Cutaneous Melanoma

Cancer Centre of Southeastern Ontario
Standard Management Guidelines

Intended for use by Clinicians and Health Care Providers involved in the Management or Referral of adult patients with Cutaneous Melanoma

Section	Activity	Activity Description	Details	Reference(s)
AA	Cancer Centre Referrals	Melanoma multidisciplinary clinic	• Post- excisional biopsy or after definitive surgery/sentinel node procedure. • Central pathology review recommended. • Referral directly to medical oncology if presentation with metastatic disease. • Referral directly to radiation oncology if presentation with brain metastasis.	
A	Diagnosis	Biopsy type, procedure	• Excisional biopsy	1, 2
B	Pathology of diagnostic specimen	Synoptic report	• As per College of American Pathologists (CAP) guideline • BRAF mutational analysis if requested – standard for all metastatic melanoma • Other mutational analysis as clinically indicated (eg NRAS, CKit)	CAP Guideline Melanoma Synoptic Template
C	History and Physical exam		If negative for evidence of satellites, other primaries and clinical nodal involvement go to D. **If suspicious for metastatic disease, proceed to G (investigations)**	1, 2
D	Definitive Curative Intent Surgery (if applicable)		Wide excision with ideal margins measured clinically: • 1 cm for < 1.0 mm depth where possible • 1- 2 cm > 1.0 mm < 4 mm where possible • 2 cm for > 4 mm where possible Sentinel node biopsy offered - for melanoma > 1 mm following discussion of risks and benefits	1-4

Section	Activity	Activity Description	Details	Reference(s)
E	Pathology of final surgical specimen (if applicable)	Synoptic report content	*Wide excision specimen*: Indicate if: Remaining tumour present margins *Sentinel lymph node(s)*: Presence/absence of melanoma If present: • Number of nodes involved • Measured Size of metastases • Presence of extranodal involvement	1, 2
F	**Assign Post-Surgical Primary Stage**			Appendix I
G	Investigations		Stage I, IIA: no further investigations unless indicated by symptoms or findings on physical exams All other patients: Baseline lab tests (CBC, LFT, LDH) and imaging of head and body – MRI head (CT if MRI not possible) and CT chest, abdomen and pelvis. Other imaging if patient symptomatic (e.g. bone scan) PET scan – only if equivocal results from baseline imaging or if excision of metastasis considered to rule out occult diffuse metastatic disease.	1, 2, 5
H	Post-investigation management	Curative intent:	Stage IA, B, IIA– routine follow up (H) Stage III – Complete node dissection followed by observation or high dose interferon alpha or clinical trial	1-3, 6

Section	Activity	Activity Description	Details	Reference(s)
			Interferon alfa only to be offered to >1 macroscopically node positive patients and/or those with tumour > 4mm deep with adequate performance status and no medical contraindications. (AJCC T4 or T1-3, N1b or higher, M0) Adjuvant Radiation to be considered in cases of : • Any single node size of ≥3 cm (axilla or groin) and ≥2 cm (head and neck) • Any extracapsular extension • Number of lymph nodes (at least one with macrometastatic deposit) ≥1 parotid node, ≥2 axillary or neck nodes, ≥3 inguinal nodes • Resected recurrent nodal disease • Doubt regarding adequacy of lymph node dissection All patients meeting above criteria should be discussed at Multidisiplinary Case Conference for review	
I	Post-investigation management	Advanced Disease:	Stage IV: If no brain metastases a. Solitary or subcutaneous (<3) – consider surgical resection. PET scan may be helpful to determine absolute number and location of metastatic disease to ensure it is surgically resectable. b. Multiple metastases or not resectable	Cancer Care Ontario Drug Formulary

Section	Activity	Activity Description	Details	Reference(s)

			Systemic First line
			• If asymptomatic, may consider observation
			• If symptomatic or observation not appropriate:
			  o If BRAF mutated – BRAF inhibitor or MEK inhibitor or clinical trial
			  o If BRAF negative or not suitable for BRAF inhibitor– DTIC or temozolomide
			Systemic Second Line
			• Consider ipilimumab if suitable
			• Consider BRAF inhibitor if not already exposed
			• Consider DTIC or temozolomide if not already exposed
			• Clinical trial
			
			Brain metastasis
			Consider surgical resection or stereotactic radiation if possible, typically followed by whole brain radiotherapy.
			
			If not consider for Palliative whole brain radiation.
			
			If brain metastases are stable or resected treat as b.
			
			If brain metastases are not stable.
			• Consider temozolomide if not already exposed
			• Consider clinical trial	

Section	Activity	Activity Description	Details	Reference(s)
			Symptom management Palliative radiation and medical management for symptomatic disease as indicated	
J	Follow up with no evidence of disease		Stage I-III– regular skin surveys (typically only patients with high risk stage II and III melanoma would be followed at the cancer clinic but all patients with a diagnosis of melanoma need skin surveys regularly by dermatology, family doctor, surgeon or oncologist). For those followed at the cancer centre they would be examined for new primaries and evidence recurrence of disease following resection: • Q 3 months x 4 • Q 6 months x 4 • Q 12 months x 2 • Investigations as clinically indicated	
K	Controversies		• Therapeutic advantage of removing an involved SLN • Completion lymph node dissection after the identification of a microscopically positive SLN • Role of high dose interferon for T3bN0 melanoma • Role of mitotic rate in melanoma in assigning high risk • Role of PET scanning • Radiation of asymptomatic incidentally identified brain metastases	

Section	Activity	Activity Description	Details	Reference(s)
			• Sequence of targeted therapies versus immune treatments for metastatic disease • The role of BRAF testing in initial management of stage 1-3 melanoma	
L	Clinical Trials	Adjuvant	No Current Trials	
		Metastatic	No Current Trials	
		Supportive Care	No Current Trials	

References

1. NCCN Guidelines, Melanoma Version 2.2014 (September 2013)
2. Revised UK guidelines for the management of cutaneous melanoma 2010, Marsden JA et al. Br J Dermatology 2010; 163: 238-56.
3. ASCO Guidelines : Sentinel Lymph node biopsy for melanoma: American Society of Clinical Oncology and Society of Surgical Oncology Joint Clinical Practice Guideline. (Found at http://www.asco.org/guidelines/snbmelanoma)
4. Primary Excision Margins and Sentinel Lymph Node Biopsy in Clinically Node-Negative Cutaneous Melanoma of the Trunk or Extremities. CCO program in EBC https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=73876
5. PET Imaging in Melanoma: Recommendations (IN REVIEW). https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=152462
6. Systemic Adjuvant Therapy for Patients at High Risk for Recurrent Melanoma. CCO program in EBC: https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14216
7. Lancet Oncology 2012. 13: 589-97
8. Lee et al. Int J Radiation Oncol Biol Phys 2000; 46(20): 467-74.
9. IJROBP 2012; 83(1):310-16.

Appendix I – Melanoma of the Skin Staging

American Joint Committee on Cancer

Melanoma of the Skin Staging

7th EDITION

Definitions

Primary Tumor (T)

- **TX** Primary tumor cannot be assessed (for example, curettaged or severely regressed melanoma)
- **T0** No evidence of primary tumor
- **Tis** Melanoma in situ
- **T1** Melanomas 1.0 mm or less in thickness
- **T2** Melanomas 1.01–2.0 mm
- **T3** Melanomas 2.01–4.0 mm
- **T4** Melanomas more than 4.0 mm

NOTE: a and b subcategories of T are assigned based on ulceration and number of mitoses per mm^2, as shown below:

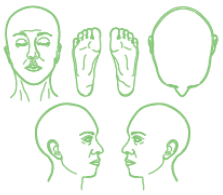
T CLASSIFICATION	THICKNESS (mm)	ULCERATION STATUS/MITOSES
T1	≤1.0	a: w/o ulceration and mitosis <1/mm^2 b: with ulceration or mitoses ≥1/mm^2
T2	1.01–2.0	a: w/o ulceration b: with ulceration
T3	2.01–4.0	a: w/o ulceration b: with ulceration
T4	>4.0	a: w/o ulceration b: with ulceration

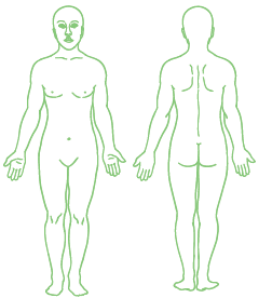
Regional Lymph Nodes (N)

- **NX** Patients in whom the regional nodes cannot be assessed (for example, previously removed for another reason)
- **N0** No regional metastases detected
- **N1-3** Regional metastases based upon the number of metastatic nodes and presence or absence of intralymphatic metastases (in transit or satellite metastases)

NOTE: N1–3 and a–c subcategories assigned as shown below:

N CLASSIFICATION	NO. OF METASTATIC NODES	NODAL METASTATIC MASS
N1	1 node	a: micrometastasis[1] b: macrometastasis[2]
N2	2–3 nodes	a: micrometastasis[1] b: macrometastasis[2] c: in transit met(s)/satellite(s) *without* metastatic nodes
N3	4 or more metastatic nodes, or matted nodes, or in transit met(s)/satellite(s) with metastatic node(s)	





Distant Metastatis (M)

- **M0** No detectable evidence of distant metastases
- **M1a** Metastases to skin, subcutaneous, or distant lymph nodes
- **M1b** Metastases to lung
- **M1c** Metastases to all other visceral sites or distant metastases to any site combined with an elevated serum LDH

NOTE: Serum LDH is incorporated into the M category as shown below:

M CLASSIFICATION	SITE	SERUM LDH
M1a	Distant skin, subcutaneous, or nodal mets	Normal
M1b	Lung metastases	Normal
M1c	All other visceral metastases	Normal
	Any distant metastasis	Elevated

ANATOMIC STAGE/PROGNOSTIC GROUPS

	Clinical Staging[3]				Pathologic Staging[4]			
Stage 0	Tis	N0	M0		0	Tis	N0	M0
Stage IA	T1a	N0	M0		IA	T1a	N0	M0
Stage IB	T1b	N0	M0		IB	T1b	N0	M0
	T2a	N0	M0			T2a	N0	M0
Stage IIA	T2b	N0	M0		IIA	T2b	N0	M0
	T3a	N0	M0			T3a	N0	M0
Stage IIB	T3b	N0	M0		IIB	T3b	N0	M0
	T4a	N0	M0			T4a	N0	M0
Stage IIC	T4b	N0	M0		IIC	T4b	N0	M0
Stage III	Any T	≥ N1	M0		IIIA	T1-4a	N1a	M0
						T1-4a	N2a	M0
					IIIB	T1-4b	N1a	M0
						T1-4b	N2a	M0
						T1-4a	N1b	M0
						T1-4a	N2b	M0
						T1-4a	N2c	M0
					IIIC	T1-4b	N1b	M0
						T1-4b	N2b	M0
						T1-4b	N2c	M0
						Any T	N3	M0
Stage IV	Any T	Any N	M1		IV	Any T	Any N	M1

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Notes

[1] Micrometastases are diagnosed after sentinel lymph node biopsy and completion lymphadenectomy (if performed).

[2] Macrometastases are defined as clinically detectable nodal metastases confirmed by therapeutic lymphadenectomy or when nodal metastasis exhibits gross extracapsular extension.

[3] 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.

[4] Pathologic staging includes microstaging of the primary melanoma and pathologic information about the regional lymph nodes after partial or complete lymphadenectomy. Pathologic Stage 0 or Stage IA patients are the exception; they do not require pathologic evaluation of their lymph nodes.

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