

高雄榮民總醫院

皮膚癌(melanoma)診療原則

修訂日期:2025.05.20

melanoma 診療指引審視修訂會議討論日期

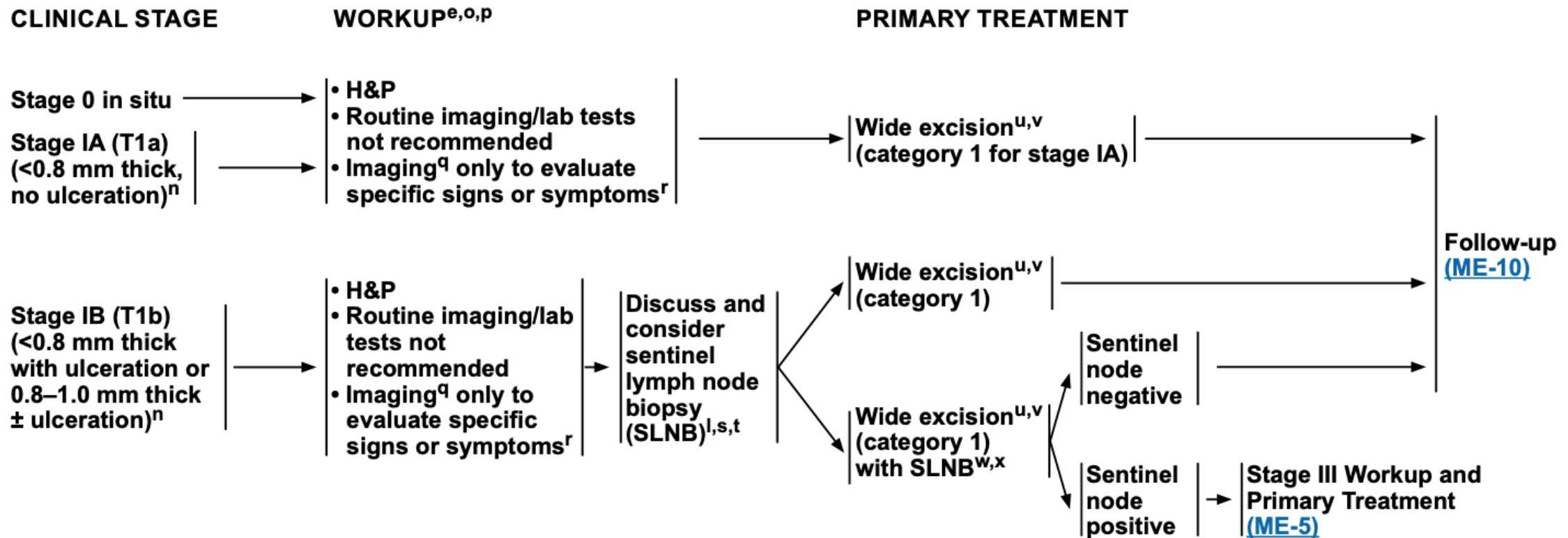
- 前次會議： 2024/04/19
- 本共識經審視：



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

上一版	新版
NCCN Guidelines 2024年版	更換附件為:NCCN Guidelines 2025年版





- **Stage IA (T1a <0.8 mm, non-ulcerated) : 不建議 SLNB 。**
- **Stage IB (T1b, <0.8 mm 有潰瘍或 0.8–1 mm ± ulceration) : 建議「討論並考慮 SLNB」。**
- **T1a 但伴隨 high-risk features (年輕 ≤42 歲、頭頸部、LVI、mitotic rate ≥2/mm²) : 也要考慮 SLNB 。**

ⁿ If a patient's risk of a positive sentinel lymph node (SLN) is <5%, NCCN does not recommend SLNB. This would include stage IA, T1a melanoma (Breslow depth of <0.8 mm, nonulcerated) without other adverse features, unless there is significant uncertainty about the adequacy of microstaging (due to positive deep margins or limited sampling of a larger lesion). If a patient's risk of a positive SLNB is 5%–10%, NCCN recommends discussing and considering SLNB. This would include clinical stage IB, T1b melanoma (Breslow depth <0.8 mm with ulceration or 0.8–1 mm with or without ulceration), or T1a lesions with Breslow depth >0.5 mm and other adverse features (age ≤42 years, head/neck location, lymphovascular invasion, and/or mitotic rate ≥2/mm²), with additive increased risk when multiple adverse features are present (Shannon AB, et al. J Am Acad Dermatol 2023;88:52-59). Ongoing prospective investigation will further inform the utility of gene expression profiling (GEP) tests and multivariable nomograms/risk calculators (eg, melanomarisks.org.au/snland; mskcc.org/nomograms/melanoma/sentinel_lymph_node_metastasis), and other decision analytical models for SLNB risk prediction (Miller JR 3rd, et al. JAMA Netw Open 2023;6:e236356 and Bartlett EK, et al. Ann Surg Oncol 2024 Oct 29. Epub ahead of print. doi: 10.1245/s10434-024-16379-2).

Note: All recommendations are category 2A unless otherwise indicated.

黑色素細胞癌(melanoma)



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

- 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)

Stage I

Stage II

Stage III

Stage IV

- **Stage IA (T1a <0.8 mm, non-ulcerated) : 不建議 SLNB 。**
- **Stage IB (T1b, <0.8 mm 有潰瘍或 0.8–1 mm ± ulceration) : 建議「討論並考慮 SLNB」。**
- **T1a 但伴隨 high-risk features (年輕 ≤42 歲、頭頸部、LVI、mitotic rate ≥2/mm²) : 也要考慮 SLNB 。**

§ : 可選擇

△ : 建議 whole body PET / CT + brain MRI





PRINCIPLES OF SURGICAL MARGINS FOR WIDE EXCISION OF PRIMARY MELANOMA

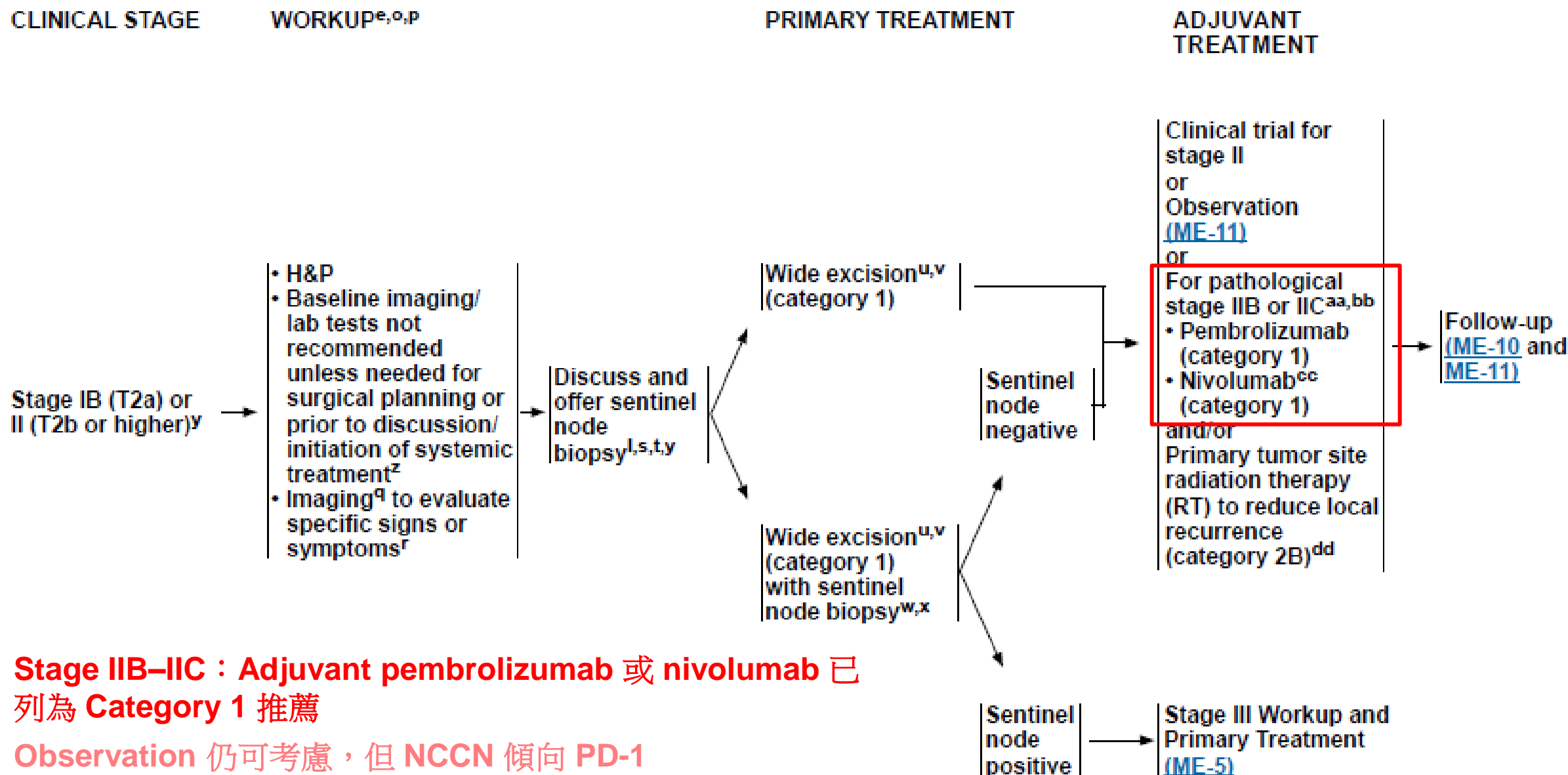
Tumor Thickness	Recommended Peripheral Surgical Margins ^{a,1-10}
In situ ^{b,c}	0.5–1 cm
≤1.0 mm	1 cm (category 1)
>1.0–2.0 mm	1–2 cm (category 1)
>2.0–4.0 mm	2 cm (category 1)
>4.0 mm	2 cm (category 1)

- There are no randomized trials to inform peripheral surgical margins or depth of wide excision for MIS.
 - ▶ Depth of excision into the subcutaneous fat may be adequate and considered in anatomic locations where excision to fascia would cause significant morbidity.
- For invasive melanoma, wide 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.¹¹ However, narrower-than-recommended margins may increase the risk for margin positivity and/or local recurrence.
 - ▶ The safety and efficacy of narrower surgical margins is being prospectively studied in a randomized controlled trial (NCT03860883) to compare 1-cm versus 2-cm margins for stage II melanoma (1–2 mm with ulceration [T2b] and >2 mm [T3a–T4b]). However, this trial excludes patients with melanoma distal to the metacarpophalangeal joint (including subungual melanoma); on the nasal tip, eyelids, or ear; and on noncutaneous sites.
- The gold standard for histologic assessment of excised melanoma is use of permanent sections. If complex reconstruction is anticipated, wound closure should generally be delayed until histologic margin assessment is complete.
- Mohs micrographic surgery (MMS) is not recommended for primary treatment of invasive cutaneous melanoma when standard clinical margins can be obtained.
 - ▶ MMS 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,12}
 - ▶ If MMS is performed, the central debulking specimen should be analyzed histologically via permanent sections (preferred) or frozen sections with immunostaining to provide complete staging information.¹³
- 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 Few trials included head/neck melanomas, and none included acral melanomas.
- In the setting of an adequate biopsy, digit-sparing surgery (via wide excision or MMS) may be an option for subungual MIS and select thin tumors (<0.8 mm), although further investigation is needed.¹⁴

[Footnotes on ME-E 1A of 3](#)

[References on ME-E 2 of 3](#)

- **NCCN 強調避免 >2 cm，因為無額外存活益處。**
- **Mohs surgery (MMS)：仍非標準，但在臉、耳、指甲床等部位可考慮 staged excision 或 MMS。**



Stage IIB–IIC : Adjuvant pembrolizumab 或 nivolumab 已列為 Category 1 推薦

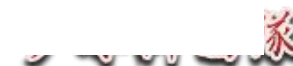
Observation 仍可考慮，但 NCCN 傾向 PD-1

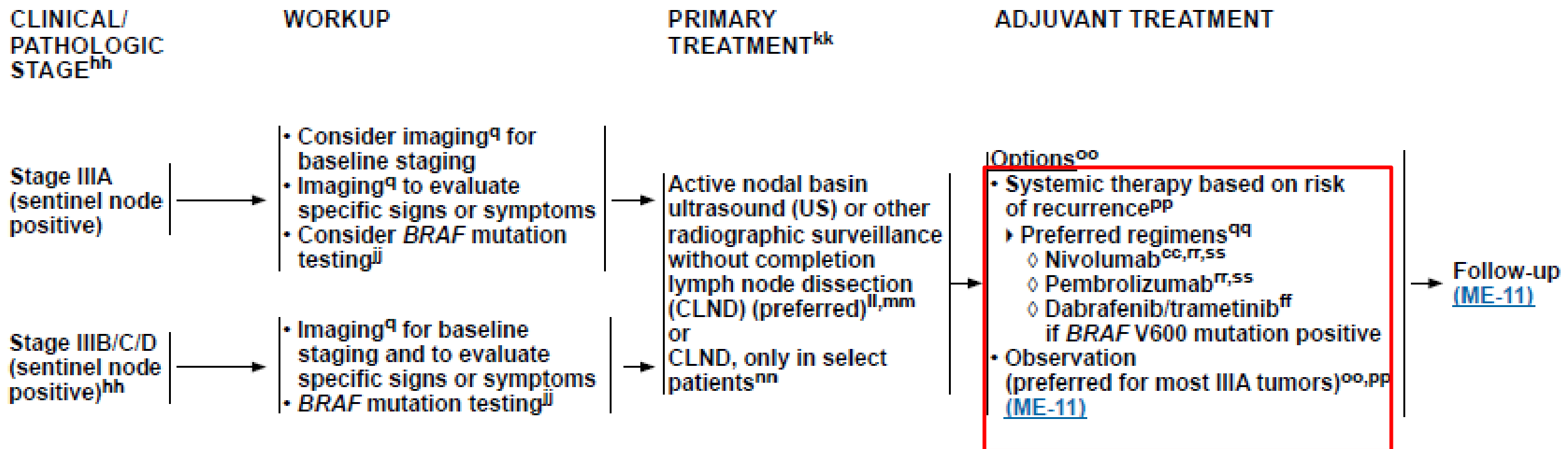
[Additional footnotes on ME-3A](#)

^y Microsatellitosis, when present in the initial biopsy or wide excision specimen, defines at least N1c and at least stage IIB disease. Although less well-studied than other stage III patient populations, SLN status does have prognostic significance in patients with microsatellitosis, with a positive SLN upstaging a patient to at least N2c, stage IIIC. SLNB should be considered in patients with microsatellitosis, especially if it will alter disease management decisions.

^z For patients with stage IIB/IIC disease being considered for adjuvant therapy, baseline/pre-treatment imaging is appropriate.

Note: All recommendations are category 2A unless otherwise indicated.





Pembrolizumab (Cat.1)
Nivolumab (Cat.1)
BRAF V600+ : 可選 dabrafenib + trametinib
Observation : 僅限於 very low-risk stage IIIA (例如 SLN tumor volume 極低)

[Additional footnotes on ME-5A](#)

^{qq} Adjuvant dabrafenib/trametinib and pembrolizumab were tested in AJCC 7th Edition stage IIIA with SLN metastasis ≥ 1 mm or stage IIIB/C disease. Adjuvant nivolumab was studied in AJCC 7th Edition stage IIIB/C disease (category 1 for all agents). Clinical efficacy of these agents has been demonstrated across AJCC 8th Edition stage III disease.

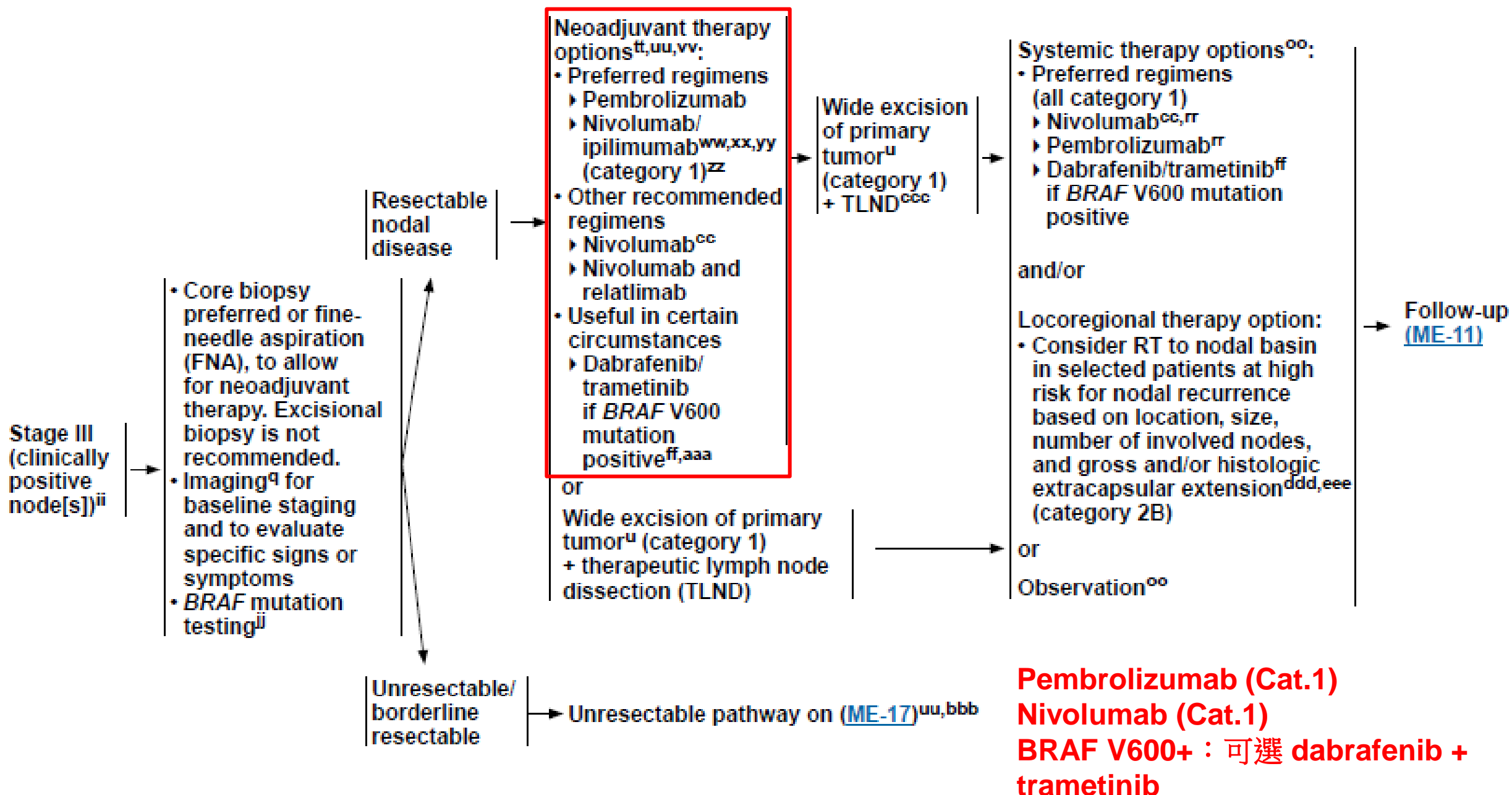
Note: All recommendations are category 2A unless otherwise indicated.

CLINICAL/
PATHOLOGIC
STAGE

WORKUP

PRIMARY TREATMENT

ADJUVANT TREATMENT



[Footnotes on ME-6A](#) [Neoadjuvant references on ME-6B](#)

Note: All recommendations are category 2A unless otherwise indicated.

SYSTEMIC THERAPY FOR METASTATIC OR UNRESECTABLE DISEASE^{a,b,c}

FIRST-LINE THERAPY

SECOND-LINE OR SUBSEQUENT THERAPY^P

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)^{f,g}
- Anti-PD-1 monotherapy^{d,f,g}
 - ▶ Pembrolizumab (category 1)
 - ▶ Nivolumab (category 1)ⁱ

Other recommended regimens

- Combination targeted therapy if *BRAF* V600 mutation positive^{j,k,l,m,n}
 - ▶ Dabrafenib/trametinib (category 1)
 - ▶ Vemurafenib/cobimetinib (category 1)
 - ▶ Encorafenib/binimetinib (category 1)
- Pembrolizumab/low-dose ipilimumab^o (category 2B)

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

Preferred regimens

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

Other recommended regimens

- Ipilimumab^f
- 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^l/intralesional T-VEC (category 2B)
 - Combination *BRAF*/*MEK* + PD(L)-1 checkpoint inhibitors (eg, dabrafenib/trametinib + pembrolizumab or vemurafenib/cobimetinib + atezolizumab^x if *BRAF* V600 mutation positive)^y
 - Cytotoxic agents ([MELSYS 2 of 7](#))
 - Consider best supportive care for poor performance status ([NCCN Guidelines for Palliative Care](#))

首選免疫治療：

PD-1 單藥 (pembro 或 nivo)

Nivo + Ipi (CTLA-4)

Nivo + Relatlimab (LAG-3) → 已列為 preferred

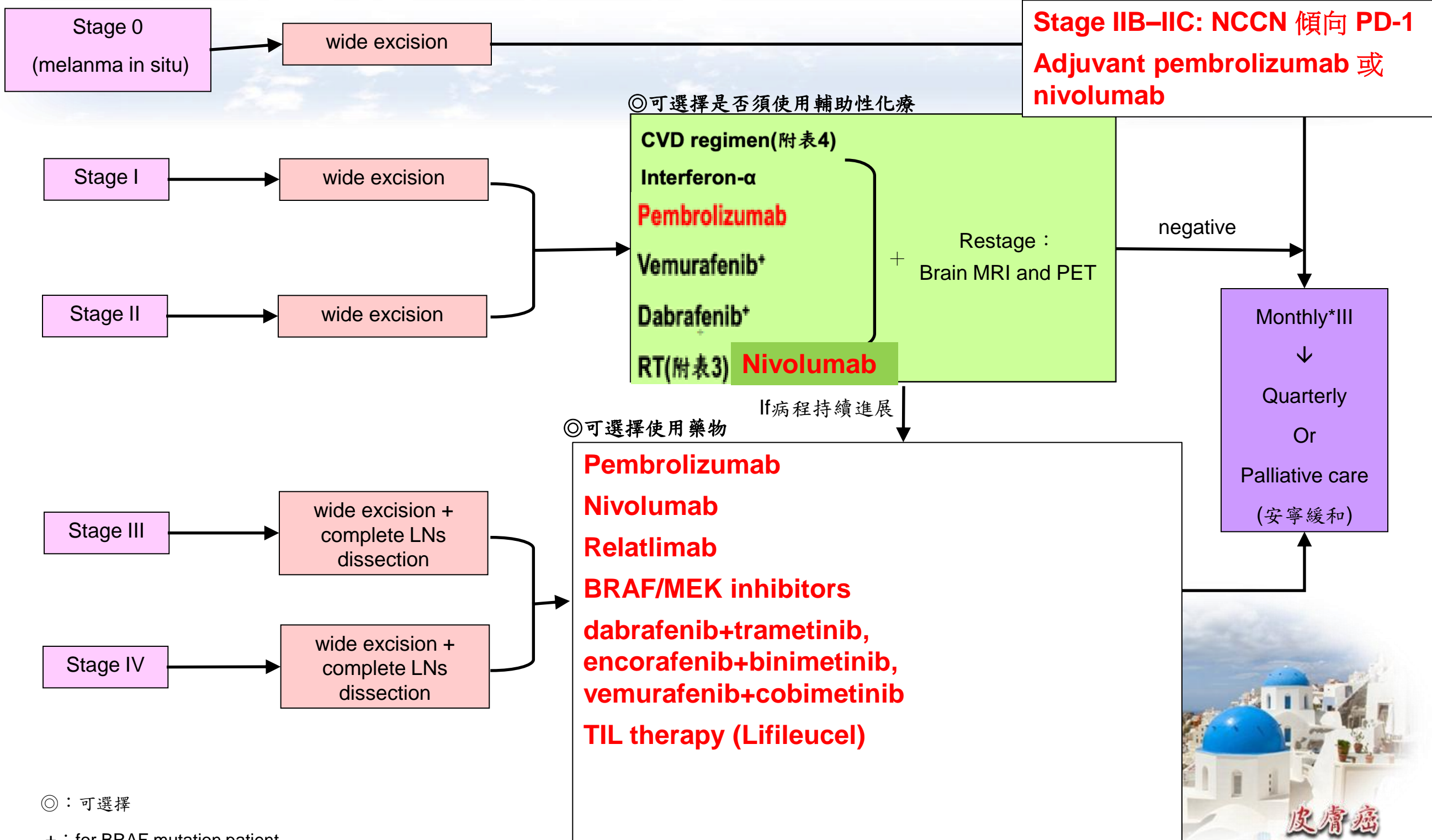
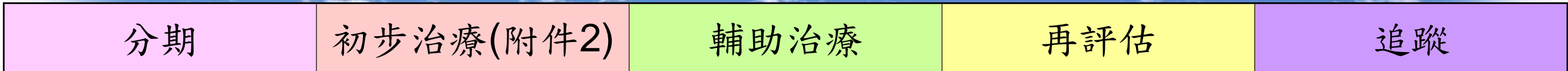
BRAF V600+ 病人：可用 BRAF/MEK inhibitors

[Footnotes on MELSYS 1A of 7](#)

- TIL therapy (Lifileucel) → 已納入，推薦於曾接受 PD-1 ± BRAF/MEK 後仍進展者。
- 傳統化療 (如 CVD, DTIC) → 僅限特殊情境，已降為 Category 2B

Note: All recommendations are category 2A unless otherwise indicated.

黑色素細胞癌(melanoma)



◎：可選擇
+：for BRAF mutation patient



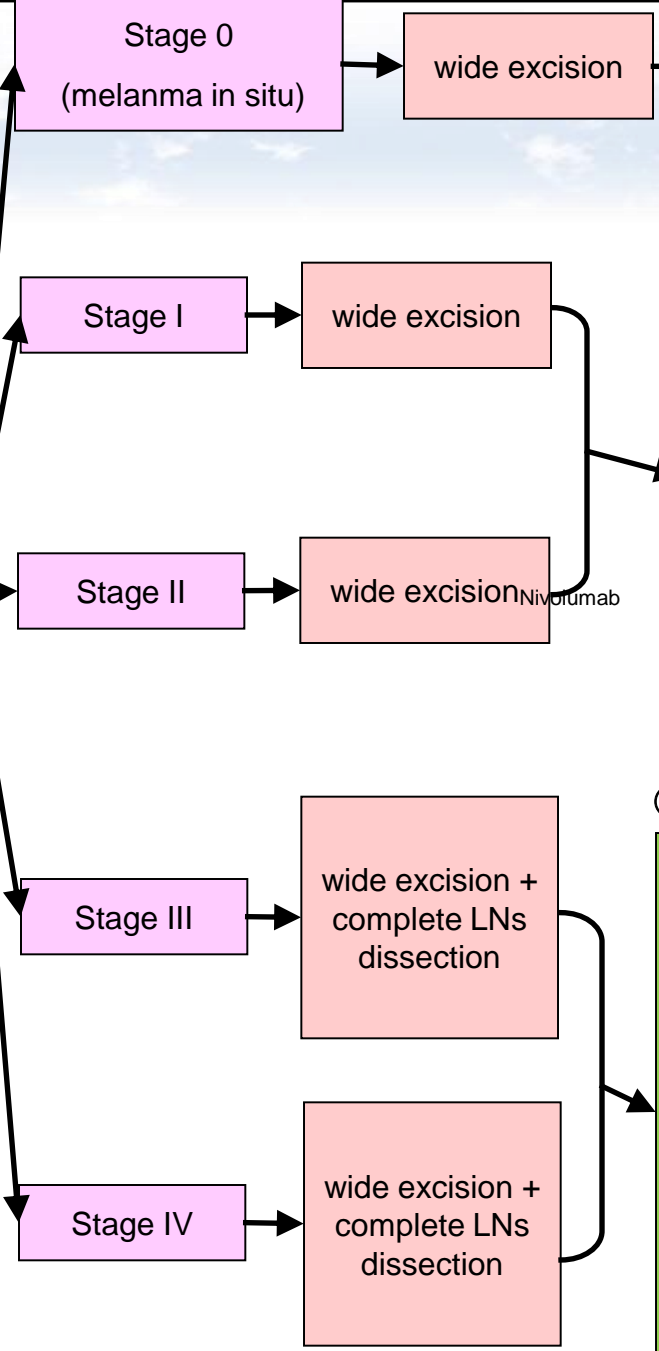
皮膚癌
多專科團隊

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



◎可選擇使用藥物

- CVD regimen(附表4)
- Pembrolizumab**
 - Nivolumab**
 - Relatlimab**
 - BRAF/MEK inhibitors**
 - dabrafenib+trametinib,**
 - encorafenib+binimetinib,**
 - vemurafenib+cobimetinib**
 - TIL therapy (Lifileucel)**
- RT(附表5)
- Restage :
Brain MRI and PET
- if 病程持續進展

◎可選擇使用藥物

- Dantmouth regimen(附表5)
- Pembrolizumab**
 - Nivolumab**
 - Relatlimab**
 - BRAF/MEK inhibitors**
 - dabrafenib+trametinib,**
 - encorafenib+binimetinib,**
 - vemurafenib+cobimetinib**
 - TIL therapy (Lifileucel)**
- Clinical trial、RT(附表3)
- Temozolomide、Palliative surgery
- + Restage :
Brain MRI and PET

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

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。



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/m ² , IV, D1	Q28d * 6 cycles
Cisplatin 20mg/m ² , IV, D2-5	Q28d * 6 cycles
Vinblastine 1.6mg/m ² , 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/m ² , IV, D1	Q28d * 6 cycles
Vinblastine 1.6mg/m ² , 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/m ² , IV, D1	Q28d * 6 cycles
Dacarbazine 220mg/m ² , IV, D1-3	Q28d * 6 cycles
Cisplatin 25mg/m ² , 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/m ² , IV, D1-3	Q28d * 6 cycles
Cisplatin 25mg/m ² , 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/m ² , IV, D1-3	Q28d * 6 cycles
Dacarbazine 220mg/m ² , 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/m ² , 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



Reference

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皮膚癌
多專科團隊