高 雄 榮 民 總 醫 院

皮膚癌(melanoma)診療原則

2015年09月29日 第二版

皮膚癌醫療團隊擬定

注意事項：這個診療原則主要作為醫師和其他保健專家診療癌症病人參考之用。假如你是一個癌症病人，直接引用這個診療原則並不恰當，只有你的醫師才能決定給你最恰當的治療。

修訂指引

- 本共識依下列參考資料修改版本
  - NCCN 2015版 診療指引

Summary of the Guidelines Updates（與上一版差異）

上一版:	新版:
無癌症藥物停藥準則	新增**癌症藥物停藥準則**

黑色素細胞癌(melanoma)

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臨床診療指引 2015第二版

診斷	初步評估	分期(附表1)	評估

臨床診斷之可疑病灶，經皮膚切片及病理組織學證實。

1、病史
2、理學檢查
(1)完整皮膚檢查。
(2)淋巴結檢查。
3、黑色素細胞癌危險因子評估
4、實驗室檢查
(1)CBC/DC
(2)Biochemistry(包括LDH)
(3)HBV/HCV
5、初步影像學檢查§
(1)CXR
(2)Regional LNs, echo

Stage 0 (melanma in situ)

1、影像學檢查△
(1)CT
(2)MRI
(3)Gallium scan
(4)Bone scan
(5)PET / CT
2、sentinel LNs biopsy

Stage I
Stage II
Stage III
Stage IV

§： 可選擇

△：建議 whole body PET / CT + brain MRI

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分期	初步治療(附表2)	輔助治療	再評估	追蹤

Stage 0 (melanma in situ) → wide excision → Monthly*III ↓ Quarterly Or Palliative care (安寧緩和)

Stage I → wide excision
Stage II → wide excision

◎ CVD regimen(附表4)
Interferon-α
Ipilmumab
Vemurafenib+
Dabrafenib+
RT(附表3)
＋ Restage：Brain MRI and PET
negative → Monthly*III ↓ Quarterly Or Palliative care (安寧緩和)

If病程持續進展

Stage III → wide excision + complete LNs dissection
Stage IV → wide excision + complete LNs dissection

◎ Dantmouth regimen(附表5)
Interferon-α
Ipilmumab
Vemurafenib+
Dabrafenib+
Interleukin-2
Palliative symptom management,
Clinical trial、RT(附表3)
Temozolomide、Palliative surgery
＋ Restage：Brain MRI and PET → Monthly*III ↓ Quarterly Or Palliative care (安寧緩和)

◎：可選擇

+：for BRAF mutation patient

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復發

1、病史
2、理學檢查
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1、影像學檢查△
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Stage 0 (melanma in situ) → wide excision

Stage I → wide excision

Stage II → wide excision

Stage III → wide excision + complete LNs dissection

Stage IV → wide excision + complete LNs dissection

◎
CVD regimen(附表4)
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癌症藥物停藥準則

- 根據CTCAE (Common Terminology Criteria for Adverse Events, Version 4.0 Published: May 28, 2009 【v4.03: June 14, 2010】)，出現Grade 3 ~ Grade 4 adverse event。
- 停藥至adverse event回復至Grade 1或Baseline時可再次用藥，但有些患者必須調整用藥劑量。
- 使用BRAF inhibitor時可能產生cutaneous SCC。此現象雖被CTCAE列為Grade 3 toxic effect, 但此現象不必停藥或調整劑量
- 特定藥物治療下疾病仍持續進展，根據追蹤及評估顯示疾病對此特定藥物治療無效(考慮停止投藥並選擇其他治療方法)。
- 病患要求 (Hospice care或其他因素)
- 病患死亡

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附件一-1:

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2015 Staging Melanoma

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Table 1

American Joint Committee on Cancer (AJCC)
TNM Staging System for Melanoma (7th ed., 2010)

Primary Tumor (T)

TX	Primary tumor cannot be assessed (eg, 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 sub categories 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 $\geq 1/mm^2$
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 lymph nodes cannot be assessed (eg, 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 sub categories are assigned as shown below:

N Classification	*No. of Metastatic Nodes*	*Nodal Metastatic Mass*
N1	1 node	a: micrometastasis* b: macrometastasis**
N2	2-3 nodes	a: micrometastasis* b: macrometastasis** 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)	

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

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

Continue

附件一-2:

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2015 Staging Melanoma

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Distant Metastasis (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*

Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T3a	N0	M0
Stage IIB	T3b	N0	M0
	T4a	N0	M0
Stage IIC	T4b	N0	M0
Stage III	AnyT	≥N1	M0
Stage IV	Any T	Any N	M1

*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.

Pathologic Staging**

Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T3a	N0	M0
Stage IIB	T3b	N0	M0
	T4a	N0	M0
Stage IIC	T4b	N0	M0
Stage IIIA	T(1–4)a	N1a	M0
	T(1–4)a	N2a	M0
Stage IIIB	T(1–4)b	N1a	M0
	T(1–4)b	N2a	M0
	T(1–4)a	N1b	M0
	T(1–4)a	N2b	M0
	T(1–4)a	N2c	M0
Stage IIIC	T(1–4)b	N1b	M0
	T(1–4)b	N2b	M0
	T(1–4)b	N2c	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1

**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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PRINCIPLES OF SURGICAL MARGINS FOR WIDE EXCISION OF PRIMARY MELANOMA

Tumor Thickness	Recommended Clinical Margins[2]
In situ[1]	0.5-1.0 cm
≤1.0 mm	1.0 cm (category 1)
1.01-2 mm	1-2 cm (category 1)
2.01-4 mm	2.0 cm (category 1)
>4 mm	2.0 cm (category 1)

- **Margins may be modified to accommodate individual anatomic or functional considerations.**

[1]For large melanoma in situ (MIS), lentigo maligna type, surgical margins >0.5 cm may be necessary to achieve histologically negative margins; techniques for more exhaustive histologic assessment of margins should be considered. For selected patients with positive margins after optimal surgery, consider topical imiquimod (for patients with MIS) or RT (category 2B).
[2]Excision recommendations are based on measured clinical margins taken at the time of surgery and not gross or histologic margins, as measured by the pathologist (category 1).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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附件三：

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PRINCIPLES OF RADIATION THERAPY FOR MELANOMA

Consider RT in the following situations:[1]

PRIMARY DISEASE

- Adjuvant treatment in selected patients with factors including, but not limited to deep desmoplastic melanoma with narrow margins, extensive neurotropism or locally recurrent disease.

REGIONAL DISEASE[2]

- Adjuvant treatment in selected patients following resection of clinically appreciable nodes (category 2B)[3] if
  - LDH <1.5 x upper limit of normal AND
  - Extranodal tumor extension AND/OR
    - Parotid: ≥1 involved node, any size of involvement
    - Cervical: ≥2 involved nodes and/or ≥3 cm tumor within a node
    - Axillary: ≥2 involved nodes and/or ≥4 cm tumor within a node
    - Inguinal: ≥3 involved nodes and/or ≥4 cm tumor within a node
- Palliative
  - Unresectable nodal, satellite, or in-transit disease

METASTATIC DISEASE

- Brain metastases (see NCCN Guidelines for Central Nervous System Cancers)
  - Stereotactic radiosurgery either as adjuvant or primary treatment
  - Whole brain radiation therapy, either as adjuvant (category 2B) or primary treatment[4]
- Other symptomatic or potentially symptomatic soft tissue and/or bone metastases[2]

[1]Interactions between radiation therapy and systemic therapies (eg, *BRAF* inhibitors and interferon alfa-2b) need to be very carefully considered as there is potential for increased toxicity.
[2]A wide range of radiation dose/fractionation schedules is effective. Hypofractionated regimens may increase the risk for long-term complications.
[3]Adjuvant nodal basin RT is associated with reduced lymph node field recurrence but has no impact on relapse-free or overall survival, and its benefits must be weighed against the increased probability of long-term skin and regional toxicities and potential reduced quality of life.
[4]Adjuvant whole brain radiation following resected melanoma brain metastasis is controversial and should be considered on an individual patient basis. An ongoing randomized clinical trial (ANZMTG 01-07, ACTRN12607000512426, NCT01503827) is currently investigating adjuvant whole brain radiation (Fogarty G, Morton RL, Vardy J, et al. Whole brain radiotherapy after local treatment of brain metastases in melanoma patients--a randomised phase III trial. BMC Cancer. 2011;17:142.)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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附件四-1:CVD regimen

化學治療處方

CVD regimen

published C/T regimens	schedule
Dacarbazine 800mg/m2, IV, D1	Q28d * 6 cycles
Cisplatin 20mg/m2, IV, D2-5	Q28d * 6 cycles
Vinblastine 1.6mg/m2, IV, D1-5	Q28d * 6 cycles

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附件四-2:CVD regimen, CCr < 60

化學治療處方

CVD regimen, CCr < 60	
published C/T regimens	**schedule**
Dacarbazine 800mg/m2, IV, D1	**Q28d * 6 cycles**
Vinblastine 1.6mg/m2, IV, D1-5	**Q28d * 6 cycles**
Paraplatin auc*1.25mg, IV, D2-5	**Q28d * 6 cycles**

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附件五-1：Dartmouth regimen (Odd)

化學治療處方

Dartmouth regimen (Odd)	
published C/T regimens	**schedule**
Carmustine 150mg/m2, IV, D1	**Q28d * 6 cycles**
Dacarbazine 220mg/m2, IV, D1-3	**Q28d * 6 cycles**
Cisplatin 25mg/m2, IV, D1-3	**Q28d * 6 cycles**
Nolvadex 10mg, PO, D1-3	**Q28d * 6 cycles**

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附件五-2：Dartmouth regimen (Even)

化學治療處方

Dartmouth regimen (Even)	
published C/T regimens	**schedule**
Dacarbazine 220mg/m2, IV, D1-3	**Q28d * 6 cycles**
Cisplatin 25mg/m2, IV, D1-3	**Q28d * 6 cycles**
Nolvadex 10mg, PO, D1-3	**Q28d * 6 cycles**

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附件五-3：Dartmouth regimen (Odd), CCr < 60

化學治療處方

Dartmouth regimen (Odd), CCr < 60	
published C/T regimens	**schedule**
Carmustine 150mg/m2, IV, D1-3	**Q28d * 6 cycles**
Dacarbazine 220mg/m2, IV, D1-3	**Q28d * 6 cycles**
Paraplatin auc*1.6mg, IV, D1-3	**Q28d * 6 cycles**
Nolvadex 10mg, PO, D1-3	**Q28d * 6 cycles**

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附件五-4：Dartmouth regimen (Even),CCr < 60

化學治療處方

Dartmouth regimen (Even),CCr < 60	
published C/T regimens	**schedule**
Dacarbazine 220mg/m2, IV, D1-3	**Q28d * 6 cycles**
Paraplatin auc*1.6mg, IV, D1-3	**Q28d * 6 cycles**
Nolvadex 10mg, PO, D1-3	**Q28d * 6 cycles**

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附件六：melanoma with brain metastasis

化學治療處方

melanoma with brain metastasis	
published C/T regimens	**schedule**
Temodal 150mg/m2/, IV, D1-5	**Q28d * 6 cycles**

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