



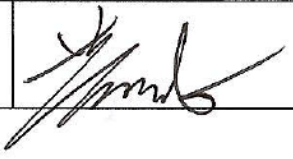
中山醫學大學附設醫院

皮膚癌診療指引

本臨床指引參考美國NCCN及台灣皮膚科醫學會共識版本

皮膚癌多專科醫療團隊編修

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癌症委員會主任委員	癌症委員會執行長	癌症中心主任	抗癌藥物安全小組	團隊負責人
詹光川		楊軒	呂昭儒	邱足滿



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一、前言

常見的皮膚癌有基底細胞癌(Basal Cell Carcinoma)、鱗狀細胞癌(Squamous Cell Carcinoma)、黑色素細胞癌(Melanoma)。基底細胞癌源自於皮膚表皮底層的柱狀基底細胞，是人類最常見的癌症，臨床可見 Pearly border 與微血管擴張，少數有 Rodent ulcer，基底細胞癌侵襲性與轉移性皆低，通常手術切除乾淨與定期追蹤，預後通常都不錯並且有極高的生存率。鱗狀細胞癌源自於皮膚表皮層的棘狀細胞，臨床常見有角化與色澤形狀不一的腫瘤，有時有 Marjolin's ulcer，預後與腫瘤大小、位置、是否有神經侵犯、是否有淋巴與遠端器官轉移有關。黑色素癌是轉移性高且死亡率也高的皮膚癌，在臺灣的發生率約為十萬分之零點八。東方人的黑色素癌好發在手指尖或是腳掌，稱為肢端型黑色素癌(acral lentiginous type of melanoma)。警覺心不足或忽略檢查腳底有無異常黑點，常會延誤診斷而耽誤治療。黑色素癌的厚度與是否有淋巴結或器官轉移，影響了患者的預後，早期黑色素癌，以手術與前哨淋巴結檢查切除，為最佳治療方式，然而，轉移型黑色素癌的治療則相當不容易，黑色素癌容易轉移到肺部，腦部，骨頭，肝臟等。傳統藥物化療藥物 Dacarbazine 對第四期轉移性黑色素癌的療效有限，平均存活時間大約只有 6 至 7 個月。而傳統免疫藥物 IFN α 2b 與高劑量 IL-2 的副作用多，包括高燒、寒顫、低血壓、心跳過速等等不舒服的症狀，往往讓患者難以承受而放棄治療。



然而，自人類基因解序幫助科學家對疾病致病機轉更加地瞭解，轉移型黑色素癌治療在 2010 年有了新的突破。整個癌症治療指引也有了重大改變。發展中的新治療主要分成兩個部分，一個是標靶治療，另一個則是新型的免疫治療，並以合併治療為趨勢。標靶治療主要是針對黑色素癌細胞生長所需的訊息傳遞因子(標的)給予抑制，例如 BRAF 基因 V600E 的突變對黑色素癌細胞生長非常重要，標靶治療針對 BRAF 抑制的藥物有日沛樂/Zelboraf (Vemurafenib)以及泰伏樂/Tafinlar (Dabrafenib)，日沛樂於 2014 年在台灣上市，有健保給付，用於治療 BRAF V600E 突變陽性 WHO 體能狀態小於等於二，且罹患無法切除(第ⅢC 期)或轉移性(第Ⅳ期)黑色素癌之病人。在 BRAF 基因 V600E 突變陽性的轉移型黑色素癌病患，標靶治療可以讓腫瘤快速地縮小，但對生存率的延長沒有顯著幫忙。

在腫瘤微環境研究發現，癌細胞為了能逃避免疫細胞的追殺，會用各種方法去干擾身體的免疫系統。其中一種方式就是藉由活化免疫系統的控制因子(免疫檢查點蛋白)，進而讓免疫系統失能，無法攻擊黑色素癌細胞。新的免疫療法就是想辦法去抑制這些控制因子，減弱免疫檢查點蛋白的抑制能力，讓免疫系統能夠恢復原本的功能，去攻擊黑色素癌細胞。臺灣有抑制 CTLA-4 的益伏/Yervoy (ipilimumab)與抑制 PD-1 的吉舒達 Keytruda (Pembrolizumab)及抑制 PD-1 的保疾伏 Opdivo (Nivolumab)。對於轉移性黑色素癌的新進展，著實另人振奮，但仍有許多待解決的問題例



如亞洲病患標靶基因突變比率偏低、抗藥性、副作用、健保給付、昂貴藥費等等。如何結合目前所有的各種標靶治療，免疫治療，找出病人最適合的治療藥物組合，成了當前最大挑戰。

二、皮膚癌分期

(1) 基底細胞癌(Basal cell carcinoma)

Stage 0: Cancer involves only the epidermis and has not spread to the dermis

Stage I: Cancer is not large (ie, < 2 cm) and has not spread to the lymph nodes or other organs

Stage II: Cancer is large (ie, >2 cm) but has not spread to lymph nodes or other organs

Stage III: Cancer has spread to tissues beneath the skin (eg, muscle, bone, cartilage), and/or to regional lymph nodes but not to other organs.

Stage IV: Cancer can be any size and has spread to other organs



(2) 鱗狀上皮細胞癌(TNM Staging Classification for Cutaneous Carcinoma of the Head and Neck (8th ed., 2017))

T	Primary Tumor	
TX		Primary tumor cannot be assessed
Tis		Carcinoma <i>in situ</i>
T1		Tumor smaller than or equal to 2 cm in greatest dimension
T2		Tumor larger than 2 cm, but smaller than or equal to 4 cm in greatest dimension
T3		Tumor larger than 4 cm in maximum dimension or minor bone erosion or perineural invasion or deep invasion*
T4		Tumor with gross cortical bone/marrow, skull base invasion and/or skull base foramen invasion
	T4a	Tumor with gross cortical bone/marrow invasion
	T4b	Tumor with skull base invasion and/or skull base foramen involvement
*Deep invasion is defined as invasion beyond the subcutaneous fat or >6 mm (as measured from the granular layer of adjacent normal epidermis to the base of the tumor); perineural invasion for T3 classification is defined as tumor cells within the nerve sheath of a nerve lying deeper than the dermis or measuring 0.1 mm or larger in caliber, or presenting with clinical or radiographic involvement of named nerves without skull base invasion or transgression.		

Clinical N (cN)

cN	Regional Lymph Nodes	
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(-)
N2		Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-);



		<i>or</i> metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-); <i>or</i> in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-)
	N2a	Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-)
	N2b	Metastases in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(-)
	N2c	Metastases in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-)
N3		Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-); <i>or</i> metastasis in any node(s) and clinically overt ENE [ENE(+)]
	N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-)
	N3b	Metastasis in any node(s) and ENE (+)

Note: A designation of “U” or “L” may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological extranodal extension (ENE) should be recorded as ENE(-) or ENE(+).

Pathological N (pN)

pN	Regional Lymph Nodes	
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(-)
N2		Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(+); <i>or</i> larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-); <i>or</i> metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-); <i>or</i> in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension, ENE(-)
	N2a	Metastasis in single ipsilateral node 3 cm or smaller in greatest dimension and ENE(+); <i>or</i> a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-)
	N2b	Metastases in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(-)
	N2c	Metastases in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension and ENE(-)
N3		Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-); <i>or</i> in a single ipsilateral node larger than 3 cm



		in greatest dimension and ENE(+); <i>or</i> multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+); <i>or</i> a single contralateral node of any size and ENE(+)
	N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-)
	N3b	Metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); <i>or</i> multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+); <i>or</i> a single contralateral node of any size and ENE(+)
Note: A designation of “U” or “L” may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological extranodal extension (ENE) should be recorded as ENE(-) or ENE(+).		

M	Distant Metastasis
M0	No distant metastasis
M1	Distant metastasis

G	Histologic Grade
GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0



Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IV	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	Any T	N3	M0
	T4	Any N	M0
	Any T	Any N	M1

(3) 黑色素細胞癌(Melanoma)

Definition of Primary Tumor (T)

T Category	Thickness	Ulceration status
TX:primary tumor thickness cannot be assessed(e.g., diagnosis by curettage)	Not applicable	Not applicable
T0:no evidence of primary tumor(e.g.,unknown primary or completely regressed melanoma)	Not applicable	Not applicable
Tis(melanoma <i>in situ</i>)	Not applicable	Not applicable
T1	$\leq 1.0\text{mm}$	Unknown or unspecified
T1a	$<0.8\text{mm}$	Without ulceration
T1b	$<0.8\text{mm}$ $0.8-1.0\text{mm}$	With ulceration With or without ulceration
T2	$>1.0-2.0\text{mm}$	Unknown or unspecified
T2a	$>1.0-2.0\text{mm}$	Without ulceration
T2b	$>1.0-2.0\text{mm}$	With ulceration
T3	$>2.0-4.0\text{mm}$	Unknown or unspecified



T3a	>2.0-4.0mm	Without ulceration
T3b	>2.0-4.0mm	With ulceration
T4	>4.0mm	Unknown or unspecified
T4a	>4.0mm	Without ulceration
T4b	>4.0mm	With ulceration

Definition of Reginal Lymph Node(N)

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(e.g., SLN biopsy not performed, regional nodes previously removed for another reason) Exception: pathological N category is not required for T1 melanomas ,use cN.	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	No
N1a	One clinically occult (i.e.,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(i.e.,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 (i.e., 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

Definition of Distant Metastasis(M)

M Category	M Criteria	
	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



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)**

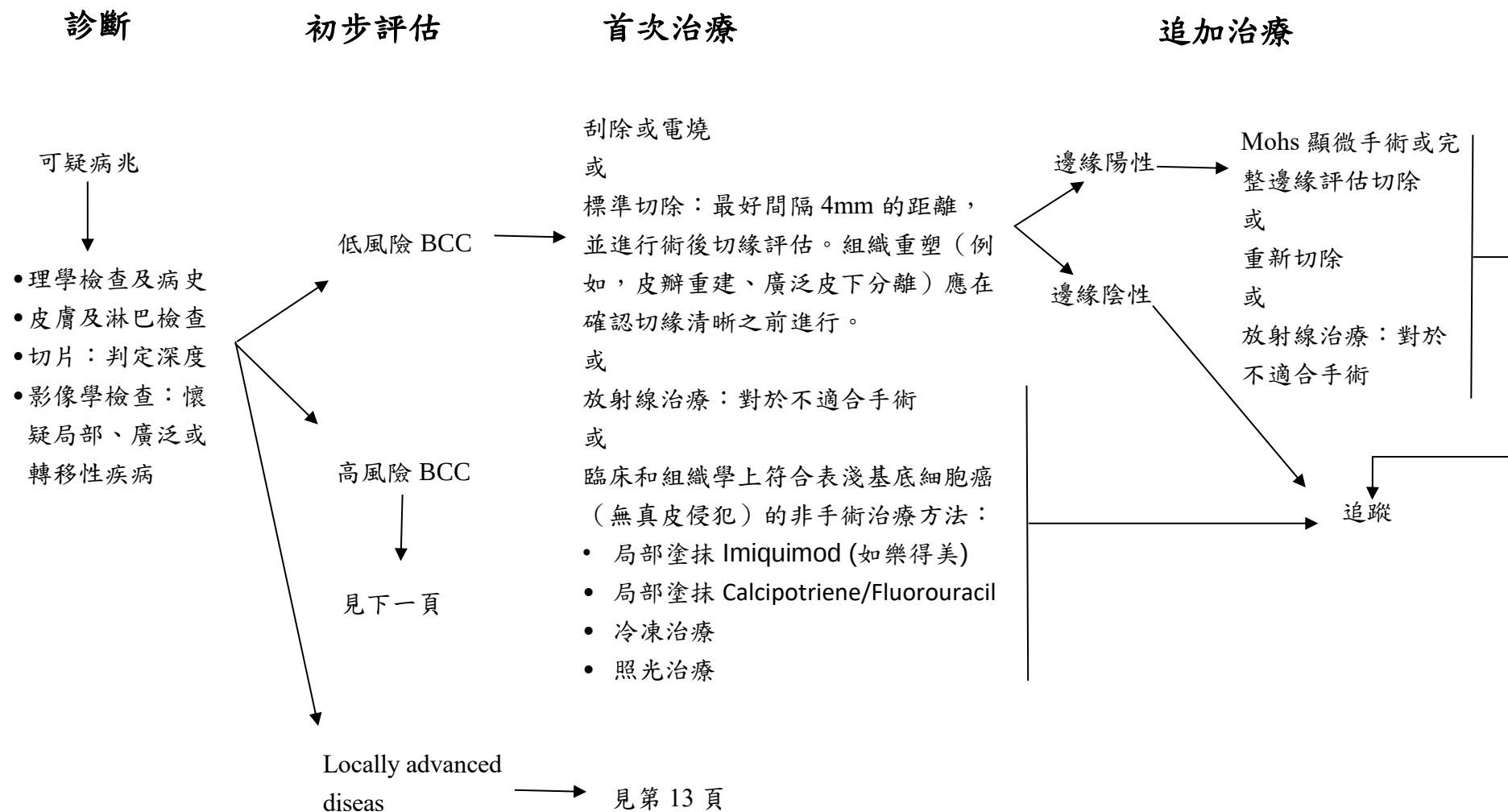
	T	N	M
Stage 0†	Tis	N0	M0
Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T3a	N0	M0
Stage IIB	T3b	N0	M0
	T4a	N0	M0
Stage IIC	T4b	N0	M0
Stage IIIA	T1a/b, T2a	N1a, N2a	M0
Stage IIIB	T0	N1b, N1c	M0
	T1a/b, T2a	N1b/c, N2b	M0
	T2b, T3a	N1a/b/c, N2a/b	M0
Stage IIIC	T0	N2b/c, N3b/c	M0
	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 (melanoma in situ) and T1 do not require pathological evaluation of lymph nodes to complete pathological staging; use cN information to assign their pathological stage.

Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing. (For complete information and data supporting the staging tables, visit www.springer.com.)

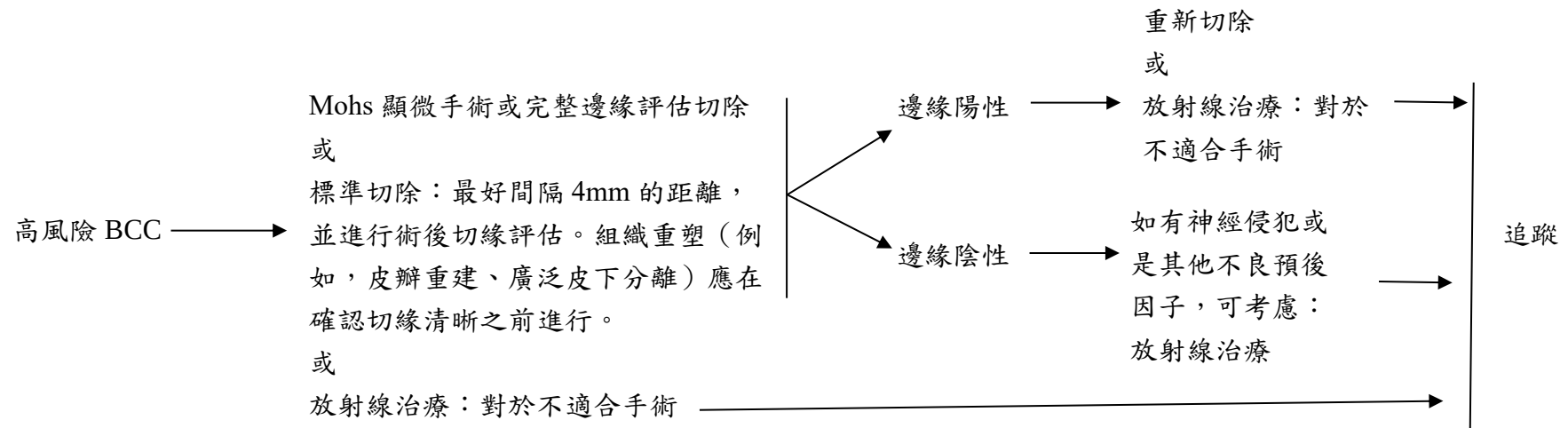
三、基底細胞癌



初步評估

首次治療

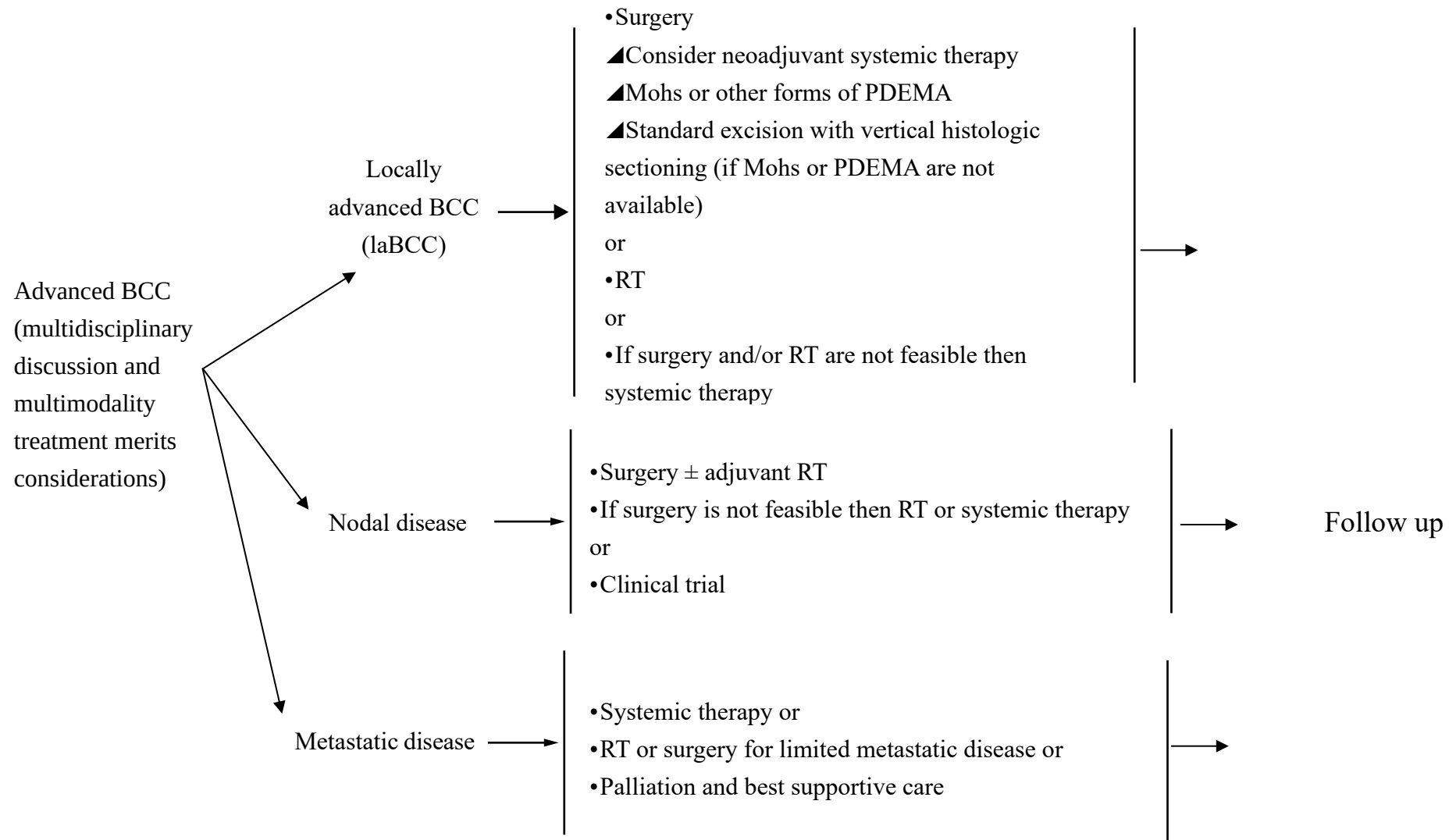
輔助治療





初步評估

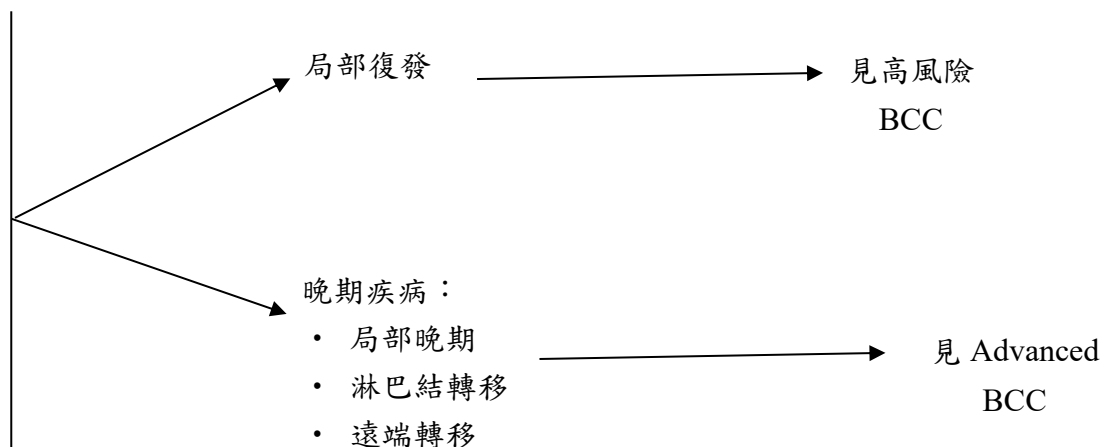
首次治療



追蹤

- 前 5 年每 6-12 個月進行一次完整的皮膚檢查，之後至少每年一次，直至終生
- 如果臨床檢查不足以追蹤病情，考慮影像學檢查
- 病患教育：
 - 防曬
 - 自我檢查

復發





附件一、局部復發的危險因子

病史及理學檢查	低風險	高風險
位置/大小	Area L < 20 mm Area M < 10 mm	Area L ≥ 20 mm Area M ≥ 10 mm Area H 任何大小
邊緣	界限分明	界線模糊
原發/續發	原發	續發
免疫抑制	無	有
病灶位置曾接受過放射治療	無	有
神經侵犯	無	有
病理分類	Nodular , superficial keratotic , infundibulocystic , fibroepithelioma of Pinkus ,	Morpheaform , basosquamous (metatyoical) ,sclerosing , Mixed infiltrative , micronodular

Area Low risk: trunk and extremities(excluding hands, feet, pretibial area)

Area Medium risk: pretibial area, face other than mask area (cheek, forehead, scalp, neck)

Area High risk: face mask area+ hands+feet+genitalia (mask area: central face, eyelid, eyebrow, nose, lips-cutaneous and vermillion, chin, mandible, preauricular/postauricular skin sulci, temple, ear)

Area H 的腫瘤不論大小都屬於高風險。這些地方通常為了美觀，margin 不夠大，易造成復發。建議使用 Mohs micrographic surgery 可達到邊緣乾淨，且最小切除範圍。對於<6mm 的腫瘤，沒有其他危險因子，建議至少要切除 4mm 的 margin。

Area H 的腫瘤不論大小都屬於高風險。這些地方通常為了美觀，margin 不夠大，易造成復發。建議使用 Mohs micrographic surgery 可達到邊緣乾淨，且最小切除範圍。對於<6mm 的腫瘤，沒有其他危險因子，建議至少要切除 4mm 的 margin。



附件二、PRINCIPLES OF TREATMENT FOR BASAL CELL SKIN CANCER

• The primary treatment goals of BCC is the complete removal of the tumor and the maximal preservation of function and cosmesis. All treatment decisions should be customized to account for the particular factors present in the individual case and for the patient's preference.

基底細胞癌 (BCC) 的主要治療目標是徹底切除腫瘤，並最大限度地保留功能和外觀。所有治療計畫應根據個別病例的具體情況和患者意願進行個人化制定。

• Surgical approaches often offer the most effective and efficient means for accomplishing cure, but considerations of function, cosmesis, and patient preference may lead to choosing RT/topical therapy/systemic therapy as primary treatment in order to achieve optimal overall results.

手術通常是根治性治療最有效的方式，但考慮到功能、外觀和患者意願，可能會選擇放射治療/局部治療/全身治療作為主要治療方式，以達到最佳的整體療效。

• In certain patients at high risk for multiple primary tumors (eg, basal cell nevus syndrome [Gorlin syndrome], xeroderma pigmentosum, history of RT), increased surveillance and consideration of prophylactic measures may be indicated. Refer patients with suspected basal cell nevus syndrome or xeroderma pigmentosum for genetic evaluation.

對於某些有多發性原發性腫瘤高風險的患者（例如，basal cell nevus syndrome [Gorlin syndrome], xeroderma pigmentosum、有放射治療史），可能需要加強監測並考慮採取預防措施。疑似 basal cell nevus syndrome 或 xeroderma pigmentosum 的患者應進行基因檢測。

• In patients with superficial basal cell skin cancer, nonsurgical modalities may be considered. (See 低風險 BCC)

對於表淺性基底細胞皮膚癌患者，可以考慮非手術治療。（參見 低風險 BCC）

附件三、PRINCIPLES OF RADIATION THERAPY FOR BASAL CELL SKIN CANCER

Primary Tumor	RT Dosing	Common Examples
Adjuvant RT		
• Conventional fractionation (1.8–2 Gy/fraction)	BED10 of 60–79 Gy	• 60–66 Gy in 2 Gy/fraction • 60–66 Gy in 1.8 Gy/fraction (reserved for areas with poor wound healing, [eg, lower extremity])
• Hypofractionation	BED10 of 48–70 Gy	• 2.5 Gy x 20 fractions • 3 Gy x 15–17 fractions to 45–51 Gy • 6 Gy x 5 fractions (non-consecutive days)
Definitive EBRT		



• Conventional fractionation (1.8–2 Gy/fraction)	BED10 of 70–84 Gy	• 60 Gy (for cosmetically sensitive areas) • 66–70 Gy (for locally advanced tumors involving bone or cartilage)
• Hypofractionation	BED10 of 48–72 Gy	• Tumors <2 cm: 2.5 Gy x 20 fractions • Tumors ≥2 cm: 2.5–3 Gy x 20–22 fractions • 3 Gy x 17–18 fractions to 51–54 Gy • 4.4 Gy x 10 fractions, 4 fractions per week • 6–7 Gy x 5 fractions, 2 treatments per week
Regional Disease		
• Conventional fractionation (1.8–2 Gy/fraction) Macroscopic/gross residual lymph nodes Lymph node + dissected nodal basins PNTS	66–70 Gy 60 Gy 50–66 Gy	

- Conventionally fractionated radiotherapy consists of five daily treatments per week.
- Hypofractionated radiotherapy consists of fewer treatments with larger fraction size

附件四、藥物治療

1. Inductions and Usage for Erivedge

Erivedge capsule is indicated for the treatment of adults with metastatic basal carcinoma, or with locally advanced basal cell carcinoma that has recurred following surgery or who are not candidates for surgery, and who are not candidates for radiation.

Erivedge Dosage nad Administration

The recommended dose of Erivedge is 150mg taken orally once daily until disease progression or until unacceptable toxicity.

Erivedge may be taken with or without food. Swallow capsules wholes. Do not open or crush capsules.

If a dose of Erivedge is missed, do not make up that dose.

Dosage Forms and Strengths

Erivedge (vismodegib) capsules, 150mg. The capsule has a pink opaque body and a gery opaque cap, with “150mg” printed on the capsule body and “VISMO” printed on the capsule cap in black ink.



2. Clinical trial

3. Cisplatin + paclitaxol (self pay)

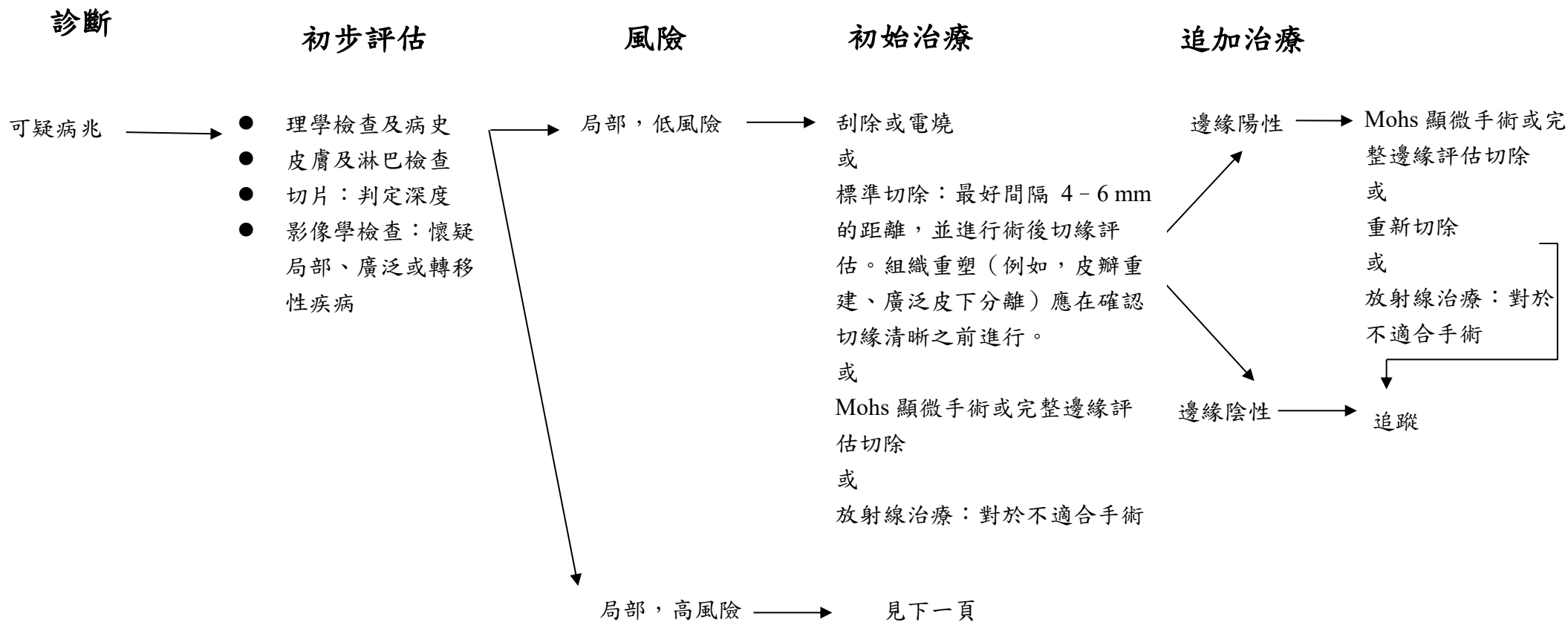
cisplatin (75 mg/m²) and paclitaxel (135 mg/m², 3 h infusion) every 3 weeks

Ref: Metastatic basal cell carcinoma: rapid symptomatic response to cisplatin and paclitaxel. ANZ J Surg. 2004 Aug;74(8):704-5.

4. Treat as recurrent/metastatic head and neck squamous cell carcinoma



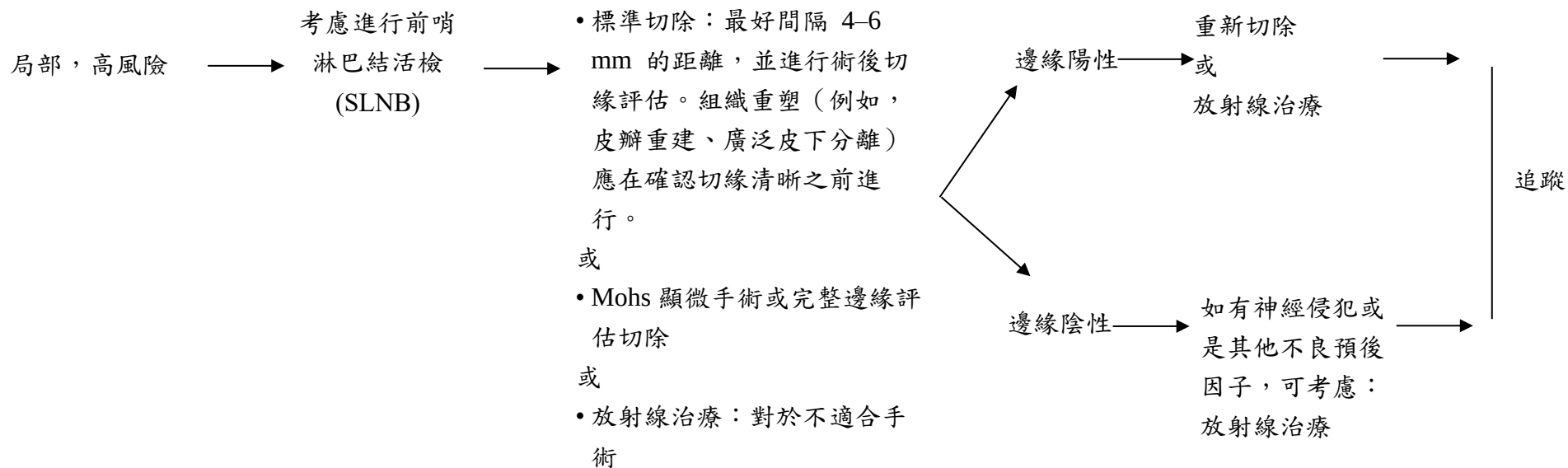
鱗狀上皮細胞癌



治療前評估

初始治療

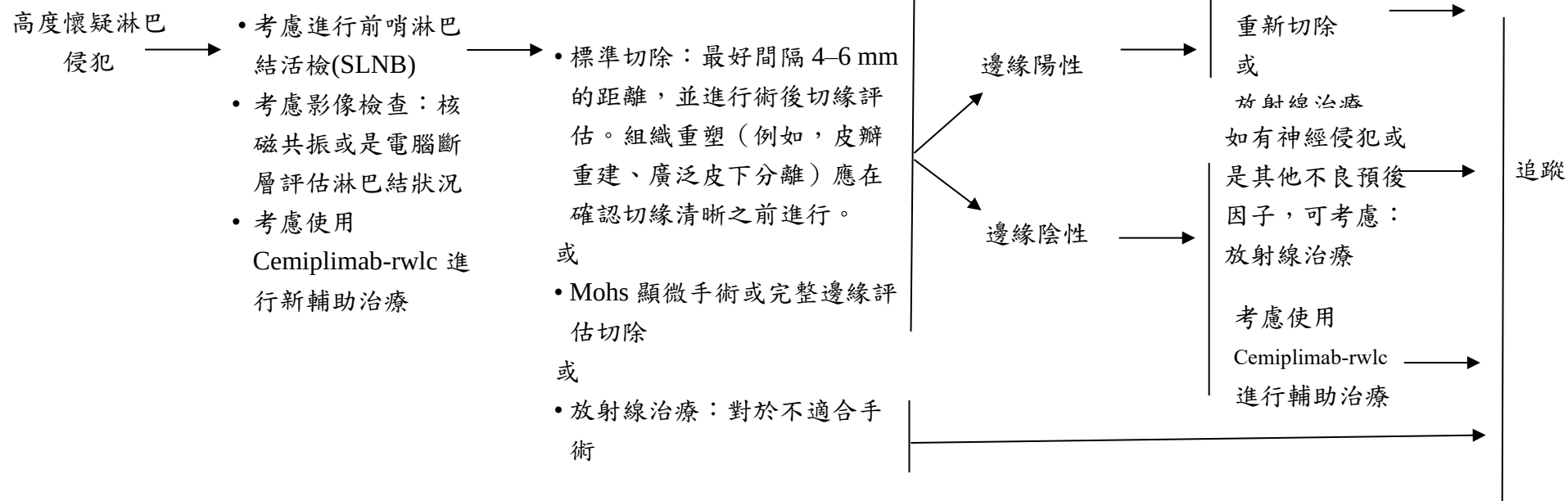
追加治療



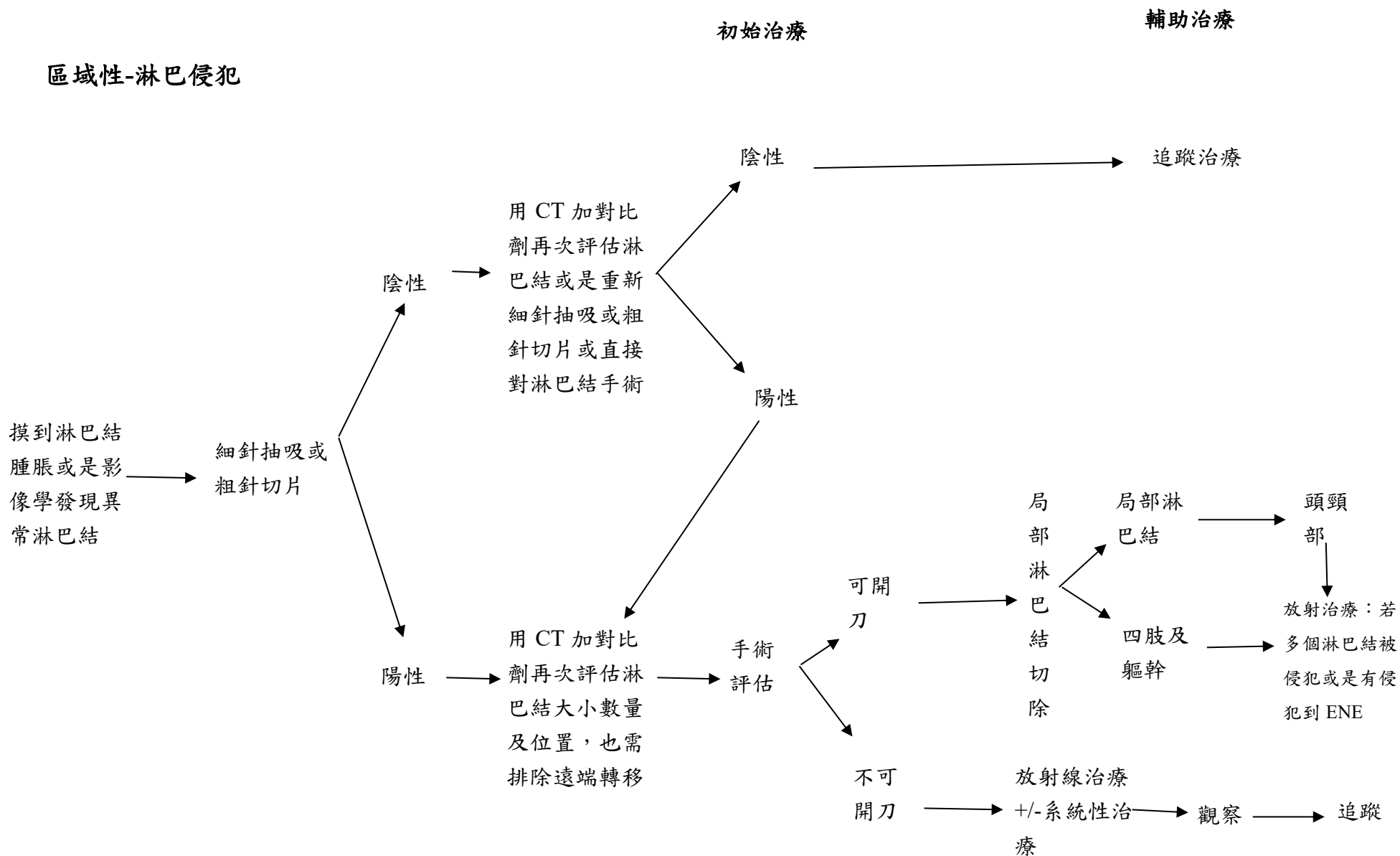
治療前評估

初始治療

追加治療



區域性-淋巴侵犯

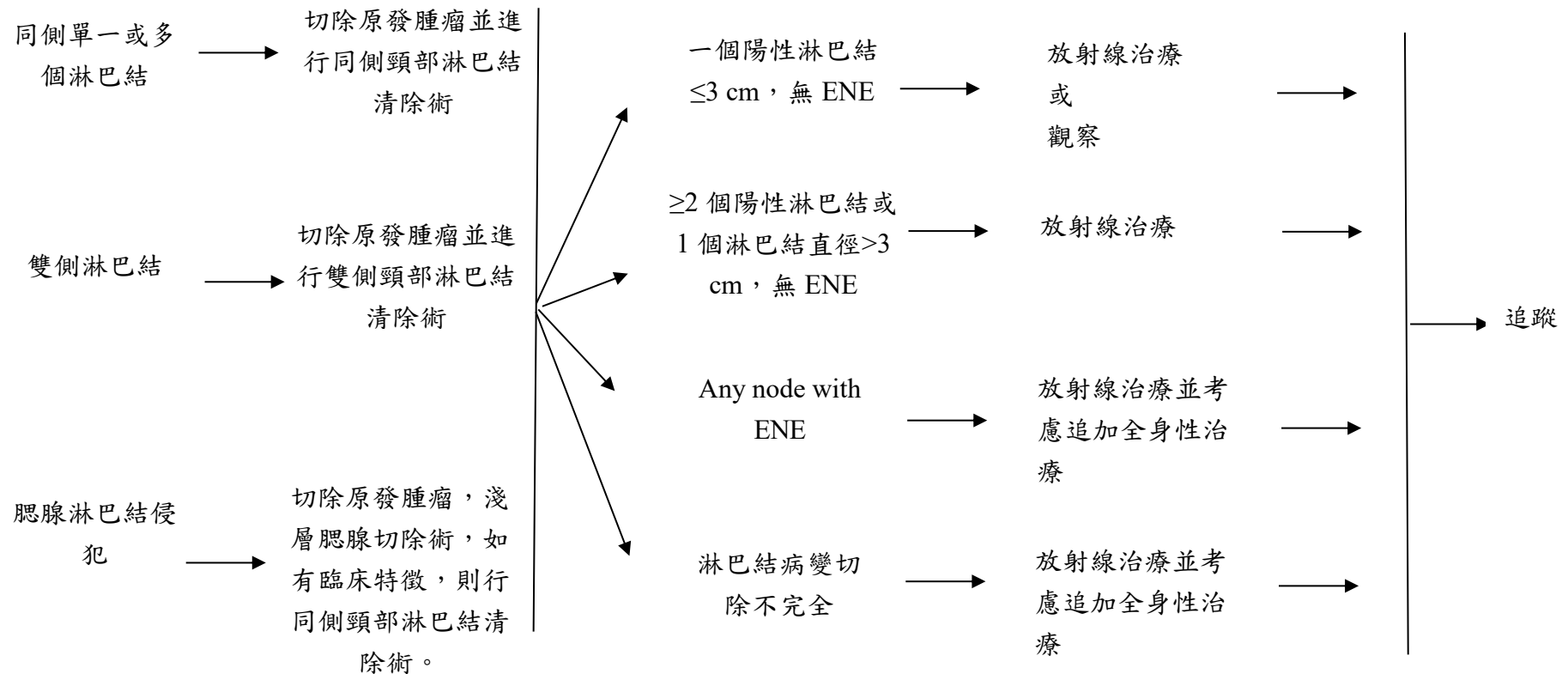


局部淋巴結

頭頸部治療

病理檢查

輔助性治療



追蹤

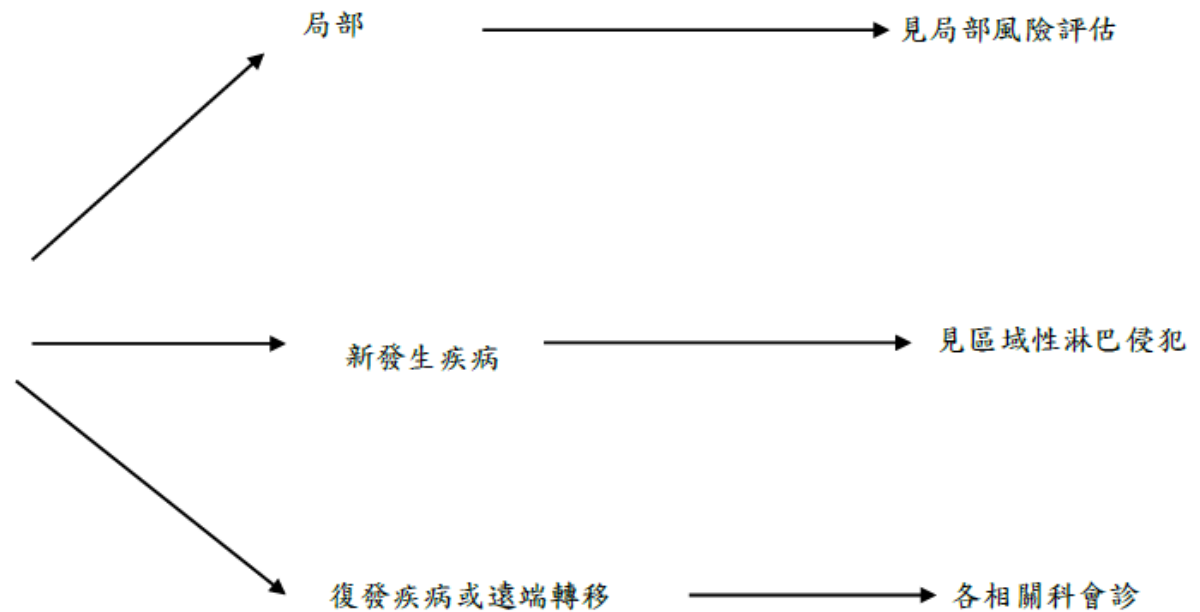
Local disease :

- 前2年：3-12個月追蹤
- 第3年：6-12個月追蹤
之後每年追蹤一次
- 病人衛教
 - 防曬
 - 自我皮膚檢測

Regional disease :

- 第1年：1-3個月追蹤
- 第2年：2-4個月追蹤
- 第3年：4-6個月追蹤
之後每年6-12個月追蹤一次
- 病人衛教
 - 防曬
 - 自我皮膚及淋巴結檢測

復發及病程進展





附件一、局部，高低風險判斷標準

病史及理學檢查	低風險	高風險
位置/大小	Area L < 20mm Area M < 10mm	Area L ≥ 20mm Area M ≥ 10mm Area H 任何大小
邊緣	界限分明	界線模糊
原發/續發	原發	續發
免疫抑制	無	有
病灶位置曾接受過放射線治療或慢性發炎狀態	無	有
生長快速	無	有
神經、血管、淋巴侵犯	無	有
神經學症狀	無	有
病理分類	分化良好	分化不良 (Adenoid-acantholytic, adenosquamous-mucin production, desmoplastic, metaplastic-carcinosarcomatous type)
深度	<2mm or Clark level I II III	≥2mm or Clark level IV V
Area Low risk: trunk and extremities(excluding hands, feet, pretibial area) Area Medium risk: pretibial area, face other than mask area (cheek, forehead, scalp, neck) Area High risk: face mask area+ hands+feet+genitalia (mask area: central face, eyelid, eyebrow, nose, lips-cutaneous and vermillion, chin, mandible, preauricular/postauricular skin sulci, temple, ear) Area H 的腫瘤不論大小都屬於高風險。這些地方通常為了美觀，margin 不夠大，易造成復發。建議使用 Mohs micrographic surgery 可達到邊緣乾淨，且最小切除範圍。對於<6mm 的腫瘤，沒有其他危險因子，建議至少要切除 4mm 的 margin。		



附件二、PRINCIPLES OF RADIATION THERAPY FOR SQUAMOUS CELL SKIN CANCER

Primary Tumor	RT Dosing	Common examples
Adjuvant RT		
• Conventional fractionation (1.8–2 Gy/fraction)	BED10 of 60–79 Gy	• 60–66 Gy in 2 Gy/fraction • 60–66 Gy in 1.8 Gy/fraction (reserved for areas with poor wound healing [eg, lower extremity])
• Hypofractionation	BED10 of 48–70 Gy	• 2.5 Gy x 20 fractions • 3 Gy x 15–17 fractions to 45–51 Gy • 6 Gy x 5 fractions (non-consecutive days)
Definitive EBRT		
• Conventional fractionation (1.8–2 Gy/fraction)	BED10 of 70–84 Gy	• 60 Gy (for small tumors in cosmetically sensitive areas) • 66–70 Gy (for locally advanced tumors involving bone or cartilage)
• Hypofractionation	BED10 of 48–72 Gy	• Tumors <2 cm: 2.5 Gy x 20 fractions • Tumors ≥2 cm: 2.5–3 Gy x 20–22 fractions • 3 Gy x 17–18 fractions to 51–54 Gy • 4.4 Gy x 10 fractions, 4 fractions per week • 6–7 Gy x 5 fractions, 2 treatments per week
Regional Disease		
• Conventional fractionation (1.8–2 Gy/fraction) Macroscopic/gross residual lymph nodes Lymph node + dissected nodal basins PNTS	66–70 Gy 60 Gy 50–66 Gy	
• Undissected at-risk nodal basins	1.8–2 Gy x 25–30 fractions	
Satellitosis/In-Transit Metastasis (S-ITM)		
• Resected	50–60 Gy over 5 to 6 weeks	
• Unresected	60–70 Gy over 6 to 7 weeks	

Conventionally fractionated radiotherapy consists of five daily treatments per week.

Hypofractionated radiotherapy consists of fewer treatments with larger fraction size.

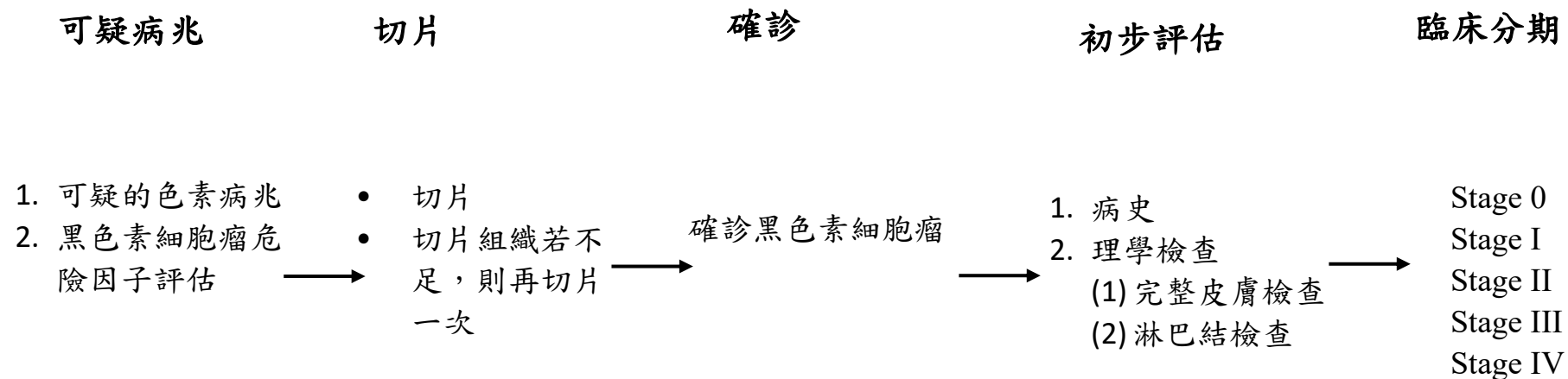


附件三、藥物治療

Chemotherapy regimen	
Published C/T regimens	schedule
Cisplatin 100mg/m ² IV D1	Q21 days *6cycles
5-FU 1g/m ² IV D1-4	Q21 days *6cycles
<i>Khansur T, Kennedy A. Cisplatin and 5-fluorouracil for advanced locoregional and metastatic squamous cell carcinoma of the skin. Cancer 1991;67:2030-2032.</i>	
EGFR inhibitors	
Published C/T regimens	schedule
Cetuximab, 400mg/m ² IV Week 1, then 250mg/m ² QW	Till IV or unacceptable toxicity
<i>Maubec E, Petrow P, Scheer-Senarich I, et al. Phase II study of cetuximab as first-line single-drug therapy in patients with unresectable squamous cell carcinoma of the skin. J Clin Oncol 2011;29:3419-3426.</i>	



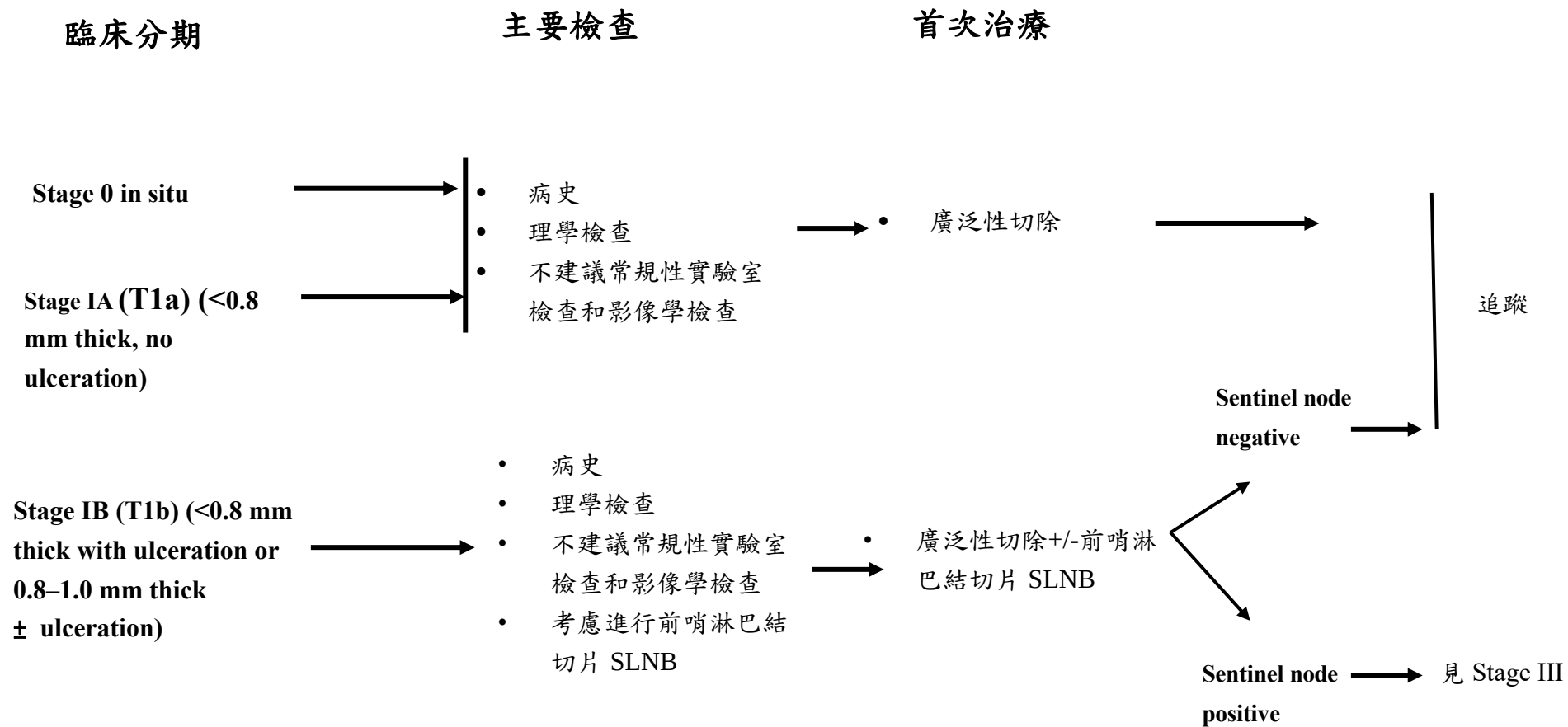
四、黑色素細胞癌



切片病理組織學證實：

- Breslow thickness
- Ulceration status (present or absent)
- Dermal mitotic rate ($\#/mm^2$)
- Assess deep and peripheral margin status
- Microsatellitosis (present or absent)
- Pure desmoplasia if present
- Lymphovascular/ angiolymphatic invasion
- Neurotropism/perineural invasion

ME-1 流程圖



ME-2 流程圖

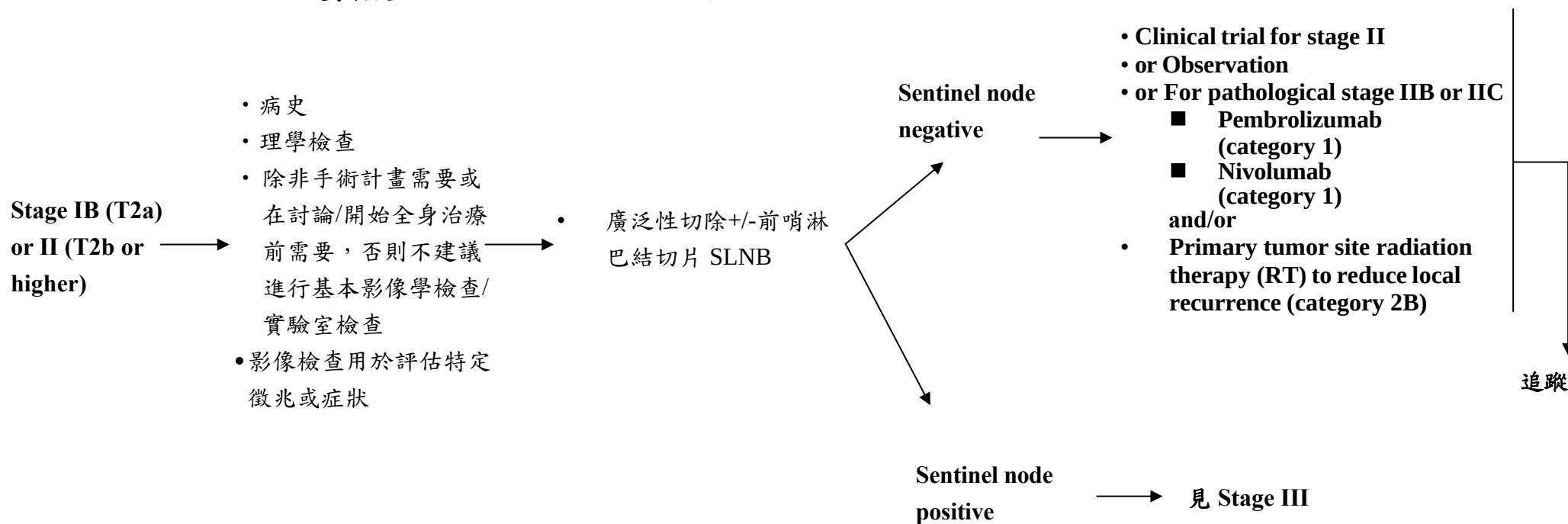


臨床分期

主要檢查

首次治療

輔助治療



ME-3 流程圖

**臨床分期**
(At least stage IIIB)**主要檢查****首次治療****輔助治療**

原發病灶切片
標本(ME-1 流
程圖檢查後的
病理報告)

- 病史及理學檢查
- 不建議進行基本實驗室檢查
- 影像檢查用於評估特定徵兆或症狀

廣泛性切除後
Sentinel node
negative 或是未取淋
巴結 (ME-2 或
ME-3 流程圖手術
後的病理報告)

- BRAF mutation testing
if considering adjuvant
therapy or clinical trial

廣泛性切除後
Sentinel node positive
(ME-2 或 ME-3 流
程圖手術後的病理
報告)

見 ME-5 流程圖

• 廣泛性切除+/-前哨淋
巴結切片 SLNB

如之前沒做前哨淋巴
結切片 SLNB 者，考
慮完成 SLNB

Sentinel node
negative

Sentinel node
positive

Sentinel node
negative 或未
取淋巴結

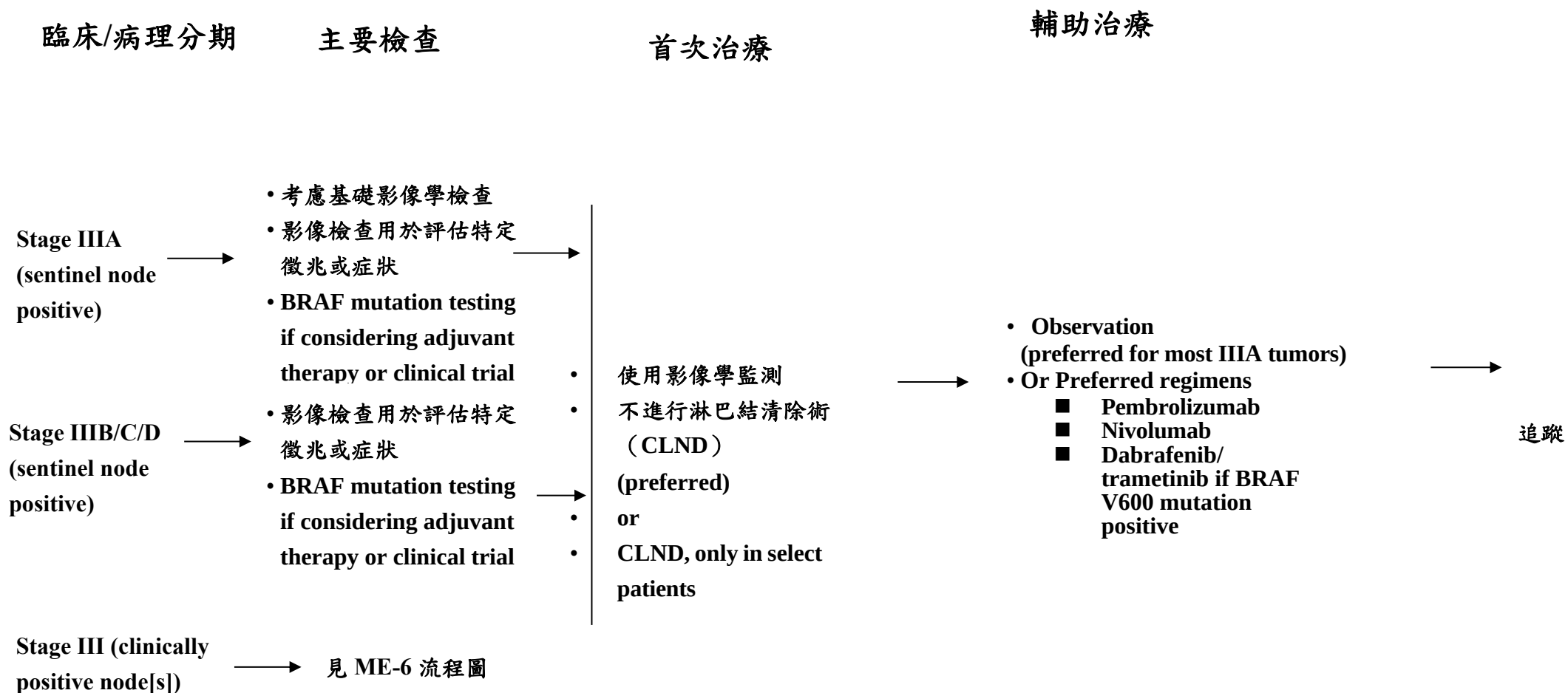
- Clinical trial for stage II
- or Observation
- or For pathological stage IIB or IIC
 - Pembrolizumab
 - Nivolumab
 - Dabrafenib/
trametinib if BRAF
V600 mutation
positive

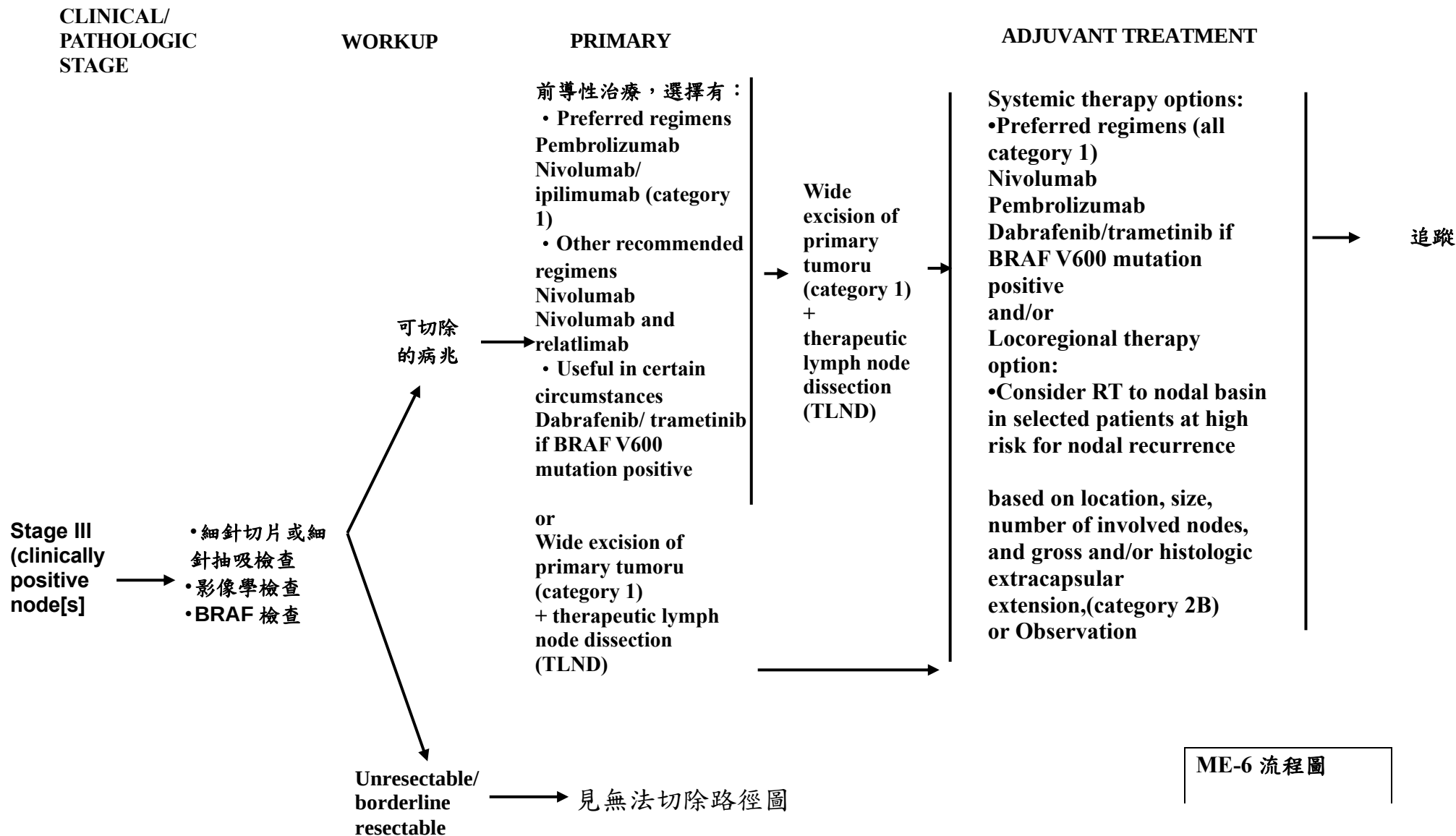
見 ME-5 流程圖

- Clinical trial for stage II
- or Observation
- or For pathological stage IIB or IIC
 - Pembrolizumab
 - Nivolumab
 - Dabrafenib/
trametinib if BRAF
V600 mutation
positive

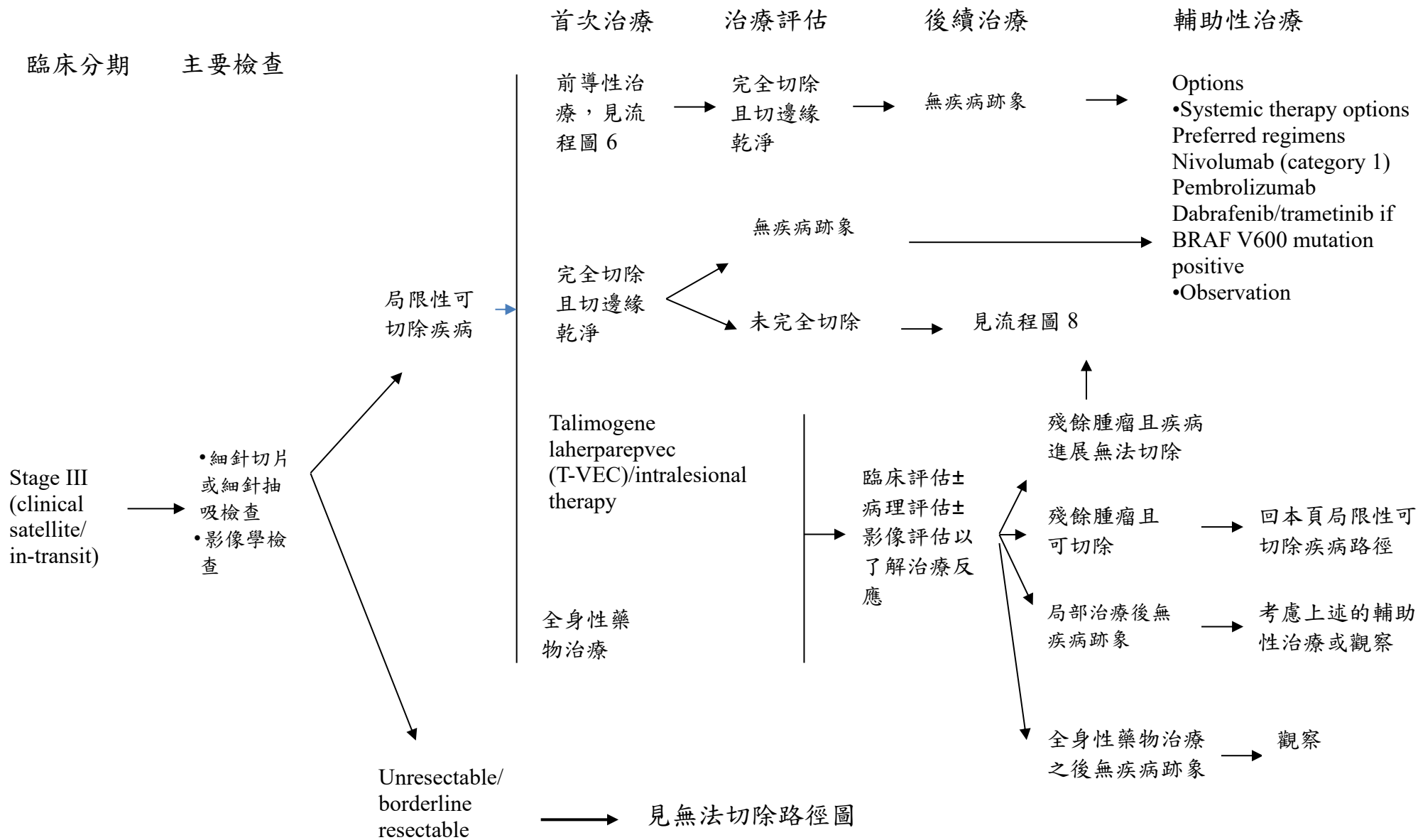
ME-4 流程圖

追蹤

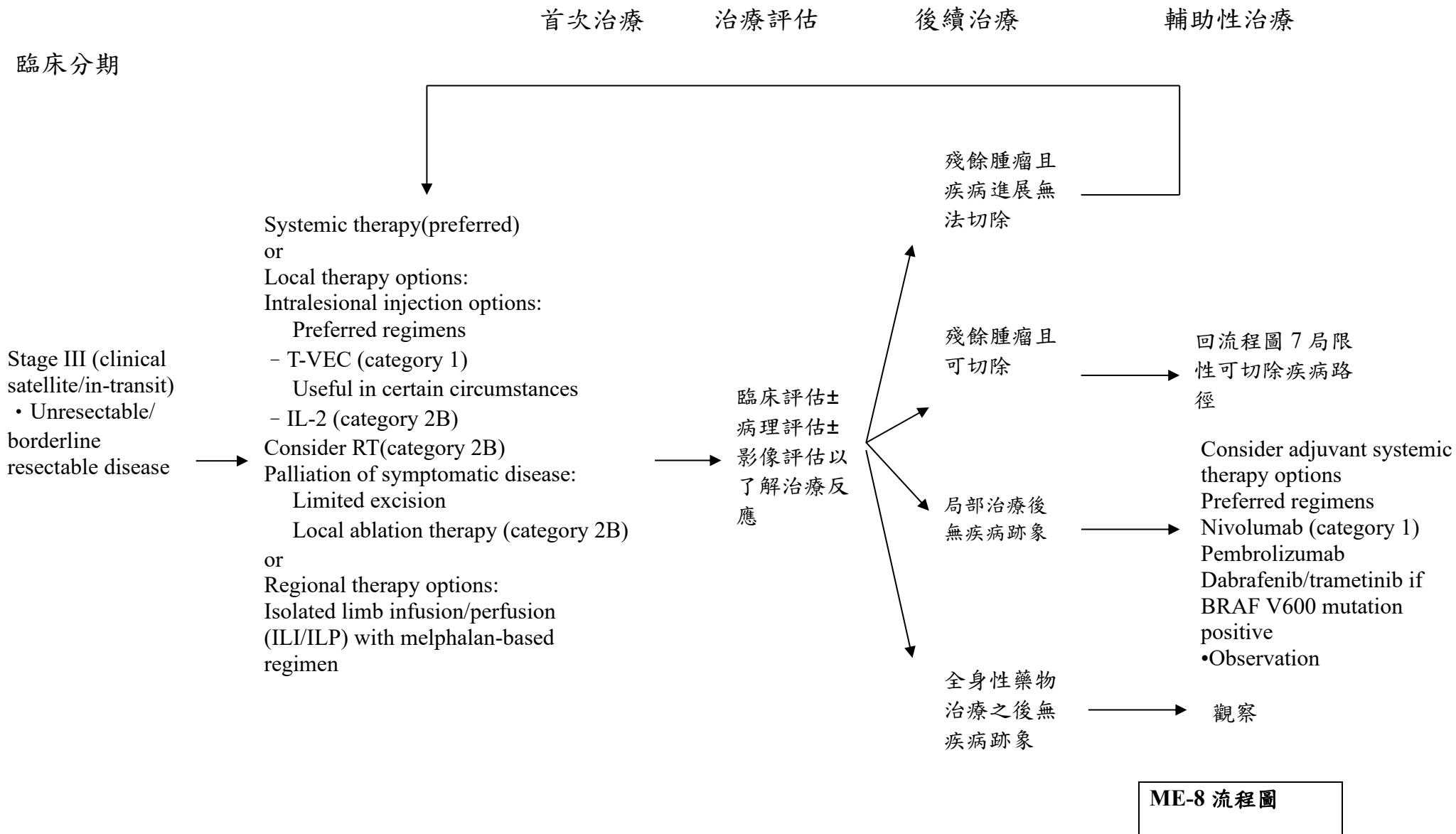


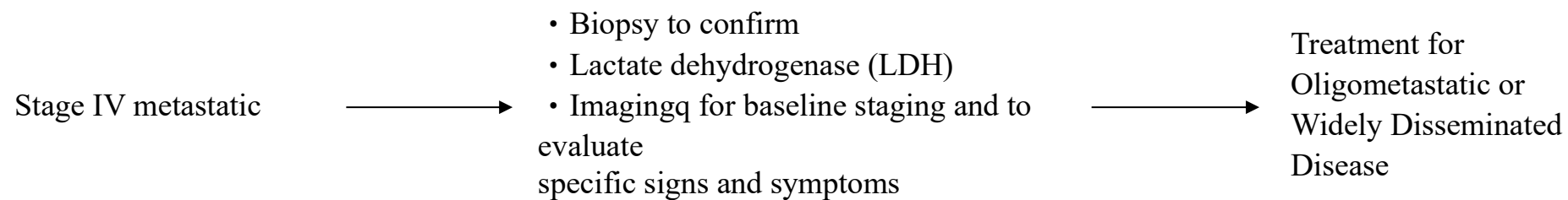


ME-6 流程圖



ME-7 流程圖



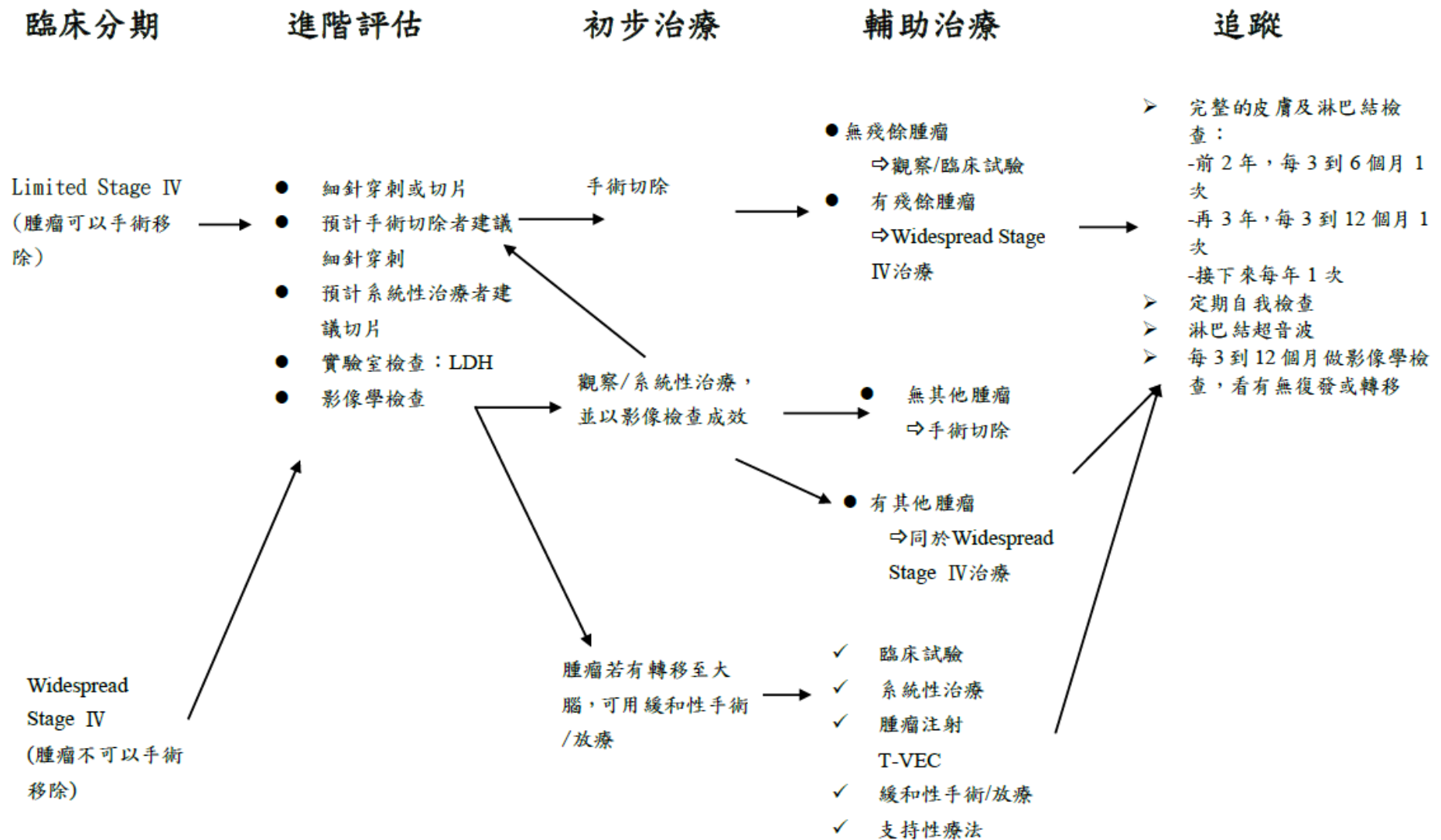


ME-9 流程圖

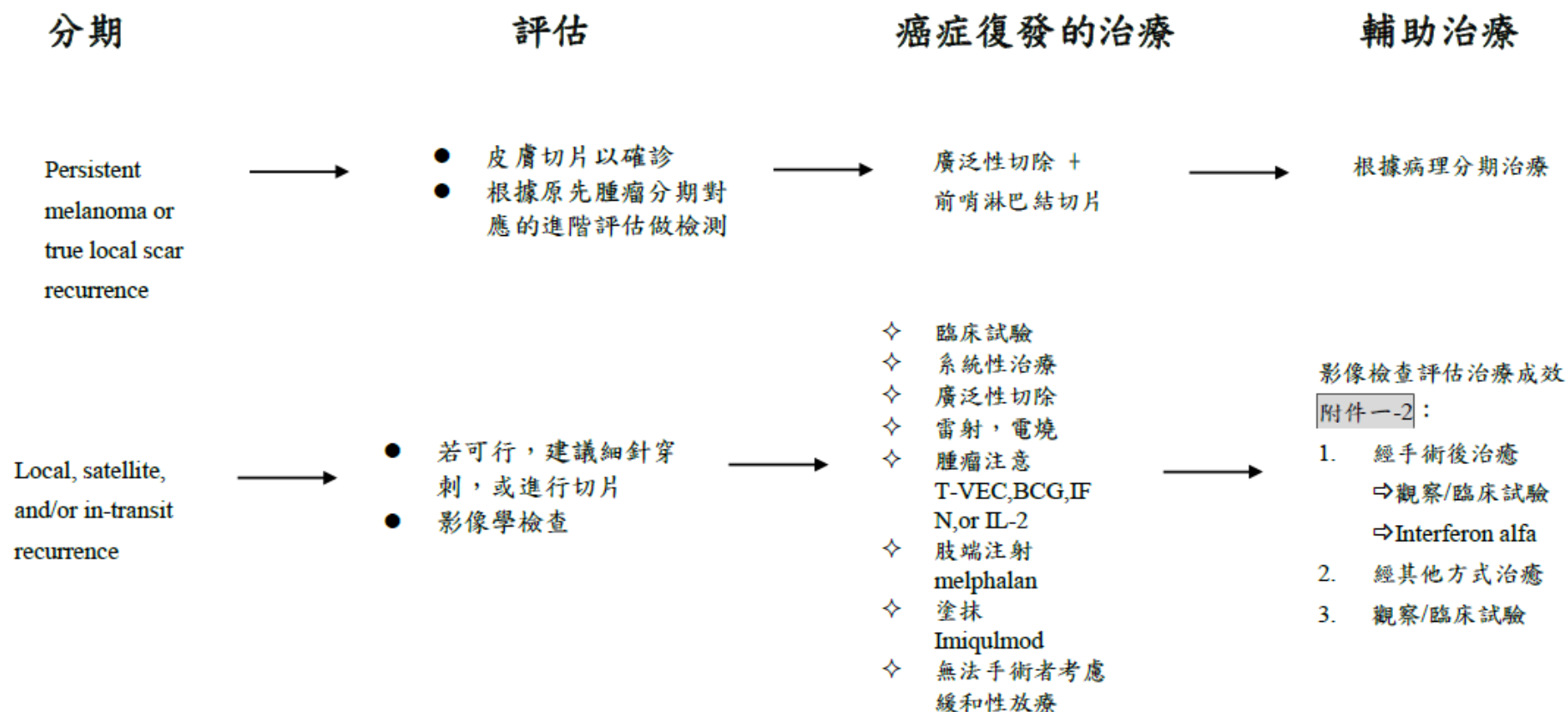


追蹤

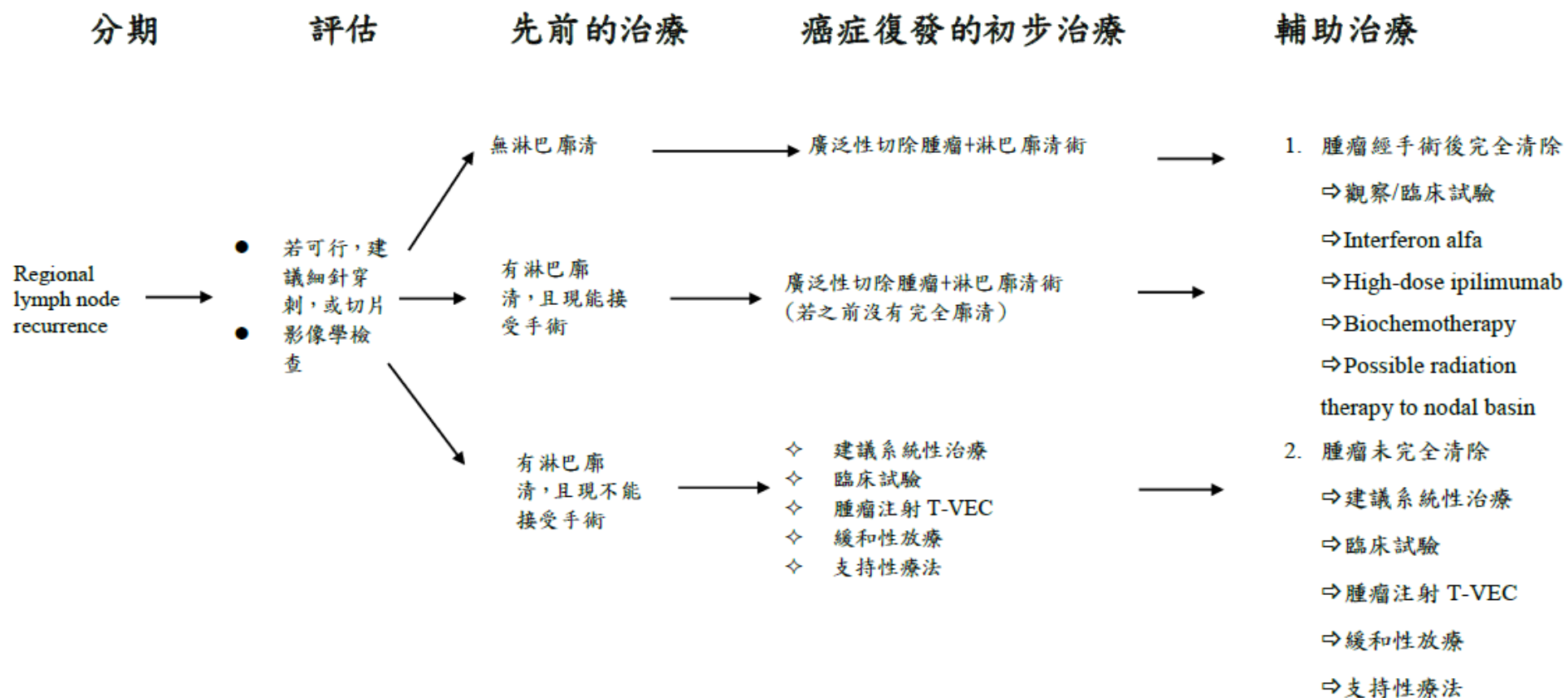
Stage 0 in situ	Stage IA–IIA NED	Stage IIB–IV NED
• See Common Follow-up Recommendations for All Patients • H&P (with emphasis on skin) at least annually • Routine blood tests are not recommended • Routine imaging to screen for asymptomatic recurrence or metastatic disease is not recommended	• See Common Follow-up Recommendations for All Patients • H&P (with emphasis on nodes and skin) every 6–12 mo for 5 y, then annually as clinically indicated • Routine blood tests are not recommended • Routine imaging to screen for asymptomatic recurrence or metastatic disease is not recommended • Imaging as indicated to investigate specific signs or symptoms	• See Common Follow-up Recommendations for All Patients • H&P (with emphasis on nodes and skin) every 3–6 mo for 2 y, then every 3–12 mo for 3 y, then annually as clinically indicated • Routine blood tests are not recommended, unless indicated for post- treatment monitoring • Imaging as indicated to investigate specific signs or symptoms • Consider imaging every 3–12 months for 2 years, then every 6–12 months for another 3 yearsxxx (unless otherwise mandated by clinical trial participation) to screen for recurrence or metastatic disease (category 2B) • Routine imaging to screen for asymptomatic recurrence or metastatic disease is not recommended after 3–5 years, depending on risk of relapse



Node-negative recurrence treatment



Regional lymph node recurrence treatment





PRINCIPLES OF RADIATION THERAPY FOR MELANOMA

- Consider RT in the following situations:
 - Interactions between radiation therapy and systemic therapies (eg, BRAF inhibitors, interferon alfa-2b, immunotherapies, checkpoint inhibitors) need to be very carefully considered as there is potential for increased toxicity
- 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
 - Adjuvant treatment in selected patients following resection of clinically appreciable nodes (category 2B) If 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
 - ◆ Stereotactic radiosurgery as primary treatment
 - ◆ Stereotactic radiosurgery as adjuvant treatment
 - ◆ Whole brain radiation therapy as primary treatment
 - ◆ Whole brain radiation therapy as adjuvant treatment (category 3)
 - Other symptomatic or potentially symptomatic soft tissue and/or bone metastases



附件三、系統性治療

ADJUVANT Chemotherapy

Pembrolizumab

Drug Combination	Dosage	Route of administration	Times	Frequency/Duration
Pembrolizumab	200 mg	IV	drip 30 mins, Day 1 of a 21-day	cycle for 2 cycle (up to 6 weeks) prior to surgery
Ref.	1. Robert C, Hamid O, Daud A, Hodi FS, et al. Five-year survival outcomes for patients with advanced melanoma treated with pembrolizumab in KEYNOTE-001. <i>Ann Oncol.</i> 2019;30(4):582–588. 2. Pembrolizumab in Chinese patients with advanced melanoma: 3-year follow-up of the KEYNOTE-151 study. <i>PubMed.</i> 2022; (NCT02821000). 3. Pembrolizumab (Keytruda) in advanced melanoma: a review of efficacy evidence. <i>PubMed.</i> 2023. 4. Efficacy of pembrolizumab for advanced/metastatic melanoma: a meta-analysis. <i>PubMed.</i> 2021. 5. Pembrolizumab: A Review in Advanced Melanoma. <i>PubMed.</i> 2016.			

Nivolumab

Drug Combination	Dosage	Route of administration	Times	Frequency/Duration
Nivolumab	200 mg fix	IVD	drip 60 mins, d1	Q2W
Ref.	1. Weber JS, D'Angelo SP, Minor D, et al. Nivolumab versus chemotherapy in patients with advanced melanoma who progressed after anti-CTLA-4 treatment (CheckMate 037): a randomised, controlled, open-label, phase 3 trial. <i>Lancet Oncol.</i> 2015;16(4):375–384.			



	2. Wolchok JD, Chiarion-Sileni V, Gonzalez R, et al. Overall survival with combined nivolumab and ipilimumab in advanced melanoma (CheckMate 067): 10-year follow-up results. <i>N Engl J Med</i>. 2024; doi:10.1056/NEJMoa2208661. 3. National Cancer Institute. Nivolumab-based treatments for advanced melanoma: Summary of efficacy and survival data from CheckMate trials. <i>Cancer.gov</i>.
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For BRAF V600E-mutated tumors

Dabrafenib and Trametinib

藥名	Dabrafenib 150 mg PO twice daily Trametinib 2 mg PO daily
Ref.	1. Long GV, Stroyakovskiy D, Gogas H, et al. Dabrafenib and trametinib versus dabrafenib and placebo for Val600 BRAF-mutant melanoma: a multicentre, double-blind, phase 3 randomised controlled trial. <i>Lancet</i>. 2015;386(9992):410-419. doi:10.1016/S0140-6736(15)60972-2. 2. Robert C, Karaszewska B, Schachter J, et al. Improved overall survival in melanoma with combined dabrafenib and trametinib. <i>N Engl J Med</i>. 2015;372(1):30-39. 3. Sun C, Wang L, Huang S. Dabrafenib and trametinib, alone and in combination for BRAF-mutant metastatic melanoma. <i>Oncologist</i>. 2014;19(8): 846-854.



OTHER SYSTEMIC THERAPIES

Cytotoxic Regimens for Metastatic Disease¹

- Dacarbazine
- Temozolomide
- Paclitaxel
- Albumin-bound paclitaxel
- Carboplatin/paclitaxel

Biochemotherapy for Metastatic Disease¹

- Dacarbazine or temozolomide, and cisplatin or carboplatin, with or without vinblastine or nitrosourea, and IL-2 and interferon alfa-2b

Biochemotherapy for Adjuvant Treatment of High-Risk Disease

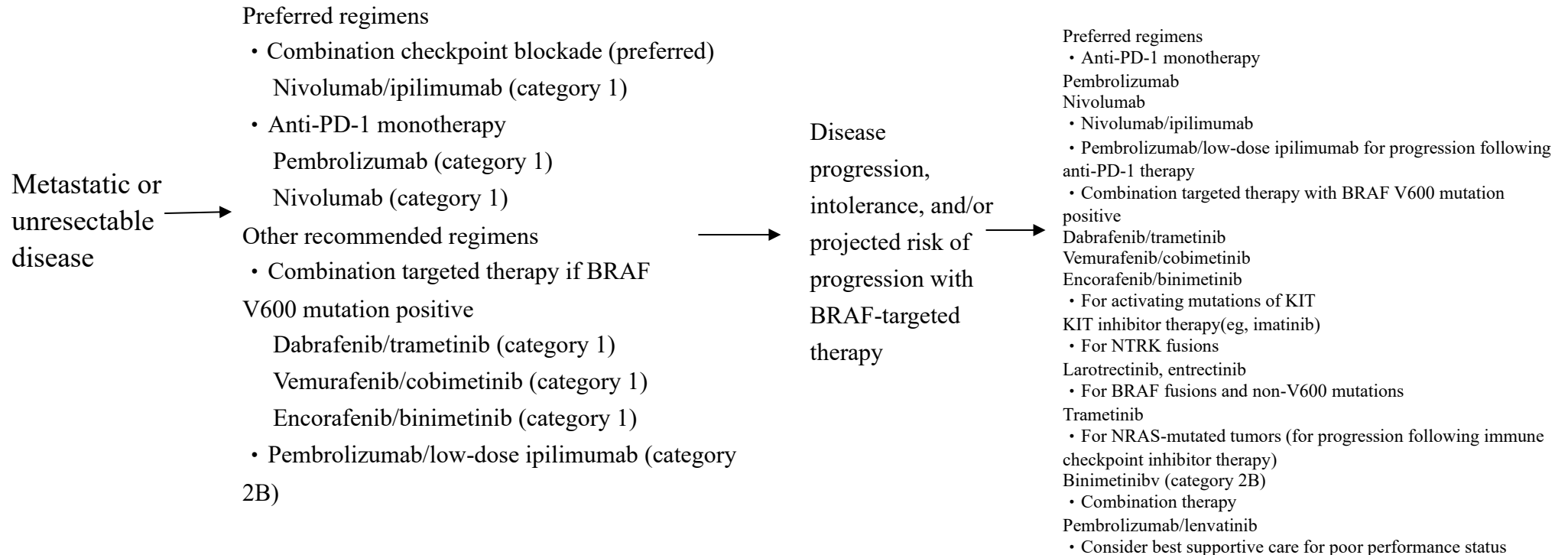
- Dacarbazine, cisplatin, vinblastine, IL-2, and interferon alfa-2b (category 2B)



附件四、對於轉移性或不可切除黑色素瘤的全身治療 Systemic therapy for metastatic or unresectable diseases

FIRST-LINE THERAPY

SECOND-LINE OR SUBSEQUENT THERAPY





五、其他細胞型態(皮膚 T 細胞淋巴瘤 mycosis fungoides,MF)參照台灣皮膚醫學會共識手冊

診斷：皮膚切片評估、常規血液檢查、影像學檢查(包含電腦斷層或是核磁共振、正子攝影)

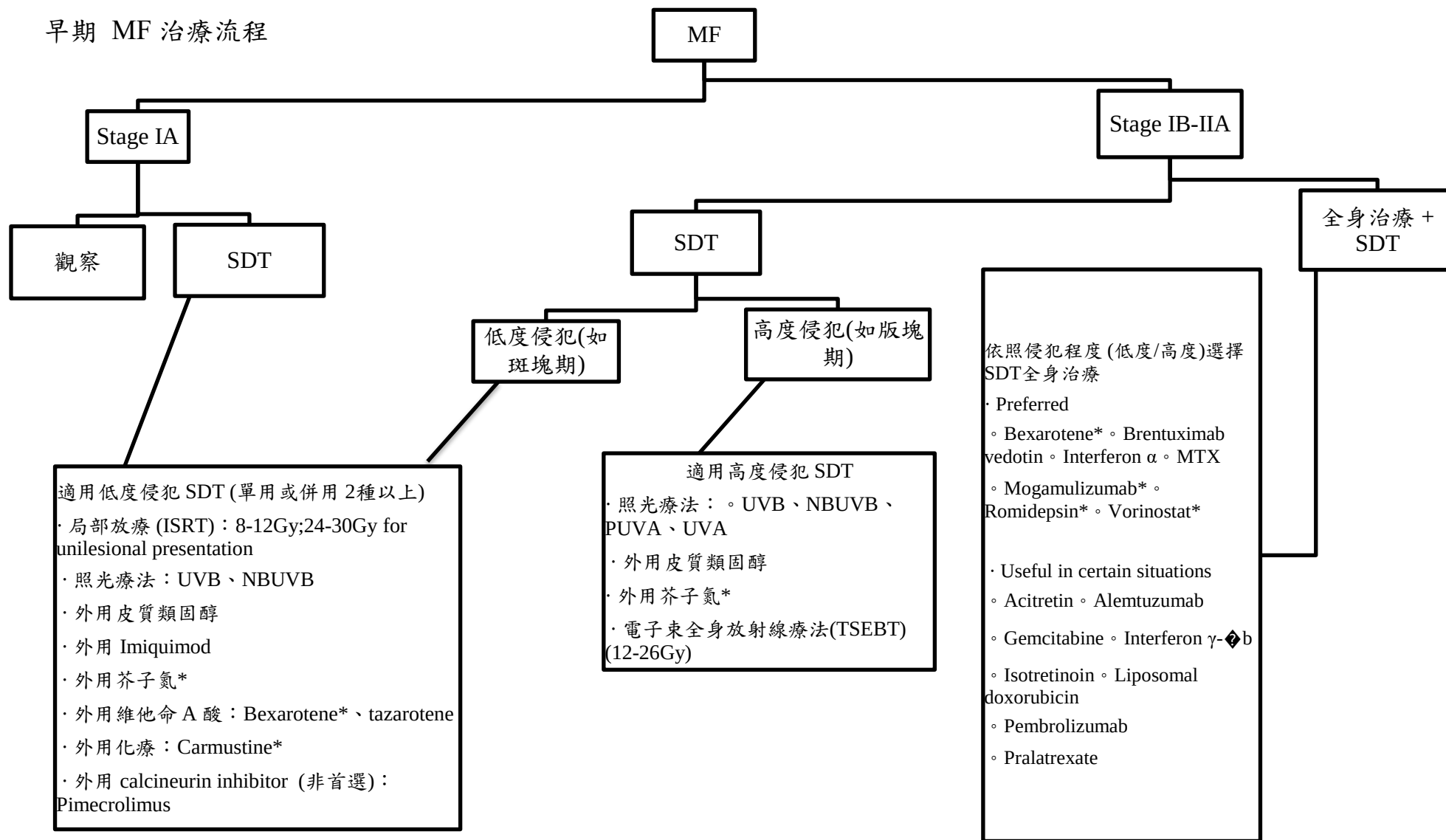
分期：

Skin(T)	T0	Absence of clinically suspicious lesions		
	T1	Patches, plaques, or papules,	T1a	Patch only lesions
			T1b	Plaque/papule+/- patch lesions
	T2	Patches, plaques, or papules ≥10% BSA	T2a	Patch only lesions T2B Plaque/papule+/- patch lesions
			T2b	Patch only lesions T2B Plaque/papule+/- patch lesions
	T3	One or more tumors≥1 cm diameter		
T4	Confluence of erythema covering ≥80% BSA			
Nodes (N)	N0	No clinically abnormal LN; no biopsy necessary		
	N1	N1a	Pathology Dutch grade 1 or NCI LN 0-2: clone negative or equivocal	
		N1b	Pathology Dutch grade 1 or NCI LN 0-2: clone positive and identical to skin	
	N2	N2a	Dutch grade 2, NCI LN3: clone negative or equivocal	
		N2b	Dutch grade 2, NCI LN3: clone positive and identical to skin	
	N3 (lymphoma)	N3a	Dutch grade 3-4, NCI LN4: clone negative or equivocal	
		N3b	Dutch grade 3-4, NCI LN4: clone positive and identical to skin	
Nx	Clinically abnormal peripheral or central lymph node but no pathologic determination of representative LN. Other surrogate means of determining involvement may be determined by Tri-Society consensus			
Viscera	M0	No visceral involvement		



(M)	M1a	BM only involvement	Clone positive and identical to skin	
			Clone negative or indeterminate	
	M1b	Non-BM visceral involvement	Clone positive and identical to skin	
			Clone negative or indeterminate	
	Mx	Visceral involvement is neither confirmed nor refuted by available pathologic or imaging assessment		
Blood (B)	B0	B0A	Clone negative or equivocal	Absence of significant blood involvement
		B0B	Clone positive and identical to skin	
	B1	B1A	Clone negative or equivocal	Low blood tumor burden
		B1B	Clone positive and identical to skin	
	B2	B2A	Clone negative or equivocal	High blood tumor burden
		B2B	Clone positive and identical to skin	
	Bx	BxA	Clone negative or equivocal	Unable to quantify blood involvement according to agreed upon guidelines
		BxB	Clone positive and identical to skin	

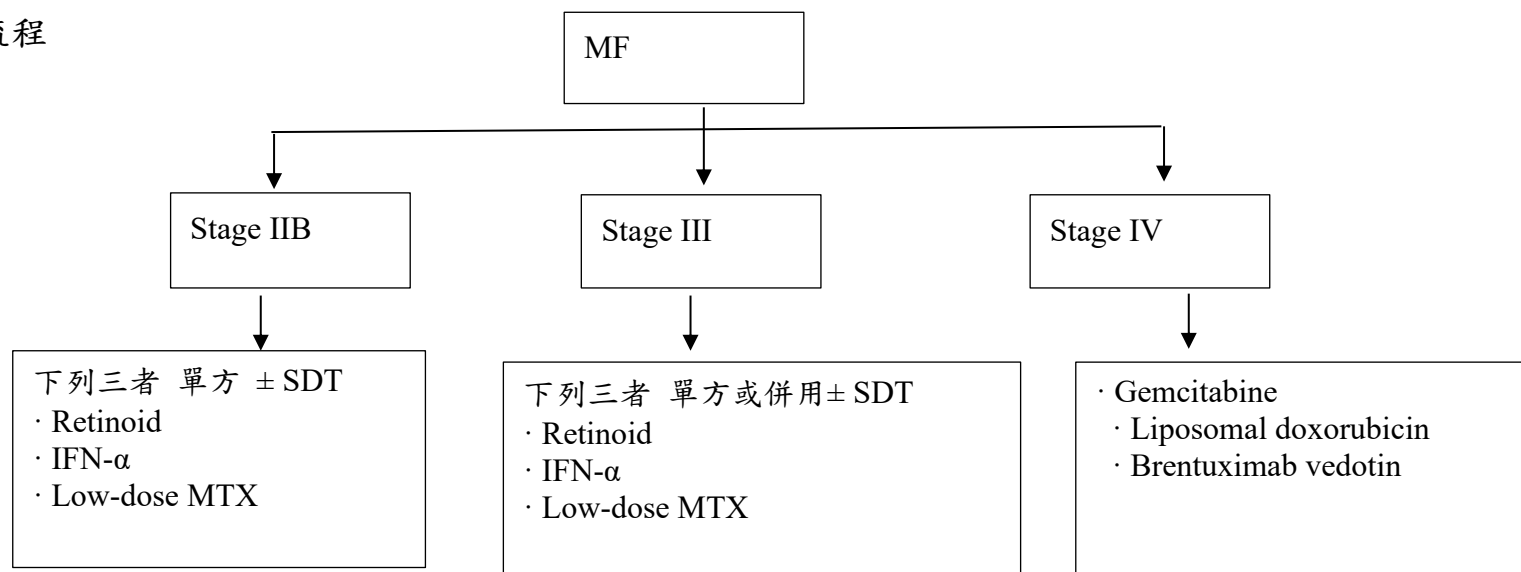
早期 MF 治療流程



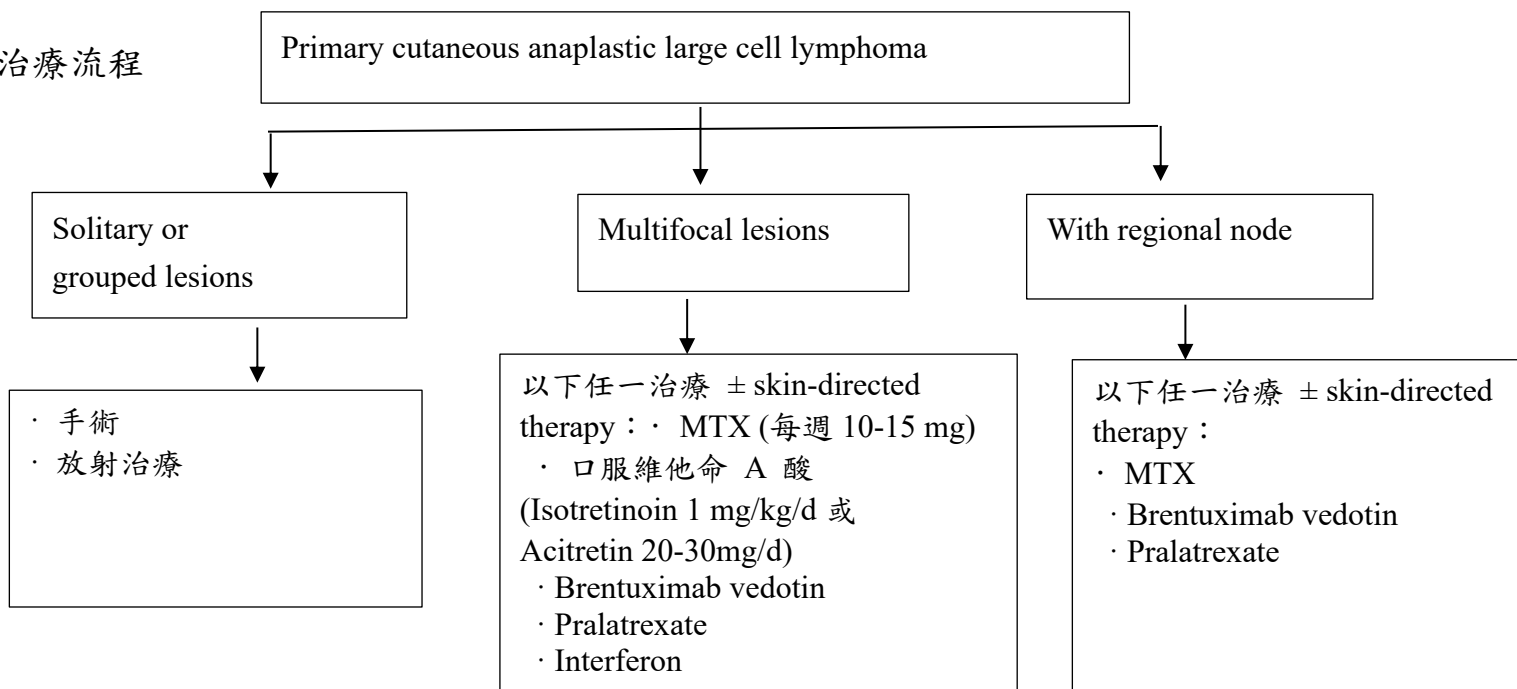


*該品項截至 2023 年 12 月於台灣未取得藥物許可證

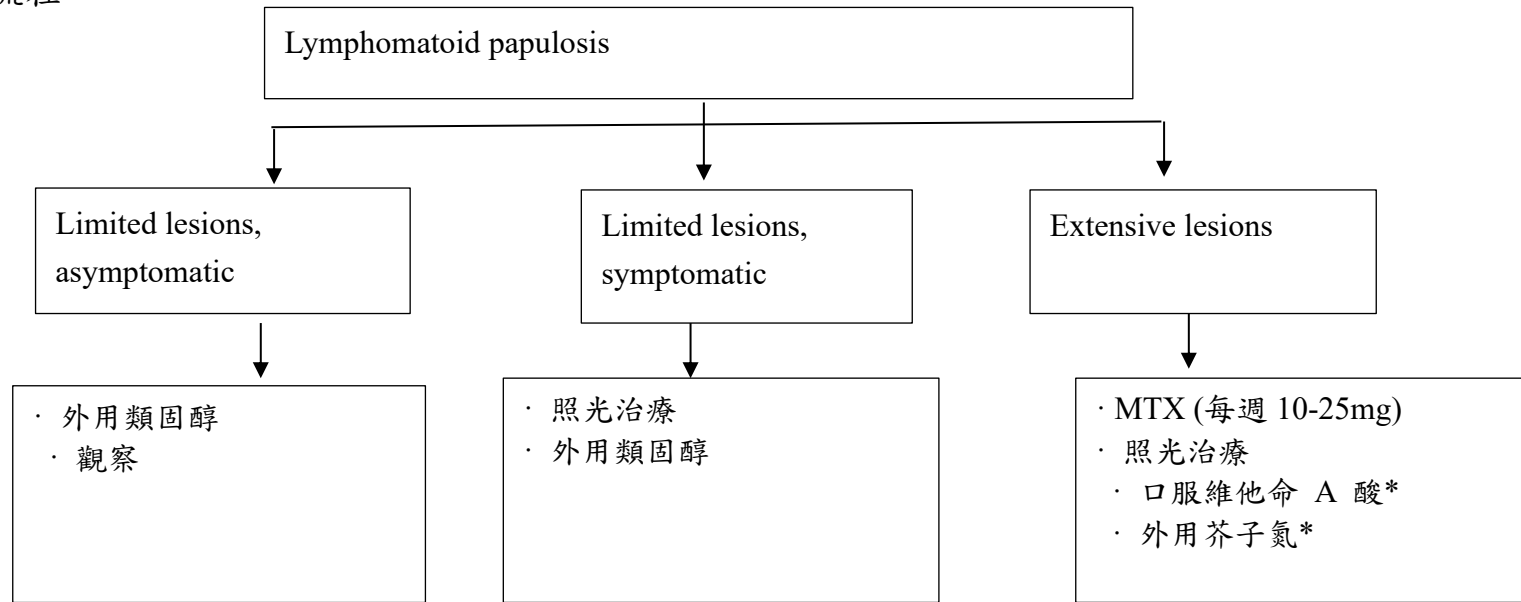
MF 治療流程



PC-ALCL 治療流程



LyP 治療流程



* Bexarotene、外用芥子氮截至 2023 年 12 月於台灣未取得藥品許可證

其他細胞型態(Dermatofibrosarcoma Protuberans, DFSP)

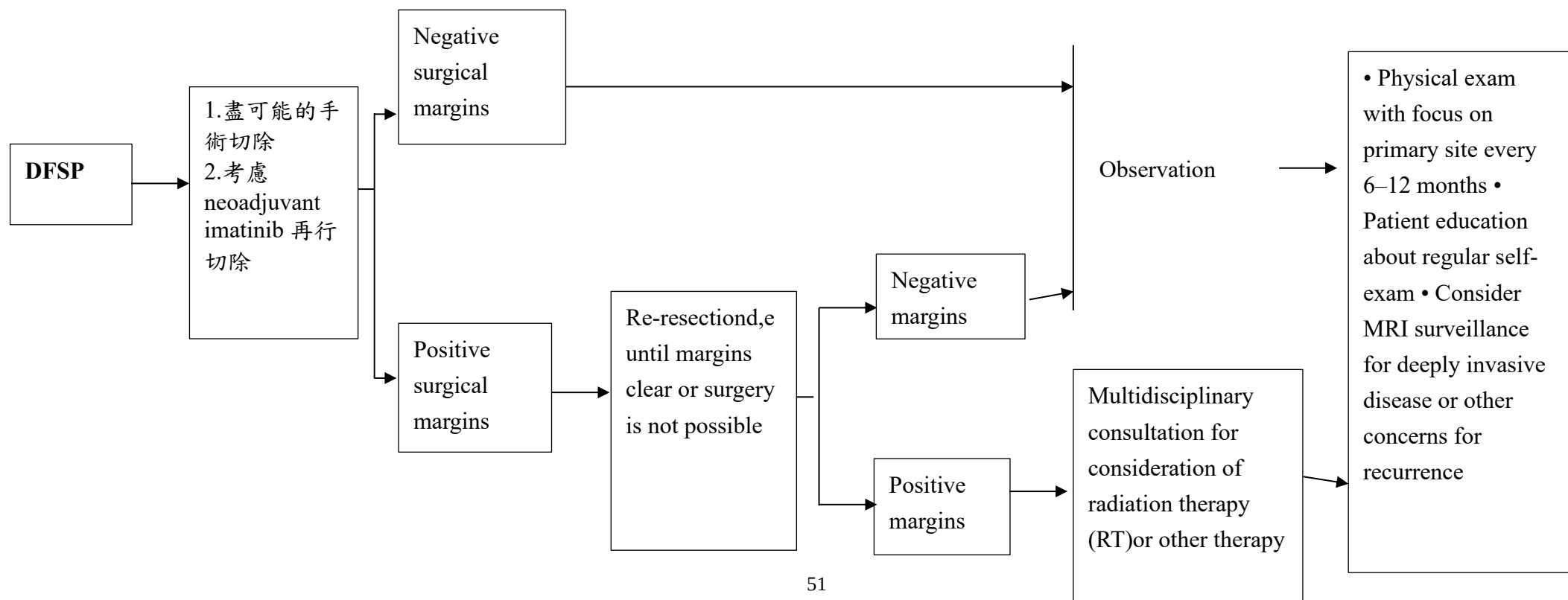
診斷：皮膚切片評估、常規血液檢查、影像學檢查(選擇性)

DIAGNOSIS

TREATMENT

ADJUVANT TREATMENT

FOLLOW-UP





六、安寧緩和照護原則

若預期疾病難以治癒時，病人存活期小於 6 個月便適合安寧療護(Pomeranz & Brustman, 2005；Waldrop & Rinfrette, 2009)。若藉由症狀、檢驗數據、及確切的腫瘤診斷，證實臨床上該惡性腫瘤已經廣泛侵犯、或進展快速；功能分數（Palliative Performance Scale）低於 70%；拒絕進一步腫瘤治癒性治療，或者在治療之下仍持續惡化者，即可轉介緩和醫療團隊（彭等，2006）。



七、參考文獻

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2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016;66:7-30. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26742998>.
3. Rogers HW, Weinstock MA, Feldman SR, Coldiron BM. Incidence estimate of nonmelanoma skin cancer (keratinocyte carcinomas) in the U.S. population, 2012. JAMA Dermatol 2015;151:1081-1086. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25928283>.
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皮膚癌各期治療完治定義

細胞型態	期別	治療方式	完治定義	備註
基底細胞癌 鱗狀上皮細胞癌	無遠端轉移	1.外科治療(手術切除、刮除或電燒) 2.不適合手術者：放射線治療	1.手術邊緣乾淨 2.完成放射線治療	
	有遠端轉移	全身性治療(化療)	完成醫師規劃之療程	
黑色素細胞瘤	0、I	手術切除	手術邊緣乾淨	
	II	手術切除佐以輔助性治療(免疫治療或是放射線治療)	手術邊緣乾淨且完成輔助性治療	
	III	1.前導性治療後手術切除，佐以輔助性治療(免疫治療或是放射線治療) 2. 手術切除，佐以輔助性治療(免疫治療或是放射線治療)		
	IV	全身性治療合併手術切除或是放射線治療	完成醫師規劃之療程	

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