Skin and Soft Tissue Tumors

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Surgical Oncology
Surgeons Group of Baton Rouge
OLOL Physician Group
LSU Department of Surgery
Skin Cancer Incidence

More than 4 million skin cancers in over 3 million people are diagnosed annually.
Skin Cancer: General Information

- Non Melanoma
  - Basal Cell Carcinoma
  - Squamous Cell Carcinoma
  - Merkel Cell Carcinoma
  - Other
- Melanoma
Basal Cell Carcinoma

- 2.5 Million per year

- Arise in the skin’s basal cells, which line the deepest layer of the epidermis

- Open sores, red patches, pink growths, shiny bumps, or scars

- Can be disfiguring
55 year old with a nodular basal cell carcinoma
Squamous Cell Carcinoma

- 700,000 each year in the US

- Arising in the squamous cells, which compose most of the skin’s upper layers (the epidermis).

- Scaly red patches, open sores, elevated growths with a central depression, or warts;

- May crust or bleed.
Merkel Cell Carcinoma

- Rare - .5/100,000
- Neural crest origin
- Nontender, rapidly growing, painless, single, red to violaceous, firm intradermal papule
- Asymptomatic
- Expanding
- Immunosuppressed
- Older
- Ultraviolet-exposed fair skin
Melanoma

Melanoma is a malignant tumor of melanocytes, which are the cells that make the pigment melanin and are derived from the neural crest.
Melanoma

• Estimated new cases and deaths from melanoma in the United States in 2013:

• New cases: 76,690
• Deaths: 9,480

Background

ABCDE Guidelines

• Asymmetry
• Border irregularity
• Color changes
• Diameter > 6 millimeters
• Evolving
Figure 16.1
SEER Observed Incidence, SEER Delay Adjusted Incidence and US Death Rates
Melanoma of the Skin, White, by Sex

Male

Rate per 100,000

SEER Incidence APCs
Delay Adj, 1986-10 = 3.2*
Observed, 1986-10 = 3.1*

US Mortality APC
2002-10 = 1.0*

Year of Diagnosis/Death

Female

Rate per 100,000

Delay-Adjusted Incidence
Observed Incidence
Mortality

SEER Incidence APCs
Delay Adj, 1980-10 = 2.8*
Observed, 2005-10 = 1.2

US Mortality APC
1986-10 = -0.3*

Year of Diagnosis/Death
Role of skin cancer screening

Surgical advances in melanoma
Role of skin cancer screening

Surgical advances in melanoma
Screening for Cancer

- Cervical
- Endometrial
- Breast
- Prostate
- Colorectal
- Lung
- Skin??
Role of Screening

Characteristics of a good screening test

- Has to be both sensitive and specific
- Has to be sufficient yield
- Has to be readily available
- Has to improve outcomes
Systematic skin cancer screening in Northern Germany
Systematic skin cancer screening in Northern Germany

SCREEN Project

- Target Screening Population Schleswig-Holstein
- Physicians
  - Nondermatologists – 8 hour training course
  - Dermatologists
- Recruitment
  - Doctor – Patient communication
  - Mass Media
    - Public ads
    - Billboards, Newspaper, Web page
    - Telephone Hotline
- 2003-2004
Systematic skin cancer screening in Northern Germany

Target population in Schleswig-Holstein: 1,880,095

SCREEN project participants: 360,288

Exam by a Non-dermatologist: 278,741

Exam by a Dermatologist: 81,032

Pts with Excisions: 15,983 (4%)

Benign: 11,870
Malignant: 2,911 (0.8%)

Systematic skin cancer screening in Northern Germany

Benign: 11,870
Malignant: 2,911

<table>
<thead>
<tr>
<th>Histology</th>
<th>No</th>
<th>Per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma</td>
<td>585</td>
<td>1.6</td>
</tr>
<tr>
<td>Basal Cell</td>
<td>1961</td>
<td>5.4</td>
</tr>
<tr>
<td>Squam Cell</td>
<td>392</td>
<td>1.1</td>
</tr>
<tr>
<td>Other</td>
<td>165</td>
<td>0.5</td>
</tr>
</tbody>
</table>
Systematic skin cancer screening in Northern Germany

Skin cancer screening was effective at identifying more skin cancers
Systematic skin cancer screening in Northern Germany

Mortality following SCREEN study was less than expected

![Graph showing melanoma mortality trends for men and women in Northern Germany](graph.png)
Systematic skin cancer screening in Northern Germany

Conclusions

- Reduction in skin cancer burden is possible
- For melanoma – reduction in mortality
- For non-melanoma– reduction morbidity, increase QOL
Systematic skin cancer screening in Northern Germany

Boniol M. BMJ Open. 2015 Sep 15;5(9)
CONCLUSIONS AND RECOMMENDATION  The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of visual skin examination by a clinician to screen for skin cancer in adults (I statement).
Societal recommendations

American Academy of Family Physicians
American College of Preventive Medicine
American Academy of Dermatology (AAD)
American College of Physicians
American Academy of Family Physicians
American College of Preventive Medicine,
American College of Physicians

American Cancer Society*
- persons age 21 years and older have a cancer-related checkup at their periodic health examination, including possibly an examination for skin cancer

No specific recommendation for skin cancer screening

MBPCC Skin Cancer Screening Results

Jan 2014 – October 2014

23 events
1,116 patients screened

109 navigated

Malignant: 4

<table>
<thead>
<tr>
<th>Histology</th>
<th>No</th>
<th>Per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma</td>
<td>1</td>
<td>1.1</td>
</tr>
<tr>
<td>Basal Cell</td>
<td>2</td>
<td>1.7</td>
</tr>
<tr>
<td>Squam Cell</td>
<td>1</td>
<td>1.1</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Role of Screening

Insufficient evidence $\neq$ Evidence of no benefit

Identify High Risk Patients
Skin Cancer Screening

Screening - high risk patients:

- Personal history of melanoma
- Family history of melanoma (especially first-degree relatives are multiple family members)
- Atypical mole syndrome
- Increased number of moles (> 25)
- Immunocompromise patients (Immunosuppressive medications, HIV/AIDS, certain malignancies, transplant patients)
- History of excessive exposure to ultraviolet radiation
- Tanning bed exposure
## Inherited Susceptibility to Melanoma

<table>
<thead>
<tr>
<th>Feature</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal hx of skin cancer</td>
<td></td>
</tr>
<tr>
<td>Melanoma</td>
<td>4.2</td>
</tr>
<tr>
<td>NMSC</td>
<td>4.2</td>
</tr>
<tr>
<td>Family history of skin cancer</td>
<td></td>
</tr>
<tr>
<td>Parent</td>
<td>2.4</td>
</tr>
<tr>
<td>Sibling</td>
<td>2.9</td>
</tr>
<tr>
<td>2 1° Relatives</td>
<td>8.9</td>
</tr>
<tr>
<td>Atypical Nevi</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Common Nevi</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>2.2</td>
</tr>
<tr>
<td>50-100</td>
<td>4</td>
</tr>
<tr>
<td>&gt;100</td>
<td>6.8</td>
</tr>
</tbody>
</table>
Atypical Nevus Syndrome
# Inherited Susceptibility to Melanoma

## Melanoma Predominant Syndromes
- CDKN2A
- CDK4
- TERT
- POT-1
- BAP1

## Melanoma Inclusive Syndromes
- BRCA-2
- Rb-1
- MC1R
- XP
- Li-fraumeni
- PTEN
- MITF
CDKN2A

- Chromosome 9p21
- Tumor suppressor
- AD inheritance
- Contains 8 exons
- Encodes two proteins
  - (p16)INK4A and (p14)ARF
G0 = Cell rests (it’s not dividing) and does its normal work in the body

G1 = RNA and proteins are made for dividing

S = Synthesis (DNA is made for new cells)

G2 = Apparatus for mitosis is built

M = Mitosis (the cell divides into 2 cells)

p16 inhibits CDK4 and CDK6
Skin cancer screening
Features associated with germline CDKN2A mutations: a GenoMEL study of melanoma-prone families from three continents

- Melanoma Genetics Consortium
- Identified 385 high risk families
- Evaluation of
  - Mutations as a function of:
    - Number of family members with melanoma
    - Number of primary melanomas in a family
    - Incidence of pancreas cancer
    - Age

Skin cancer screening
Skin cancer screening

Features associated with germline CDKN2A mutations: a GenoMEL study of melanoma-prone families from three continents

- 3 CMM
- 4 CMM
- 5 CMM
- ≥6 CMM

p < 0.001

- No MPM
- 1 MPM
- 2 MPM
- ≥3 MPM

p < 0.001

Goldstein A. J Med Genet. 2007
Features associated with germline CDKN2A mutations: a GenoMEL study of melanoma-prone families from three continents

Goldstein A. J Med Genet. 2007
Skin cancer screening

Features associated with germline CDKN2A mutations: a GenoMEL study of melanoma-prone families from three continents

Mutations are most likely to be present in the following settings:

• Multiple family members w melanoma
• Early onset of melanoma (<50)
• Multiple primaries
• Occurrence of other malignancies (ie pancreas cancer)
CDKN2A

• Lifetime risk of melanoma
  – Bt 30-90%

• Stage for stage
  – Worse MSS
Skin cancer screening

CDK4

- Ch 12q14.1
- AD
- Nervous tumors
- CDKN2A Phenotype
Skin cancer screening

Other Melanoma Predominant Syndromes

• POT-1
  – Ch 9q31.33
  – Assoc w gliomas

• TERT
  – Ch 5p15.33
  – Ovary, GU, Lung
Who to offer genetic testing?

<table>
<thead>
<tr>
<th>Low melanoma incidence area (United Kingdom)</th>
<th>≥2</th>
<th>2 relatives(^\dagger) with melanoma or 1 with melanoma and 1 with pancreatic cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate to high incidence melanoma area (US and Australia)</td>
<td>≥3</td>
<td>3 melanomas or 2 melanomas and 1 pancreatic cancer or 1 melanoma and 2 pancreatic cancers</td>
</tr>
</tbody>
</table>
How to manage these patients?

At least yearly skin cancer screening (no consensus)

Genetic counseling
  Ensure family members are evaluated
  Ensure that other associated malignancies are being considered
Known Human Carcinogens*

It’s a known human carcinogen

- Aflatoxins
- Arsenic
- Asbestos (all forms)
- Benzene
- Epstein-Barr virus infection
- Helicobacter pylori infection
- Hepatitis B virus infection
- Hepatitis C virus infection
- HIV-1 infection
- HPV
- Ionizing radiation (all types)
- Outdoor air pollution
- Plutonium
- Radium-224 and its decay products
- Radium-226 and its decay products
- Radium-228 and its decay products
- Radon-222 and its decay weeps
- Sulfur mustard
- 2,3,7,8-Tetrachlorodibenzo-p-dioxin
- Thiotepa
- Thorium-232 and its decay products
- Tobacco, smokeless
- Tobacco smoke, secondhand
- Tobacco smoking
- Ultraviolet (UV) radiation, including UVA, UVB, and UVC rays
- Ultraviolet-emitting tanning devices
- Vinyl chloride

* Not a complete list
Skin Cancer Screening

UV Radiation

UVA

UVB

95% of Radiation
- Longer rays (deeper)
- Regardless of Time of Day
- Penetrates glass/clouds
- Responsible for Aging
- Responsible for Tanning

5% of Radiation
- Shorter rays
- Prevalent at peak hours
- Responsible of Burning
- Responsible for SPF

UV Radiation and the Skin
Sun Protection

- Limiting ultraviolet (UV) exposure

- Seek shade
- Protect your skin with clothing
- Wear a hat
- Wear sunglasses
- Avoid tanning beds and sunlamps
- Use sunscreen
  - Zinc Oxide
  - Titanium Dioxide
  - SPF 30
  - Reapply every 2 hours
Conclusions

- There is no data to support screening all patients
- Everyone should probably have at least one baseline skin exam
- Subset of high risk patients should be identified and seen more frequently
Role of skin cancer screening

Surgical advances in melanoma
Case 1

Punch Biopsy:
- 1.4 mm superficial spreading melanoma
- Ulceration – Yes
- Mitosis < 2
- Clarks – 4
- Tumor Infiltrating Lymphocytes – None
- Angio - lymphatic invasion – None
Technique of Sentinel Node Biopsy

1. Radiolabelled protein is injected into the tumor.
2. A nuclear medicine picture (called a lymphoscintogram) is done to see exactly where the protein travelled.
3. Blue dye is injected into the tumor.
4. Audio and visual cues are used at surgery to identify “hot, blue” sentinel lymph nodes.
Surgical advances in melanoma

Case 1
Technique of SLNB
Case 1
## NCCN Guidelines Version 1.2017
### Melanoma

#### CLINICAL/PATHOLOGIC STAGE

<table>
<thead>
<tr>
<th>Stage III (sentinel node positive)</th>
<th>Stage III (clinically positive node[s])</th>
</tr>
</thead>
</table>

#### WORKUP

- **Stage III (sentinel node positive):**
  - Consider imaging for baseline staging (category 2B)
  - Imaging to evaluate specific signs or symptoms

- **Stage III (clinically positive node[s]):**
  - FNA preferred, if feasible, or core, incisional, or excisional biopsy
  - Imaging for baseline staging and to evaluate specific signs or symptoms

#### PRIMARY TREATMENT

- Discus and offer complete lymph node dissection

- **Stage III (sentinel node positive):**
  - Wide excision of primary tumor (category 1) and complete therapeutic lymph node dissection

- **Stage III (clinically positive node[s]):**
  - Wide excision of primary tumor (category 1) and complete therapeutic lymph node dissection

#### ADJUVANT TREATMENT

- Clinical trial
- Observation
- Interferon alfa
- High-dose ipilimumab for SLN metastasis >1 mm

- Locoregional option:
  - Consider RT to nodal basin in selected high-risk patients based on location, size, and number of involved nodes, and/or macroscopic extranodal extension (category 2B)

- Systemic options:
  - Clinical trial
  - Observation
  - Interferon alfa
  - High-dose ipilimumab
  - Biochemotherapy (category 2B)

---

*See Follow-up (ME-9)*
Surgical advances in melanoma

Videoscopic Inguinal Node Dsxn

- Inguinal ligament
- Nodal packet held up to transect last remaining attachments
- Artery
- Vein
- Pectineus muscle visible below posterior femoral sheath
- Femoral Sheath
- Sartorius m.
- Adductor longus m.
Melanoma: A clinical overview

Videoscopic Inguinal Node Dsxn
Surgical advances in melanoma

Videoscopic Inguinal Node Dsxn

Table — Selected Studies of Wound Complications Following Open Inguinal Lymphadenectomy for Melanoma

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Overall Wound Complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shaw</td>
<td>58</td>
<td>43</td>
</tr>
<tr>
<td>Coit</td>
<td>42</td>
<td>64</td>
</tr>
<tr>
<td>Beitsch</td>
<td>168</td>
<td>51</td>
</tr>
<tr>
<td>Karakousis</td>
<td>205</td>
<td>52</td>
</tr>
<tr>
<td>Serpell</td>
<td>27</td>
<td>71</td>
</tr>
<tr>
<td>de Vries</td>
<td>14</td>
<td>35</td>
</tr>
<tr>
<td>van Akkooi</td>
<td>129</td>
<td>29</td>
</tr>
<tr>
<td>Sabel</td>
<td>212</td>
<td>19</td>
</tr>
<tr>
<td>Guggenheim</td>
<td>43</td>
<td>48</td>
</tr>
<tr>
<td>Poos</td>
<td>129</td>
<td>21</td>
</tr>
<tr>
<td>Chang</td>
<td>53</td>
<td>77</td>
</tr>
</tbody>
</table>
Surgical advances in melanoma

Videoscopic Inguinal Node Dsxn
Oncologic Outcomes of Patients Undergoing Videoscopic Inguinal Lymphadenectomy for Metastatic Melanoma

Benjamin M Martin, MD, Joanna W Etra, BA, Maria C Russell, MD, Monica Rizzo, MD, FACS, David A Kooby, MD, FACS, Charles A Staley, MD, FACS, Viraj A Master, MD, PhD, FACS, Keith A Delman, MD, FACS

• Single institution series (Emory)
• VIL (n=40) vs. Open superficial inguinal lymphadenectomy (n=40)
• Same Surgeon (KAD)
• 2005 to 2012 Median follow-up
  – VIL 19.1 mos
  – OIL 33.9 mos
• Outcomes
  – Morbidity
  – Pathologic
  – Survival

**Oncologic Outcomes of Patients Undergoing Videoscopic Inguinal Lymphadenectomy for Metastatic Melanoma**

**Table 1.** Demographic Data of Patients Undergoing Inguinal Lymphadenectomy, via Videoscopic or Open Approach, for Regionally Metastatic Melanoma

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>VIL (n = 40)</th>
<th>Open (n = 40)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age ± SD</td>
<td>49.9 ± 16.1</td>
<td>50.9 ± 17.2</td>
<td>0.777</td>
</tr>
<tr>
<td>Range</td>
<td>16–85</td>
<td>16–81</td>
<td></td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female sex</td>
<td>60.0</td>
<td>47.5</td>
<td>0.262</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>92.5</td>
<td>94.1</td>
<td>0.782</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean BMI ± SD</td>
<td>28.2 ± 6.5</td>
<td>27.2 ± 8.1</td>
<td>0.570</td>
</tr>
<tr>
<td>Range</td>
<td>18.4–48.7</td>
<td>19.8–59.8</td>
<td></td>
</tr>
<tr>
<td>Smoker, %</td>
<td>25.0</td>
<td>16.9</td>
<td>0.799</td>
</tr>
<tr>
<td>Mean Charlson Comorbidity Index calculated 10-year mortality, %</td>
<td>82.5</td>
<td>76.3</td>
<td>0.305</td>
</tr>
</tbody>
</table>

*Calculated as 10-year mortality in study.
Oncologic Outcomes of Patients Undergoing Videoscopic Inguinal Lymphadenectomy for Metastatic Melanoma

Table 3. Comparison of Perioperative and Pathologic Data Between Videoscopic Inguinal Lymphadenectomy and Open Superficial Inguinal Lymphadenectomy Patients with Melanoma

<table>
<thead>
<tr>
<th>Variable</th>
<th>VIL (n = 40)</th>
<th>Open (n = 40)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median operative time, min (range)</td>
<td>181.3 (85–343)</td>
<td>155.9 (103–318)</td>
<td>0.008*</td>
</tr>
<tr>
<td>Mean lymph node retrieval count, n (range)</td>
<td>12.6 (3–24)</td>
<td>14.2 (4–23)</td>
<td>0.131</td>
</tr>
<tr>
<td>Total positive lymph nodes, mean, n (range)</td>
<td>1.78 (1–9)</td>
<td>1.22 (1–3)</td>
<td>0.035*</td>
</tr>
<tr>
<td>Total positive sentinel lymph nodes, n, mean†</td>
<td>1.39</td>
<td>1.22</td>
<td>0.177</td>
</tr>
<tr>
<td>Total additional lymph nodes removed at completion lymphadenectomy, n, mean†</td>
<td>0.53</td>
<td>0.03</td>
<td>0.056</td>
</tr>
<tr>
<td>Largest lymph node removed, cm, mean (range)</td>
<td>2.9 (1.5–5.0)</td>
<td>2.5 (0.9–4.5)</td>
<td>0.196</td>
</tr>
<tr>
<td>Mean LOS, d</td>
<td>1.4</td>
<td>1.5</td>
<td>0.086</td>
</tr>
<tr>
<td>Duration of drain, d, mean</td>
<td>19.8</td>
<td>17.2</td>
<td>0.359</td>
</tr>
</tbody>
</table>
Oncologic Outcomes of Patients Undergoing Videoscopic Inguinal Lymphadenectomy for Metastatic Melanoma

Table 4. Complications after Videoscopic Inguinal Lymphadenectomy and Open Superficial Inguinal Lymphadenectomy for Regionally Metastatic Melanoma

<table>
<thead>
<tr>
<th>Complication</th>
<th>VIL, % (n = 40)</th>
<th>Open, % (n = 40)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications</td>
<td>47.5</td>
<td>80.0</td>
<td>0.002**</td>
</tr>
<tr>
<td>Infection</td>
<td>40.0</td>
<td>65.0</td>
<td>0.025**</td>
</tr>
<tr>
<td>Flap necrosis/dehiscence</td>
<td>2.5</td>
<td>15.0</td>
<td>0.047*</td>
</tr>
<tr>
<td>Seroma</td>
<td>22.5</td>
<td>35.0</td>
<td>0.217</td>
</tr>
</tbody>
</table>

*Statistically significant (p < 0.05).
Oncologic Outcomes of Patients Undergoing Videoscopic Inguinal Lymphadenectomy for Metastatic Melanoma

Recurrence Free Survival - Sentinel Lymph Node Positive

No. at Risk
- Videoscopic Inguinal Lymphadenectomy: 36
- Open Inguinal Lymphadenectomy: 37

Percent Survival

- VIL
- Open

p=0.361

Months
0 12 24 36 48 60 72 84 96

Case 1

1 year later he represents with:
Surgical advances in melanoma

Isolated Limb Infusion
Surgical advances in melanoma

Outcomes Following Isolated Limb Infusion for Melanoma. A 14-Year Experience

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>84%</td>
</tr>
<tr>
<td>CR</td>
<td>70 (85%)</td>
</tr>
<tr>
<td>PR</td>
<td>84 (46%)</td>
</tr>
<tr>
<td>SD</td>
<td>18 (10%)</td>
</tr>
<tr>
<td>Time to BR</td>
<td>1.4 mos</td>
</tr>
<tr>
<td>Duration of Response</td>
<td>13 mos</td>
</tr>
</tbody>
</table>
Outcomes Following Isolated Limb Infusion for Melanoma. A 14-Year Experience

Probability of response duration

Months

Patients at risk

CR 70
PR 86

CR
PR

p = .012
Role of skin cancer screening
Surgical advances in melanoma
New systemic therapies
Soft tissue sarcomas
New Systemic Therapies

Oncolytic viral therapy

Immune checkpoint inhibition

Targeted therapy
Viral oncolytic therapy

Talimogene laherparepvec (T-vec)
**T-VEC Treatment for Melanoma**

**genetically-modified virus features**

- **Herpes virus altered so it doesn’t cause cold sores**
- **Virus targets only cancer cells, killing them and not healthy cells**
- **Virus attracts immune cells to help fight the cancer**

---

**New Systemic Therapies**

**Viral oncolytic therapy**
Viral oncolytic therapy

New Systemic Therapies

Overall Survival (%)

Study Month

No. at risk
GM-CSF 141 124 100 83 63 52 46 36 27 15 5
T-VEC 295 269 230 187 159 145 125 95 66 36 16 2

Events/n (%) Median (95% CI) OS in months
T-VEC 189/295 (64) 23.3 (19.5 to 29.6)
GM-CSF 101/141 (72) 18.9 (16.0 to 23.7)

Log-rank \( P = .051 \)
Hazard ratio, 0.79 (95% CI, 0.62 to 1.00)
### New Systemic Therapies

#### Immune Checkpoint inhibition

<table>
<thead>
<tr>
<th>Anti CTLA-4 antibodies</th>
<th>Anti PD-1 antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipilimumab</td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td></td>
<td>Nivolumab</td>
</tr>
<tr>
<td></td>
<td>Atezolizumab</td>
</tr>
</tbody>
</table>
New Systemic Therapies

Anti-CTLA
Ipilimumab in Melanoma

A. Overall Survival

- **Median OS (months)**
  - Ipi + gp 100: 10.0
  - Ipi alone: 10.1
  - gp 100 alone: 6.4

- **HR for death for Ipi + gp100 vs. gp100 alone**: 0.68, \( p < 0.001 \)

- **HR for death for Ipi alone vs. gp 100 alone**: 0.66, \( p = 0.003 \)

### No. at Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>403</th>
<th>297</th>
<th>223</th>
<th>163</th>
<th>115</th>
<th>81</th>
<th>54</th>
<th>42</th>
<th>33</th>
<th>24</th>
<th>17</th>
<th>7</th>
<th>6</th>
<th>4</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipi plus gp100</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipi</td>
<td>137</td>
<td>106</td>
<td>79</td>
<td>56</td>
<td>38</td>
<td>30</td>
<td>24</td>
<td>18</td>
<td>13</td>
<td>13</td>
<td>8</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>gp100</td>
<td>136</td>
<td>93</td>
<td>58</td>
<td>32</td>
<td>23</td>
<td>17</td>
<td>16</td>
<td>7</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
New Systemic Therapies

Anti-PD 1
New Systemic Therapies

Anti-PD 1

Progression-free survival (%)

Number at risk

<table>
<thead>
<tr>
<th>Treatment</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
<th>14</th>
<th>16</th>
<th>18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab 2 mg/kg</td>
<td>180</td>
<td>152</td>
<td>84</td>
<td>58</td>
<td>32</td>
<td>15</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pembrolizumab 10 mg/kg</td>
<td>181</td>
<td>156</td>
<td>101</td>
<td>65</td>
<td>47</td>
<td>19</td>
<td>7</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>179</td>
<td>127</td>
<td>47</td>
<td>23</td>
<td>14</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
New Systemic Therapies

MAPK pathway

Inhibitors:
- Imatinib
- Nilotinib
- Dasatinib

Inhibitors:
- Vemurafenib
- Dabrafenib
- Encorafenib

Inhibitors:
- Trametinib
- Selumetinib
- Binimetinib

Melanoma cell

Mutant KIT → RAS → Mutant BRAF → CRAF → MEK → ERK → Cyclin D1 → Growth and survival
Role of skin cancer screening
Surgical advances in melanoma
New systemic therapies
Soft tissue sarcomas
Soft Tissue Sarcoma

- Malignant tumors of mesenchymal cells
- About 10,000 per year in US
- 1% of adult malignancies
Soft tissue sarcoma

U.S. Soft Tissue Sarcoma Incidence by Age

Incidence per 100,000


Age < 20 Age ≥ 20

https://www.cancer.gov/research/progress/snapshots/sarcoma
Skin Cancer Screening

Sarcoma cell of origin

- Pluripotential mesenchymal cell
- SOX9
- CBFA1
- OSX inactivation
- osteopontin
- osteocalcin
- PPARγ2
- myo D
- myogenin
- myf-5
- MRF4
- MEF2
- Skeletal muscle
- Fat cells
- Osteoblasts
Soft tissue sarcoma

Behavior based on location

Soft tissue sarcoma

**Behavior based on histiotype**

[Graph showing survival rates based on histiotype with legend: Myxoid, Well-differentiated, Round cell, Pleomorphic, Dedifferentiated.]
Soft tissue sarcoma

Behavior based on grade

[Graph showing disease-specific survival based on grade.]

- Low Grade n=1120
- High Grade n=1814

Time (years)

Disease Specific Survival

n=2934

p<0.005

Soft tissue sarcoma

Work up – trunk/extremity

Size < 3cm

Size > 3cm
# Lymph Node Metastasis

## Table 1. HISTOLOGIC TYPE OF SARCOMAS AND LYMPH NODE METASTASIS

<table>
<thead>
<tr>
<th>Histologic Findings</th>
<th>No. of Nodal Metastases/All Sarcoma Patients</th>
<th>% of All Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Weingrad*</td>
<td>Mazeron†</td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td>55/1083</td>
<td>54/215</td>
</tr>
<tr>
<td>Malignant fibrous histiocytoma</td>
<td>1/30</td>
<td>84/823</td>
</tr>
<tr>
<td>Undifferentiated spindle cell</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>108/888</td>
<td>201/1354</td>
</tr>
<tr>
<td>Embryonal rhabdomyosarcoma</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>10/94</td>
<td>21/524</td>
</tr>
<tr>
<td>Neurofibrosarcoma/MPNT</td>
<td>0/60</td>
<td>3/476</td>
</tr>
<tr>
<td>Vascular</td>
<td>—</td>
<td>43/376</td>
</tr>
<tr>
<td>Angiosarcoma</td>
<td>Ni</td>
<td>—</td>
</tr>
<tr>
<td>Hemangiopericytoma</td>
<td>3/23</td>
<td>—</td>
</tr>
<tr>
<td>Lymphangiosarcoma</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>20/327</td>
<td>—</td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Synovial sarcoma</td>
<td>91/535</td>
<td>117/851</td>
</tr>
<tr>
<td>Epithelioid sarcoma</td>
<td>—</td>
<td>14/70</td>
</tr>
<tr>
<td>Liposarcoma</td>
<td>15/288</td>
<td>16/504</td>
</tr>
<tr>
<td>Alveolar soft part sarcoma</td>
<td>6/62</td>
<td>3/24</td>
</tr>
<tr>
<td>Clear cell sarcoma</td>
<td>—</td>
<td>11/40</td>
</tr>
<tr>
<td>Other</td>
<td>11/125</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td>320/3515</td>
<td>567/5257</td>
</tr>
</tbody>
</table>
The Treatment of Soft-tissue Sarcomas of the Extremities

Prospective Randomized Evaluations of (1) Limb-sparing Surgery Plus Radiation Therapy Compared with Amputation and (2) the Role of Adjuvant Chemotherapy

STEVEN A. ROSENBERG, M.D., Ph.D.,* JOEL TEPPER, M.D.,† ELI GLATSTEIN, M.D.,† JOSE COSTA, M.D.,‡ ALAN BAKER, M.D.,* MURRAY BRENNAN, M.D.,* ERNEST V. DEMOSS, M.D.,* CLAUDIA SEIPP, R.N.,* WILLIAM F. SINDELAR, M.D., Ph.D.,* PAUL SUGARBAKER, M.D.,* ROBERT WESLEY, Ph.D.§
42 year old Russian female with right leg mass
Pathology - 19 cm myxoid round cell (5%) liposarcoma, negative margins
72 year old man with a mass and wrist drop in his left arm
72 year old man with a mass and wrist drop in his left arm
Nomogram to predict local recurrence
Work up – RP/intraabdominal

Imaging
CT Chest, Abdomen, Pelvis
Soft tissue sarcoma

Work up – RP/intraabdominal

<table>
<thead>
<tr>
<th>Sarcoma subtype</th>
<th>No. patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liposarcoma</td>
<td>350</td>
<td>31.5</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>315</td>
<td>28.4</td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td>114</td>
<td>10.3</td>
</tr>
<tr>
<td>Malignant fibrous histiocytoma</td>
<td>101</td>
<td>9.1</td>
</tr>
<tr>
<td>MNPT/neurogenic sarcoma</td>
<td>57</td>
<td>5.1</td>
</tr>
<tr>
<td>Hemangiopericytoma/angiosarcoma</td>
<td>25</td>
<td>2.3</td>
</tr>
<tr>
<td>Other</td>
<td>149</td>
<td>13.4</td>
</tr>
</tbody>
</table>

Abbreviation: MPNT, malignant peripheral nerve tumor.


MSKCC Data says it’s usually ab 40-45%
64 year old male RP WD/DD Liposarcoma
Caval and R Iliac Artery Involvement
### Work up – RP/intraabdominal

**Table 19.3** Overview of the literature with respect to the recent series reporting 5-year and 10-year survival rates after complete resection of retroperitoneal soft tissue sarcoma

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients</th>
<th>Complete resection</th>
<th>5-year overall survival</th>
<th>10-year overall survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lewis et al. 1998</td>
<td>231</td>
<td>80%</td>
<td>54%</td>
<td>35%</td>
</tr>
<tr>
<td>Stoeckle et al. 2001</td>
<td>145a</td>
<td>65%</td>
<td>49%</td>
<td>ND</td>
</tr>
<tr>
<td>Ferrario and Karakousis 2003</td>
<td>130</td>
<td>95%</td>
<td>60%</td>
<td>48%</td>
</tr>
<tr>
<td>Gronchi et al. 2004</td>
<td>167</td>
<td>88%</td>
<td>54%</td>
<td>27%</td>
</tr>
<tr>
<td>Hassan et al. 2004</td>
<td>99</td>
<td>78%</td>
<td>51%</td>
<td>36%</td>
</tr>
<tr>
<td>Erzen et al. 2005</td>
<td>102</td>
<td>95%</td>
<td>52%</td>
<td>36%</td>
</tr>
<tr>
<td>Pierie et al. 2006</td>
<td>103</td>
<td>64%</td>
<td>62%</td>
<td>52%</td>
</tr>
<tr>
<td>Chen et al. 2007</td>
<td>132</td>
<td>74%</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

ND, not determined

*National survey

Complete rsxn means all gross tumor removed, but there can be R0 and R1 complete rsxns

---

Treatment of Bone and Soft Tissue Sarcomas. 179, 301 Springer-Verlag Berlin Heidelberg 2009

Mary Bird Perkins Cancer Center
Soft tissue sarcoma

RP/intraabdominal

40 year old man with an MRI for back pain
Soft tissue sarcoma

RP/intraabdominal

- Ureter
- Vena Cava
- Psoas Muscle
- Right Colon
Soft tissue sarcoma

RP/intraabdominal
52 year old female with a soft tissue tumor of the left pelvis causing disabling incontinence and radiculopathy.
87 year old female abdominal distention and lower extremity DVT
THANK YOU

FREE CANCER SCREENINGS:
- BREAST CANCER
- COLORECTAL CANCER
- ORAL CANCER
- PROSTATE CANCER
- SKIN CANCER

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Many cancers can be detected with regular screenings.

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MARY BIRD PERKINS
OUR LADY OF THE LAKE
CANCER CENTER

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