough or headache. Sixty percent of recurrences are discovered by physical examination with changes primarily being found between the site of the original disease and the regional lymph nodes.<sup>1,4-7</sup> A full skin review with examination of the soft tissues, regional lymph nodes and organomegaly constitutes the appropriate standard of assessments of patients who have had a malignant melanoma.

## **GUIDELINE GOALS AND OBJECTIVES**

To improve overall survival, disease-free survival, and quality of life for adult patients with high-risk malignant melanoma who are rendered disease-free following resection

## **GUIDELINE QUESTIONS**

- Which patients should be referred to the cancer treatment centre?
- What should the referral consist of?
- What is the appropriate duration of follow-up?
- What are the recommended follow-up intervals?
- What should be assessed during follow-up?
- Who should conduct the follow-up?

## DEVELOPMENT PANEL

This guideline was reviewed and endorsed by the Alberta Cutaneous Tumour Team. Members of the Alberta Cutaneous Tumour Team include medical oncologists, radiation oncologists, surgical oncologists, dermatologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Cutaneous Tumour Team and a Knowledge Management Specialist from the Guideline Utilization Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the [Guideline Utilization Resource Unit Handbook](#).

## SEARCH STRATEGY

The MEDLINE (1966 through January 2011), CINAHL, Cochrane, ASCO Abstracts and proceedings, and CANCELIT databases were searched. The search included practice guidelines, systematic reviews, meta-analyses, randomized controlled trials, and clinical trials. Search terms included: monitoring, surveillance, follow up, ultrasound or ultrasonography, referral, and malignant melanoma.

For the 2013 update of the guideline, PubMed was searched for evidence on follow-up in cutaneous melanoma. The search term “melanoma” was used and results were limited to clinical trials, published between January 2012 and January 2013. Citations were hand-searched for relevant studies. Following a review of the evidence by the Alberta Cutaneous Tumour Team, no changes to the recommendations were made.

## TARGET POPULATION

The recommendations outlined in this guideline apply to adults over the age of 18 years with malignant melanoma. Different principles may apply to pediatric patients.

## RECOMMENDATIONS

For staging please refer to the Appendix.<sup>8</sup>

### Referral

- All patients who have malignant melanoma could be seen at a cancer treatment centre for assessment.
  - Referral is strongly encouraged for all patients with lesions 1 mm in thickness or greater, Clark IV or Clark V or if ulcerated.
  - All patients with lesions less than 1 mm depth of invasion should be followed by their referring physician.
- It is expected that a referral will be forwarded to the cancer treatment centre regarding the patient's assessment. The referral will include the following:<sup>9</sup>
  - Letter describing the clinical disease
  - Pathology reports (e.g. melanoma biopsy or excision, lymph node dissection, and all previous reports of skin lesions)
  - Operative reports (e.g. lymph node dissection and wide excision)

- Laboratory reports (e.g. LFT)
- Information regarding other malignancies
- Imaging reports (e.g. chest x-ray)

### **Follow-up and Surveillance**<sup>10</sup>

- All patients are to be informed of signs of locoregional recurrence.
- Physicians who wish to be involved in the long-term follow-up of their patients may do so.
- Manual skin examination to be conducted by dermatologist.

Stage-specific recommendations follow:

#### ***In situ malignant melanoma***

- At least annual skin exam for life
- Educate patient on monthly skin self exam
- The patient may be seen in the cancer clinic then discharged to the referring physician.
  - History and physical exam (with emphasis on nodes and skin)
  - Exam should ensure adequate excision of the original lesion and include a review of skin self examination.
  - No routine investigation is indicated; radiologic imaging may be used to investigate specific signs or symptoms.

#### ***Lesions less than 1 mm***

- At least annual skin exam for life
- H & P (with emphasis on nodes and skin) every 6-12 months in the first year, with subsequent full skin exams annually for life.
- Educate patient in monthly self skin and lymph node exam
- The patient may be seen in the cancer clinic then discharged to the referring physician.
  - The patient should have a history and physical examination with full skin review carried out every six months for the first year and then annually.
  - No routine investigation is indicated; radiologic imaging may be used to investigate specific signs or symptoms; an initial chest x-ray for documentation and future comparison is optional.

#### ***Intermediate and thick lesions*** (lesions <1.0 mm with ulceration or lesions 1.0-4.0 mm and >4 mm)

- At least annual skin exam for life
- Educate patient in monthly self skin and lymph node exam
- The patient may be seen in the cancer clinic then discharged to the referring physician.
  - History and physical examination (with emphasis on nodes and skin) at least every six months for the first three years, annually for the next two years, and then annually as clinically indicated
  - CT scan to follow-up for specific signs and symptoms

### ***Proven nodal metastases***

- The patient should be followed at the cancer centre at a frequency determined by the attending physician depending on the treatment plan.
- History and physical examination (with emphasis on nodes and skin) every 3-6 months for three years, then every four to twelve months for two years, then annually as clinically indicated.
- Additional investigations (e.g. blood work, imaging, etc.) as per symptoms.

### ***Stage IV: Lesions of any thickness with proven distant metastases***

- The patient should be followed at the cancer centre at a frequency determined by the attending physician depending on the treatment plan.
- History and physical examination (with emphasis on nodes and skin) every 3-6 months for three years, then every 4-12 months for two years, then annually as clinically indicated
- Additional investigations (e.g. blood work, imaging, etc.) as per symptoms.

### ***Patients receiving Interferon therapy***

- The patient will be seen by the attending medical oncologist monthly during the year of treatment, every three months for two more visits and then every six months thereafter in the outpatient clinic.

### ***Ocular Melanoma***

- Patients with ocular melanoma will be assessed by the referring ophthalmologist and receive an initial assessment in the clinic.
- Subsequent follow up will be once yearly for five years and consist of a history and physical exam, liver function studies, a chest x-ray and an ultrasound.
- For uveal melanoma, a reasonable consensus protocol is six-monthly follow up, with full clinical examination. Liver imaging, liver function tests and possibly a plain chest radiograph may be undertaken regularly or intermittently as clinically indicated.<sup>11</sup>
- For conjunctival melanoma, due to the high likelihood of recurrence or new ocular lesions, indefinite biannual assessment is recommended; these patients should be followed-up for life.<sup>11</sup>

## **DISCUSSION**

The best evidence currently available on the follow-up and surveillance of malignant melanoma is low-level evidence, as no prospective randomized controlled trials have yet been performed. Despite a lack of convincing evidence that regional control, quality of life, or overall survival is increased through follow-up, it is assumed that earlier treatment is likely to result in improvements in these outcomes.

From the patient's perspective, there may be preference for being seen more often, if reassurance is needed; alternatively, a patient may prefer to be seen less often if the appointment brings about anxiety or is associated with significant time and monetary expenses.<sup>3</sup> According to a study in the UK by Dancey, et al. (2005), more often the former is the case and patients feel reassured by clinic visits.<sup>12</sup>

As the majority of recurrences are discovered by the patient (47-67%) or by the physician during physical examination (21-26%),<sup>13,14,15</sup> a thorough history and physical examination is a key component of follow-up. The history should evaluate the patient's general well being, any changes in weight, and specific symptoms, such as cough or headache. A full skin review with examination of the soft tissues, regional lymph nodes and organomegaly constitutes the appropriate standard of physical examination of patients who have had a malignant melanoma.

Routine radiologic imaging and blood tests do not have a role in the follow-up of patients, unless clinically indicated at the discretion of the physician. The yield from imaging in this setting is low, while false positive rates and cumulative exposure to imaging radiation are of concern.<sup>10,16,17</sup> Retrospective studies have revealed recurrence detection rates between 7 and 32%, using any radiologic imaging.<sup>13,14</sup> However, PET-CT has demonstrated high sensitivity rates (73-100%),<sup>18-21</sup> while the sensitivity of chest x-ray is far lower (8-48%).<sup>22,23</sup>

Blood tests are also of little use, unless specific signs or symptoms warrant investigation.<sup>10</sup> A prospective study among 97 high risk melanoma patients showed that neither LDH, nor S-100B, was a strong indicator of in-transit metastases; and that clinically apparent lymph nodes were rarely detected using these indicators (e.g. detection rates of 29.4% and 11.8% for S-100B and LDH, respectively).<sup>24</sup> Therefore, routine laboratory investigations are not recommended for the routine follow-up of melanoma patients.

## GLOSSARY OF ABBREVIATIONS

Acronym	Description
LDH	lactate dehydrogenase
LFT	liver function tests
mets	metastases

## DISSEMINATION

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

## MAINTENANCE

A formal review of the guideline will be conducted at the Alberta Cutaneous Tumour Team Annual Meeting in 2015. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

## CONFLICT OF INTEREST

Participation of members of the Alberta Cutaneous Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to

advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Cutaneous Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

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**APPENDIX**
**AJCC 2009 (7th Edition) Anatomic Stage Groupings for Cutaneous Melanoma<sup>8</sup>**

	Clinical Staging <sup>a</sup>				Pathologic Staging <sup>b</sup>			5-year Survival (%)
	T	N	M		T	N	M	
0	Tis	N0	M0	0	Tis	N0	M0	100%
IA	T1a	N0	M0	IA	T1a	N0	M0	95%
IB	T1b T2a	N0	M0	IB	T1b T2a	N0	M0	90%
IIA	T2b T3a	N0	M0	IIA	T2b T3a	N0	M0	78%
IIB	T3b T4a	N0	M0	IIB	T3b T4a	N0	M0	65%
IIC	T4b	N0	M0	IIC	T4b	N0	M0	45%
III	Any T	N > N0	M0	IIIA	T1-4a	N1a	M0	66%
				IIIB	T1-4a	N2a	27%	
					T1-4b	N1a		
					T1-4b	N2a		
				IIIC	T1-4a	N1b		
					T1-4a	N2b		
T1-4a	N2c							
					T1-4b	N1b		
					T1-4b	N2b		
					T1-4b	N2c		
					Any T	N3		
IV	Any T	Any N	M1	IV	Any T	Any N	M1	13%

<sup>a</sup> Clinical staging includes microstaging of the primary melanoma and clinical/radiologic evaluation for metastases. By convention, it should be used after complete excision of the primary melanoma with clinical assessment for regional and distant metastases.

<sup>b</sup> Pathologic staging includes microstaging of the primary melanoma and pathologic information about the regional lymph nodes after partial (i.e., sentinel node biopsy) or complete lymphadenectomy. Pathologic stage 0 or IA patients are the exception; they do not require pathologic evaluation of their lymph nodes.

**AJCC 2009 (7<sup>th</sup> Edition) TNM Staging Categories for Cutaneous Melanoma<sup>8</sup>**

T	Thickness (mm)	Ulceration Status/Mitoses
Tis	NA	NA
T1	≤ 1.00	a: without ulceration and mitosis < 1/mm <sup>2</sup> b: with ulceration or mitoses ≥ 1/mm <sup>2</sup>
T2	1.01-2.00	a: without ulceration b: with ulceration
T3	2.01-4.00	a: without ulceration b: with ulceration
T4	> 4.00	a: without ulceration b: with ulceration
N	Number of Metastatic Nodes	Nodal Metastatic Burden
N0	0	NA
N1	1	a: micrometastasis <sup>a</sup> b: macrometastasis <sup>b</sup>
N2	2-3	a: micrometastasis <sup>a</sup> b: macrometastasis <sup>b</sup> c: in transit metastases/satellites without metastatic nodes
N3	4+ metastatic nodes, or matted nodes, or in transit metastases/satellites with metastatic nodes	
M	Site	Serum LDH (lactate dehydrogenase)
M0	No distant metastases	not applicable
M1a	Distant skin, subcutaneous or nodal metastases	Normal
M1b	Lung metastases	Normal
M1c	All other visceral metastases	Normal
	Any distant metastases	Elevated

<sup>a</sup> Micrometastases are diagnosed after sentinel lymph node biopsy.

<sup>b</sup> Macrometastases are defined as clinically detectable nodal metastases confirmed pathologically.