Drug and Device Combinations in Light Based Therapy to Achieve Optimal Results

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Disclosures: Off-label uses will be discussed
Drug donated for research: Light Sciences Oncology
Light Sources donated for research or to clinic: Light Sciences Oncology; Solta; CoolTouch/NewStar
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Why Combination Therapy?

• To achieve enhanced results
• To prevent or delay recurrence
• Resolve or minimize side effects

Overview on Uses of Combination Therapy involving light based therapy

• Combination Phototherapy in History
• Port Wine Birthmarks
• Infantile Hemangiomas
• Angiofibromas
• Trichoepitheliomas
• Actinic Keratoses
• Rosacea
• Scars (Dr. Jill Waibel)
• Future indications to consider

PDL + Rapamycin

• 23 patients with SWS and facial PWB
• Placebo; PDL + Placebo; 1% Rapamycin alone; PDL + Rapamycin
• Analysis at 6, 12, and 18 weeks after intervention
• PDL + Rapamycin yielded the lowest digital photographic image score (greatest improvement) and lowest percentage of blood vessels on histologic analysis
• Well tolerated; rapamycin was detected in the blood

Port Wine Birthmarks

Ancient Egyptians: Treated vitiligo with sunlight and ingested plant extract Ammi Majus
Ancient Hindus: Treated leukoderma with Psoralea coryllifolia and sunlight


Topical rapamycin combined with PDL in the treatment of capillary vascular malformations in SWS: Phase II, randomized double-blind, intra-individual placebo controlled clinical trial
JAAD 2015 72:152-158.
**Port Wine Birthmarks: PDL + Rapamycin**

Placebo PDL + Placebo; PDL + Rapamycin
Analyzed at 6, 12, and 18 weeks after intervention.

PDL + Rapamycin yielded the lowest digital photographic image score (greatest improvement) and lowest percentage of blood vessels on histologic analysis.

Well tolerated; rapamycin was detected in the blood.

Photographs taken before treatment (A), after 6 weeks (B), and after 12 weeks (C). The lateral part of port wine stain was treated with laser, and in the patient, according to the randomization, the rapamycin treatment was applied in the superior half.

Topical rapamycin combined with PDL in the treatment of capillary vascular malformations in SWS: Phase II, randomized double-blind, intradividual placebo controlled clinical trial. JAAI 2015 72:152-158

**Photodynamic Therapy (PDT)**

A photosensitizing drug is administered which can be "selectively" accumulated in the target (vasculature).

After a pre-selected time interval, lesion is exposed to light at a wavelength absorbed by the photosensitizer.

**Photodynamic Therapy for Port Wine Birthmarks**

<table>
<thead>
<tr>
<th>Photosensitive Period</th>
<th>RPDR</th>
<th>RPDR 1 cm²</th>
<th>RPDR 2 cm²</th>
<th>RPDR 3 cm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment spot</td>
<td></td>
<td>1 cm²</td>
<td>1 cm²</td>
<td>1 cm²</td>
</tr>
<tr>
<td>Light dose rate</td>
<td>100 mW/cm²</td>
<td>100 mW/cm²</td>
<td>100 mW/cm²</td>
<td>100 mW/cm²</td>
</tr>
<tr>
<td>Total effective light dose</td>
<td>85 J/cm²</td>
<td>75-96 J/cm²</td>
<td>350 J/cm²</td>
<td></td>
</tr>
<tr>
<td>Total effective treatment time</td>
<td>~11 minutes</td>
<td>~12-16 minutes</td>
<td>~60 minutes</td>
<td></td>
</tr>
<tr>
<td>Photosensitive period</td>
<td>3 days</td>
<td>5-7 days</td>
<td>&gt; 7 days</td>
<td></td>
</tr>
</tbody>
</table>

**Infantile Hemangiomas**

Facial-segmental IH treated with propranolol and PDL demonstrated more rapid and complete clearance and required a lower cumulative propranolol dose to achieve near-complete clearance.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Combined (6/12)</th>
<th>PDL (2/5)</th>
<th>Propranolol (1/5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of propranolol until near-complete clearance</td>
<td>Concurrent 92 days</td>
<td>Propranolol 288 days</td>
<td></td>
</tr>
</tbody>
</table>

**Infantile Hemangiomas : Propranolol and PDL**


**Angiofibromas**
Angiofibromas: Laser (PDL/AFR) + Rapamycin

Pulsed-dye laser treatment 10 mm; 1.5 ms; 7.5 J/cm²; 30 ms cooling
Ablative fractional resurfacing (AFR) 15 mm; 70 mJ; 40%
Pinpoint electrocautery to papular fibrotic lesions
0.2% topical sirolimus ointment bid

2% topical formulation ointment versus gel versus vehicle applied bid for 12 weeks


Trichoepitheliomas

- 2 siblings case report – both with multiple trichoepitheliomas
- One carbon dioxide laser ablation and topical sirolimus (8 year old with more lesions and larger) and the other topical sirolimus alone (6 year old with smaller lesions)
- Both had improvement with no side effects


Actinic Keratoses

Daylight Photodynamic Therapy (PDT)

Acknowledgements to Merete Haedersdal, Chris Zachary, Brandon Coakley, Melissa Shive

Latitude matters

- In AK literature, need at least 8J/cm² for PPIX activation
- Irvine: 33.6°N, Boston, 42°N, Seattle 47°N, Anchorage 63° N
- Decrease in effective light dose with cloud cover:
  - Partly Cloudy Day: 25% decrease
  - Cloudy Day: 50% decrease
  - Rain: 75% decrease

**Topical PDT for Acne**

### Indications
- Patients who can’t or won’t use traditional medications
  - Antibiotic allergy
  - History of Head Injury or Severe Migraines where tetracyclines or isotretinoin contraindicated

### Contraindications
- Must be able to stay indoors after the procedure
- Must be able to follow directions

Please note that teenagers often have difficulties with both.

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### 0.33% Brimonidine topical gel

- FDA approved August 2013
- Indicated for topical treatment of erythematotelangiectatic subtype of rosacea, which is characterized by flushing and persistent facial erythema
- Alpha 2 adrenergic agonist
- Apply a pea-sized amount once daily to each of the 5 areas of the face
- Most common adverse events include erythema, flushing, skin burning sensation and contact dermatitis

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### Topical Brimonidine Tartrate 0.33% gel effectively reduces the post-treatment erythema of daylight-activated PDT

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### Topical Brimonidine Tartrate 0.33% on Postlaser Erythema: Our experience and review of literature

- 55 year old women – 1927 nonablative fractional resurfacing (5 mj; 30% density; 6 passes)
- 21 year old IPL (14-18 J/cm², 15 x 35 mm spot)

Topical BT was applied to one side immediately post which led to significant reduction in erythema within 30 minutes

Topical BT then applied to other side of face

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### Topical Brimonidine Tartrate 0.33% on Postlaser Erythema: Our experience and review of literature

- 21 year old man with acne scars underwent fraction CO₂ laser (14-18 mj/cm²); BT applied immediately post to reduce erythema
- Patient began to doze off and at 30 minutes not able to sit up
- Transferred to emergency department VSS; Discharged after 4 hours a
- BT crosses the blood brain barrier leading to CNS depression
- Ablative laser facilitate cutaneous absorption and recommended does is 1 pea sized amount and more was applied
- While mild toxicity may self resolve; patients may require an opiate antagonist
Rosacea

Types of Rosacea

- Erythematotelangiectatic
  - Light based devices
- Papulopustular – inflammatory
  - Anti-inflammatory agents/antibiotics
- Phymatous
- Ocular

1% Oxymetazoline cream

- Available since May 2017
- Indicated for persistent facial erythema
- Alpha 1 agonist - different from previously available alpha 2 agonists
- Apply a pea-sized amount once daily in a thin layer to cover the entire face
- Data now available up to 52 weeks of continued use
- Most common side effects are application site dermatitis, erythema, pruritus or pain and worsening inflammatory lesions of rosacea

Combination treatment for Rosacea?

- Could oxymetazoline be used in combination with PDL to achieve an enhanced response
- Studies on going but possibly
- Need to consider carefully because oxymetazoline may decrease the rosacea target and minimize laser effect

Scars

Medications applied post-AFR to augment Scar treatment results

- Keep in mind you should only consider this for medications that you would safely inject into the skin or blood stream
- Medications to consider
  - Triamcinolone for injection
  - 5-Fluorouracil
  - Bimatoprost – to repigment
  - Poly-L-lactic acid

Future Indications to Consider

Basal Cell Carcinomas
Could Imiquimod be used post laser treatment of basal cell carcinoma to enhance results?

Gynecologic Dermatology?
Could topicals be applied post – ablative fractional treatment to further increase atrophy improvement

Summary
• Light based therapies have been used in combination with medications to enhance/prolong results
• There can be safety issues so potential risks do need to be considered
• Clinicians can improve patient satisfaction by considering combination treatments and implementing cautiously

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