

高雄榮民總醫院

皮膚癌(SCC、Keratoacanthoma)

診療原則

修訂日期:2024.05.14

癌委會公告日期:2024.06.03

SCC診療指引審視修訂會議討論日期

● 前次會議：2023/05/23

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



鱗狀上皮細胞癌(SCC、Keratoacanthoma)

診斷

初步評估

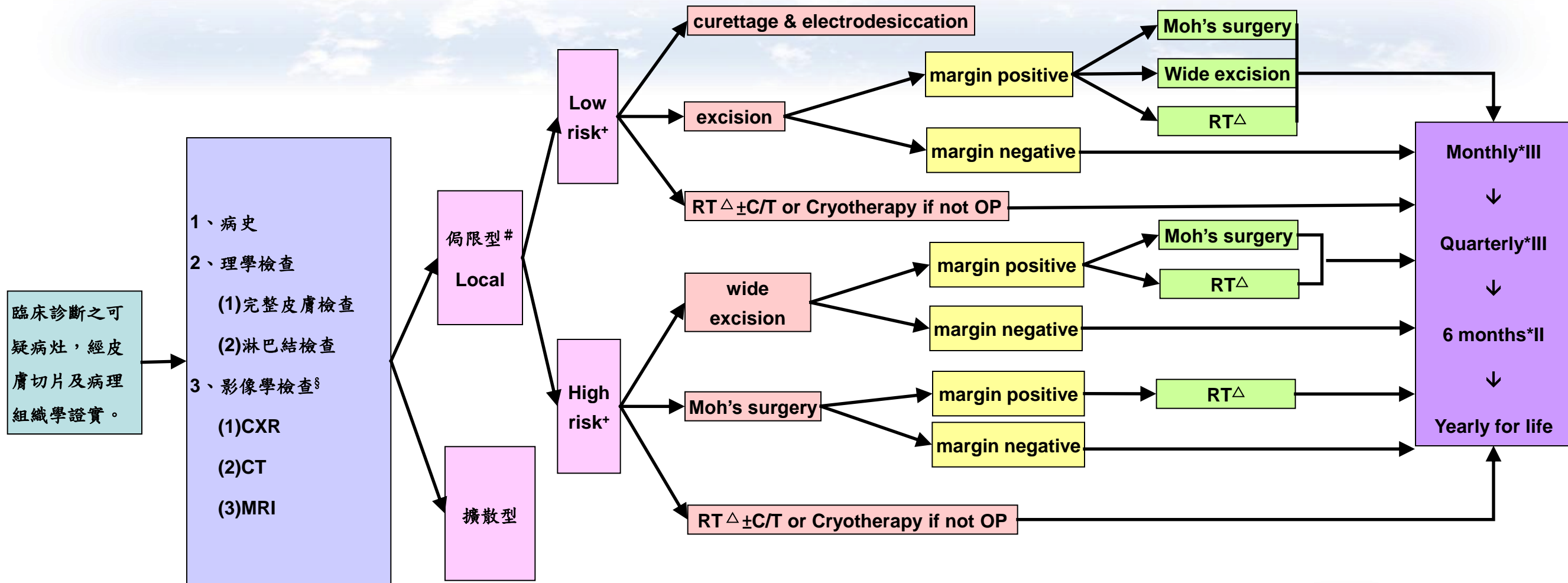
分期

初始治療

療效評估

輔助治療

追蹤



§ : Image studies is indicated for extensive disease (deep structural involvement such as bone, deep soft tissue, perineural disease)

+ : 附件一

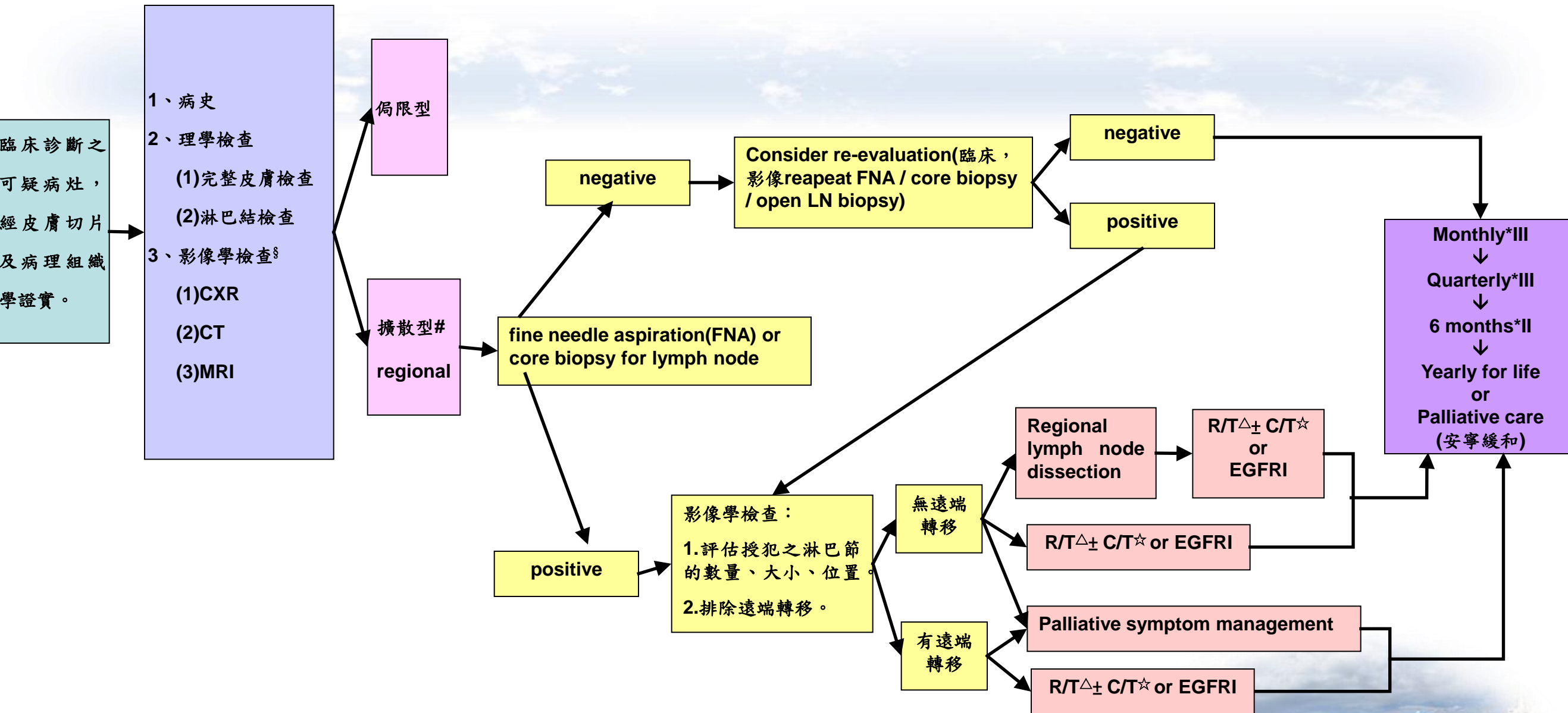
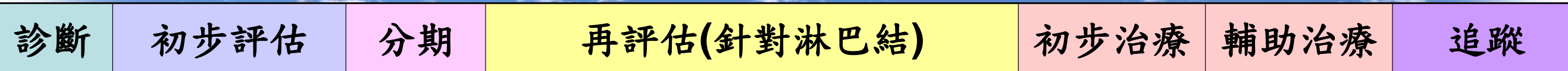
△ : RT主要針對手術不適用之情形, 附件二

: T any, N0, M0, 附件三



皮膚癌
多專科團隊

鱗狀上皮細胞癌(SCC、Keratoacanthoma)



§ : Image studies is indicated for extensive disease (deep structural involvement such as bone, deep soft tissue, perineural disease) if perineural disease is suspected, MRI is preferred.

≡ : Palliative symptom management, including salvage C/T

△ : RT主要針對手術不適用之情形, 附件二

: Palpable regional lymph node(s) or abnormal lymph nodes identified by image studies. (擴散型的“初始皮膚病灶”治療同局限型中high risk)

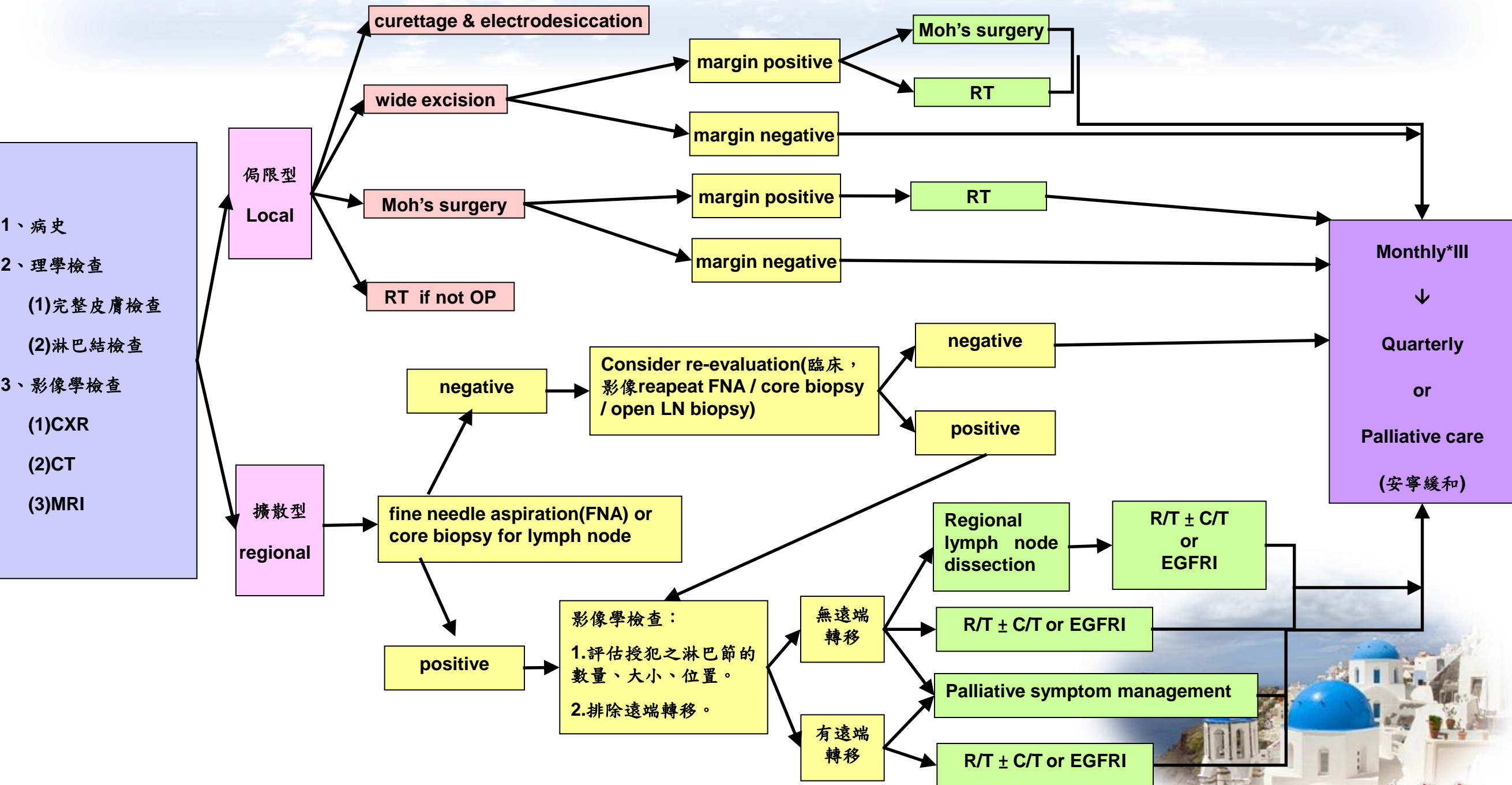
T any, N1, M0 or M1 (附件三)

☆ : chemotherapy regimen & EGFR, 附件四



鱗狀上皮細胞癌(SCC、Keratoacanthoma)

復發



鱗狀上皮細胞癌(SCC、Keratoacanthoma)

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。



PRIMARY TREATMENT^{i,j,k,l}

Field cancerization^g/
Confluent epidermal
dysplasia

- **Prevention^{m,n}:**
 - ▶ **Daily sunscreen^o**
 - ▶ **Nicotinamide^p**
- **Accepted treatment modalities**
 - ▶ **Topical:**
 - ◇ **5-fluorouracil (5-FU)-based regimens are preferred**
 - **Topical 5-FU ± calcipotriol (calcipotriene)^{q,r,s}**
 - ▶ **Destructive:**
 - ◇ **Ablative laser vermilionectomy (may be of value in the treatment of extensive actinic cheilitis)**
 - ◇ **Ablative skin resurfacing (eg, laser, dermabrasion)**
 - ◇ **Chemical peels (trichloroacetic acid)**
 - ◇ **Cryotherapy^t**
 - ◇ **Curettage and electrodesiccation (C&E)**
 - ▶ **Other modalities that may be considered:**
 - ◇ **Photodynamic therapy (PDT) (eg, topical aminolevulinic acid [ALA], porfimer sodium)**
 - ◇ **Systemic retinoids (eg, acitretin,ⁿ isotretinoin)**
 - ◇ **Capecitabine^{l,u} (for severe refractory disease that has progressed on oral retinoids)**

^g Field cancerization defined as UV induced confluent dysplasia clinically manifested as diffuse actinic keratoses and superficial (in situ) SCC. Willenbrink TJ, et al. J Am Acad Dermatol 2020;83:709-717.

ⁱ [Principles of Systemic Therapy \(SCC-F 1 of 4\)](#).

^j Actinic keratoses that have an atypical clinical appearance or do not respond to appropriate therapy should be biopsied for histologic evaluation.

^k Actinic keratoses should be treated at first development.

^l Comejo CM, et al. J Am Acad Dermatol 2020;83:719-730.

^m Use of oral retinoids (eg, acitretin, isotretinoin) is a therapeutic option used to reduce the development of actinic keratoses. Side effects of oral retinoids may be significant, especially in patients of childbearing potential, and therapeutic benefits are limited to the duration of the regimen. Topical retinoids were shown not to reduce development of actinic keratosis.

ⁿ Badri O, et al. Dermatol Surg 2021;47:125-126.

^o Green AC, et al. J Clin Oncol 2011;29:257-263.

^p Oral nicotinamide may be effective in reducing the development of CSCCs.

^q The longest duration of prophylaxis against SCC has been demonstrated with topical 5-FU plus calcipotriol.

^r Cunningham TJ, et al. J Clin Invest 2017;127:106-116.

^s Jansen MHE, et al. N Engl J Med 2019;380:935-946.

^t Afsar FS, et al. Postepy Dermatol Alergol 2015;32:88-93.

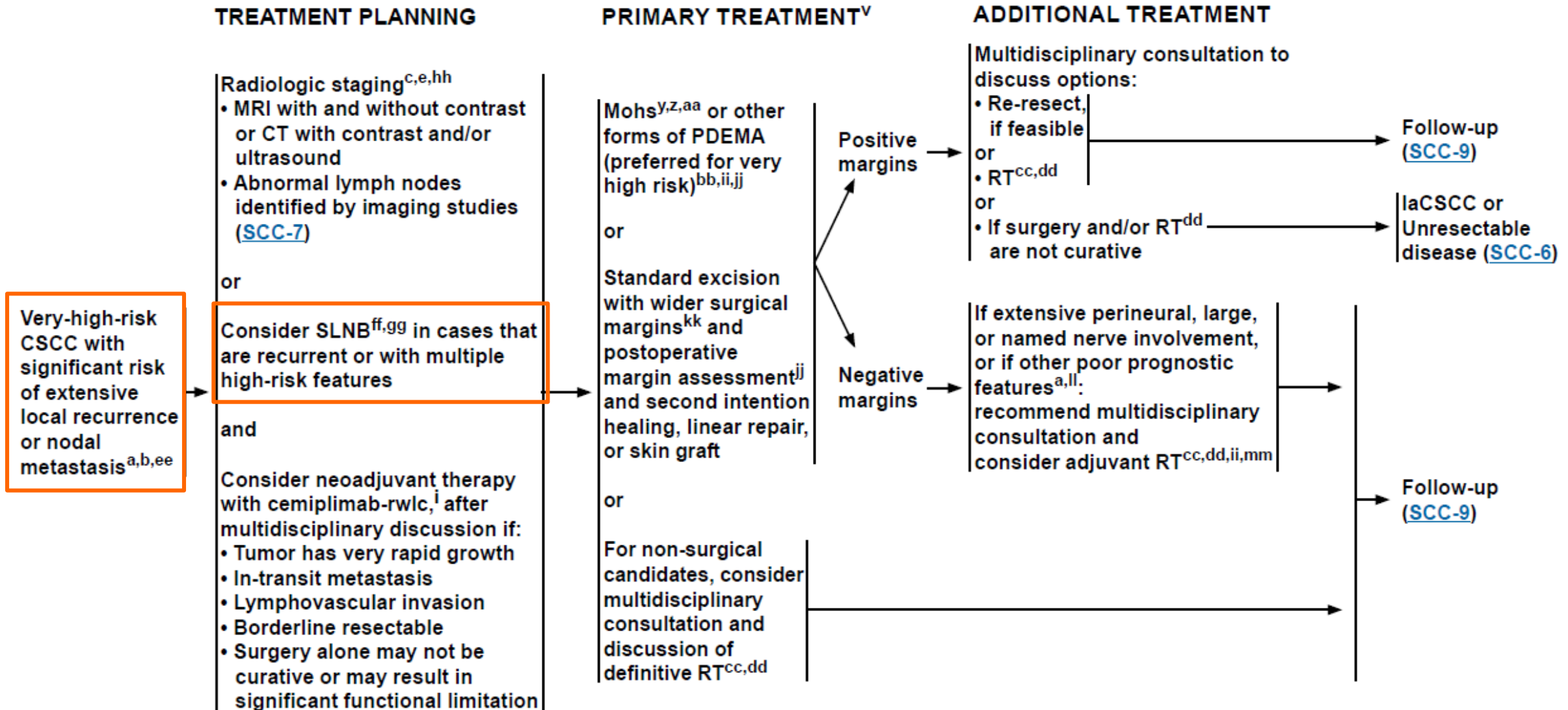
^u Endrizzi B, et al. Dermatol Surg 2013;39:634-645.

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.



NCCN Guidelines Version 1.2024 Squamous Cell Skin Cancer



Very-high-risk CSCC with significant risk of extensive local recurrence or nodal metastasis^{a,b,ee}

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 on SCC-5A](#)



鱗狀上皮細胞癌(SCC)_ regional disease

附件一：



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022 Squamous Cell Skin Cancer

[NCCN Guidelines Index](#)
[Table of Contents](#)
[Discussion](#)

STRATIFICATION TO DETERMINE TREATMENT OPTIONS AND FOLLOW-UP FOR LOCAL CSCC BASED ON RISK FACTORS FOR LOCAL RECURRENCE, METASTASES, OR DEATH FROM DISEASE

Risk Group ¹	Low Risk	High Risk	Very High Risk
Treatment options	See SCC-2	See SCC-3	See SCC-3
H&P			
Location/size ²	Trunk, extremities ≤2 cm	Trunk, extremities >2 cm – ≤4 cm	>4 cm (any location)
		Head, neck, hands, feet, pretibia, and anogenital (any size) ⁵	
Borders	Well-defined	Poorly defined	
Primary vs. recurrent	Primary	Recurrent	
Immunosuppression	(-)	(+)	
Site of prior RT or chronic inflammatory process	(-)	(+)	
Rapidly growing tumor	(-)	(+)	
Neurologic symptoms	(-)	(+)	
Pathology (See SCC-A)			
Degree of differentiation	Well or moderately differentiated		Poor differentiation
Histologic features: Acantholytic (adenoid), adenosquamous (showing mucin production), or metaplastic (carcinosarcomatous) subtypes	(-)	(+)	Desmoplastic SCC
Depth ^{3,4} : Thickness or level of invasion	≤6 mm and no invasion beyond subcutaneous fat		>6 mm or invasion beyond subcutaneous fat
Perineural involvement	(-)	(+)	Tumor cells within the nerve sheath of a nerve lying deeper than the dermis or measuring ≥0.1 mm
Lymphatic or vascular involvement	(-)	(-)	(+)

[See footnotes on SCC-B \(2 of 2\)](#)

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.

Version 1.2022, 11/17/21 © 2021 National Comprehensive Cancer Network® (NCCN®). All rights reserved. NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN.



STRATIFICATION TO DETERMINE TREATMENT OPTIONS AND FOLLOW-UP FOR LOCAL CSCC BASED ON RISK FACTORS FOR LOCAL RECURRENCE, METASTASES, OR DEATH FROM DISEASE

Risk Group ^a	Low Risk	High Risk	Very High Risk
Treatment options	SCC-2	SCC-3	SCC-3
H&P			
Location/size ^b	Trunk, extremities ≤2 cm	Trunk, extremities >2 cm – ≤4 cm	>4 cm (any location)
		Head, neck, hands, feet, pretibia, and anogenital (any size) ^e	
Clinical extent	Well-defined	Poorly defined	
Primary vs. recurrent	Primary	Recurrent	
Immunosuppression	(-)	(+)	
Site of prior RT or chronic inflammatory process	(-)	(+)	
Rapidly growing tumor	(-)	(+)	
Neurologic symptoms	(-)	(+)	
Pathology (SCC-A)			
Degree of differentiation	Well or moderately differentiated		Poor differentiation
Histologic features: Acantholytic (adenoid), adenosquamous (showing mucin production), or metaplastic (carcinosarcomatous) subtypes	(-)	(+)	Desmoplastic SCC
Depth ^{c,d} : Thickness or level of invasion	<2 mm thick and no invasion beyond subcutaneous fat	2–6 mm depth	>6 mm or invasion beyond subcutaneous fat
Perineural involvement	(-)	(+)	Tumor cells within the nerve sheath of a nerve lying deeper than the dermis or measuring ≥0.1 mm
Lymphatic or vascular involvement	(-)	(-)	(+)

Footnotes on [SCC-B \(2 of 2\)](#)

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.





PRINCIPLES OF TREATMENT

- The primary goals of treatment of CSCCs are 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.
- 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 as primary treatment in order to achieve optimal overall results.
- In certain patients at high risk for multiple primary tumors, increased surveillance and consideration of prophylactic measures may be indicated. ([Identification and Management of Patients at High Risk for Multiple Primary CSCCs \[SCC-C\]](#)).
- In patients with CSCC in situ (Bowen disease), alternative therapies such as topical 5-FU, topical imiquimod, photodynamic therapy (eg, ALA, porfimer sodium), or vigorous cryotherapy may be considered although cure rates may be lower than with surgical treatment modalities. **Focal squamous in situ arising within actinic keratosis is not appropriate for surgery and should be treated topically.**
- When Mohs with margin assessment is being performed and the preoperative biopsy is considered insufficient for providing all the staging information required to properly treat the tumor, submission of the central specimen for vertical paraffin-embedded permanent sections or documentation of staging parameters in Mohs report is recommended.

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.



鱗狀上皮細胞癌(SCC)_ regional disease

附件二



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022 Squamous Cell Skin Cancer

[NCCN Guidelines Index](#)
[Table of Contents](#)
[Discussion](#)

PRINCIPLES OF RADIATION THERAPY

General Principles

- Protracted fractionation is associated with improved cosmetic results and should be utilized for poorly vascularized or cartilaginous areas.
- For extensive perineural invasion, clinically evident perineural involvement, or involvement of named nerves (particularly in the head and neck region), consider including the course of the local nerves proximally.
- RT is contraindicated for genetic conditions predisposing to skin cancer (eg, basal cell nevus syndrome) and relatively contraindicated for patients with connective tissue diseases (eg, scleroderma).
- Given higher complication rates, re-irradiation should not be routinely utilized for recurrent disease within a prior radiation field.
- Isotope-based brachytherapy can be an effective treatment for certain sites of disease, particularly on the head and neck.
- There are insufficient long-term efficacy and safety data to support the routine use of electronic surface brachytherapy.

General Treatment Information

Primary Tumor	Examples of Dose Fractionation and Treatment Duration
Definitive RT	
Tumor diameter <2 cm	60–64 Gy over 6 to 7 weeks 50–55 Gy over 3 to 4 weeks 40 Gy over 2 weeks 30 Gy in 5 fractions over 2 to 3 weeks
Tumor diameter ≥2 cm, T3/T4, or those with invasion of bone or deep tissue	60–70 Gy over 6 to 7 weeks 45–55 Gy over 3 to 4 weeks
Postoperative Adjuvant RT	
60–64 Gy over 6 to 7 weeks 50 Gy over 4 weeks	
Regional Disease	
• Lymph node regions, after lymph node dissection	
▶ Negative margins, no ECE	50–60 Gy over 5 to 6 weeks
▶ Positive margins or ECE	60–66 Gy over 6 to 7 weeks
• Lymph node regions, without lymph node dissection	
▶ Clinically negative, at risk	50 Gy over 5 weeks
▶ Clinically positive	60–70 Gy over 6 to 7 weeks
• Clinically at-risk nerves	50–60 Gy over 5 to 6 weeks

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.

Version 1.2022, 11/17/21 © 2021 National Comprehensive Cancer Network® (NCCN®). All rights reserved. NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN.

SCC-E



鱗狀上皮細胞癌(SCC)_ regional disease

附件三-1

American Joint Committee on Cancer (AJCC)
TNM Staging Classification for Cutaneous Carcinoma of the Head and Neck (8th ed., 2017)^{1,2}

Table 1. Definitions for T, N, M

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

Clinical N (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(-); or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-); or 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(-); or 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 (+)

*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.

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(+).

¹ These staging tables are for cutaneous squamous cell carcinoma, cutaneous carcinoma, basal cell carcinoma of the head and neck, and all other nonmelanoma skin carcinomas of the head and neck (except Merkel cell carcinoma). Anatomic site of external vermilion lip is included because it has a more similar embryologic origin to skin, and its etiology—which is often based on ultraviolet exposure—is more similar to other nonmelanoma skin cancers. The AJCC Staging Manual, Eighth Edition does not include staging for cutaneous carcinoma outside the head and neck.
² Used with the 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

[Continued](#)



鱗狀上皮細胞癌(SCC)- regional disease

附件三-2:



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022 Squamous Cell Skin Cancer

[NCCN Guidelines Index](#)
[Table of Contents](#)
[Discussion](#)

American Joint Committee on Cancer (AJCC)
TNM Staging Classification for Cutaneous Carcinoma of the Head and Neck (8th ed., 2017)^{1,2}

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(+); or larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-); or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(-); or 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(+); or 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(-); or in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); or multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+); or 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(+); or multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+); or 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

Table 2. AJCC Prognostic Stage Groups

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

¹ These staging tables are for cutaneous squamous cell carcinoma, cutaneous carcinoma, basal cell carcinoma of the head and neck, and all other nonmelanoma skin carcinomas of the head and neck (except Merkel cell carcinoma). Anatomic site of external vermilion lip is included because it has a more similar embryologic origin to skin, and its etiology—which is often based on ultraviolet exposure—is more similar to other nonmelanoma skin cancers. The AJCC Staging Manual, Eighth Edition does not include staging for cutaneous carcinoma outside the head and neck.

² Used with the 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.



鱗狀上皮細胞癌(SCC)- regional disease

附件四-1:chemotherapy regimen or **metastasis**

化學治療處方

chemotherapy regimen

published C/T regimens	schedule
Cisplatin, 100 mg/m ² IV D1	Q 21-28 days x 4 cycles
5-FU, 1 g/m ² IV D1-3	Q 21-28 days x 4 cycles



鱗狀上皮細胞癌(SCC)_ regional disease

附件四-2:chemotherapy regimen & EGFRi or **metastasis**

化學治療處方

chemotherapy regimen & EGFRi

published C/T regimens	schedule
Cisplatin 100 mg/m ² IV D1	Q 21 days * 6 cycles
5-FU 1 g/m ² IV D1-4	Q 21 days * 6 cycles
* Cetuximab 400 mg/m ² ; 250 mg/m ² IV	400 mg/m ² * Week 1 ; then 250 mg/m ² * QW

* Cetuximab could be continued as long as the response or the stabilization persisted



鱗狀上皮細胞癌(SCC)_ regional disease

附件四-3:EGFRI or metastasis

化學治療處方

EGFRI

published C/T regimens	schedule
•Cetuximab, 400 mg/m ² IV Week 1, then 250 mg/m ² QW	Till IV or unacceptable toxicity

* Cetuximab could be continued as long as the response or the stabilization persisted





PRINCIPLES OF SYSTEMIC THERAPY

Local Disease (Including Multiple Primaries) Amenable to Curative Surgery

- Systemic therapy is not recommended.

Primary and Recurrent Locally Advanced Disease in Non-Surgical Candidates (See SCC-3)

- For patients who have residual disease and further surgery is not feasible, recommend RT, and multidisciplinary teams can consider concurrent systemic therapy in select cases (Table 1).
- For patients who have complicated cases of locally advanced disease in which curative surgery and curative RT are not feasible,¹ recommend multidisciplinary consultation to consider systemic therapy alone (Table 2).

New Regional Disease (See SCC-4 and SCC-5)

- For most cases of fully resected regional disease, adjuvant systemic therapy is not recommended, unless within a clinical trial.
- For patients with resected high-risk regional disease, consider RT ± systemic therapy (Table 1).
- For patients with unresectable, inoperable, or incompletely resected disease, multidisciplinary consultation is needed to consider:
 - ▶ RT ± systemic therapy (Table 1)
 - ▶ Systemic therapy alone if curative RT not feasible¹ (Table 2)

Regional Recurrence or Distant Metastatic Disease (See SCC-6)

- For regional recurrence or distant metastases, multidisciplinary team can consider systemic therapy alone (Table 2) or in combination with RT (Table 1).

Table 1: Systemic Therapy Options for Use with RT

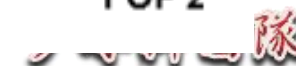
Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
<ul style="list-style-type: none"> • Cisplatin² • Clinical trial^{3,4} 	<ul style="list-style-type: none"> • None 	<ul style="list-style-type: none"> • EGFR inhibitors (eg, cetuximab)² • Cisplatin + 5-FU² • Carboplatin ± paclitaxel^{2,5,6}

Table 2: Options for Systemic Therapy Alone

Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
<ul style="list-style-type: none"> • Cemiplimab-rwlc^{3,4} (if curative RT or surgery is not feasible¹ for locally advanced, recurrent, or metastatic disease) • Pembrolizumab^{3,4} (if curative RT or surgery is not feasible¹ for locally advanced, recurrent, or metastatic disease) • Clinical trial^{3,4} 	<ul style="list-style-type: none"> • If ineligible for or progressed on immune checkpoint inhibitors and clinical trials, consider: <ul style="list-style-type: none"> ▶ Carboplatin + paclitaxel 	<ul style="list-style-type: none"> • If ineligible for or progressed on immune checkpoint inhibitors and clinical trials, consider: <ul style="list-style-type: none"> ▶ EGFR inhibitors (eg, cetuximab)² ▶ Capecitabine ▶ Cisplatin² ▶ Cisplatin + 5-FU² ▶ Carboplatin²

[See Footnotes and References on SCC-F \(2 of 2\)](#)

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.





PRINCIPLES OF SYSTEMIC THERAPY

Local Disease (Including Multiple Primaries) Amenable to Curative Surgery

- Systemic therapy is not recommended.

Primary and Recurrent Locally Advanced Disease in Non-Surgical Candidates (SCC-3)

- For patients who have residual disease and further surgery is not feasible, recommend RT, and multidisciplinary teams can consider concurrent systemic therapy in select cases (Table 1).
- For patients who have complicated cases of locally advanced disease in which curative surgery and curative RT are not feasible,^a recommend multidisciplinary consultation to consider systemic therapy alone (Table 2).

New Regional Disease (SCC-4 and SCC-5)

- For most cases of fully resected regional disease, adjuvant systemic therapy is not recommended, unless within a clinical trial.
- For patients with resected high-risk regional disease, consider RT ± systemic therapy (Table 1).
- For patients with unresectable, inoperable, or incompletely resected disease, multidisciplinary consultation is needed to consider:
 - RT ± systemic therapy (Table 1)
 - Systemic therapy alone if curative RT not feasible^a (Table 2)

Regional Recurrence or Distant Metastatic Disease (SCC-6)

- For regional recurrence or distant metastases, multidisciplinary team can consider systemic therapy alone (Table 2) or in combination with RT (Table 1).

Table 1: Systemic Therapy Options for Use with RT

Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
<ul style="list-style-type: none"> • Cisplatin^b • Clinical trial 	<ul style="list-style-type: none"> • None 	<ul style="list-style-type: none"> • EGFR inhibitors (eg, cetuximab)^b • Cisplatin + 5-FU^b • Carboplatin ± paclitaxel^{b,1,2}

Table 2: Options for Systemic Therapy Alone

Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
<ul style="list-style-type: none"> • Cemiplimab-rwlc^{c,d} (if curative RT or surgery is not feasible^a for locally advanced, recurrent, or metastatic disease) • Pembrolizumab^{c,d} (if curative RT or surgery is not feasible^a for locally advanced, recurrent, or metastatic disease) • Clinical trial 	<ul style="list-style-type: none"> • If ineligible for or progressed on immune checkpoint inhibitors and clinical trials, consider: <ul style="list-style-type: none"> ▸ Carboplatin + paclitaxel 	<ul style="list-style-type: none"> • Neoadjuvant cemiplimab-rwlc^e • If ineligible for or progressed on immune checkpoint inhibitors and clinical trials, consider: <ul style="list-style-type: none"> ▸ EGFR inhibitors (eg, cetuximab)^b ▸ Capecitabine ▸ Cisplatin^b ▸ Cisplatin + 5-FU^b ▸ Carboplatin^b



Reference

1. [NCCN Clinical Practice Guideline in Oncology, Basal and Squamous Cell Skin Cancers, Version 1.2022](#)
2. Am J Clin Dermatol. 2016 Oct;17(5):491-508. Cutaneous Squamous Cell Carcinoma: A Review of High-Risk and Metastatic Disease.
3. Mendenhall WM, Ferlito A, Takes RP, et al. Cutaneous head and neck basal and squamous cell carcinomas with perineural invasion. Oral Oncol 2012;48:918-922.
4. Gurudutt VV, Genden EM. Cutaneous squamous cell carcinoma of the head and neck. J Skin Cancer 2011;2011:502723.
5. 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 Sep 1;29(25):3419-26
6. Lott DG, Manz R, Koch C, Lorenz RR. Aggressive behavior of nonmelanotic skin cancers in solid organ transplant recipients. Transplantation 2010;90:683-687.
7. Cranmer LD, Engelhardt C, Morgan SS. Treatment of unresectable and metastatic cutaneous squamous cell carcinoma. Oncologist 2010;15:1320-1328.
8. Brantsch KD, Meisner C, Schonfisch B, et al. Analysis of risk factors determining prognosis of cutaneous squamous-cell carcinoma: a prospective study. Lancet Oncol 2008;9:713-720.
9. Platinum-Based Chemotherapy plus Cetuximab in Head and Neck Cancer. N Engl J Med 2008;359:1116-27. Neville JA, Welch E, Leffell DJ. Management of nonmelanoma skin cancer in 2007. Nat Clin Pract Oncol 2007;4:462-469.
10. Squamous cell carcinoma developing on burn scar. Ann Plast Surg 2006;56:406-408.
11. Ross AS, Schmults CD. Sentinel lymph node biopsy in cutaneous squamous cell carcinoma: a systematic review of the English literature. Dermatol Surg 2006;32:1309-1321.
12. Veness MJ, Morgan GJ, Palme CE, Gebiski V. Surgery and adjuvant radiotherapy in patients with cutaneous head and neck squamous cell carcinoma metastatic to lymph nodes: combined treatment should be considered best practice. Laryngoscope 2005;115:870-875.