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Cross-border cooperation to foster the resilience of clinical management in cancer patients by establishing best practices in personalized molecular-based diagnostics, treatment, and long-term care

RORS00040

Clinical Insights from a Melanoma Case Presentation

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Melanoma of the Areola in a Male Patient

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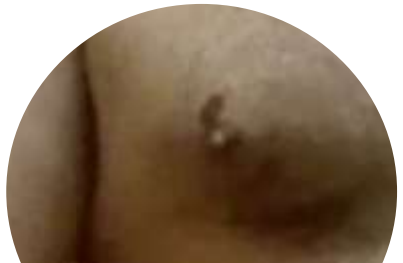
Medical History

Patient Data: D.D



- Age: 49
- Gender: Male
- Occupation: Driver

He presented in 2023 with a painless, pigmented lesion, dark brown to black, located on the areola.

Over the past 5 years, the lesion showed progressive darkening and increase in size.

He denied pain, pruritus, bleeding, or erythema.

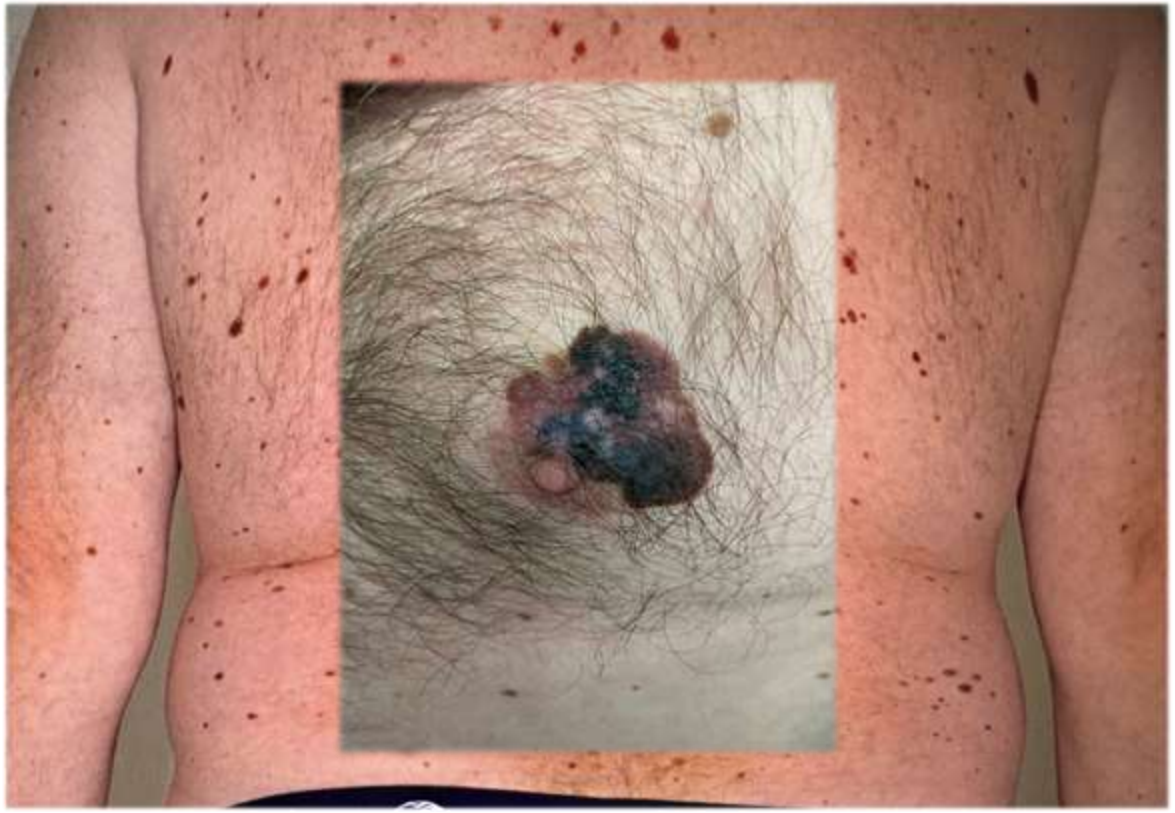
He reported no family history of skin cancer or other dermatological diseases.

Clinical Examination

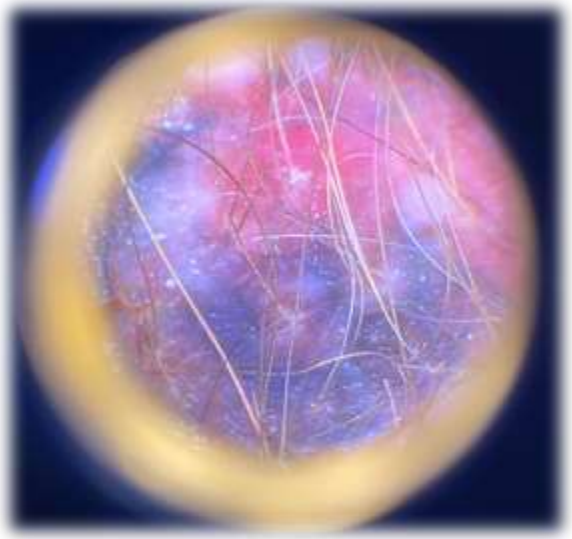
The patient had over 100 nevi

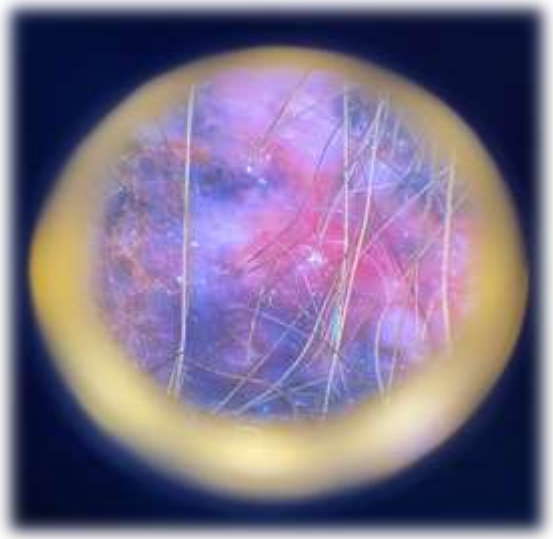
A large (2.6 × 2.6 cm), irregularly shaped brown-to-black papule on the areola, extending around the nipple and onto the surrounding skin

No palpable breast masses, nipple discharge, or axillary or supraclavicular lymphadenopathy



Clinical Examination





Dermoscopy revealed light-to-dark brown and black pigmentation with **atypical pigment network**, blotches, and a **blue-white veil.**

Clinical Diagnosis: Melanoma

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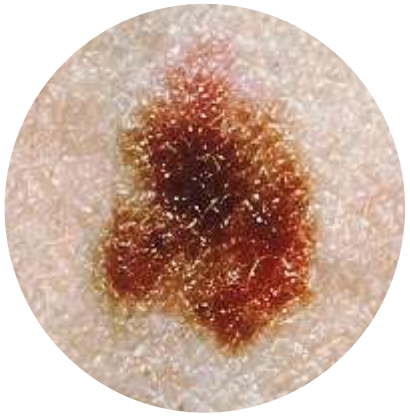
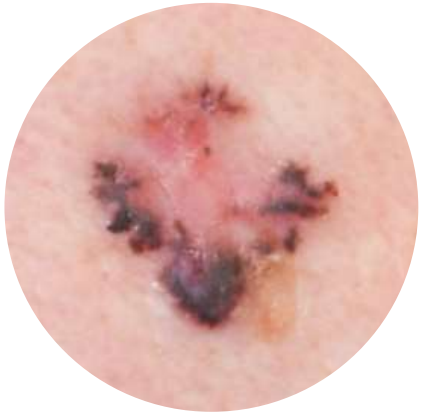
Differential Diagnosis

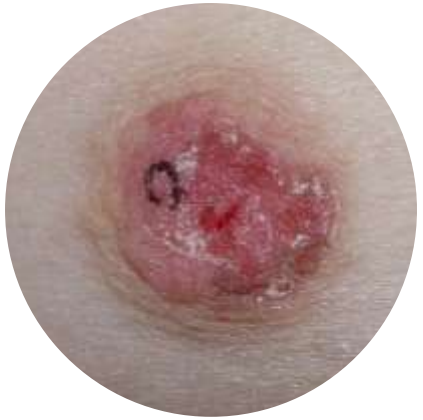


Atypical (dysplastic) nevus



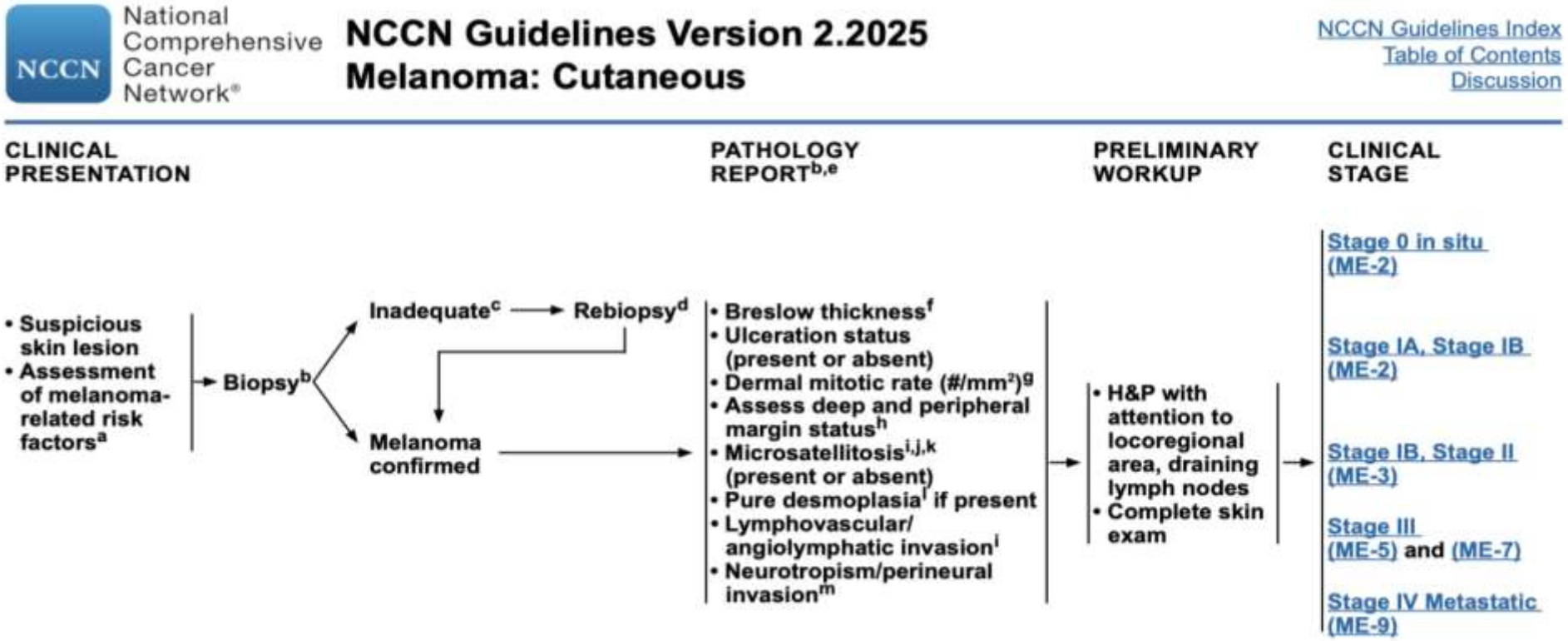
Pigmented basal cell carcinoma

Seborrheic keratosis



Paget disease of the breast

Treatment

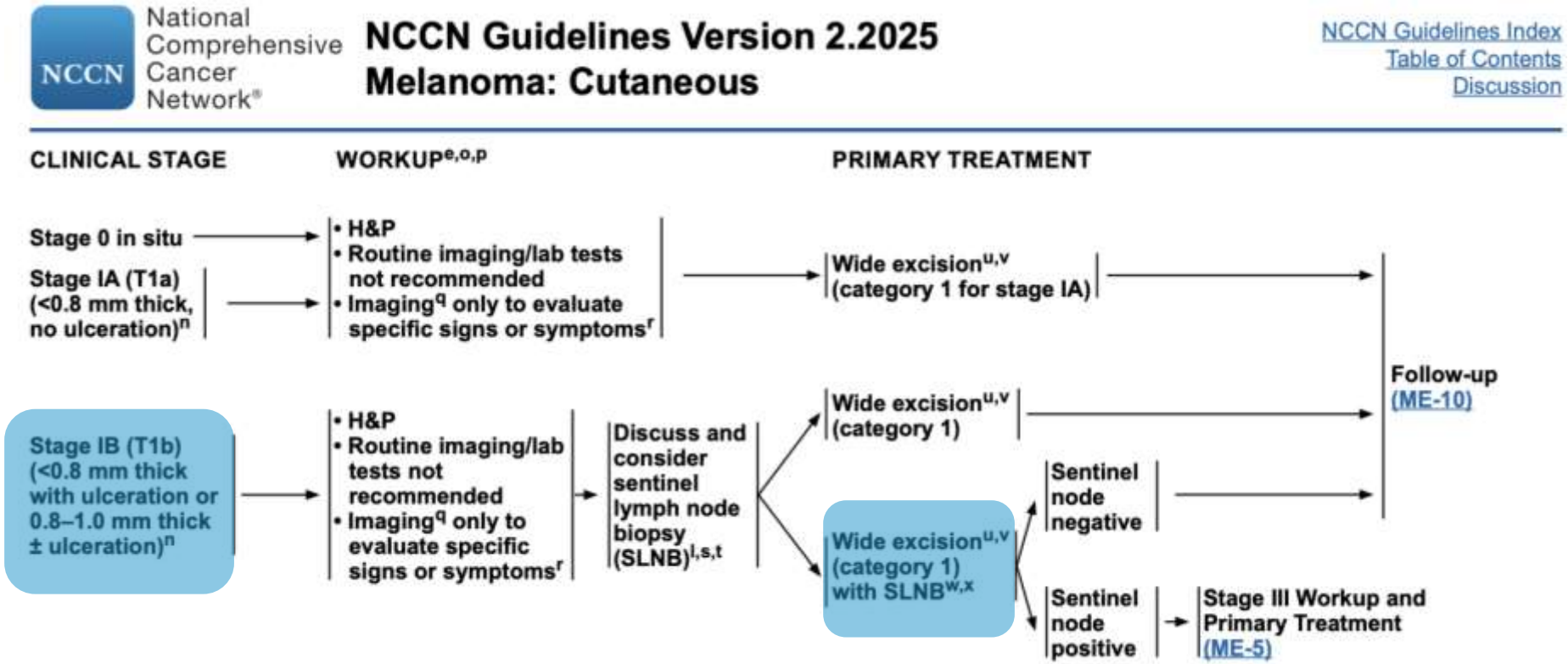


Melanoma Management - According to NCCN Guidelines:

- Identification of a suspicious lesion and risk factor assessment
- Diagnostic confirmation by biopsy
- Histopathological report: tumor thickness (Breslow index), ulceration, and other prognostic factors
- Sentinel lymph node biopsy (when indicated)

Clinical staging

Treatment



Indications for Sentinel Lymph Node Biopsy (SLNB):

- T1b melanoma: Breslow thickness <0.8 mm with ulceration or 0.8–1 mm, with or without ulceration
- Selected T1a lesions: Breslow thickness >0.5 mm with additional risk factors:
  age ≤42 years, head and neck location, lymphovascular invasion, mitotic rate ≥2/mm²

Treatment

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2025
Melanoma: Cutaneous

NCCN Guidelines Index
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Discussion

PRINCIPLES OF SURGICAL MARGINS FOR WIDE EXCISION OF PRIMARY MELANOMA

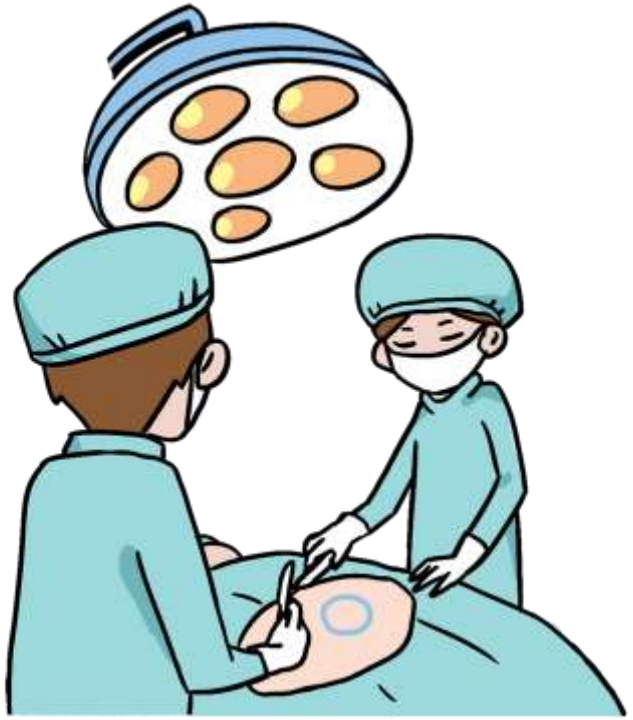
Tumor Thickness	Recommended Peripheral Surgical Margins[a,1-10]
In situ[b,c]	0.5–1 cm
≤1.0 mm	1 cm (category 1)
>1.0–2.0 mm	1–2 cm (category 1)
>2.0–4.0 mm	2 cm (category 1)
>4.0 mm	2 cm (category 1)

Wide Excision and Sentinel Lymph Node Biopsy - **Key Principles**:

- Wide excision is performed following the initial excision
- Surgical margins are determined based on tumor thickness (Breslow index)
- Sentinel lymph node biopsy (SLNB) is performed during the same procedure when indicated

Excision

- A 4 mm margin excisional biopsy of the pigmented lesion on the left pectoral region, including the nipple - areola complex, was performed
- Excision extended into the subcutaneous adipose tissue
- Hemostasis was achieved
- The wound was closed with sutures
- Sterile dressing was applied



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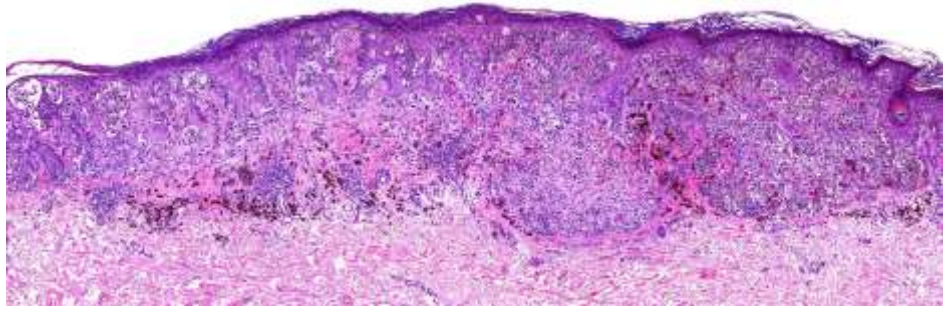
Histopathological Diagnosis

The histological findings are consistent with **malignant melanoma** with **superficial spreading** component, in the **vertical growth phase**, with extensive tumor regression.

- **Breslow thickness**: 0.8 mm, Clark level III
- 0 mitoses/mm² in the intradermal component
- **No lymphovascular** or **perineural invasion**; no satellite lesions
- Dense inflammatory infiltrate (brisk) with extensive regression features
- **No epidermal ulceration**



pT1b

Treatment

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Melanoma: Cutaneous

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

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.

Melanoma staging is driven primarily by Breslow thickness, ulceration, and nodal status.

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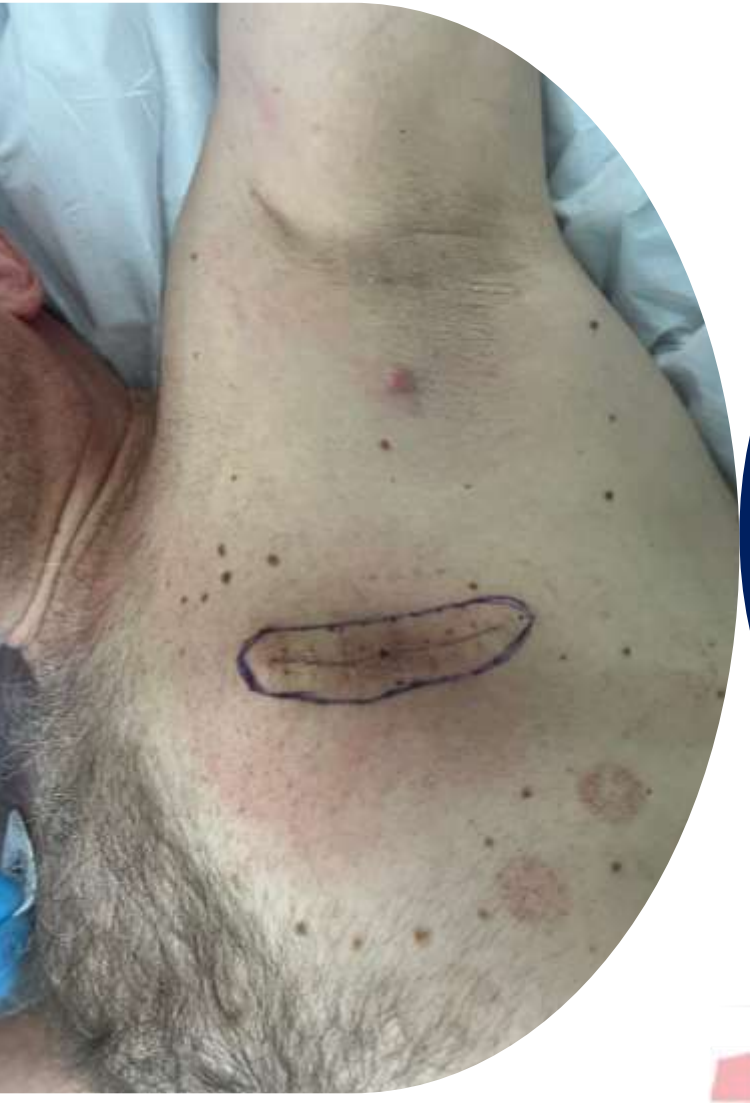
Wide Excision and Sentinel Lymph Node Biopsy



3 Weeks Later

Scar marked and intradermal injection of 1 mL **methylene blue dye**

Wide local excision of the scar with 2 cm margins

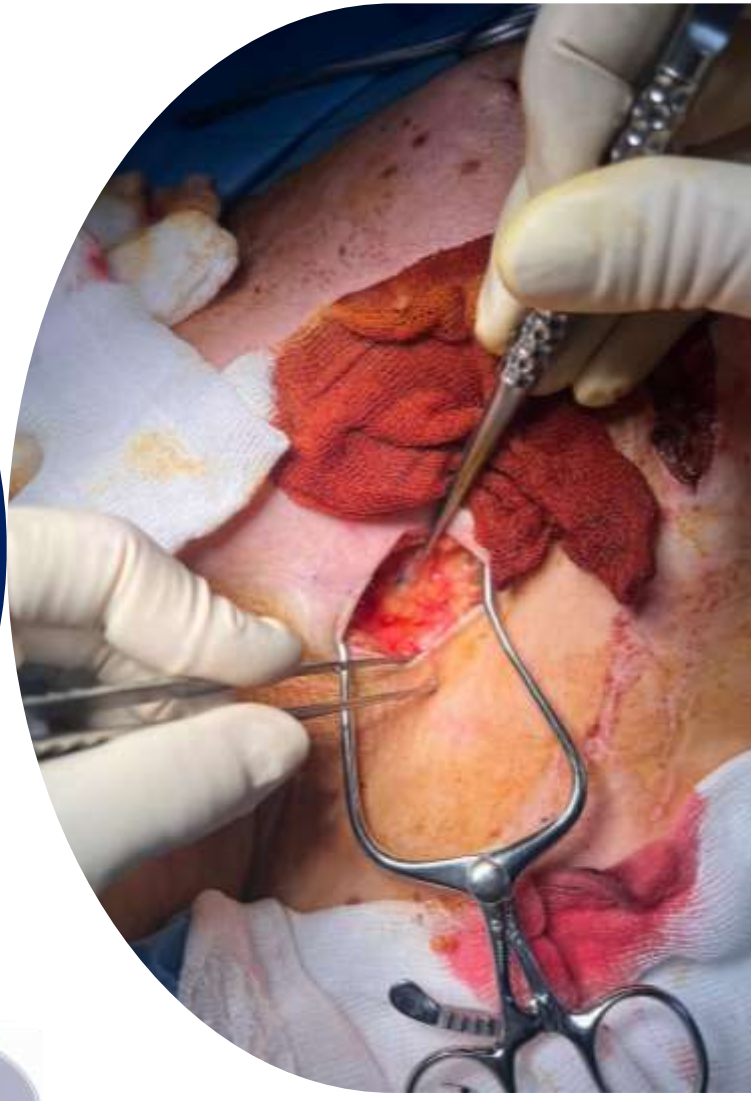
Gamma probe localization of the axillary sentinel lymph node

Identification and excision of two blue, radioactive lymph nodes

Hemostasis

Closure in layers

Dressing applied



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Histopathological Diagnosis

Sentinel lymph nodes (overall assessment)

- Melan-A negative for tumor cells
- No evidence of metastatic melanoma in the examined lymph nodes
- Final diagnosis: two sentinel lymph nodes without tumor infiltration

Malignant melanoma with a superficial spreading component in the vertical growth phase with extensive tumor regression

pT1b
N0
M0

STAGE IB

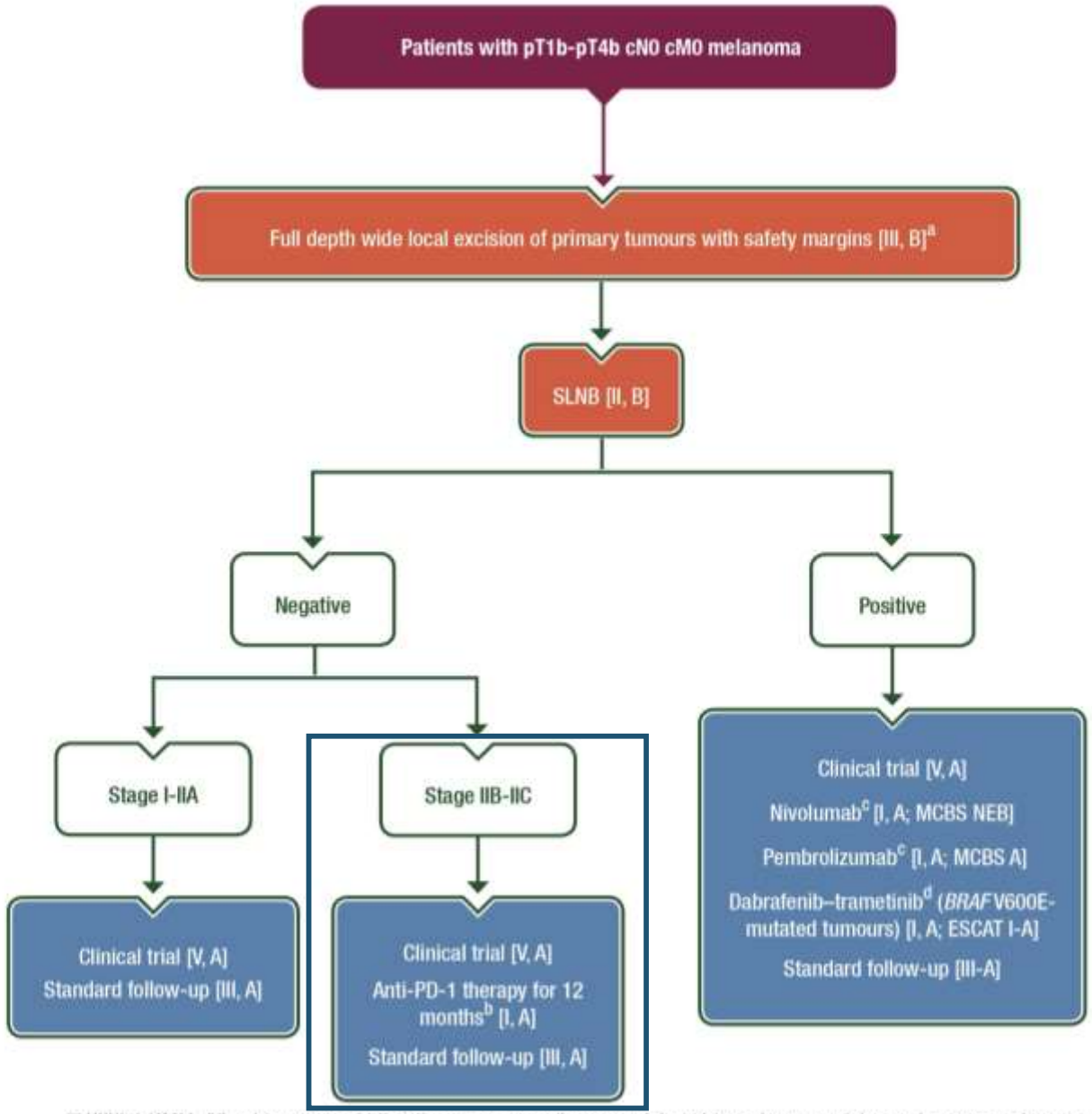
CLINICAL PRACTICE GUIDELINES

ESMO Cutaneous Melanoma Living Guideline v1.0 February 2025

Management of Patients with pT1b-pT4b cN0 cM0 Melanoma

[a]RT can be considered for local tumour control in cases of inadequate resection margins of LM [III, B] and could be discussed for patients with an R1 resection [III, C]. Adjuvant RT to the primary excision site should be considered for patients with desmoplastic or neurotropic melanoma for whom adequate (8 mm) pathological resection margins cannot be achieved [IV, C].
[b]Treatment discussions with the patient should include consideration of the RFS benefit but lack of mature OS data [I, A].
[c]Treatment discussions with the patient should consider the DMFS and RFS benefits but lack of mature OS data compared with placebo [I, A].
[d]Treatment discussions with the patient should consider the DMFS and RFS benefits and potential OS benefit for patients with *BRAF* V600E-mutated melanoma [I, A].

Adjuvant systemic therapy in stage IIB-IIC melanoma	
Adjuvant therapy with either pembrolizumab [**ESMO-MCBS v1.1 score: A**] or nivolumab [**ESMO-MCBS v1.1 score: A**] for 12 months should be considered for patients with stage IIB-IIC disease; treatment discussions with the patient should include consideration of the recurrence-free survival benefit but lack of mature overall survival data	I, A



CLINICAL PRACTICE GUIDELINES

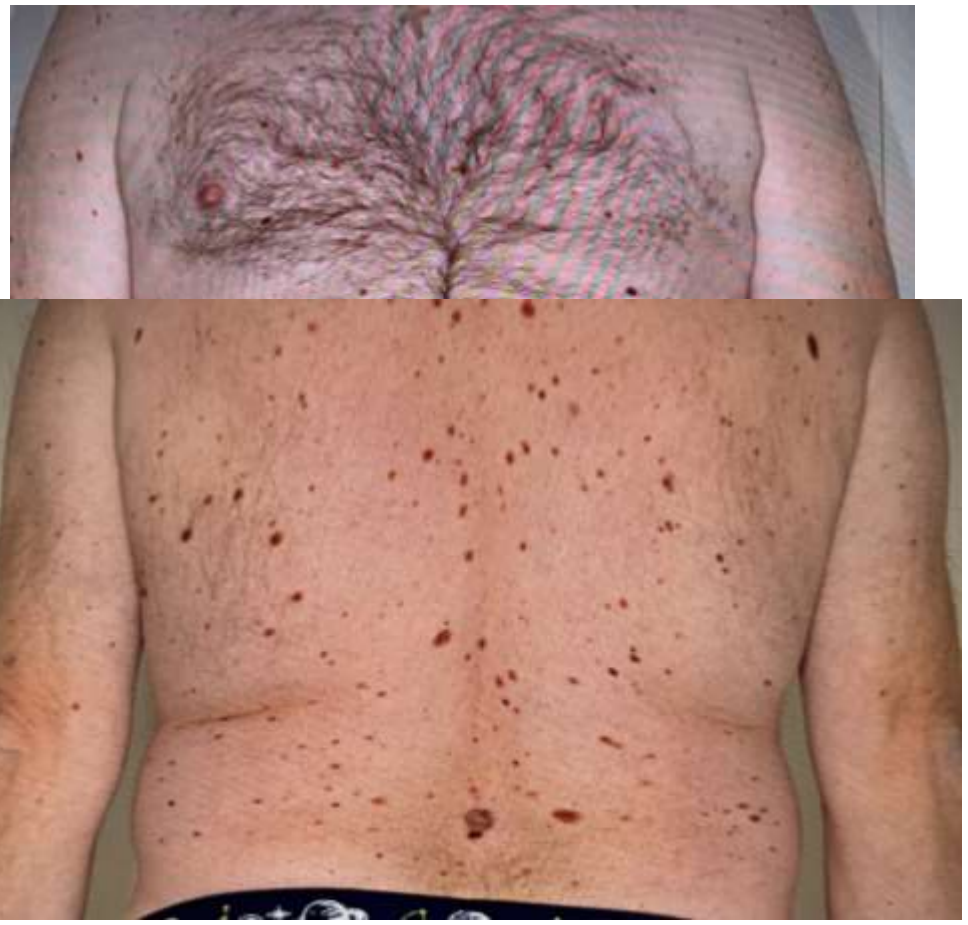
ESMO Cutaneous Melanoma Living Guideline v1.0 February 2025

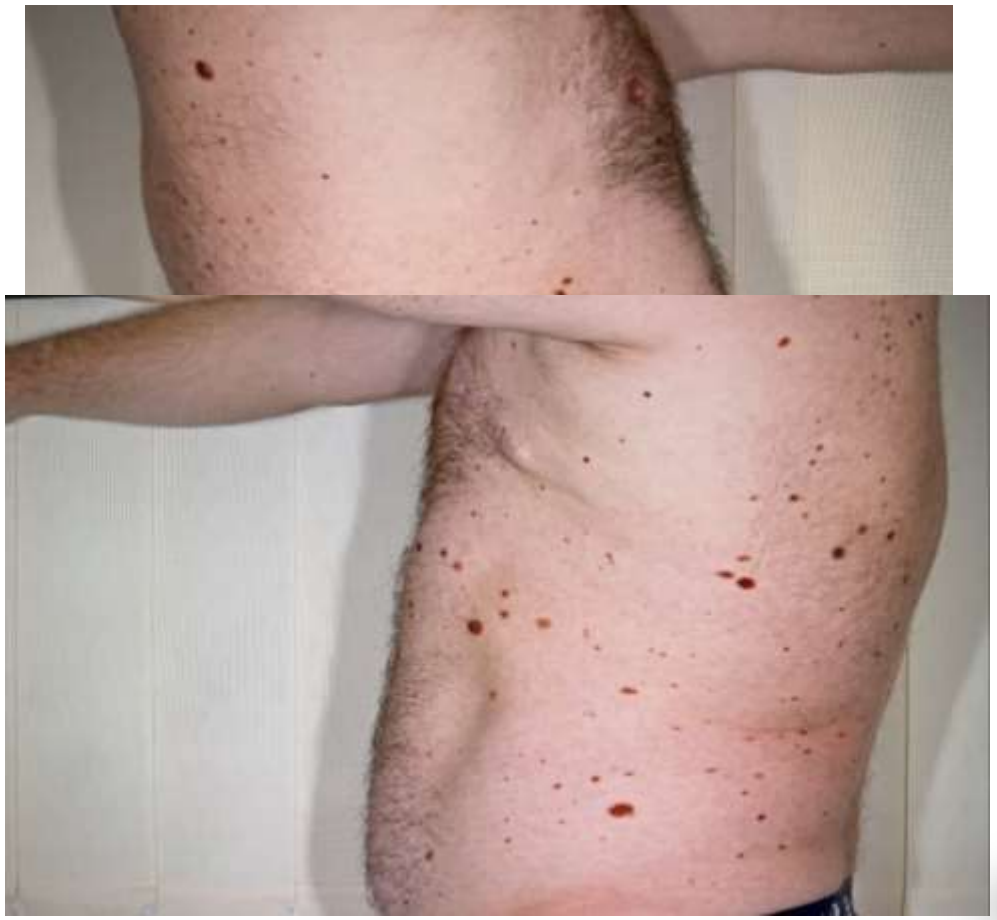
Suggested Follow-up Schedule by Disease Stage

	Stage IA	Stage IB-IIA	Stage IIB, IIIA	Stage IIC, IIIB-IIID	Stage IV NED (resected – CR)	Stage IV (M1a-M1d) (distant metastases)
Clinical-dermatological examination	Q6 mo (yr 1-3), Q12 mo (yr 4-10), Q12 mo (yr >10)	Q3-6 mo (yr 1-3), Q6 mo (yr 4-10), Q12 mo (yr >10)	Q3 mo (yr 1-3), Q6 mo (yr 4-10), Q12 mo (yr >10)	Q3 mo (yr 1-3), Q6 mo (yr 4-10), Q12 mo (yr >10)	Q3 mo (yr 1-3), Q6 mo (yr 4-10), Q12 mo (yr >10)	Individualised to each patient, depending on therapy and symptoms; otherwise, staging Q12 weeks For patients achieving CR, staging Q12 weeks (yr 1-3) after ICI discontinuation
Lymph node ultrasound	NA	Q6 mo (yr 1-3)	Q3-6 mo (yr 1-3)	Q3-6 mo (yr 1-3)	Q3-6 mo (yr 1-3)	
Laboratory examination	NA	Q3-6 mo (yr 1-3)	Q3-6 mo (yr 1-3)	Q3-6 mo (yr 1-3)	Q3-6 mo (yr 1-3)	
CT (or PET-CT) of neck, thorax, abdomen, pelvis; brain MRI	NA	NA	Q6 mo (yr 1-2) Q12 mo (yr 3-5)	Q3 mo (yr 1-2) Q6 mo (yr 3-5)	Q3 mo (yr 1-3) Q6 mo (yr 3-5)	

ESMO

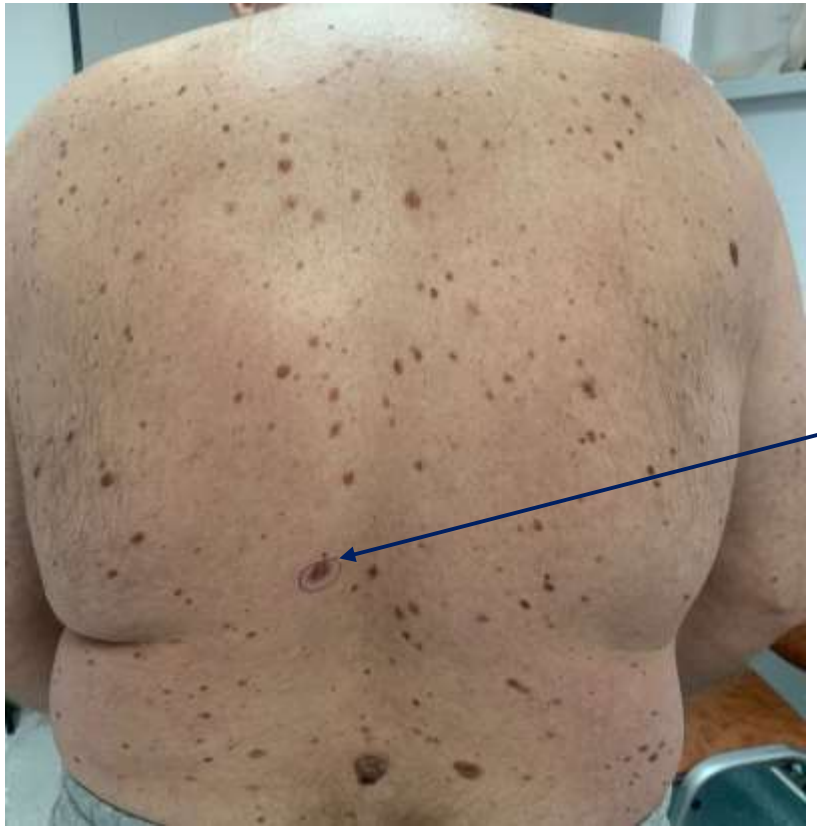
Follow up

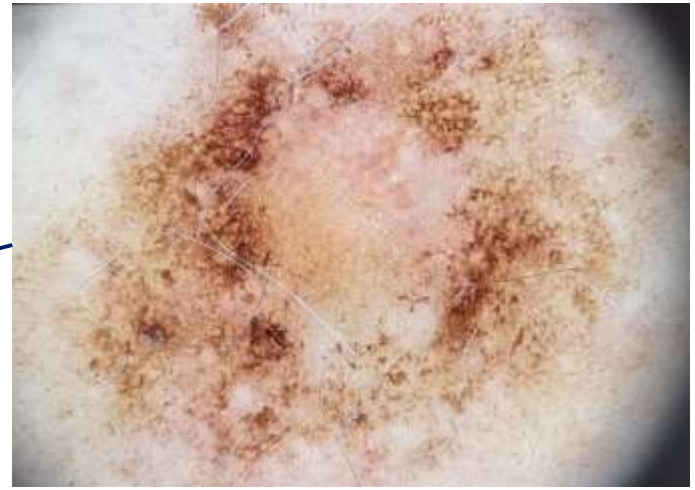




Follow up

At the FotoFinder examination in January 2026, a lesion was identified:





Dermoscopy showed an **irregular pattern** with different shades of brown and black, **asymmetry**, and areas suggesting regression and a blue-white veil.

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Surgical Excision and Histopathology

Histopathological Findings:

Junctional component with atypical melanocytic nests and lentiginous proliferation, with focal pagetoid spread
Melanocytes: medium to large size, moderate nuclear atypia, no mitotic activity
Dermal component showing maturation, without atypia or mitoses
Mild chronic inflammatory infiltrate with rare melanophages
Immunohistochemistry: HMB-45 positive in junctional component, negative in dermal component; p16 positive
Findings consistent with **melanoma in situ arising on a dysplastic compound nevus**

STAGE 0
Melanoma in situ

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Discussions

Areolar melanoma is rare and may be clinically misleading

The lesion showed a slow evolution over 5 years, suggesting a slow-growing melanoma

This likely reflects a stepwise progression from a pre-existing nevus, driven by early oncogenic mutations (e.g., BRAF)

Regression and brisk inflammatory infiltrate suggest an active host immune response

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Conclusions

Early detection improves prognosis

Patients with multiple nevi have a higher risk of new melanomas

Follow-up is crucial in melanoma patients

This case highlights that melanoma patients remain at lifelong risk of developing new primary melanomas, making follow-up essential

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Thank you!

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