PHOTODYNAMIC THERAPY:
WHAT IS POSSIBLE AND WHAT IS NOT

Heather D. Rogers
Clinical Assistant Professor of Dermatology
UW School of Medicine

RELEVANT FINANCIAL RELATIONSHIP
DISCLOSURE STATEMENT

No relationships to disclosure

I will discuss off label use of photodynamic therapy
USES OF PDT IN DERMATOLOGY

- Actinic keratoses
- Prevention of NMSC
- Treat superficial NMSC
- Acne
- Photorejuvenation
- Warts
- Grover’s disease
- Folliculitis
- Keratosis pilaris
- Striae
- Sebaceous hyperplasia

MECHANISM OF ACTION

- Topical produg containing aminolevulinic acid
- Penetrates the stratum corneum
- Enters keratinocytes, pilosebaceous units
- Increase uptake in neoplastic cells, sebaceous glands, overexpression of receptors
- Converted to protoporphyrin IX (PpIX)
- Accumulation of PpIX
- Expose to light wavelength absorbed by PpIX
- Generation cytotoxic products that destroy cells

HEME PATHWAY

Nestor MS et al. J Drugs Derm. 2006;5(2):139-153
PROTOPORPHYRIN IX

• Maximal absorption at the Soret band, 360-410nm

• Multiple smaller peaks at 500 to 635nm

VARIABLES OF PDT

• Photosensitizers
• Prepping of the skin
• Time of incubation
• Light source
• Number and timing of treatments

PHOTOSENSITIZER

• 5-Aminolevulinic Acid (ALA)
• Levulan Kerastick
  • ALA 20% topical solution
  • Hydrophilic
• FDA approval in 1999 for the treatment of minimally to moderately thick AKs of the face or scalp

Price: $300 per Kerastick
PHOTOSENSITIZER

• Methyl Aminolevulinate (MAL)
  • Metvixia
  • MAL 16% cream
  • Lipophilic
  • FDA approval in 2008 for the treatment of thin and moderately thick AKs of the face and scalp
  • January 2013: no longer available in US

PREPPING THE SKIN

• Creams: keratolytics, retinoids, chemotherapy
• Degrease the skin
• Microdermabrasion
• Tissue penetration enhancer: dimethylsulfoxide
• Curettage
• Lasers: fractional photothermolysis

LIGHT SOURCES

• Wavelength
• Irradiance
  • intensity of light in mW/cm²
• Fluence
  • dose of light in J/cm²
  • continuous wave light sources, LED
  • intense pulsed light / lasers (PDL)
LIGHT SOURCES

• Blu-U (417nm), DUSA
• Omnilux (417nm, 633nm), Photomedex
• Versaclear (420nm, 615nm), Theralight
• Aktilite (630nm), Galderma
• Clearlight (419nm), Lumenis
AKTILITE

PDT FOR ACTINIC KERATOSES

ALA-PDT FOR AKS

- FDA approved protocol
- ALA, 14-18 hours of incubation, no occlusion
- Activation with blue light source
- Dose: 10J/cm²
- Repeat in 4-8 weeks
MAL-PDT FOR AKS

- FDA approved protocol
- Curette lesions
- MAL, 3 hours of incubation under occlusion
- Activation with red light source
- Dose: 37J/cm²
- 2 sessions, 1 week apart

ALA-PDT FOR AKS

- Phase III Protocol
  - Randomized, placebo-controlled
  - 243 patients, 1909 lesions, face or scalp
  - ALA x 14-18 hours incubation
  - Vehicle cream
  - Blue light 10J/cm²

Piacquadio DJ et al. Archives of Dermatology, Jan 2004:140;41-46

- 8 weeks after single treatment
  > 77% vs. 18% with >75% lesion clearing, p <0.001
  > 66% vs. 11% with 100% lesion clearing, p<0.001

- 12 weeks after treatment(s)
  > 30% of patients received 2nd treatment
  > 89% vs. 13% with >75% lesion clearing, p <0.001
  > 73% vs. 8% with 100% lesion clearing, p <0.001

Piacquadio DJ et al. Archives of Dermatology, Jan 2004:140;41-46
**ALA-PDT FOR AKS**

- Short Incubation
  - 18 patients, at least 4 lesions on face
  - ALA x 1, 2 or 3 hours
  - Blue light for 10j/cm²
- Complete clearance of target AKs
  - 1 month after treatment (17 patients)
    - 96% 1 hour, 94% 2 hour, 85% 3 hour
  - 5 months after treatment (10 patients)
    - 87% 1 hour, 94% 2 hour


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**ALA-PDT FOR AKS**

- 38 patients with 76 AKs of face and scalp
- 2 treatments: ALA 4 hours, red light
- 6 months after, complete clearance
  - 92.1%


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**TREATMENTS FOR ACTINIC KERATOSES**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Treatment</th>
<th>Complete Clearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryotherapy</td>
<td>One freeze-thaw cycle</td>
<td>39% 5 sec</td>
</tr>
<tr>
<td></td>
<td></td>
<td>83% &gt;20 sec</td>
</tr>
<tr>
<td>5FU</td>
<td>BID for 2-4 weeks</td>
<td>84% at 24 weeks</td>
</tr>
<tr>
<td></td>
<td>Daily for 2-4 weeks</td>
<td>55% at 4 weeks</td>
</tr>
<tr>
<td>Imiquimod</td>
<td>TIW for 16 weeks / 8 weeks</td>
<td>69% / 57% at 8 weeks</td>
</tr>
<tr>
<td></td>
<td>Daily x 4 weeks (2on/2off/2on)</td>
<td>59% at 8 weeks (75%)</td>
</tr>
<tr>
<td>Diclofenac 3% gel</td>
<td>BID for 12 weeks</td>
<td>56 % at 4 weeks</td>
</tr>
<tr>
<td>Ingenol Mebutate Gel</td>
<td>0.05% 3 days to face</td>
<td>42% at 57 days</td>
</tr>
<tr>
<td></td>
<td>0.015% 2 days to extremities</td>
<td>34% at 57 days</td>
</tr>
</tbody>
</table>
**Treatments for Actinic Keratoses**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Treatment</th>
<th>Complete Clearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALA-PDT with blue light</td>
<td>One, 30% with two treatments 14-18 hours incubation</td>
<td>73% at 12 weeks</td>
</tr>
<tr>
<td></td>
<td>One treatment 1 hour incubation</td>
<td>87% at 20 weeks</td>
</tr>
<tr>
<td>ALA-PDT with red light</td>
<td>Two treatments 4 hours incubation</td>
<td>92% at 24 weeks</td>
</tr>
<tr>
<td>MAL-PDT with red light</td>
<td>Two treatments 3 hours incubation</td>
<td>89% - 91% at 12 weeks</td>
</tr>
</tbody>
</table>

**PDT for AKS**

- Only FDA approved indication for PDT
- At least one hour of incubation
  - Continuous wave light source
  - Red, blue, pink
- Works best on face, scalp, ears

2 treatments of PDT = 5% 5FU BID for 2 weeks

**My AK Protocol**

- 10 or more AKS on face, scalp, ears
- Pretreatment x 1 week with topical
- ALA with 1 hour incubation
- "Pink" light (430, 540, 615, 630nm)
  - 15 minutes, 23 j/cm²
- Repeat in 2 weeks to 1 month
- Expected results
  - 75% improvement
  - Decreased skin cancers in next year
SIDE EFFECTS OF PDT

• During treatment
  • Burning, itching

• After treatment
  • 2 days
    • Photosensitivity: avoid bright lights and sunlight
  • 2 to 4 days
    • Erythema, scale, edema

LONG TERM EFFICACY

• Depends
  • Response to treatment
  • Sun behavior
  • Use of retinoids
  • Immunostatus

PDT FOR PREVENTION OF NMSC
PDT FOR PREVENTION OF NMSC

• Peter Lee, MD, University of Minnesota
  • PDT for the prevention of SCCs in OTRs
  • 12 high risk SOTRs
  • Cyclic PDT q 4 to 8 weeks for 2 years


PDT FOR PREVENTION OF NMSC

• Acetone skin prep
  • Hyperkeratotic scales curetted
  • 20% ALA applied, one stick per extremity
  • One hour incubation with occlusion
  • Blue light

PDT FOR PREVENTION OF NMSC

• Number of SCC in 12 months prior: 235
  • Number of SCC first 12 months: 51
  • Number of SCC in second 12 months: 14
PDT FOR PREVENTION OF NMSC

- Split face trial, 45 patients
- 2 treatments
- 20% ALA cream
- 3.5 hours of incubation, occlusion
- Red light

Appalla Z et al. British J Derm 2010 162; 171-175

<table>
<thead>
<tr>
<th>Months</th>
<th>New Lesions Treatment</th>
<th>New Lesions Placebo</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>1</td>
<td>8</td>
<td>0.020</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>15</td>
<td>0.085</td>
</tr>
<tr>
<td>9</td>
<td>7</td>
<td>23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12</td>
<td>14</td>
<td>30</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

DAY LIGHT PDT
# PDT for Superficial Skin Cancers

## Superficial Basal Cell Carcinoma

<table>
<thead>
<tr>
<th>Modality</th>
<th>Treatment</th>
<th>Clearance</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
<td>Standard excision Mohs</td>
<td></td>
<td>3 - 8% at 5 years 1 - 3% at 5 years</td>
</tr>
<tr>
<td>Cryotherapy</td>
<td>2 cycles</td>
<td>19% at 4 years</td>
<td></td>
</tr>
<tr>
<td>ED&amp;C</td>
<td>3 cycles, attendings vs residents</td>
<td>79-99%</td>
<td>6 - 19% at 5 years</td>
</tr>
<tr>
<td>Radiation Brachytherapy</td>
<td>50 Gray delivered in 20 daily fractions</td>
<td>8 -15% at 5 years</td>
<td></td>
</tr>
<tr>
<td>5FU</td>
<td>BID for up to 12 weeks</td>
<td>90% at 3 weeks</td>
<td></td>
</tr>
<tr>
<td>Imiquimod cream</td>
<td>5 x week for 6 weeks</td>
<td>82% at 12 weeks</td>
<td>25% at 5 years</td>
</tr>
</tbody>
</table>

## Superficial Basal Cell Carcinoma

<table>
<thead>
<tr>
<th>Modality</th>
<th>Treatment</th>
<th>Clearance</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red light MAL-PDT</td>
<td>1-2 treatments, 3 hours incubation</td>
<td>80-97% at 3 months</td>
<td>9% at 3 years</td>
</tr>
<tr>
<td>Red light ALA-PDT</td>
<td>2 treatments same day, 4 and 6 hours incubation</td>
<td>97% at 12 months</td>
<td>11.5% at 5 years</td>
</tr>
</tbody>
</table>
MY SKIN CANCER PROTOCOL

• Invasive: Surgery
• Superficial Squamous Cell: Typically surgery

• Superficial Basal Cell: Discussion with patient
  • ED&C
  • Excision or Mohs based on location
  • Red light PDT
  • Creams
  • Educate, Educate, Educate

MY SUPERFICIAL NMSC PROTOCOL

• Curette lesions
• MAL but now ALA
  • 3 hours of incubation, occlusion
• Red light
• 2 sessions, 1 week apart
• Expected Results
  • sBCC 85% cure rate
  • SCCIS 75% cure rate

PDT VS IMIQUIMOD VS 5FU FOR THE TREATMENT OF SBCC

• 601 patients randomized
  • 202 MAL-PDT
  • 198 5% imiquimod cream
  • 201 5% FU cream

• Funded by Grant of Netherlands Organization for Scientific Research

**PDT VS IMIQUIMOD VS 5FU**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Treatment Protocol</th>
<th>Disease Free at 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAL PDT</td>
<td>2 sessions, 1 week apart</td>
<td>72.8%</td>
</tr>
<tr>
<td>5% Imiquimod</td>
<td>5 days a week for 6 weeks</td>
<td>83.4%</td>
</tr>
<tr>
<td>5% 5FU</td>
<td>BID for 4 weeks</td>
<td>80.1%</td>
</tr>
</tbody>
</table>


**Conclusions**

“Topical 5% FU was non-inferior to and imiquimod was superior to MAL-PDT in terms of treatment success after 1 year follow up.”

“In our study the proportion of successfully treated patients was lower than expected for those treated with MAL-PDT.”

**MY RESULTS TO DATE**

- 2010-2014
  - sBCC treated 140
  - Recurrences: 9 (6.4%)
  - Unknown, lost to follow up: 4 (9.2%)
PDT: THE GOOD AND THE BAD

• It works as well, if not better, than many of the modalities we use every day for the treatment and prevention of actinic keratoses and NMSCs
• High patient satisfaction and excellent cosmesis
• Time consuming, expensive and poorly reimbursed

THANK YOU
drrogers@mdinseattle.com
206-489-2530 (office)