



HemeOncJobs.com Oncology Boards Review

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Melanoma

Types of Melanomas (or "Mels" for short)

- A. Superficial Spreading
- B. Nodular
- C. Lentigo
- D. Acral → these are the ones on the palms, soles of feet, nail beds.
- E. Uveal Melanomas → these are the ones in the eyes.

Risk Factors for developing a Melanoma

Sun Exposure, sun tanning in sun tan parlors

SPF (suntan lotion sun protection factor) = the level of SPF needs to be > 15

Family history of someone in the family having developed a Melanoma

Dysplastic Nevus and Atypical moles on the skin = are "precursor lesions"

(in fact if you have **both** a positive FH **and** a Dysplastic Nevus your risk of developing a melanoma is something like = 80%)

For someone with both of these risk factors, you have to do something called "Intensive Surveillance" - i.e. keep a close eye on them.

Prognosis

Remember that the depth of invasion (i.e. the Clark's/Breslow stuff → see below) is key in terms of deciding the prognosis of a melanoma.

Some other things which characterize Mels with worse prognosis are:

- 1) **Bleeding or ulceration** → this is important
- 2) High Mitotic Rate
- 3) Involvement of regional lymph nodes → (see more about this below)
- 4) Lack of TILs (Tumor Infiltrating Lymphocytes) in them
- 5) Presence of "In Transit" lesions or "Microscopic Satellites"
- 6) Trunk or head location, male sex, older age group

Clark's and Breslow

Remember and review the whole **Clark's Level** vs **Breslow's thickness** thing.

Clark's → is how thick it goes into the **I. epidermis, II. papillary dermis III. Pappillary-Reticular level and IV. Reticular Dermis**

Breslow → is how thick the melanoma is in millimeters.
this thickness thing is **the most prognostically predictive**

Breslow Thickness	5 year survival	Treat or Not to treat
< 1 mm	95 - 100%	Do not treat
1-2 mm	80 - 96 %	Sentinel Node Bx
2-4 mm	60 - 75%	"
>4 mm	50%	Adjuvant α Interferon*

*See below for more on adjuvant α Interferon

Hereditary Considerations in Melanoma

Remember that Chromosome #9 is important in Melanomas (see below)

10% of people who get melanoma = have a **family history** of melanoma.

Genes involved/related to melanoma: **CDK/N2A** → on Chromosome 9

CDK₄

BRCA₂

BRAF → in 60% of **sporadic** Mels

NRAS → in 15% of Mels

KIT → in **Lentigo** Mels

PTEN → if you lose this = Mels

MITF

Surgery In Melanomas

For the initial excision, you only need maybe 1-2 mm margins around it.

But you must go DOWN past the **subcutaneous tissue** - down to the **fascia**.

Don't do a **shave** or a **curretage** for a melanoma → I know, I know, its nuts to even have to remind us of something like this.

Surgery In Melanomas (cont'd)

What to do following the initial excision of the primary melanoma:

Depth of the Mel found at resection	Surgical resection margins needed
In Situ	0.5 - 1 CM
< 1 mm	1 CM
1-2 mm	1 - 2 CM
2-4 mm	2 CM
> 4 mm	At least 2 CM

If the Primary Lesion had:

Primary Lesion had/was	Sentinel Node Biopsy	False Negatives
> 1 mm in depth Ulcerated or bleeding Clark's level III or IV	Do a Sentinel LN Biopsy	Remember that a Sentinel Node Bx can have 4% False Neg Rate

What is a HIGH RISK Melanoma and what do you do when you find one?

	Why it's a low/high risk	What to do about it
Low Risk Melanoma	<1.0 mm depth	No further testing, ? CXR
High Risk Melanoma	> 4 mm and/or +Lymph nodes*	CXR, Cat Scans, LFTs, LDH

* i.e. a positive sentinel LN biopsy

Note: This high risk/low risk stuff is a hot topic these days.

In this day and age of cost consciousness, the Boards are probably very much going to want you to know when you do and when you do not need to order the "million dollar work up" for a patient.

Stages in Melanomas

- I & II → Mels limited to the skin
- III → Mels that have gone to the Lymph Nodes (see box below)
- IV → Mels with Distant Mets

Stages in Melanomas (Cont'd)

What to do about **Stage III Melanomas**

→ i.e. Mels with Lymph Node involvement when 1st found

A) If the LN are **not palpable** clinically then → Doesn't help
 an elective/Prophylactic LN Dissection → No survival Benefit
 Don't do it

B) But if the LN are "clinically enlarged"
 which basically means if you → Then there is evidence
 can **feel them clinically** → that what is called a
"Therapeutic LN Dissection" helps.

↓

Doing a so-called
"Therapeutic LN Dissection" →
 Produces:

- Long Term Disease-Free survival
- Optimal local long term dz control
- Sometimes even produces a cure!

Dr. Wesley's / HemeOncJobs.com Note:

I was once had a patient who presented with a palpably enlarged left groin. She had very hard and palpable lymph nodes in her left groin. These did not feel like normal, rubbery nodes. These nodes were rock hard and worrisome. We thus sent her to get a biopsy of these hard lymph nodes. To our surprise, the biopsy showed that the nodes had metastatic Melanoma! But she had no primary lesion! Her left leg had no melanomas. We found no other skin lesions that even remotely looked like a melanomas anywhere on her body. Her CT scans and other imaging studies, labs, etc were all negative. We thus recommended a complete therapeutic lymph node dissection of the left groin and a course of adjuvant alpha Interferon. That was well over 5 years ago and she still remains disease free to this day.

In a Nutshell: Melanoma 101

What to do after you find a melanoma and remove the primary lesion:

A. Decide what will be the surgical **margins of the re-resection**

Depth of Mel (found at the 1st resection)	Surgical resection margins needed
In Situ	0.5 - 1 CM
< 1 mm	1 CM
1-2 mm	1 - 2 CM
2-4 mm	2 CM
> 4 mm	At least 2 CM

If the Primary Lesion had:

Primary Lesion had/was	Sentinel Node Biopsy	False Negatives
> 1 mm in depth Ulcerated or bleeding Clark's level III or IV	Do a Sentinel LN Biopsy	Remember that a Sentinel Node Bx can have 4% False Neg Rate

B. How much of a work up to do once you find a melanoma depends on **if its High Risk or Low Risk Melanoma:**

	Why it's a low/high risk	What to do about it
Low Risk Melanoma	< 1.0 mm depth	No further testing
High Risk Melanoma	> 4 mm and/or +Lymph nodes*	CXR, Cat Scans, LFTs, LDH, etc

* i.e. a positive sentinel LN biopsy

C. Stage III Melanomas

If the lymph nodes were positive (i.e. a positive Sentinel Node biopsy or clinically involved lymph nodes and thus a stage III disease), see the "Stage III Melanomas" box and the Sentinel Lymph Nodes boxes above to decide how much surgery to do (or not to do). Then, after you know much surgery is needed (or not), follow up with the following:

D. Treatments for **High Risk and/or Stage III Melanomas**

Surgery	Surgically remove the involved lymph nodes - but remember, only if they're clinically palpable
Radiation Therapy	Radiate the axilla/groin following resection but Do not give a course of adjuvant xrt to the axilla or groin after the resection if there was no proof of extra-capsular extension
α Interferon course (high dose)	After the surgery (or after deciding that surgery is not needed if the LN are not palpable) give a course of adjuvant α Interferon Note: Not a course of adjuvant DTIC Chemotherapy or adjuvant Interleukin-2 (IL-2) (ECOG study E1684)

E. Things to remember about **Alpha Interferon**

α Interferon: Criteria for who to give adjuvant α Interferon	<ol style="list-style-type: none"> 1) >4 mm initial depth at the time of resection 2) + Lymph Node involvement 3) "In Transit" or "Satellite Lesions" 4) Rendered "DZ-free" after a LN dissection
α Interferon Benefits when given in the adjuvant setting	<ol style="list-style-type: none"> 1) Improves RFS (Relapse Free Survival) by 10% 2) Not so sure if it improves OS (overall survival) 3) Has to be high dose - not low dose α Interferon 4) adjuvant vaccines - still no survival data
α Interferon Side Effects	<ol style="list-style-type: none"> 1) Flu like - fever, chills, fatigue 2) Myalgias, anorexia, nausea/vom, headache 3) ↓ WBC, ↑ Triglycerides, anemia 4) ↑ Hepatic enzymes - monitor LFTs weekly during induction phase monitor LFTs monthly during the maintenance phase 5) Thyroid dysfunction 6) Depression and suicidal ideation
α Interferon Side Effects (cont'd)	<ol style="list-style-type: none"> 1) If ↑ Hepatic enzymes 5 x normal Temporarily stop the αInf until values normalize Then restart the αInf at 50% the previous dose 2) If ↓ Granulocytes < 500 Temporarily stop the αInf until values normalize Then restart the αInf at 50% the previous dose

F. Treatments for **Metastatic** Melanoma

Chemotherapy	DTIC	FDA approved for metastatic Mels	Does not improve OS (overall survival)
Immunotherapy	α Interferon	Mostly used in the adjuvant setting	Does not improve OS (overall survival)
	IL-2	FDA approved for metastatic Mels	Does not improve OS (overall survival)
	Zelboraf (verumafenib)	FDA approved for metastatic Mels But only for <i>BRAF mutation + Mels</i>	Improves both PFS (progression free survival) and OS (overall survival)
	Yervoy (Ipilimumab)	monoclonal antibody Blocks CTLA-4 FDA approved for advanced Metastatic melanoma	Improves OS (overall survival)

G. **Side effects** of the treatment options available for **Metastatic** melanoma

Medication	Name	Side Effects
Chemotherapy	DTIC	Typical chemotherapy side effects: Marrow suppression, anemia, etc
Immunotherapy	α Interferon	See page 6 above
	IL-2	Rash, arthralgias, leaky lungs, etc
	Zelboraf (verumafenib)	1) arthralgia, rash, fatigue, alopecia 2) keratoacanthoma, 3) squamous cell carcinoma 4) photosensitivity 5) nausea, and diarrhea
	Yervoy (Ipilimumab)	1) Enterocolitis - severe diarrhea, etc. 2) Immune mediated Hepatitis 3) Toxic Epidermal Necrolysis 4) Severe dermatitis 5) Stevens Johnson Syndrome 6) Guillian-Barré or Myasthenia Gravis 7) Endocrinopathies (\downarrow Pit, \downarrow thyroid, \downarrow adrenals, \downarrow gonads, etc) 8) Ocular damage (think of this drug as basically causing a Graft-versus-host disease)

NOTES: