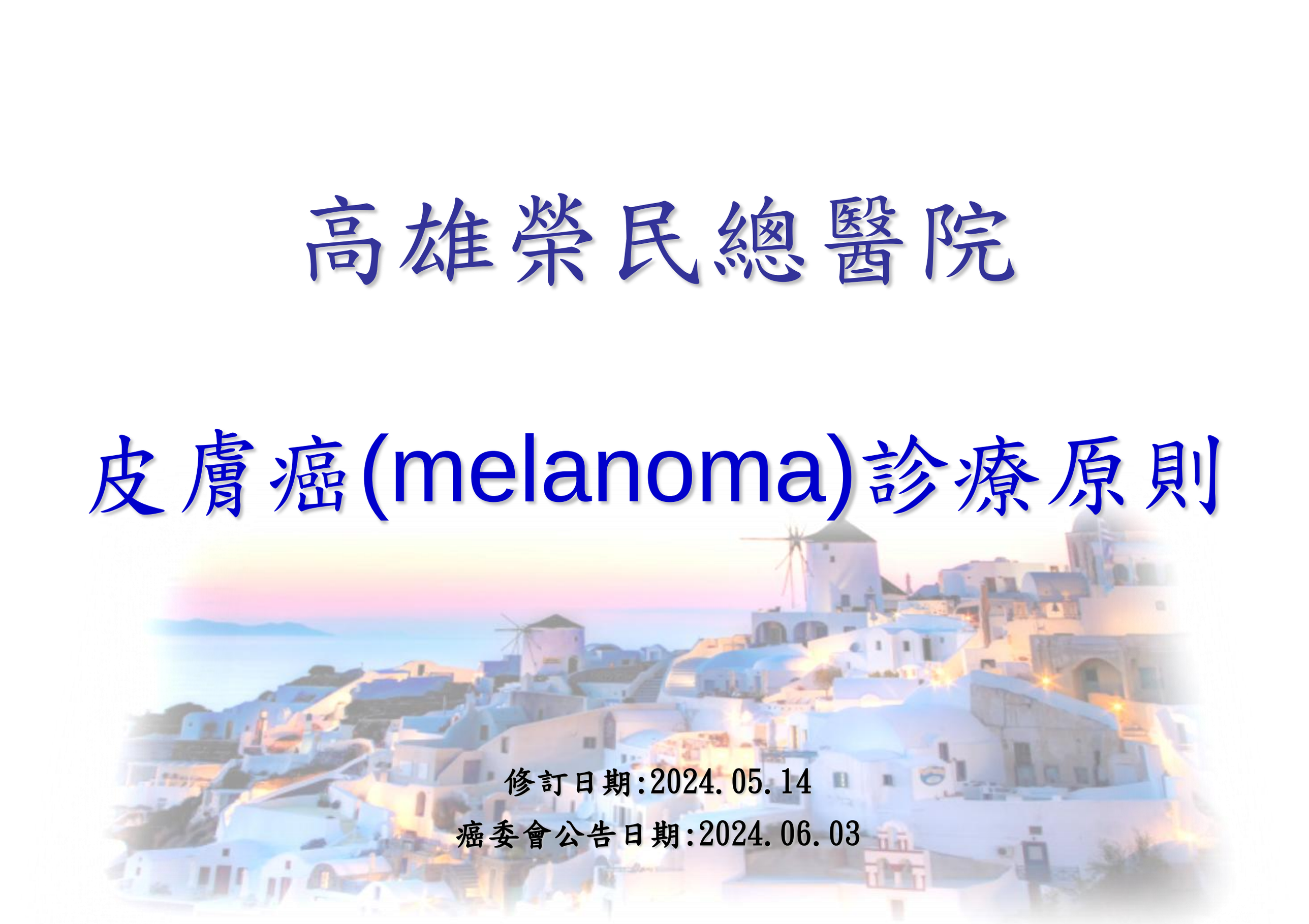
高雄榮民總醫院

皮膚癌(melanoma)診療原則



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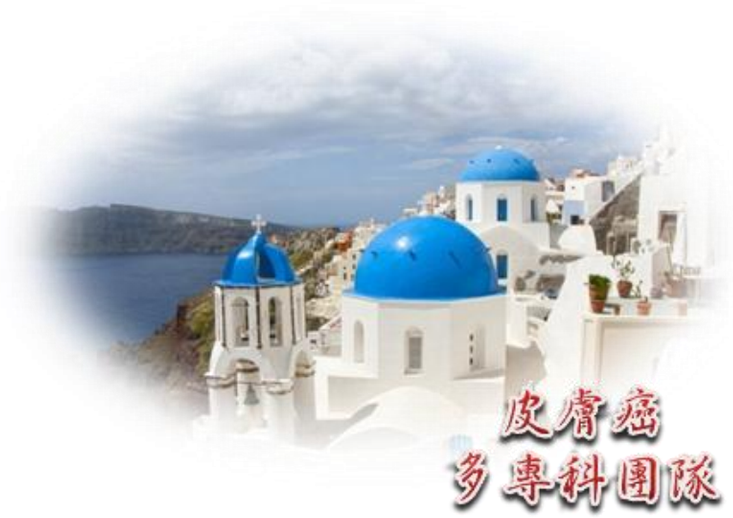
Reference: NCCN Clinical Practice Guideline in OncologyTM ,melanoma, V.1.2019

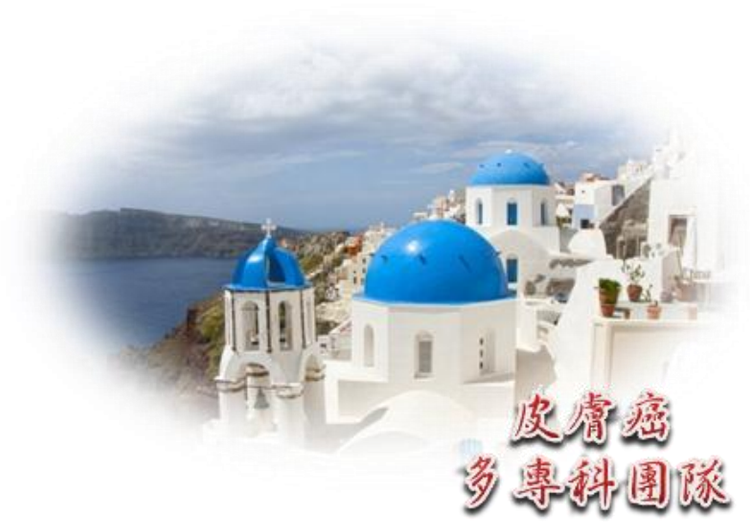
melanoma診療指引審視修訂會議討論日期

- 前次會議：2023/05/23
- 本共識經審視:



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

上一版	新版
NCCN Guidelines 2023年版	**更換附件為:NCCN Guidelines 2024年版**



黑色素細胞癌(melanoma)

診斷	初步評估	分期(附件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

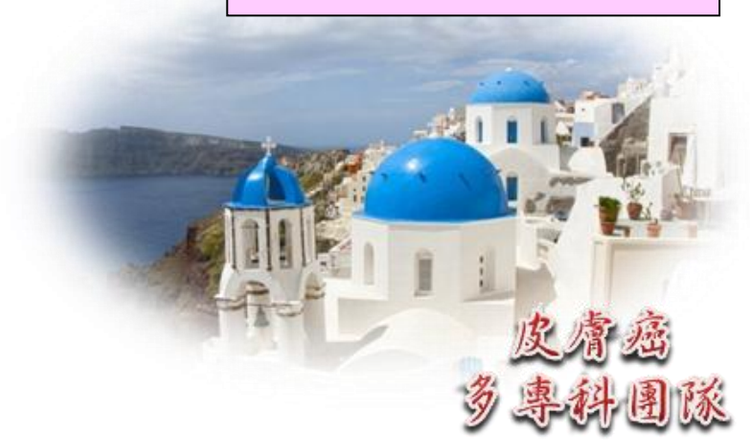
Stage 0 (melanma in situ)

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



黑色素細胞癌(melanoma)

分期	初步治療(附件2)	輔助治療	再評估	追蹤

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

Stage I → wide excision

Stage II → wide excision

◎可選擇是否須使用輔助性化療

CVD regimen(附表4)
Interferon-α
Pembrolizumab
Vemurafenib*
Dabrafenib*
RT(附表3)

＋ Restage： Brain MRI and PET

If病程持續進展

Stage III → wide excision + complete LNs dissection

Stage IV → wide excision + complete LNs dissection

◎可選擇使用藥物

Dantmouth regimen(附表5)
Interferon-α
Nivolumab'
Pembrolizumab
Vemurafenib*
Dabrafenib/trametinib*
Palliative symptom management,
Clinical trial、RT(附表3)
Temozolomide、Palliative surgery

＋ Restage： Brain MRI and PET

◎：可選擇

＋：for BRAF mutation patient

皮膚癌多專科團隊

黑色素細胞癌(melanoma)

復發

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

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

Stage 0 (melanma in situ) → wide excision

Stage I → wide excision

Stage II → wide excision Nivolumab

Stage III → wide excision + complete LNs dissection

Stage IV → wide excision + complete LNs dissection

◎可選擇使用藥物

CVD regimen(附表4)
Interferon-α
Ipilmumab
Nivolumab
Pembrolizumab
Vemurafenib+
Dabrafenib/trametinib+
RT(附表5)

＋ Restage：
Brain MRI and PET

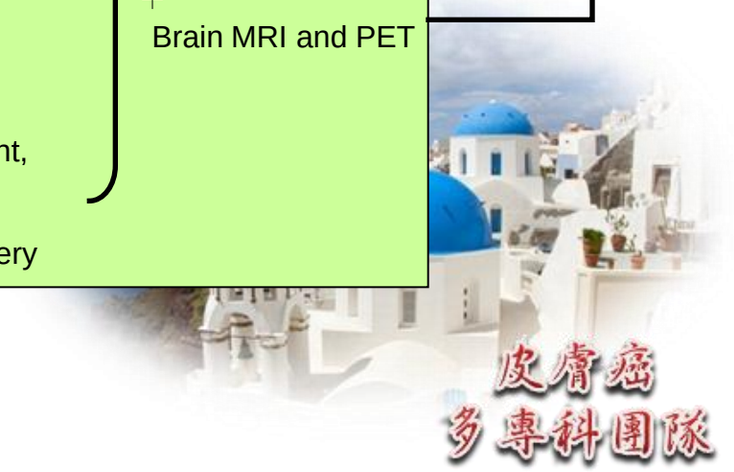
negative → Monthly*III → Quarterly Or Palliative care (安寧緩和)

if 病程持續進展

◎可選擇使用藥物

Dantmouth regimen(附表5)
Interferon-α
Ipilmumab
Nivolumab
Pembrolizumab
Vemurafenib+
Dabrafenib/trametinib+
Palliative symptom management,
Clinical trial、RT(附表3)
Temozolomide、Palliative surgery

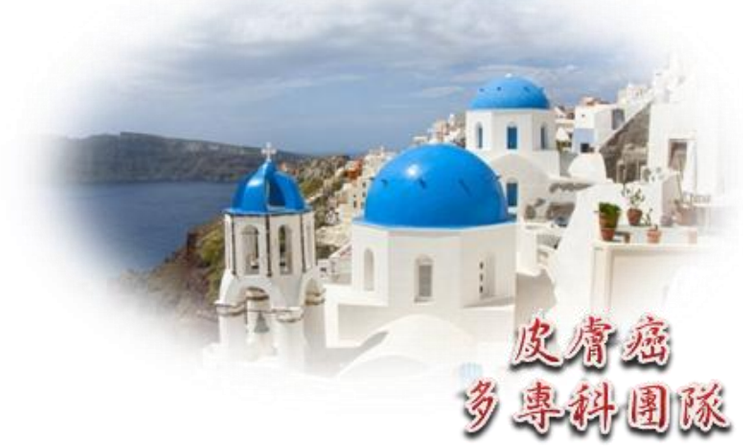
＋ Restage：
Brain MRI and PET



黑色素細胞癌(melanoma)

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。



SYSTEMIC THERAPY FOR METASTATIC OR UNRESECTABLE DISEASE[a,b,c]

FIRST-LINE THERAPY

Metastatic or unresectable disease →

Preferred regimens
- Combination checkpoint blockade[d] (preferred)
  - Nivolumab/ipilimumab (category 1)[e,f,g,h]
  - Nivolumab and relatlimab-rmbw (category 1)[e,f,i]
- Anti-PD-1 monotherapy[d,e,f,j]
  - Pembrolizumab (category 1)
  - Nivolumab (category 1)

Other recommended regimens
- Combination targeted therapy if *BRAF* V600 mutation positive[k,l,m,n,o]
  - Dabrafenib/trametinib (category 1)
  - Vemurafenib/cobimetinib (category 1)
  - Encorafenib/binimetinib (category 1)
- Pembrolizumab/low-dose ipilimumab[p] (category 2B)

→ Disease progression, intolerance, and/or projected risk of progression with *BRAF*-targeted therapy →

SECOND-LINE OR SUBSEQUENT THERAPY[q]

Preferred regimens
- Anti-PD-1 monotherapy[e,f]
  - Pembrolizumab
  - Nivolumab
- Nivolumab/ipilimumab[e,f,g,r]
- Nivolumab and relatlimab-rmbw[e,f,i]
- Pembrolizumab/low-dose ipilimumab for progression following anti-PD-1 therapy[e,f]
- Combination targeted therapy with *BRAF* V600 mutation positive[l,m,n,o]
  - Dabrafenib/trametinib
  - Vemurafenib/cobimetinib
  - Encorafenib/binimetinib
- Tumor-infiltrating lymphocyte therapy (TIL)[s]
  - Lifileucel

Other recommended regimens
- Ipilimumab[e]
- High-dose IL-2[t]

Useful in certain circumstances
- For activating mutations of *KIT*
  - KIT inhibitor therapy (eg, imatinib, dasatinib, nilotinib, ripretinib)
- For *ROS1* fusions
  - Crizotinib, entrectinib
- For *NTRK* fusions
  - Larotrectinib, entrectinib
- For *BRAF* fusions and non-V600 mutations[u]
  - Trametinib
- For *NRAS*-mutated tumors (for progression following immune checkpoint inhibitor therapy)
  - Binimetinib[v] (category 2B)
- Combination therapy
  - Pembrolizumab/lenvatinib[w]
  - Ipilimumab[e]/intralesional T-VEC (category 2B)
- Combination BRAF/MEK + PD(L)-1 checkpoint inhibitors (eg, dabrafenib/trametinib + pembrolizumab or vemurafenib/cobimetinib + atezolizumab if *BRAF* V600 mutation positive)[x]
- Cytotoxic agents (MELSYS 2 of 7)
- Consider best supportive care for poor performance status (NCCN Guidelines for Palliative Care)

Footnotes on next page

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

FOOTNOTES FOR SYSTEMIC THERAPY FOR METASTATIC OR UNRESECTABLE DISEASE

[a] Principles of Imaging–Treatment Response Assessment (ME-D).

[b] Systemic Therapy Considerations (ME-J).

[c] The order of listed systemic therapies in a given section does not reflect order of preference. The choice of a treatment is based on evaluation of the individual patient to include patient characteristics, disease presentation, prior treatment, health system resources/experience, and patient preference.

[d] Considerations for using combination nivolumab/ipilimumab or nivolumab and relatlimab-rmbw versus PD-1 monotherapy include: patient willingness to take on a higher risk of treatment-related toxicities (immune-related adverse events [irAEs]); absence of comorbidities or autoimmune processes that would elevate the risk of irAEs; and patient social support and preparedness to work with medical team to handle toxicities.

[e] See NCCN Guidelines for Management of Immunotherapy-Related Toxicities for proactive monitoring and management of toxicities in patients undergoing treatment with immune checkpoint inhibitors.

[f] Testing for tumor PD-L1 should not guide clinical decision-making. The utility of this biomarker requires further investigation.

[g] Nivolumab/ipilimumab combination therapy is associated with improved overall response rate (ORR), progression-free survival (PFS), and OS compared with single-agent ipilimumab, at the expense of significantly increased toxicity in previously untreated patients with unresectable stage III or IV melanoma. While that study was not powered to compare nivolumab plus ipilimumab and nivolumab alone, improved OS with the combination support a meaningful survival benefit of the combination compared with nivolumab monotherapy.

[h] Nivolumab/ipilimumab has demonstrated clinically meaningful intracranial activity.

[i] The combination nivolumab and relatlimab-rmbw is associated with higher PFS but more frequent and more severe toxicity than nivolumab alone. Nivolumab and relatlimab-rmbw showed a 9%–12% objective response rate in patients with PD-1/PD-L1 refractory disease.

[j] Appropriateness of single agent depends on patient fitness/frailty, comorbidities, low-volume disease, autoimmune disease history, and other factors.

[k] Positive VE1 IHC results are sufficient for starting targeted therapy in patients who are symptomatic or have rapidly progressing disease. Confirmatory *BRAF* molecular testing is encouraged. See Principles of Molecular Testing (ME-C).

[l] Management of Toxicities Associated with Targeted and Immune Therapies (ME-K).

[m] In previously untreated patients with unresectable AJCC 7th Edition stage IIIC or stage IV disease, BRAF/MEK inhibitor combination therapy was associated with improved response rate, PFS, and OS compared to BRAF inhibitor monotherapy. Similar efficacy has been demonstrated across AJCC 8th Edition unresectable stage III or stage IV disease.

[n] If BRAF/MEK inhibitor combination therapy is contraindicated, BRAF inhibitor monotherapy is an option, especially in patients who are not appropriate candidates for checkpoint immunotherapy.

[o] High-volume symptomatic disease *BRAF*+ patients may benefit from BRAF/MEK inhibition, as opposed to combination immunotherapy. Otherwise nivolumab/ipilimumab is preferred first-line over BRAF/MEK therapy due to OS benefit.

[p] Dosing used in KEYNOTE-029: Pembrolizumab 2 mg/kg IV plus ipilimumab 1 mg/kg IV every 3 weeks for four doses, followed by pembrolizumab 2 mg/kg every 3 weeks for up to 2 years or disease progression, intolerable toxicity, withdrawal of consent, or investigator decision.

[q] For patients who experience progression of melanoma during or shortly after adjuvant or first-line therapy, consider second-line agents if not used first line and if from a different class. For patients who progressed on single-agent anti-PD-1 checkpoint immunotherapy, anti-PD-1/ipilimumab or nivolumab and relatlimab combination immunotherapy, or BRAF/MEK inhibitor combination therapy are reasonable treatment options. Ipilimumab monotherapy may also be considered, though it is less effective than combination therapy. For patients who experience disease control (CR, PR, or SD) and have no residual toxicity, but subsequently experience disease progression/relapse >3 months after treatment discontinuation, reinduction with the same agent or same class of agents may be considered.

[r] A 94-patient trial randomized patients to ipilimumab and nivolumab versus ipilimumab alone following progression on anti-PD-1 therapy. The combination was associated with higher response rates (28% vs. 8%) and 6-month PFS (35% vs. 13%).

[s] For patients with good performance status who have progressed on anti-PD-1 based therapy and BRAF/MEK inhibition (if BRAF V600 mutation present), TIL therapy should be considered, based on favorable durable response rates in anti-PD-1 refractory melanoma. TIL therapy should not be considered for patients with inadequate cardiac, pulmonary, and/or renal function, poor performance status, or with untreated or active brain metastases. TIL therapy currently requires a resectable metastasis for TIL harvesting and includes the use of non-myeloablative chemotherapy and high-dose IL-2. Referral to a TIL authorized treatment center is recommended.

[t] High-dose IL-2 should not be used for patients with inadequate organ reserve, poor performance status, or untreated or active brain metastases. For patients with small brain metastases and without significant peritumoral edema, IL-2 therapy may be considered (category 2B). Therapy should be restricted to an institution with medical staff experienced in the administration and management of these regimens.

[u] Case reports and preclinical data have suggested that BRAF + MEK inhibition may be an option for certain non-V600 *BRAF* mutations, including *BRAF* L597 mutations.

[v] In patients who were previously untreated or whose disease progressed despite immunotherapy, binimetinib was associated with a response rate of 15%, and demonstrated a modest improvement in PFS with no improvement in OS compared with single-agent dacarbazine.

[w] For patients with confirmed progression or unresectable or metastatic melanoma after treatment with an anti-PD-1–/PD-L1–based therapy, including in combination with anti-CTLA-4 for ≥2 doses.

[x] Despite FDA approval in the first-line setting, these triplet regimens are recommended for second-line or subsequent therapy due to excessive toxicity with minimal additive benefit.

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

References
Continued

黑色素細胞癌(melanoma)

附件一-1:

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2022
Melanoma: Cutaneous

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Discussion

Table 1. **American Joint Committee on Cancer (AJCC) Definitions for T, N, M**

T Category	Thickness	Ulceration Status
TX: Primary tumor thickness cannot be assessed (eg, diagnosis by curettage)	Not applicable	Not applicable
T0: No evidence of primary tumor (eg, unknown primary or completely regressed melanoma)	Not applicable	Not applicable
Tis (melanoma *in situ*)	Not applicable	Not applicable
T1	≤1 mm	Unknown or unspecified
T1a	<0.8 mm	Without ulceration
T1b	<0.8 mm	With ulceration
	0.8–1.0 mm	With or without ulceration
T2	>1.0–2.0 mm	Unknown or unspecified
T2a	>1.0–2.0 mm	Without ulceration
T2b	>1.0–2.0 mm	With ulceration
T3	>2.0–4.0 mm	Unknown or unspecified
T3a	>2.0–4.0 mm	Without ulceration
T3b	>2.0–4.0 mm	With ulceration
T4	>4.0 mm	Unknown or unspecified
T4a	>4.0 mm	Without ulceration
T4b	>4.0 mm	With ulceration

Continued

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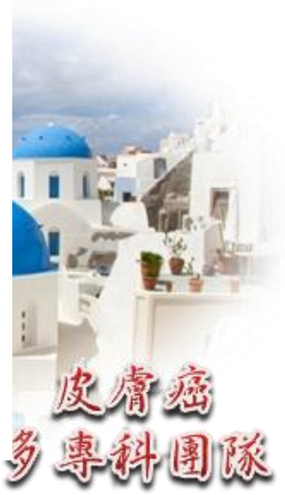

黑色素細胞癌(melanoma)

附件一-2:

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2022
Melanoma: Cutaneous

Table 1. **American Joint Committee on Cancer (AJCC) Definitions for T, N, M (*continued*)**

Extent of Regional Lymph Node and/or Lymphatic Metastasis

N Category	Number of Tumor-Involved Regional Lymph Node	Presence of In-Transit, Satellite, and/or Microsatellite Metastases
NX	Regional nodes not assessed (eg, SLN biopsy not performed, regional nodes previously removed for another reason) Exception: When there are no clinically detected regional metastases in a pT1 cM0 melanoma, assign cN0 instead of pNX	No
N0	No regional metastases detected	No
N1	One tumor-involved node or in-transit, satellite, and/or microsatellite metastases with no tumor-involved nodes	
N1a	One clinically occult (ie, detected by SLN biopsy)	No
N1b	One clinically detected	No
N1c	No regional lymph node disease	Yes
N2	Two or three tumor-involved nodes or in-transit, satellite, and/or microsatellite metastases with one tumor-involved node	
N2a	Two or three clinically occult (ie, detected by SLN biopsy)	No
N2b	Two or three, at least one of which was clinically detected	No
N2c	One clinically occult or clinically detected	Yes
N3	Four or more tumor-involved nodes or in-transit, satellite, and/or microsatellite metastases with two or more tumor-involved nodes, or any number of matted nodes without or with in-transit, satellite, and/or microsatellite metastases	
N3a	Four or more clinically occult (ie, detected by SLN biopsy)	No
N3b	Four or more, at least one of which was clinically detected, or presence of any number of matted nodes	No
N3c	Two or more clinically occult or clinically detected and/or presence of any number of matted nodes	Yes

Continued

黑色素細胞癌(melanoma)

附件一-3:

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2022
Melanoma: Cutaneous

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Table 1. **American Joint Committee on Cancer (AJCC)**

M Category	Anatomic Site	LDH Level
M0	No evidence of distant metastasis	Not applicable
M1	Evidence of distant metastasis	See below
M1a	Distant metastasis to skin, soft tissue including muscle, and/or nonregional lymph node	Not recorded or unspecified
M1a(0)		Not elevated
M1a(1)		Elevated
M1b	Distant metastasis to lung with or without M1a sites of disease	Not recorded or unspecified
M1b(0)		Not elevated
M1b(1)		Elevated
M1c	Distant metastasis to non-CNS visceral sites with or without M1a or M1b sites of disease	Not recorded or unspecified
M1c(0)		Not elevated
M1c(1)		Elevated
M1d	Distant metastasis to CNS with or without M1a, M1b, or M1c sites of disease	Not recorded or unspecified
M1d(0)		Normal
M1d(1)		Elevated

- Serum lactate dehydrogenase (LDH)
- Suffixes for M category: (0) LDH not elevated, (1) LDH elevated.
- No suffix is used if LDH is not recorded or is unspecified.

Continued

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黑色素細胞癌(melanoma)

附件一-4:

National Comprehensive Cancer Network®

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Melanoma: Cutaneous

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Table 2. **AJCC Prognostic Stage Groups**

Clinical Staging (cTNM)*

	T	N	M
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	Any T, Tis	≥N1	M0
Stage IV	Any T	Any N	M1

*Clinical staging includes microstaging of the primary melanoma and clinical/radiologic/biopsy evaluation for metastases. By convention, clinical staging should be used after biopsy of the primary melanoma, with clinical assessment for regional and distant metastases. Note that pathological assessment of the primary melanoma is used for both clinical and pathological classification. Diagnostic biopsies to evaluate possible regional and/or distant metastasis also are included. Note there is only one stage group for clinical Stage III melanoma.

Pathological Staging (pTNM)**

	T	N	M
Stage 0†	Tis	N0	M0
Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	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	T1a/b, T2a	N1a, N2a	M0
Stage IIIB	T0	N1b, N1c	M0
	T1a/b, T2a	N1b/c, N2b	M0
	T2b, T3a	N1a/b/c, N2a/b	M0
Stage IIIC	T0	N2b/c, N3b/c	M0
	T1a/b, T2a/b, T3a	N2c, N3a/b/c	M0
	T3b, T4a	Any N ≥ N1	M0
	T4b	N1a/b/c, N2a/b/c	M0
Stage IIID	T4b	N3a/b/c	M0
Stage IV	Any T, Tis	Any N	M1

**Pathological staging includes microstaging of the primary melanoma, including any additional staging information from the wide-excision (surgical) specimen that constitutes primary tumor surgical treatment and pathological information about the regional lymph nodes after SLN biopsy or therapeutic lymph node dissection for clinically evident regional lymph node disease.

†Pathological Stage 0 and pathological T1 without clinically detected regional or distant metastases (pTis/pT1 cN0 cM0) do not require pathological evaluation of lymph nodes to complete pathological staging; use cN0 to assign pathological stage.

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黑色素細胞癌(melanoma)

附件二:

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2022
Melanoma: Cutaneous

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PRINCIPLES OF SURGICAL MARGINS FOR WIDE EXCISION OF PRIMARY MELANOMA

Tumor Thickness	Recommended Peripheral Surgical Margins[b,1-10]
In situ[a]	0.5–1 cm
≤1.0 mm	1 cm (category 1)
>1.0–2.0 mm	1–2 cm (category 1)
>2.0–4.0 mm	2 cm (category 1)
>4.0 mm	2 cm (category 1)

- **Wide local excision involves removal of all tissue to the level of the fascia, which is typically preserved unless involved by tumor. Peripheral resection margins may be modified to accommodate individual anatomic or functional considerations. However, the safety and efficacy of narrower surgical margins have not been prospectively studied in a randomized controlled manner. Narrower than recommended margins may increase the risk for margin positivity and/or local recurrence.**
- **The gold standard for histologic assessment of excised melanoma is use of permanent sections. If Mohs micrographic surgery (MMS) is performed, permanent section analysis of the central debulking specimen is strongly recommended to provide complete staging information. Consider delay of complex reconstruction or wound closure until histologic margin assessment is complete.**
- **MMS is not recommended for primary treatment of invasive cutaneous melanoma when standard clinical margins can be obtained. It may be considered selectively for minimally invasive (T1a) melanomas in anatomically constrained areas (ie, face, ears, acral sites), along with other surgical methods that provide comprehensive histologic assessment, such as staged excision with permanent sections for dermatopathology review.[a,11]**
- **With respect to disease-related outcomes, there have been no prospective comparisons of different excision methods, including conventional wide excision, MMS, and staged excision with permanent sections. All randomized controlled trials of resection margins for invasive cutaneous melanoma were performed using standard wide excision technique.[1-10] Of note, few included head/neck melanomas and none included acral melanomas.**

[a] For large and/or poorly defined MIS, LM or acral lentiginous subtypes, or LM melanoma with a minimally invasive (T1a) component (also referred to as high CSD melanoma), surgical margins >0.5 cm may be necessary, and techniques for comprehensive histologic evaluation of margins (ie, complete circumferential peripheral and deep margin assessment) should be considered.[12-17] If MMS is performed, use of frozen section melanocytic immunohistochemistry stains may assist in accurate interpretation of histologic margins. For selected patients with positive margins after surgery, in whom further resection is not feasible or desirable, consider topical imiquimod (for patients with MIS/LM type) or RT.

[b] Excision recommendations for invasive melanoma are based on measured clinical margins taken at the time of surgery and not gross or histologic margins, as measured by the pathologist. However, narrower peripheral histologic margins have been associated with higher rates of local recurrence for invasive melanoma, though not worse melanoma-specific survival.[18-21] Narrow pathologic margins, particularly of the invasive component, may warrant further surgical resection.

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

ME-E
1 OF 2

皮膚癌
多專科團隊

黑色素細胞癌(melanoma)

附件三：

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2021
Melanoma: Cutaneous
NCCN Evidence Blocks™

NCCN Guidelines Index
Table of Contents
Discussion

PRINCIPLES OF RADIATION THERAPY FOR MELANOMA

General Treatment Information: Consider RT in the following situations:

- Modalities: Adjuvant nodal external beam RT (EBRT) should be delivered using a technique judged optimal by the treating radiation oncologist. Newer technologies, such as intensity-modulated RT (IMRT) may lower toxicity and should be considered when available and where appropriate.[1,2] Image-guided RT (IGRT) should be used to improve accuracy of radiotherapy delivery, where clinically appropriate.

Primary Disease:

- Definitive Therapy
  - Definitive radiation may be considered as a treatment option for MIS, LM-type (ie, high-CSD) in medically inoperable patients or those in whom surgical morbidity of complete resection would be prohibitive.[3-5]
  - Dosing Regimens: Optimal doses are not well established, but potential regimens include:[a]
    - ◊ 64–70 Gy in 32–35 fractions over 6–7 weeks
    - ◊ 50–57.5 Gy in 20–23 fractions over 4–5 weeks[4,6]
    - ◊ 35 Gy in 5 fractions over 1 week for fields <3 cm^2
    - ◊ 32 Gy in 4 fractions once per week[7]
  - There are insufficient data to support the routine use of electronic surface brachytherapy in the management of cutaneous melanoma.

- Adjuvant Therapy
  - Adjuvant radiation may be considered for select cases of high-risk desmoplastic melanoma based on a combination of risk factors for local recurrence.[b,8] (category 2B)
  - Dosing Regimens: Optimal adjuvant doses are not well established, but potential regimens include:[a]
    - ◊ 60–66 Gy in 30–33 fractions over 6–7 weeks[9,10]
    - ◊ 48 Gy in 20 fractions over 4 weeks[11]
    - ◊ 30 Gy in 5 fractions over 2 weeks (twice per week or every other day)[12]

[a]Hypofractionated regimens may increase the risk for long-term complications.
[b]Risk factors for local recurrence include location on the head or neck, extensive neurotropism, pure desmoplastic melanoma histologic subtype, close margins where re-resection is not feasible, or locally recurrent disease.

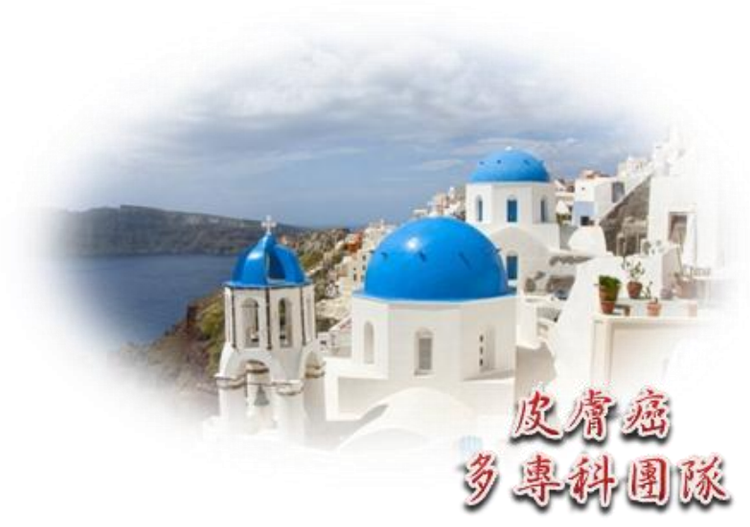
Note: For more information regarding the categories and definitions used for the NCCN Evidence Blocks™, see page EB-1.
All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Continued
References

黑色素細胞癌(melanoma)

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

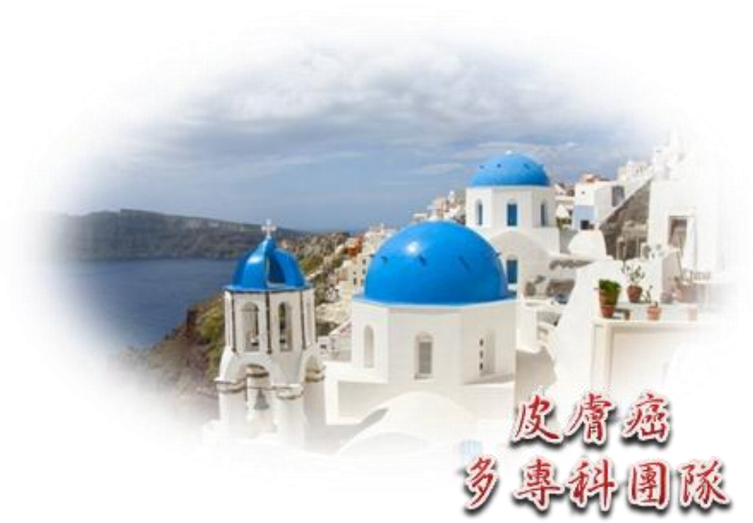


黑色素細胞癌(melanoma)

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

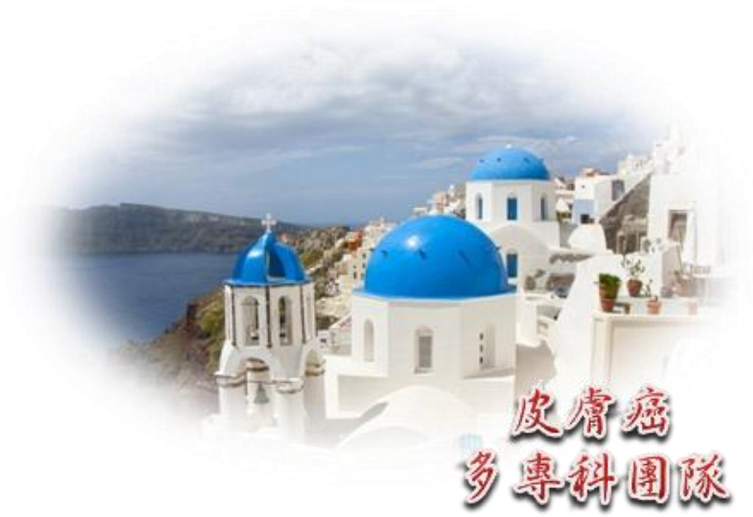


黑色素細胞癌(melanoma)

附件五-1：Dartmouth regimen (Odd) (or metastasis)

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

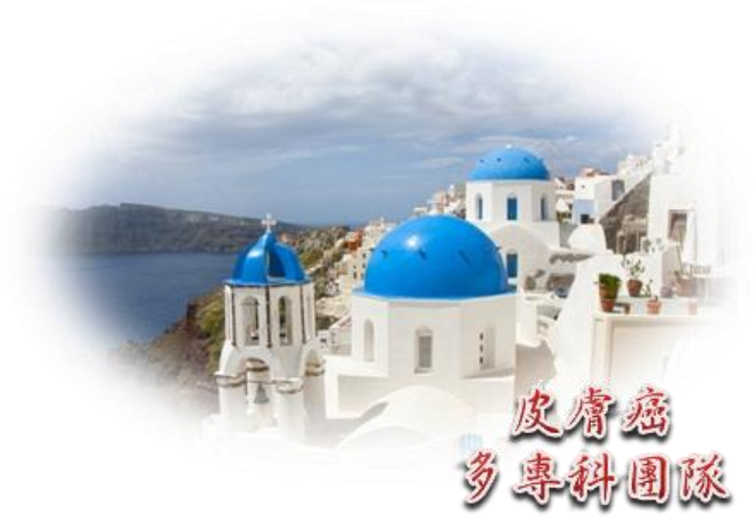


黑色素細胞癌(melanoma)

附件五-2：Dartmouth regimen (Even) (or metastasis)

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

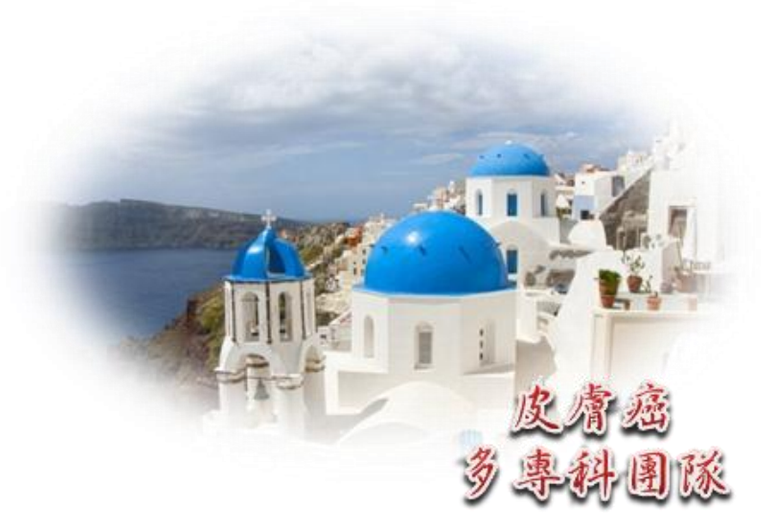


黑色素細胞癌(melanoma)

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

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

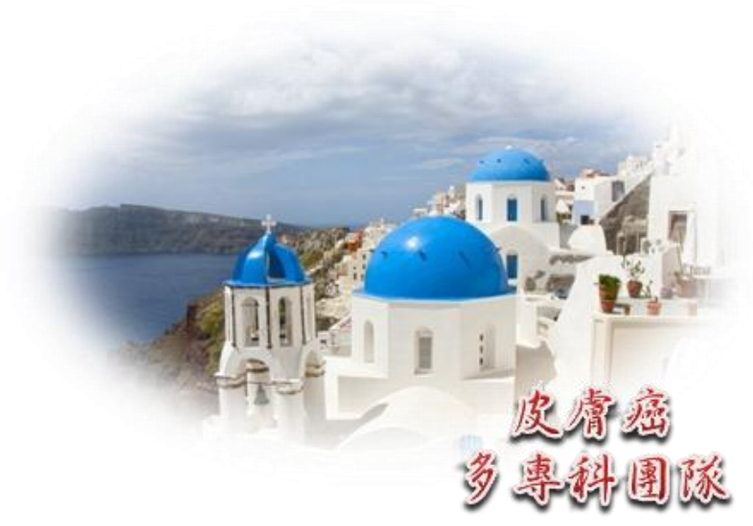


黑色素細胞癌(melanoma)

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

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

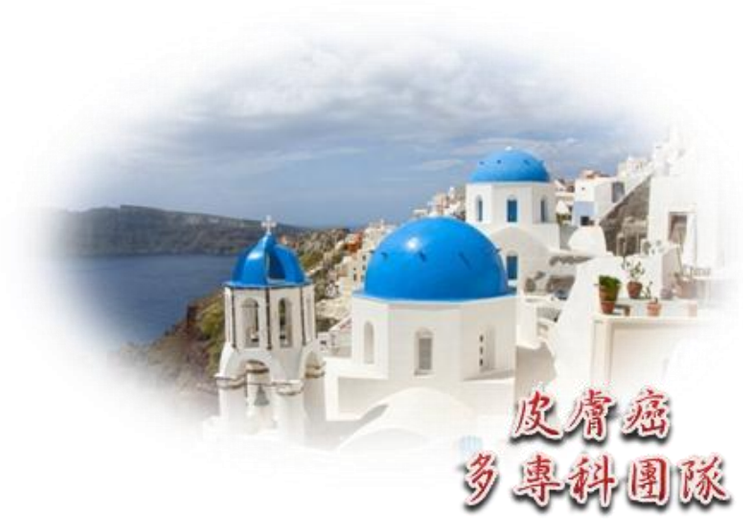


黑色素細胞癌(melanoma)

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

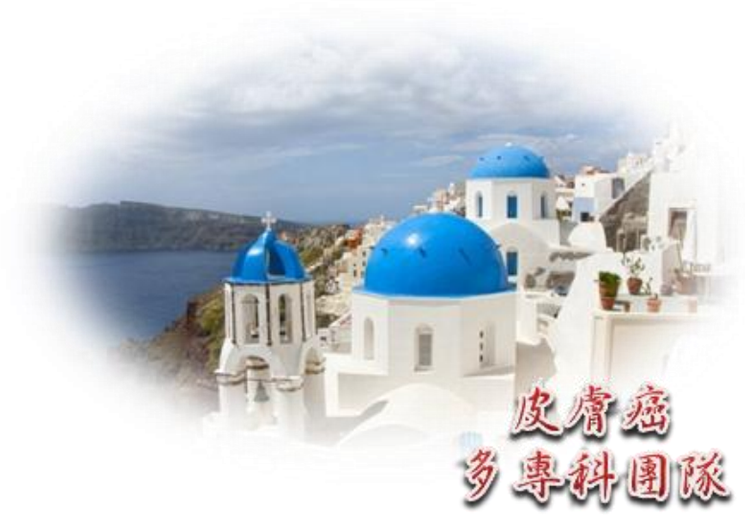


黑色素細胞癌(melanoma)

附件七：melanoma with Target therapy (or metastasis)

標靶治療處方

melanoma with Target therapy	
Target therapy	schedule
Vemurafenib 960mg, oral	Twice daily, continued

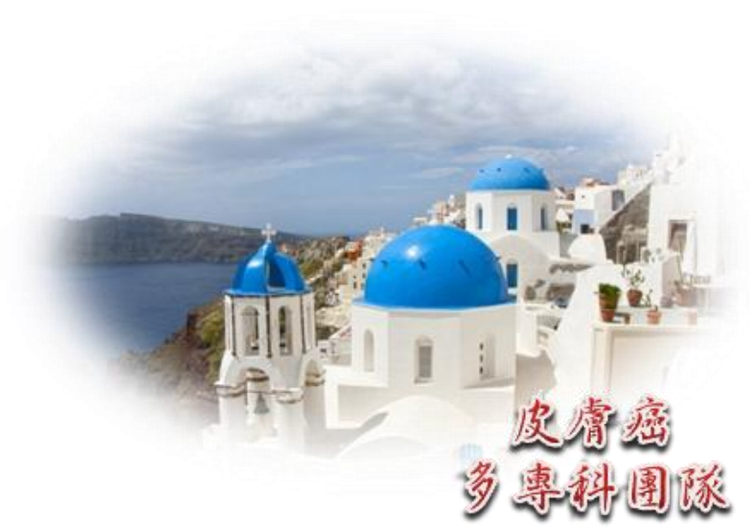


黑色素細胞癌(melanoma)

附件八：melanoma with Immunotherapy (or metastasis)

免疫治療處方

melanoma with Immunotherapy	
Immunotherapy	schedule
Ipilimumab 3mg/kg, IV	Every 3wks, 4 sessions
Nivolumab 3mg/kg, IV	Every 2 wks, at least 2 years



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