Skin Cancer in Organ Transplant Recipients

Dana Baran, M.D. FRCPC
Manish Khanna, M.D. FRCPC
Skin Cancer in Transplant Recipients

• Skin cancers are the most frequent malignancies after organ transplantation
• Squamous and basal cell carcinoma (Nonmelanoma skin cancer – NMSC) account for greater than 95% of the skin cancers
• Other uncommon tumors such as Merkel cell carcinoma, Kaposi sarcoma, and melanoma are increased
Post-transplant Malignancy Risk Varies with Cancer Type

NHL = Non-Hodgkin’s lymphoma

NMSC: Most Common Malignancy in Canadian Transplant Patients

- NMSC (41.4%)
- Genitourinary cancer (15.3%)
- Lung cancer (10.8%)
- Digestive cancer (12.6%)
- Breast cancer (2.7%)
- Sarcoma (3.6%)
- Lymphoma (2.7%)
- Other (7.3%)
- Head & neck (3.6%)
Standard Incidence Ratios of Skin Cancer in Transplant Patients

- Squamous cell carcinoma (SCC) = SIR 65
- Basal cell carcinoma (BCC) = SIR 10
- In the general population BCC is more common than SCC
- Among RTRs the SCC:BCC is reversed

Risk Factors

• Most important predisposing factors include fair skin, light eyes and hair, and susceptibility to sunburn

• Cumulative ultraviolet radiation is the primary responsible carcinogen for the induction of NMSC

• Age – 12-fold higher risk in patients receiving grafts beyond age 55

• Duration of immunosuppression

• HPV infection
Skin Cancer Epidemic

• Skin cancer is the most common human malignancy
• It is more common than cancers of the colon, lung, breast, and prostate combined
• Where as the incidence of most other cancers is decreasing, the incidence of skin cancer continues to rise
Non Melanoma Skin Cancer Statistics

Skin cancer treated by dermatologists in Quebec from 1984 to 2005

SOURCE: Pierre Ricard, RAMQ

The Gazette, May 27, 2006
SEGAL CANCER CENTRE
THE 3 MOST COMMON SKIN CANCERS

1. BASAL CELL CARCINOMA
2. SQUAMOUS CELL CARCINOMA
3. MALIGNANT MELANOMA
BASAL CELL CARCINOMA AND SQUAMOUS CELL CARCINOMA

- Environmental risk factors
  UVR (most important)
  also: arsenic, therapeutic radiation, scar, ...

- Host risk factors
  fair skin, blond or red hair
  freckling
  immunosuppression
  genetic syndromes

- Location
  85% head and neck

- Metastatic potential: rare for BCC; 2-15% for SCC
Sunlight Causes Skin Cancer
Carcinogens
Carcinogens
Fry Now... Pay Later.

There is a proven connection between sun exposure and skin cancer as well as premature wrinkling. If you must be in the sun, use sunscreen and common sense.

For more information call the American Cancer Society toll free: 1-800-ACS-2345
Patient Education is Key, But Are We Doing Enough?

This Canadian study, “suggest that many transplant recipients do not use adequate sun protection. Further study of strategies to encourage the use of sun protection among transplant patients is needed to reduce the incidence of skin cancer.”
Epidemiology – Incidence of NMSC in Transplant Patients

• Incidence of NMSC increases with time after transplant
• Incidence varies in the US and western europe from 5 to 10-27 to 40-60% at 2, 10 and 20 years respectively
• Higher figures are observed in Australia, where 20 years incidence reaches 70-82%
• Several studies have shown a 2 to 4 fold higher incidence in heart transplant compared with kidney
Clinical Features

• NMSC appear on sun exposed areas after a mean interval of 8 years after transplantation
• Often associated with multiple keratotic lesions that mimic SCC such as actinic keratoses, seborrheic keratoses, warts, and Bowen’s disease (in-situ SCC)
• Multiple keratotic skin lesions are associated with an increased risk of SCC (12 fold elevated risk with > 50 lesions) in areas of UV exposure
• Field cancerization
Actinic Keratosis

- “Pre-Cancerous” lesions induced by UVR
Disease Continuum of AK to Invasive SCC

• AK is an evolving SCC
• Genetically similar to SCC
• Morphologically, cells are identical to SCC
• AK and invasive SCC are frequently contiguous with one another
• Same anatomic distribution
Tumor Progression and Field Cancerization

- Cascade occurs at different stages at multiple sites throughout the sun-exposed skin.
Field Cancerization

• The areas of ‘field cancerization’ account for a vast majority of the NMSC-related morbidity and mortality and have become the key target of dermatologic initiatives to reduce skin cancer burden in OTR.

• **Field** adapted therapies of precursor lesions (Actinic keratoses/subclinical disease) instead of lesion-adapted to reduce the number of new cancers and recurrences.
# Treatment of AK: Lesion-Directed Options

<table>
<thead>
<tr>
<th>Treatment</th>
<th>MOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryotherapy</td>
<td>Freeze cells</td>
</tr>
<tr>
<td>Curettage and electrodessication</td>
<td>Mechanical scraping</td>
</tr>
<tr>
<td>Excision</td>
<td>Excision</td>
</tr>
<tr>
<td>Laser</td>
<td>Burn cells</td>
</tr>
</tbody>
</table>
## Treatment of AK: Topical Field-Directed Options

<table>
<thead>
<tr>
<th>Treatment</th>
<th>MOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imiquimod</td>
<td>Immune response modifier</td>
</tr>
<tr>
<td>5-Fluorouracil</td>
<td>Antimetabolite</td>
</tr>
<tr>
<td>Chemical peels</td>
<td>Destruction</td>
</tr>
<tr>
<td>Photodynamic Therapy (PDT)</td>
<td>Free radical production</td>
</tr>
</tbody>
</table>
Clinical

• A first SCC is predictive of subsequent multiple NMSC as 88% of renal transplant recipients develop multiple new tumors within 5 years
• SCC are more aggressive, grow more rapidly, recur locally in 13.4% and metastasize in 5-8%
Treatment of NMSC (SCC)

- Depends on type and number
- Surgery with histologically–controlled margins is the gold standard therapy
TREATMENT OF SCC

• Depends on **multiple factors**:
  
  • Size
  • Location
  • Histologic Type
  • Recurrent Tumors
  • Patient factors
TREATMENT OF SCC – Options:

- Curettage and Electrodesiccation
- Conventional Excision
- Mohs Micrographic Surgery
- Radiation
- Chemotherapy/Chemoprevention
- Reduction/Cessation/Alteration
- Immunosuppression
Systemic Retinoids

• *Chemoprevention* of CSCC (high-risk patients)
• Reduce the number of preexisting Actinic keratoses and new SCC’s
• Exert effect only during therapy and long-term use limited by side effects
• Treatment started at 10 mg acitretin and increased to 30 mg
Role of Immunosuppressive Agents in Causing Skin Cancer

- Decrease in immunosurveillance

- Direct oncogenic effects linked to some agents
Role of Immunosuppressive Agents

• Incidence of NMSC proportional to the level of immunosuppression

• Effect of immunosuppression reversible as a decrease in new tumor development reported after reduction or cessation of immunosuppression
Role of Immunosuppressive Agents

• Calcineurin inhibitors (CNI’s) have oncogenic properties linked to the production of cytokines that promote tumor growth, metastasis, and angiogenesis.

• By contrast, mTOR inhibitors may have antitumoral properties by blocking angiogenesis.
Sirolimus (mTOR inhibitors)

• Prospective clinical studies suggest that mTOR inhibitors could have a preventative effect on cancerogenesis

• RTR’s treated de novo with these agents or converted had a lower incidence of malignancies especially NMSC as compared with CNI’s
Immunosuppression Strategies to Reduce Risk

• Reduction in overall immunosuppression level\textsuperscript{1,2}

• Modification to immunosuppression regimen\textsuperscript{1,2}

2. EBPG. Nephrol Dial Transplant 2002;17 Suppl 4:32-6
New Immunosuppressive Strategies for Skin Cancer

• Current challenge is to determine if conversion to mTOR inhibitors is a better option than reduction of immunosuppression
New Immunosuppressive Strategies for Skin Cancer

• Several randomized prospective trials are ongoing for testing the potential antineoplastic effects of mTOR inhibitors in OTR

• All assess the burden of new skin tumors as well as graft and patient survival over at least 2 years
Switch to a Sirolimus-Based Immunosuppression in Long-Term Renal Transplant Recipients: Reduced Rate of (Pre-)Malignancies and Nonmelanoma Skin Cancer in a Prospective, Randomized, Assessor-Blinded, Controlled Clinical Trial

**Table 4a: Clinical Assessment—changes at month 12 compared to baseline findings—frequency**

<table>
<thead>
<tr>
<th>Clinical assessment (month 12)</th>
<th>Arm A (sirolimus)</th>
<th>Arm B (control)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (Patients)</td>
<td>%</td>
</tr>
<tr>
<td>1 = Marked worsening</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>2 = Worsening</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>3 = Slight worsening</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>4 = Unchanged</td>
<td>4</td>
<td>26.7</td>
</tr>
<tr>
<td>5 = Slight improvement</td>
<td>6</td>
<td>40.0</td>
</tr>
<tr>
<td>6 = Improvement</td>
<td>4</td>
<td>26.7</td>
</tr>
<tr>
<td>7 = Marked improvement</td>
<td>1</td>
<td>6.7</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Randomized Controlled Trial of Sirolimus for Renal Transplant Recipients at High Risk for Nonmelanoma Skin Cancer

Table 3: Summary of efficacy measures; intent-to-treat and on-therapy populations

<table>
<thead>
<tr>
<th>End Points</th>
<th>Sirolimus (N = 39)</th>
<th>Calcineurin Inhibitor (N = 47)</th>
<th>p-Value (^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nonmelanoma skin cancer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rate of biopsy-confirmed new lesions Inumber per patient-year</td>
<td>1.31</td>
<td>2.48</td>
<td>0.022</td>
</tr>
<tr>
<td>Overall, ITT</td>
<td>1.35</td>
<td>2.50</td>
<td>0.072</td>
</tr>
<tr>
<td>Patients with ≥1 new or recurrent biopsy-confirmed lesion, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall, ITT</td>
<td>22 (56)</td>
<td>38 (81)</td>
<td>0.015</td>
</tr>
<tr>
<td>OT</td>
<td>14 (36)</td>
<td>36 (75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Squamous cell carcinoma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rate of biopsy-confirmed new lesions Inumber per patient-year, ITT</td>
<td>0.88</td>
<td>1.71</td>
<td>0.038</td>
</tr>
<tr>
<td>Overall, ITT</td>
<td>0.95</td>
<td>1.68</td>
<td>0.145</td>
</tr>
<tr>
<td>Patients with ≥1 new biopsy-confirmed lesion, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall, ITT</td>
<td>16 (41)</td>
<td>33 (70)</td>
<td>0.006</td>
</tr>
<tr>
<td>OT</td>
<td>10 (26)</td>
<td>31 (66)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Basal cell carcinoma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rate of biopsy-confirmed new lesions Inumber per patient-year, ITT</td>
<td>0.43</td>
<td>0.77</td>
<td>0.104</td>
</tr>
<tr>
<td>Overall, ITT</td>
<td>0.41</td>
<td>0.82</td>
<td>0.095</td>
</tr>
<tr>
<td>Patients with ≥1 new biopsy-confirmed lesion, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall, ITT</td>
<td>14 (36)</td>
<td>24 (51)</td>
<td>0.163</td>
</tr>
<tr>
<td>OT</td>
<td>8 (21)</td>
<td>23 (48)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

\(^1\) Poisson regression was used to model NMSC counts using the years in study as an offset. The generalized estimated equations approach was used to estimate parameters and compare treatment differences.

ITT = intent-to-treat; OT = on-therapy.
Figure 2: Kaplan-Meier estimates of new biopsy-confirmed lesion-free survival for nonmelanoma skin cancer in the intent-to-treat population for nonmelanoma skin cancer (A), squamous cell carcinoma (B) and basal cell carcinoma (C).
<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Arm A (Sirolimus)</th>
<th>Arm B (control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aphthae</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Leg edema</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Cough</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Joint pain</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Increase in creatinine</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Anemia</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia/pneumonitis</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Increase in transaminases</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Quincke edema</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Soft tissue infection</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Septicemia</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Carcinoma of the tongue</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Mamma carcinoma</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Severe adverse event requiring</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>hospitalization</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*American Journal of Transplantation* 2010; 10: 1–9
Reduction of Immunosuppression Task Force: ITSCC and Skin Care in Organ Transplant Patients Europe

<table>
<thead>
<tr>
<th>Skin cancer scenario</th>
<th>Kidney allograft</th>
<th>Heart allograft</th>
<th>Liver allograft</th>
</tr>
</thead>
<tbody>
<tr>
<td>No history of actinic keratosis or skin cancer</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>History of actinic keratosis (no risk of mortality; marker for increased skin cancer risk in future)</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>History of ≤ 1 NMSC per year (negligible risk of mortality, ≤ 1 minor surgical procedure per year; patients handle this with ease; warning sign of possible future skin cancers)</td>
<td>Mild</td>
<td>None</td>
<td>Mild</td>
</tr>
<tr>
<td>History of 2–5 NMSCs per year (0.5% risk of mortality over 3 years, minor–moderate surgical procedure 2–5 times per year; patients can usually handle this, but it starts to bother them; likelihood of numerous future skin cancers)</td>
<td>Mild</td>
<td>Mild</td>
<td>Mild</td>
</tr>
<tr>
<td>History of 6–10 NMSCs per year (1% risk of mortality over 3 years, minor–moderate surgical procedure 6–10 times per year; patients can usually handle this, but it bothers them; high likelihood of numerous future skin cancers)</td>
<td>Mild</td>
<td>Mild</td>
<td>Mild</td>
</tr>
</tbody>
</table>

ITSCC = International Transplant Skin Cancer Collaborative
## Reduction of Immunosuppression Task Force (cont’d)

<table>
<thead>
<tr>
<th>Skin cancer scenario</th>
<th>Level of reduction of immunosuppression to consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of 11–25 NMSCs per year (2% risk of mortality over 3 years, minor–moderate surgical procedure 11–25 times per yr; this level of morbidity causes moderate distress and moderate disfigurement; depression may begin; high likelihood of severe future skin cancer)</td>
<td>Kidney allograft</td>
</tr>
<tr>
<td></td>
<td>Mild</td>
</tr>
<tr>
<td>History of &gt;25 NMSCs per year (5% risk of mortality over 3 years, moderate–severe surgical procedure &gt;25 times per yr; this level of morbidity causes severe distress, disfigurement; patients question whether transplant was worth it; depression is common; high likelihood of severe and possibly life-threatening future skin cancers)</td>
<td>Moderate</td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 1% mortality over 3 years (average-risk SCC; cutaneous and oral KS; stage IA melanoma)</td>
<td>Mild</td>
</tr>
</tbody>
</table>
Reduction of Immunosuppression Task Force (cont’d)

<table>
<thead>
<tr>
<th>Skin cancer scenario</th>
<th>Kidney allograft</th>
<th>Heart allograft</th>
<th>Liver allograft</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual high-risk skin cancer: 5% mortality over 3 years</td>
<td>Mild</td>
<td>Mild</td>
<td>Mild</td>
</tr>
<tr>
<td>(moderate-risk SCC; stage IB melanoma)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 10% mortality over 3 years</td>
<td>Moderate</td>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>(high-risk SCC; early Merkel cell carcinoma; stage IIA melanoma)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 25% mortality over 3 years</td>
<td>Moderate</td>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>(very high-risk SCC; stage IIB melanoma)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 50% mortality over 3 years</td>
<td>Severe</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 90% mortality over 3 years</td>
<td>Severe</td>
<td>Severe</td>
<td>Severe</td>
</tr>
<tr>
<td>(untreatable metastatic SCC; stage IV melanoma; metastatic Merkel cell carcinoma)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Otley C. Br J Dermatol 2006;154:395–400
Case Illustrations
<table>
<thead>
<tr>
<th>Skin cancer scenario</th>
<th>Level of reduction of immunosuppression to consider</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Skin Cancer: ITSCC and Skin Care in Organ Transplant Patients Europe</strong></td>
<td><strong>Kidney allograft</strong></td>
</tr>
<tr>
<td><strong>Heart allograft</strong></td>
<td><strong>Liver allograft</strong></td>
</tr>
<tr>
<td>No history of actinic keratosis or skin cancer</td>
<td>None</td>
</tr>
<tr>
<td>History of actinic keratosis (no risk of mortality; marker for increased skin cancer risk in future)</td>
<td>None</td>
</tr>
<tr>
<td>History of $\leq 1$ NMSC per year (negligible risk of mortality, $\leq 1$ minor surgical procedure per year; patients handle this with ease; warning sign of possible future skin cancers)</td>
<td>Mild</td>
</tr>
<tr>
<td>History of 2–5 NMSCs per year (0.5% risk of mortality over 3 years, minor–moderate surgical procedure 2–5 times per year; patients can usually handle this, but it starts to bother them; likelihood of numerous future skin cancers)</td>
<td>Mild</td>
</tr>
<tr>
<td>History of 6–10 NMSCs per year (1% risk of mortality over 3 years, minor–moderate surgical procedure 6–10 times per year; patients can usually handle this, but it bothers them; high likelihood of numerous future skin cancers)</td>
<td>Mild</td>
</tr>
</tbody>
</table>

ITSCC = International Transplant Skin Cancer Collaborative
Skin Cancer: ITSCC and Skin Care in Organ Transplant Patients Europe (cont’d)

<table>
<thead>
<tr>
<th>Skin cancer scenario</th>
<th>Level of reduction of immunosuppression to consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual high-risk skin cancer: 5% mortality over 3 years (moderate-risk SCC; stage IB melanoma)</td>
<td>Kidney allograft: Mild, Heart allograft: Mild, Liver allograft: Mild</td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 10% mortality over 3 years (high-risk SCC; early Merkel cell carcinoma; stage IIA melanoma)</td>
<td>Kidney allograft: Moderate, Heart allograft: Mild, Liver allograft: Moderate</td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 25% mortality over 3 years (very high-risk SCC; stage IIB melanoma)</td>
<td>Kidney allograft: Moderate, Heart allograft: Mild, Liver allograft: Moderate</td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 50% mortality over 3 years</td>
<td>Kidney allograft: Severe, Heart allograft: Moderate, Liver allograft: Moderate</td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 90% mortality over 3 years (untreatable metastatic SCC; stage IV melanoma; metastatic Merkel cell carcinoma)</td>
<td>Kidney allograft: Severe, Heart allograft: Severe, Liver allograft: Severe</td>
</tr>
</tbody>
</table>
## Skin Cancer: ITSCC and Skin Care in Organ Transplant Patients Europe (cont’d)

<table>
<thead>
<tr>
<th>Skin cancer scenario</th>
<th>Kidney allograft</th>
<th>Heart allograft</th>
<th>Liver allograft</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of 11–25 NMSCs per year (2% risk of mortality over 3 years, minor–moderate surgical procedure 11–25 times per yr; this level of morbidity causes moderate distress and moderate disfigurement; depression may begin; high likelihood of severe future skin cancer)</td>
<td>Mild</td>
<td>Mild</td>
<td>Mild</td>
</tr>
<tr>
<td>History of &gt;25 NMSCs per year (5% risk of mortality over 3 years, moderate–severe surgical procedure &gt;25 times per yr; this level of morbidity causes severe distress, disfigurement; patients question whether transplant was worth it; depression is common; high likelihood of severe and possibly life-threatening future skin cancers)</td>
<td>Moderate</td>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 1% mortality over 3 years (average-risk SCC; cutaneous and oral KS; stage IA melanoma)</td>
<td>Mild</td>
<td>None</td>
<td>Mild</td>
</tr>
</tbody>
</table>

Otley C. *Br J Dermatol* 2006;154:395–400
Skin Cancer: ITSCC and Skin Care in Organ Transplant Patients Europe (cont’d)

<table>
<thead>
<tr>
<th>Skin cancer scenario</th>
<th>Kidney allograft</th>
<th>Heart allograft</th>
<th>Liver allograft</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual high-risk skin cancer: 5% mortality over 3 years (moderate-risk SCC; stage IB melanoma)</td>
<td>Mild</td>
<td>Mild</td>
<td>Mild</td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 10% mortality over 3 years (high-risk SCC; early Merkel cell carcinoma; stage IIA melanoma)</td>
<td>Moderate</td>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 25% mortality over 3 years (very high-risk SCC; stage IIB melanoma)</td>
<td>Moderate</td>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 50% mortality over 3 years</td>
<td>Severe</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Individual high-risk skin cancer: 90% mortality over 3 years (untreatable metastatic SCC; stage IV melanoma; metastatic Merkel cell carcinoma)</td>
<td>Severe</td>
<td>Severe</td>
<td>Severe</td>
</tr>
</tbody>
</table>

Otley C. Br J Dermatol 2006;154:395–400
Strategies to Reduce Risk of Post-transplant Malignancy

1. Early screening
2. Immunosuppression
   - Reduction in immunosuppression level
   - Modification to immunosuppression regimen
3. Patient education (eg, sun protection)
4. Multidisciplinary approach
Prevention

• OTR can reduce NMSC risk by avoiding sun exposure

• Specialized dermatology clinics for OTR have improved compliance with photoprotective measures through education
Specialized OTR Clinic for Skin Cancer

- Encourage sun protective practices
- Identify those at increased risk
- Consider prophylaxis for high-risk patients
  - eg, Topical retinoids, 5%-fluorouracil cream, photodynamic therapy
- Encourage monthly self-exam
  - Lymph node self exam for patients with a history of SCC or melanoma
- Follow patient closely at regular intervals based on risk

# Skin Cancer Screening Recommendations:
Dermatological Follow up for Transplant Patients

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Dermatologic exam interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>No history of skin cancer or actinic keratosis</td>
<td>Initial dermatology consult followed by annual examination by transplant physicians until lesions arise. Patients at high risk for skin cancer may benefit from annual exam by dermatologist.</td>
</tr>
<tr>
<td>History of actinic keratosis</td>
<td>6 months</td>
</tr>
<tr>
<td>History of one NMSC</td>
<td>6 months</td>
</tr>
<tr>
<td>History of multiple NMSCs</td>
<td>2–4 months</td>
</tr>
<tr>
<td>History of high-risk SCC or melanoma</td>
<td>3 months</td>
</tr>
<tr>
<td>History of metastatic SCC or melanoma</td>
<td>2 months</td>
</tr>
</tbody>
</table>
Collaborative Approach is Best

• “With all strategies, a collaborative approach between transplant physicians, dermatologists, oncologic surgeons, pathologists, medical oncologists, and radiation oncologists with experience with aggressive tumours in organ transplant recipients is optimal”

Summary – Post-transplant Skin Cancer

• Growing cause of morbidity and mortality
• Cutaneous SCC is most frequent
• Relative risk of SCC is about 65 X
• Risk of malignancy increases over time
• Most important non-immunosuppressant–related risk factor is exposure to UVR pre and post transplant
• Modification of immunosuppressant regimen may help improve outcomes