



MELANOMDA EVRELEME VE İZLEM

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III. DERMATOONKOLOJİ GÜNDEMİ

BAKÜ, 2014

EVRELEME

- Prognostik Öngörü
- Tedavi Stratejisi Belirleme
- Klinik Çalışma Dizaynı

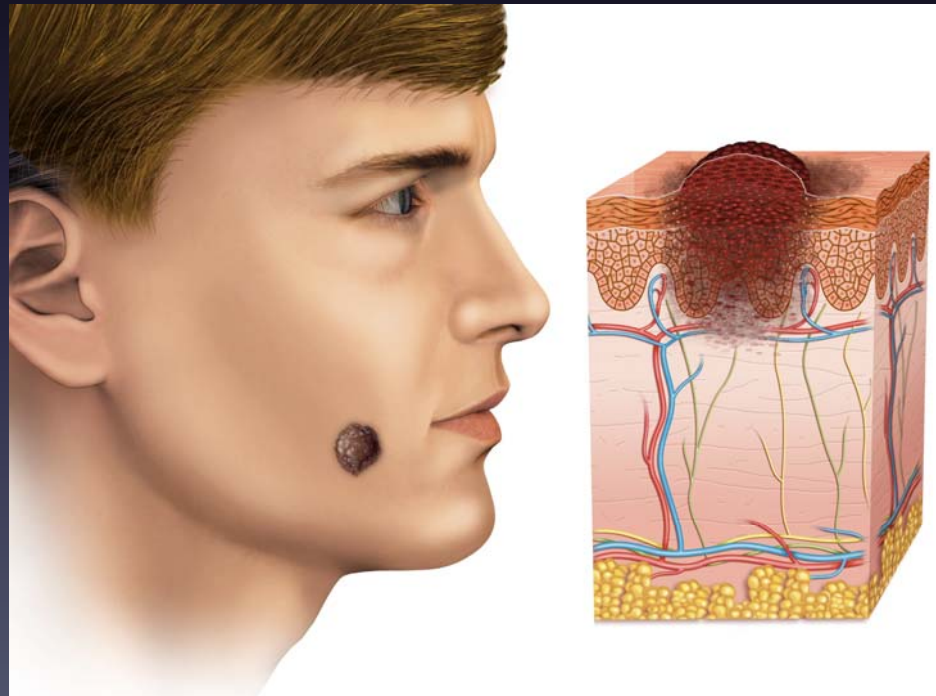
Prognostik faktörlerin idantifikasyonu ve analizi

Wallace H. CLARK

1969

Alexander BRESLOW

1970



PROGNOSTİK FAKTÖRLER

- Primer tumor;
 - BRESLOW Tumor kalınlığı
 - Mitoz oranı
 - Ulserasyon
 - CLARK seviyesi
 - Anatomik bölge

- Lenf Nodu;
 - LN sayısı
 - Mikroskopik
 - Makroskopik

- Yaş
- Cins
- Immun yetmezlik

- Metastaz;
 - Uzak
 - Kutan, subkutan
 - Akc met

Table 4
Multivariate Cox regression analysis of prognostic factors in 10,233 patients with localized cutaneous melanoma (stage I and II)

Variable	Chi-Square Value (1 df)	P	HR	95% CI
Tumor thickness	84.6	<.0001	1.25	1.19–1.31
Mitotic rate	79.1	<.0001	1.26	1.20–1.32
Ulceration	47.2	<.0001	1.56	1.38–1.78
Age	40.8	<.0001	1.16	1.11–1.22
Gender	32.4	<.0001	0.70	0.62–0.79
Site	29.1	<.0001	1.38	1.23–1.54
Clark level	8.2	.0041	1.15	1.04–1.26

AJCC

AMERICAN JOINT COMMITTEE ON CANCER MELANOMA STAGING GUIDELINES

- 1998
- 2002; TNM sistemi
- 2009; Son versiyon

Table 3
Differences between the sixth edition (2002) and the seventh edition (2009) of the melanoma staging system



Factor	Sixth Edition Criteria	Seventh Edition Criteria	Comments
Thickness	Primary determinant of T staging	Same	Thresholds of 1.0, 2.0, and 4.0 mm
Level of invasion	Used only for defining T1 melanomas	Same	Used as a default criterion only if mitotic rate cannot be determined
Ulceration	Included as a secondary determinant of T and N staging	Same	Signifies a locally advanced lesion; dominant prognostic factor for grouping stages I, II, and III
Mitotic rate per mm ²	Not used	 Used for categorizing T1 melanoma	Mitosis $\geq 1/\text{mm}^2$ used as a primary criterion for defining T1b melanoma
Satellite metastases	In N category	Same	Merged with in transit lesions
Immunohistochemical detection of nodal metastases	Not included	 Included	Must include at least 1 melanoma-associated marker (eg, HMB-45, Melan-A, MART-1) unless diagnostic cellular morphology is present
0.2 mm threshold of defined N+	Implied	No lower threshold of staging N+ disease	Isolated tumor cells or tumor deposits <0.1 mm meeting the criteria for histologic or immunohistochemical detection of melanoma should be scored as N+
Number of nodal metastases	Primary determinant of N staging	Same	Thresholds of 1 vs 2–3 vs 4+ nodes
Metastatic volume	Included as a second determinant of N staging	Same	Clinically occult (microscopic) nodes are diagnosed at sentinel node biopsy vs clinically apparent (macroscopic) nodes diagnosed by palpation or imaging studies, or by the finding of gross (not microscopic) extracapsular extension in a clinically occult node
Lung metastases	Separate category as M1b	Same	Has a better prognosis than other visceral metastases
Increased serum LDH level	Included as a second determinant of M staging	Same	Recommend a second confirmatory LDH level if increased
Clinical vs pathologic staging	Sentinel node results incorporated into definition of pathologic staging	Same	Large variability in outcome between clinical and pathologic staging; sentinel node staging encouraged for standard patient care, should be required before entry into clinical trials

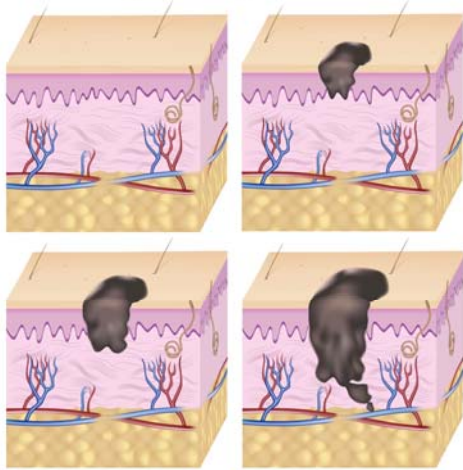
Table 6
Multivariate Cox regression analysis of pathologic factors by T category for stage I and II melanoma

T Category	Tumor Thickness		Ulceration		Mitotic Rate		Clark Level	
	χ^2	P	χ^2	P	χ^2	P	χ^2	P
T1	12.8	.0003	3.8	.05	20.8	<.0001	1.9	.17
T2	4.9	.03	16.2	<.0001	15.9	<.0001	0.2	.65
T3	4.1	.04	15.4	<.0001	12.2	.0005	1.4	.24
T4	0.2	.69	14.2	.0002	9.1	.003	2.7	.10

Table 1
TNM staging categories for cutaneous melanoma

T	Thickness (mm)	Ulceration Status and Mitoses
T is	Not applicable	Not applicable
T1	≤1.00	T1a: without ulceration and mitoses <1/mm ² T1b: with ulceration or mitoses ≥1/mm ²
T2	1.01–2.00	T2a: without ulceration T2b: with ulceration
T3	2.01–4.00	T3a: without ulceration T3b: with ulceration
T4	≥4.01	T4a: without ulceration T4b: with ulceration
N	No. of Metastatic Nodes	Nodal Metastatic Burden

The stages of malignant melanoma



TUMOR

- Kalınlık
- Mitoz
- Ulserasyon

Kalınlık

T₁ ≤ 1 mm

- Uls. yok **ve** Mitoz < 1 / mm²
- Uls. var **veya** Mitoz ≥ 1 / mm²

T₂ 1.01-2.00

- Uls. Yok
- Uls. var

T₃ 2.00-4.00

- Uls. Yok
- Uls. var

T₄ ≥ 4.00 mm

- Uls. Yok
- Uls. var

KALINLIK

Intraokuler mikrometre

Granüler tabaka üst seviyesinden en alttaki tumor hücresine dek

Ulserasyon varsa; ulser tabanından.....

1 mm. ye dek; İnce / 1-4mm ; Orta / 4mm. üstü ; Kalın

ULSERASYON

Travma & cerrahi olmaksızın;

Epidermisin tüm kalınlığındaki defekt... (T; a...b'ye)

Ulserasyon yüzdesi; Tumor çapı ve ulserasyon çapı ölçülür.

% 5 den az ulserasyon varsa yaşam şansı daha yüksektir.

DERMAL MITOZ

Hot spot; Dermiste en çok mitotik figürün görüldüğü alan.

'Hot spot'ta mitoz sayılır.

Sayım 1 mm² lik alana genişletilir.

1 /mm² ; Mitojenik

0 / mm²; Nonmitojenik

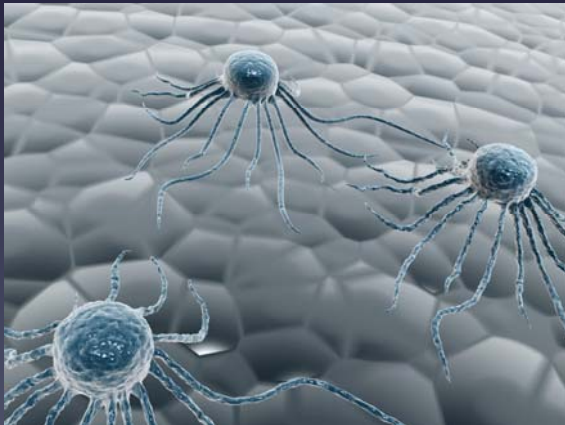


Table 7
2008 AJCC melanoma staging database data on mitotic rate and survival

Number of Mitoses/mm ²	n	Survival Rate \pm SE	
		5 y	10 y
0–0.99	3312	0.973 \pm 0.004	0.927 \pm 0.007
1.00–1.99	2117	0.920 \pm 0.007	0.842 \pm 0.012
2.00–4.99	3254	0.869 \pm 0.007	0.754 \pm 0.012
5.00–10.99	2049	0.781 \pm 0.011	0.680 \pm 0.018
11.00–19.99	673	0.695 \pm 0.022	0.576 \pm 0.027
≥ 20.0	259	0.594 \pm 0.039	0.476 \pm 0.050
Total	11,664 ^a		

Ki 67

Antifosfohiston H₃; Anti- PHH₃

DERMAL MİTOZ

1. Prognostik bilgi
2. Cerrahi sınır genişliği planlaması

Mitotik aktivite yüksekliği; SLN pozitifliği (≥ 1 /mm² ise SLN biyopsisi ince melanomda bile önerilmektedir)

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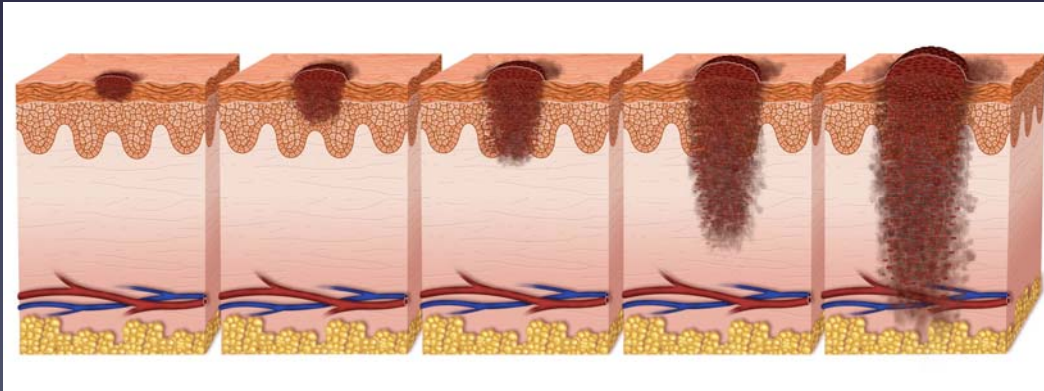
CLARK SEVİYESİ

Mitotik hızın belirlenemediği durumlarda

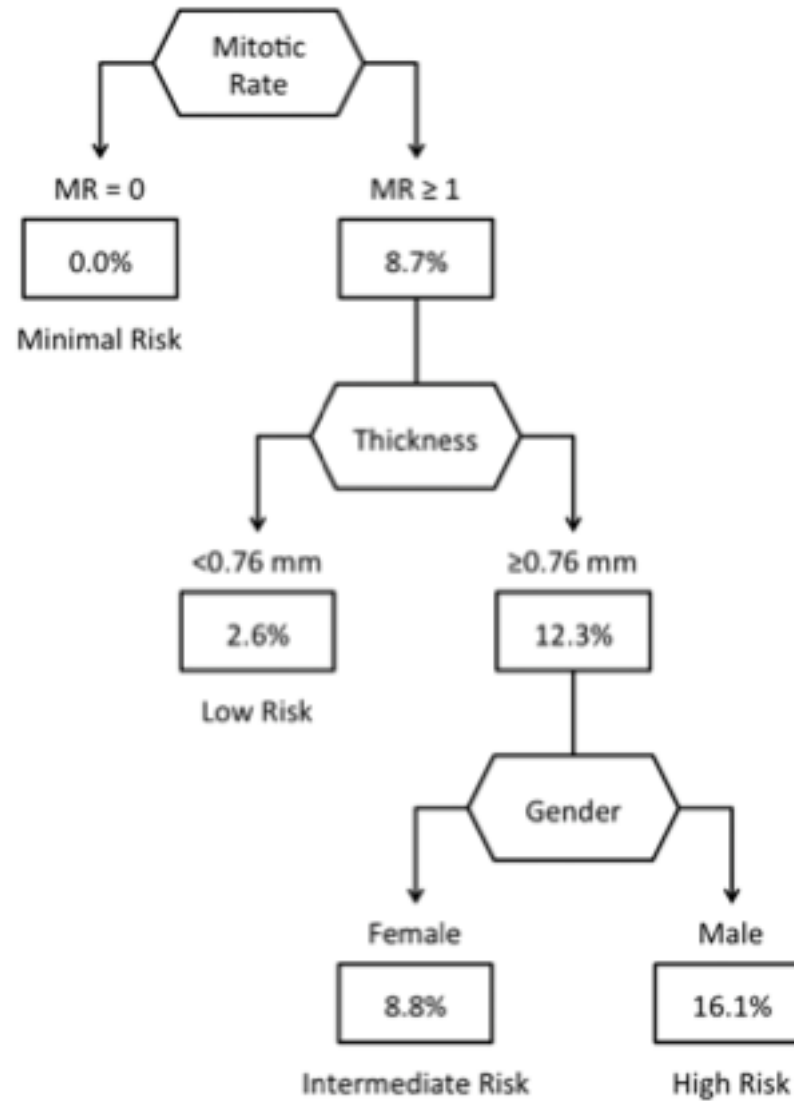
Table 5
Clark levels of invasion

I	Tumor confined to the epidermis
II	Tumor invading into the upper papillary dermis
III	Tumor filling the papillary dermis with no extension into the reticular dermis
IV	Tumor invading into the reticular dermis
V	Tumor invading into the subcutaneous tissue

CLARK IV ve V; Tumor 1mm altında bile olsa T₁ üzerine çıkar



Risk Belirleme



LENF NODU

- Sayı
- Mikrometastaz
- Makrometastaz

Table 1
TNM staging

T		
T is		
T1		
T2		
T3		
T4		
N		
N0	0	Not applicable
N1	1	N1a: micrometastasis ^a N1b: macrometastasis ^b
N2	2-3	N2a: micrometastasis ^a N2b: macrometastasis ^b N2c: in transit metastases/satellites without metastatic nodes
N3	4+ metastatic nodes, or matted nodes, or in transit metastases/satellites with metastatic nodes	
M	Site	Serum Lactate Dehydrogenase
M0	No distant metastases	Not applicable
M1a	Distant skin, subcutaneous, or nodal metastases	Normal
M1b	Lung metastases	Normal
M1c	All other visceral metastases	Normal
	Any distant metastasis	Increased

^a Micrometastases are diagnosed after sentinel lymph node biopsy.

^b Macrometastases are defined as clinically detectable nodal metastases confirmed pathologically.

Data from Edge SB, Byrd DR, Compton CC, et al, editors. AJCC cancer staging manual. 7th edition. Chicago: Springer; 2009. p. 332.

Sayı

N1 1

- Mikrometastaz
- Makrometastaz

N2 2-3

- Mikrometastaz
- Makrometastaz
- In-transit metastaz/
Satellit (LN yok)

N3 4

4 den fazla lenf nodu veya in-transit metastaz/ satellit (LN var)

Table 9
Multivariate Cox regression analysis of prognostic factors in 1338 stage III patients in the 2008 melanoma staging database

Variable	Chi-Square Values (1 df)		
	All Patients with Stage III (n = 1338)	Patients with Micrometastasis (n = 1070)	Patients with Macrometastasis (n = 268)
Number of positive nodes	27.4	27.8	5.0
Ulceration	17.5	13.5	2.1
Tumor thickness	9.1	9.4	1.1
Tumor burden (micro vs macro)	4.7	—	—
Mitotic rate	4.4	12.7	0.2
Age	24.8	15.8	7.1
Site	4.3	4.7	0.4
Gender	0.5	0.4	0.2
Clark level	0.1	0.0	0.2

Adapted from Balch CM, Gershenwald JE, Soong SJ, et al. Melanoma of the skin. In: Edge SB, Byrd DR, Compton CC, et al, editors. AJCC staging manual. 7th edition. New York: Springer; 2010. p. 325–44; with permission.

İNTRALENFATİK METASTAZ

- Satellit

- Mikrosatellit

- Melanom hücre grupları

- 0.05mm den büyük
 - Tumor kitlesinden en az 0.3 mm uzakta

- Klinik satellit

- Primer lezyondan 5 cm



Beraberinde lenf nodu yoksa N2c.....Lenf nodu varsa N3

İNTRALENFATİK METASTAZ

- In-transit metastaz
 - 5 cm.den uzaktaki lezyonlar
 - Lenf drenajının proksimali

Beraberinde lenf nodu yoksa N2c.....Lenf nodu varsa N3

SENTINEL LENF NODU METASTAZI

- Klinik olarak gizli lenf nodu metastazi
- Lenfatik drenaj paterni
- Isosulfan blue dye, Technetium-99m

Rotterdam Kriterleri

Lenf nodunda tumorun boyutu

- < 0.1 mm
- $0.1 - 1.0$ mm
- > 1.0 mm

Dewar Kriterleri

Lenf nodunda tumorun lokalizasyonu

- Subkapsüler
- Parankimal
- Multifokal
- Kombine
- Yaygın
- Bilinmeyen

0.1 altında tumor boyutunda;
Subkapsüler tutulum; %95
Non subkapsüler tutulum; % 88

Lenf nodu patolojisi; İmmunohistokimyasal inceleme

- Melanom Marker

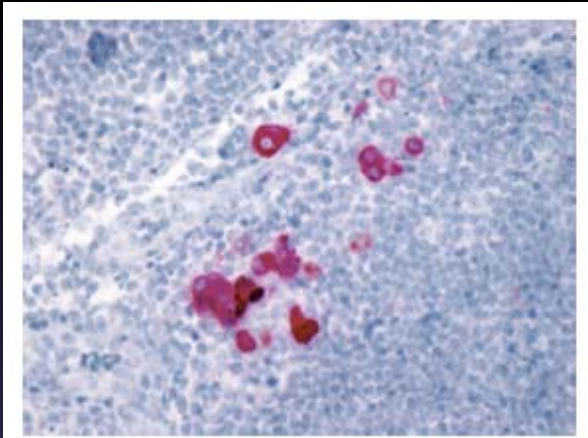


Fig. 4. Metastatic cells in the lymph node parenchyma. The tumor cells stain for Melan-A (red chromogen) and show irregular and pleomorphic nuclei. Some of the cells show multinucleation (×600).

- S 100
- Melanoma antigen; **Melan A**
- Melanoma antigen recognized by T cells;
MART-1
- Human Melanoma Black 45; HMB 45
- Microphthalmia- associated transcription factor; MITF

0.1 mm.den daha az boyuttaki mikrometastazlar saptanabilir.

METASTAZ

- Yeri
- LDH

Table 1
TNM staging

T		
T is		
T1		
T2		
T3		
T4		
N		
N0		
N1		
N2		
N3		
M		
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Yeri

M1 a

Uzak Kutan / Subkutan veya
Nodal metastaz / LDH normal

M1 b

Akciğer metastazı/ LDH normal

M1 c

Diğer organ metastazı

LDH Yüksekliği

Herhangi bir uzak metastaz

Metastaz sayısı da önemli; Evrelemede yok

Metastazlar

- Deri
- Yumuşak Doku
- Akciğer
- Beyin
- Kemik
- GIS

LDH yüksekse metastaz yeri önemli değil, yaşam şansı azalır

Table 10
Impact of serum LDH on median survival by site of disease

Site of Disease	LDH <200 U/L			LDH >200 U/L			P Value
	Number of Patients	Number of Deaths	Median Survival	Number of Patients	Number of Deaths	Median Survival	
Skin/subcutaneous/ distant nodal	49	32	16 (13–21)	5	5	9 (2–n/r)	.10
Lung	83	71	14 (12–17)	15	12	9 (4–17)	.008
Other viscera	114	91	9 (7–10)	105	95	5 (4–7)	.003

Adapted from Neuman HB, Patel A, Ishill M. A single-institution validation of the AJCC staging system for stage IV melanoma. *Ann Surg Oncol* 2008;15:2034–41; with permission.

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Data from Edge SB, Byrd DR, Compton CC, et al, editors. AJCC cancer staging manual. 7th edition. Chicago: Springer; 2009. p. 332.

Table 2
TNM melanoma staging

	Clinical Staging ^a				Pathologic Staging ^b		
	T	N	M		T	N	M
0	Tis	N0	M0	0	Tis	N0	M0
IA	T1a	N0	M0	IA	T1a	N0	M0
IB	T1b	N0	M0	IB	T1b	N0	M0
	T2a	N0	M0		T2a	N0	M0
IIA	T2b	N0	M0	IIA	T2b	N0	M0
	T3a	N0	M0		T3a	N0	M0
IIB	T3b	N0	M0	IIB	T3b	N0	M0
	T4a	N0	M0		T4a	N0	M0
IIC	T4b	N0	M0	IIC	T4b	N0	M0
III	Any T	N > N0	M0	IIIA	T14a	N1a	M0
				IIIB	T14a	N2a	M0
					T14b	N1a	M0
					T14b	N2a	M0
					T14a	N1b	M0
					T1-4a	N2b	M0
					T14a	N2c	M0
				IIIC	T1-4b	N1b	M0
					T14b	N2b	M0
					T14b	N2c	M0
					Any T	N3	M0
IV	Any T	Any N	M1	IV	Any T	Any N	M1

Patolojik Evreleme

- Tumor kalınlığı
- Ulserasyon
- Mitoz hızı
- Sınırların durumu
- Clark seviyesi
- Mikrosatellitler

Mutlak Bakılmalıdır !

Patolojik Evreleme

- Anjiolenfatik
(Lenfovaskuler)invazyon

- Histolojik subtip

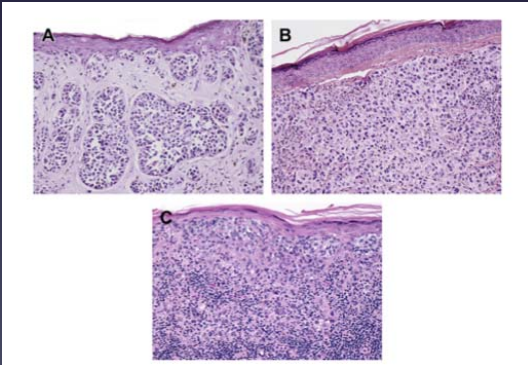
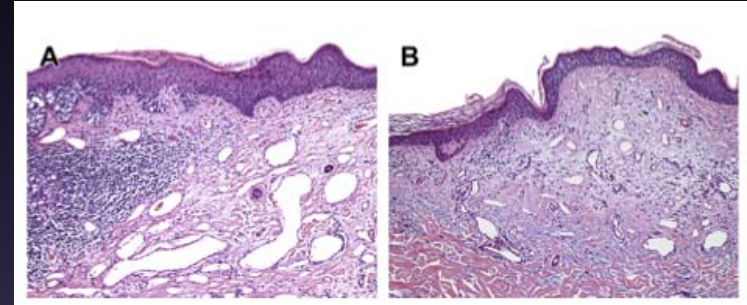
- Nörotrofizm

- Regresyon

- İnfiltrate lenfositler (Sitotoksik T hüç)

- Vertikal büyüme fazı

REGRESYON



INFILTRE LENFOSITLER

Opsiyonel

Table 11
Optional melanoma histologic features with prognostic value found in the dermatopathology report

Histologic Feature	Description	Impact on Prognosis
Angiolymphatic Invasion	Presence of tumor cells within a vessel lumen	Potential marker for hematologic/lymphatic spread of melanoma cells, but there is a high potential for misinterpretation in the presence of torturous vessels; Prognostic power overlaps with angiotropism
Histologic Subtype	SSM NM LMM ALM	LMM and SSM have been found to have a better prognosis than NM and ALM, but when controlling for tumor thickness, studies have not consistently found a significant difference between the subtypes There is also significant variance in categorization criteria among dermatopathologists
Neurotropism	Neoplastic infiltration of nerve fibers	Found to increase risk for local recurrence with an unclear role in metastatic disease, but there is limited data reported in the literature
Regression	Partial or complete absence of tumor cells in both the dermis and epidermis found within a melanoma; There is a residual variable combination of fibrosis, degenerative melanoma cells, melanophages, lymphocytes, and telangiectasia. Thought to be caused by interaction between the host immune response and the tumor cells	Unclear prognostic value because of inconsistencies in definition and measurement and lack of control of other histologic variables Several studies have shown that severe regression correlates with a worsening DFS, whereas other studies have found that regression in thin melanomas had a decreased metastatic risk
Angiotropism	Melanoma cells cuffing the external surface of vessels	Potential source for hematologic spread of melanoma cells, but there is limited data to evaluate whether angiotropism is an independent risk factor for metastasis or survival
Tumor Infiltrating Lymphocytes	Brisk: diffuse infiltrate of lymphocytes throughout the dermal tumor cells or the presence of lymphocytes along 90% of the circumference of the lesion base Non-Brisk: focal infiltrate of lymphocytes Absent: no lymphocytes are admixed with melanoma cells, but may be present perivascularly	Presence of a host inflammatory response is generally associated with a better prognosis, but prognostic power is limited because of the inconsistency in controlling for other prognostic features in previous studies There is lack of research on the functional status of lymphocytic infiltrates to determine whether they are operating as an active vs anergic immune response
Vertical Growth Phase	Presence of aggregates of tumor cells in the dermis with at least one nest in the dermis being larger than the largest intraepidermal nest, or the presence of mitoses	Indicates a worse prognosis, but its value as an independent risk factor has not been consistently validated; confounding factors are Breslow thickness and mitotic rate, with significant controversy in thin melanomas

Abbreviations: ALM, acral-lentiginous melanoma; LMM, lentigo maligna melanoma; NM, nodular melanoma; SSM, superficial spreading melanoma.

Data from Payette MJ, Katz M, Grant-Kels JM. Melanoma prognostic factors found in the dermatopathology report. J Clin Dermatol 2009;27:53–74.

STAGE	PATHOLOGIC STAGE GROUPING	10-YEAR SURVIVAL RATE	
		2002	2010
Stage 0	Tis N0 M0		
Stage IA	T1a N0 M0	88	94
Stage IB	T1b–T2a N0 M0	80	85
Stage IIA	T2b–T3a N0 M0	64	67
Stage IIB	T3b–4a N0 M0	52	56
Stage IIC	T4b N0 M0	32	40
Stage III	Stage IIIA T1–4a N1a/N2a M0	60	68
	Stage IIIB T1b–T4b N1a/N2a M0	42	44
	• T1a–T4a N1b/N2b M0	40	44
	• T1a–T4a/b N2c M0		52
	Stage IIIC T1–T4b N1b/2b M0	20	30
	• T1a–T4b N3 M0	18	26
	• Any T N3 M0		
Stage IV	Any T Any N M1	2.5–10	2.5–5

Abbreviations: *is=in situ*

Adapted from Balch CM, Gershenwald JE, Soong S, Thompson JF, Atkins MB, Byrd DR, et al. Final Version of 2009 AJCC Melanoma Staging Guidelines. *J Clin Oncol*. 2009;27(61):6199-6206.

İZLEM

- Rekurrens
- Metastaz
- Yeni primer tumor

(ikinci yeni melanom için yaşam boyu risk; %4-8)

İZLEM

- NCCN; National Comprehensive Cancer Network
- ESMO; European Society for Medical Oncology
- AAD; American Academy of Dermatology
- BAD; British Association of Dermatologists
- Swiss Melanoma Guidelines
- German Cancer Society and German Dermatologic Society
- Guidelines for the Management of Melanoma in Australia and New Zealand

Evre

NCCN
BAD
Swiss Guideline
German Guideline
Australia- New Zaeland Guideline

AAD
ESMO

Bireysel risk

	PROVIDER OR SPECIALTY	BASIS OF FOLLOW-UP GUIDELINES	FOLLOW-UP GUIDELINES			
			STAGE/ BRESLOW THICKNESS	H&P	IMAGING/ LABORATORY EVALUATION	COMMENTS
NCCN	Not discussed	Stage specific	Stage 0	H&P annually for life	None	<ul style="list-style-type: none"> Lifelong clinical exams Routine blood tests not recommended Frequency of H&P given in ranges and should be adjusted based on risk factors Self-skin exams should include self-lymph node exams
			Stage IA-IIA	H&P every 3–12 months for 5 years and then annually as clinically indicated	Not recommended	
			Stage IIB–IV	H&P every 3–6 months for 2 years and then every 3–12 months for 3 years and then annually as clinically indicated	Consider CXR, CT+/-PET every 3–12 months and annual MRI of brain. No imaging in asymptomatic patients after 5 years	
ESMO	Not discussed	Risk	Low risk/ thin melanomas	No specific recommendations	Not recommended	<ul style="list-style-type: none"> Emphasis on patient education and lifelong regular self-exams
			High risk	No specific recommendations	CT +/- PET recommended	

AAD	Not discussed	General recommendations	NA	H&P at least annually, possibly every 3–12 months	<ul style="list-style-type: none"> Not recommended in asymptomatic patients Directed imaging and lab work not recommended after 5 years in high-risk patients 	<ul style="list-style-type: none"> Lifelong clinical exams Follow-up should be based on individual risk factors Not stage-specific recommendations
BAD	Specialist skin cancer multidisciplinary teams	Stage specific	<i>in situ</i> Stage IA	Self-exam H&P 2–4 times for 12 months	No specific recommendations	No follow-up required for MIS
			Stage IB–IIIA	H&P every 3 months for 3 years then every 6 months for 2 years	No specific recommendations	—
			Stage IIIB–IV (resected)	H&P every 3 months for 3 years, every 6 months for the next 2 years and then annually for the next 5 years	Consider CT	—
			Stage IV (unresected)	Per patient need	No specific recommendations	Not discussed

Bireysel kontrol

NCCN
BAD
Swiss Guideline
German Guideline
Australia- New Zaeland Guideline

Optimal izlem süresi

1 yıl.....yaşam boyu

İzlem sıklığı

3 ay.....12 ay

BAD

İnsitu; yok
IA; 1 yıl
IB-III A; 5 yıl
IIIB-IV; 10 yıl

GERMAN

Tüm evrelerde;
10 yıl

PROVIDER OR SPECIALTY	BASIS OF FOLLOW-UP GUIDELINES	FOLLOW-UP GUIDELINES			
		STAGE/ BRESLOW THICKNESS	H&P	IMAGING/ LABORATORY EVALUATION	COMMENTS
German Cancer Society and German Dermatologic Society	Not discussed	Stage I <1mm	H&P every 6 months for years 1-5 then every 6-12 months for years 6-10	No imaging or blood work	<ul style="list-style-type: none"> Limit clinical exams to 10 years Use of LNS, S100β levels emphasized
			H&P every 3 months for years 1-5 then every 6-12 months for years 6-10	LNS every 6 months for years 1-5	
		Stage III	H&P every 3 months for years 1-5 then every 6 months for years 6-10	S100 β level every 3-6 months for years 1-5 No additional imaging studies LNS every 3-6 months for years 1-5	
				S100 β level every 3-6 months for years 1-5 Abdominal sonography and CXR or CT, MRI, or PET every 6 months for years 1-5	

Swiss Guidelines	Not discussed	Stage specific	Stage I (\leq T1N0)	H&P every 6 months for years 1-3 then annually from years 6-10	None	<ul style="list-style-type: none"> Lifelong clinical surveillance is recommended Use of LNS emphasized Abdominal sonography and CXR on individual basis for Stage I (T2N0)-IV melanomas
			Stage I (T2N0)-IIB	H&P every 3 months for years 1-3, every 6 months for years 4-5, then every 6-12 months for years 6-10	LNS and S100 every 6-12 months for years 1-5	
			Stage IIC-III	H&P every 3 months for years 1-5 then every 6 months for years 6-10	LNS and S100 every 6 months for years 1-5 CT, MRI, PET or PET-CT every 6-12 months for years 1-5	
			Stage IV	Individual	Individual	
Guidelines for Management of Melanoma in Australia and New Zealand	Patients themselves and/or preferred health professional	Stage specific	Stage I	H&P every 6 months for 5 years	<ul style="list-style-type: none"> Ultrasound may be used in conjunction with clinical examination only in patients with more advanced primary disease No lab tests are recommended 	<ul style="list-style-type: none"> Self examinations are essential and all patients should be properly educated on how to perform them Individual patient's needs must be considered before appropriate follow-up is offered
			Stage II, III	H&P every 3-4 months for 5 years then annually thereafter		
			Stage IV	Not discussed		

NCCN
AAD
SWISS

Yaşam Boyu

EVRE I
5 yıl

Diğer;
Yaşam boyu

Risk Faktörleri Değerlendirilmeli

Evre

Breslow kalınlığı

Açık ten

Atipik nevus varlığı

Aile öyküsü

Entellektüel düzey

Psikolojik durum, anksiyete

İlk 5 yıl önemli
Yılda 2 kez
Yaşam boyu

Kim ?

- a. Dermatolog
- b. Onkolog
- c. Plastik Cerrah
- d. Genel Cerrah

Kim ?

a. Dermatolog

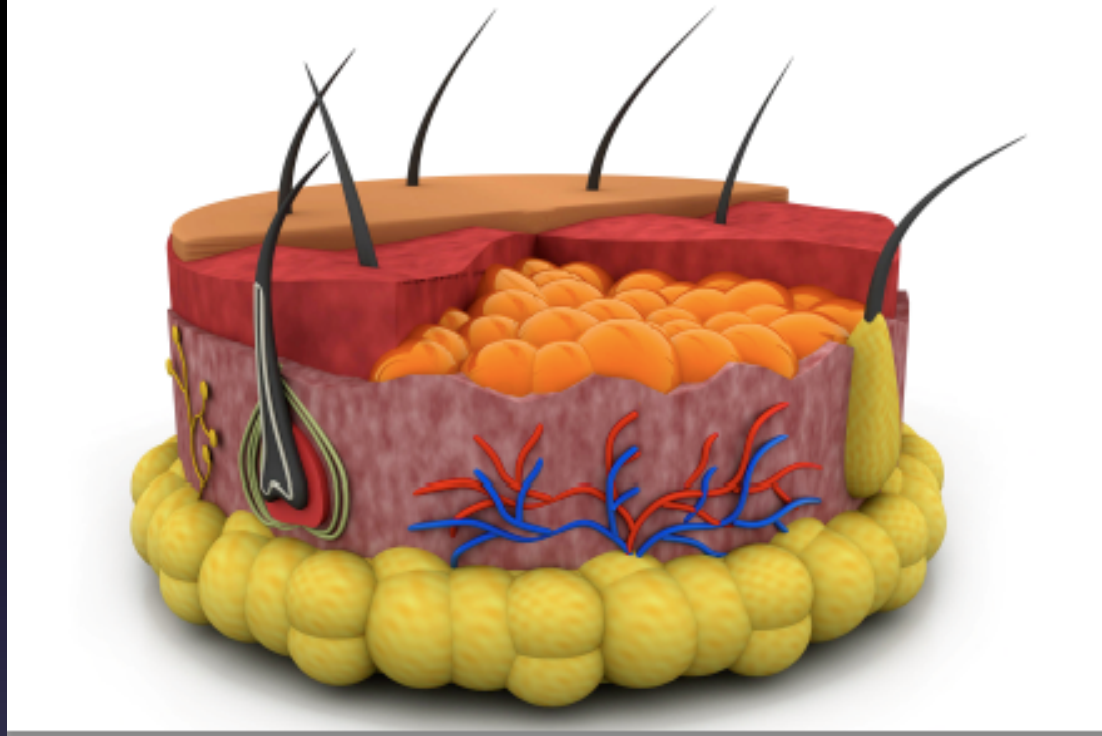
b. Onkolog

c. Plastik Cerrah

d. Genel Cerrah

McKenna ve ark. Br J Dermatol 2004

a. Dermatolog



Saygılarımla.....