New and Emerging Therapies for Acne and Rosacea

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Disclosures

• Allergan
• Galderma
• Ortho Derm
• Almirall
• Ferndale
• J & J
• L’Oreal

• Aclaris
• P & G
• Dermira
• Sienna
• Revance
• Sonoma
Acne Topical Combinations

- Erythromycin 3% - BP 5% pak
  - 8 month shelf life, no refrigeration

- Adapalene 0.3% - BP 2.5%
  - Decrease number and size atrophic scars

- Tretinoin - BP
  - Stability issues, dual chamber pump
New Topical Retinoids

• Tretinoin lotion 0.05%
  – micronized, small $\rightarrow$↑ penetration follicle
  – polymerized emulsion, meshlike network
  – vehicle – hydrating agents
    – glycerin, HA, soluble collagen
    – spreads and absorbs easily

• Tazarotene lotion
  – emulsion technology
  – phase 3

• Trifarotene
  – 4$^{th}$ generation retinoid
  – RAR $\gamma$ selective binding
  – phase 3 – face and trunk
New Topicals

• Hypochlorous Acid antimicrobial facial cleanser
  – bacteria, virus, fungus, spores, MRSA
  – anti-inflammatory - ↓ mast cell degranulation
  – mild – moderate acne
Acne – New Topicals
Minocycline

- Gel (BPX – 01) – 2%
  - fully solubilized minocycline
  - bioavailable in hydrophilic gel
  - penetrates epidermis and pilosebaceous unit
  - lipophilic, improved drug delivery
  - achieved primary endpoint phase 2b randomized multicenter clinical trial
  inflammatory acne – 59% reduction
  - at least 2 grade reduction (secondary endpoint) > 25% patients
• Foam (fmx 101) 4%
  - micronized in triglyceride – based foam technology
  - 2 randomized placebo controlled phase 3 trials
  - 12 weeks, 961 patients
  - met primary and secondary efficacy endpoints (number lesions, IGA, percent reduction)
  - third phase 3 study
New Topicals - Antiandrogen

• Clascoterone 17 alpha propionate 1% cream
  – steroid
  – topical potent peripherally selective antiandrogen
  – targets AR in sebocytes and hair papilla cells within pilosebaceous unit
  – competes with androgen receptor
    → displaces hormones (DHT) from binding
  – no inhibition of 5 – alpha – reductase, no systemic side effects
  – inhibits sebum production and inflammation (cytokines)
  – higher activity than finasteride and flutamide, equal to cyproterone acetate
– phase 2 study
– statistical significance primary endpoints
– 17% IGA improvement 35.7% TLC reduction
– phase 3 – 12 weeks twice daily vs. placebo
  – 1400 patients
– statistically significant IGA treatment success
– statistically significant reductions non-inflammatory and inflammatory lesion counts
– will also evaluate potential for long term safety (adrenal suppression)
New Oral for Acne

• Sarecycline
  – narrow spectrum tetracycline – derived antibiotic with antiinflammatory properties
  – once daily with or without food
  – weight based dosing
  – approved age 9
  – chest and back acne
• Sarecycline
  – 2 phase 3 trials – moderate to severe acne
  – co-primary endpoints and inflammatory lesion count secondary endpoints both met
  – low incidence side effects
Lidose – isotretinoin without food

- Phase 4 study of long term efficacy and safety – 166 patients
- Examined relapse rates 104 weeks after 20 weeks of treatment on empty stomach
- 83% required no further treatments
Acne Controversies - Isotretinoin

- Delaying procedures post treatment
  - Consensus recommendations based on expert survey over 100 dermatologists
  - Insufficient evidence to support delaying: superficial chemical peels, skin surgery, LHR, fractional nonablative laser procedures, vascular and pigmented lesion lasers

- Blood test monitoring – may not be necessary to repeat after 2-3 months if all stable
  - CK and GGT may be more useful than AST and ALT

- New Iplede “qualifying” exemption for partial hysterectomy patients – no longer required to have pregnancy test (AADA advocacy)
• Microbiome imbalance – barrier defect and ↓ healthy microbiome
  – C. acnes is present in most people
  – virulence – related genes are involved in production and transport of bacterial toxins that are more abundant in acne patients
  – C. acnes also have health benefits for skin
    – produce short-chain fatty acids that contain antimicrobial properties (staph and strep)
    – maintain low skin PH
  – treatment goal – restore balance of microbiome
  – probiotics are more targeted than antibiotics (kill both beneficial and harmful bacteria)
    – antibiotics with probiotics may improve acne
Acne Controversies - Diet

- High glycemic index foods
  - sugars, refined grains, starches, white rice, corn
- Skim milk – contains milk proteins whey and casein
  - stimulates insulin – like GF – 1
  - increase insulin levels
- Benefits of mediterranean diet
  - fruits, vegetables, whole grains, healthy fats
- Low glycemic diet
  - lower androgen bioavailability
  - altered sebum production
  - ↓ inflammation
Devices – Particle Assisted Laser Treatment

- Topical suspensions of gold and silver coated silica microparticles are absorbed and activated by laser → heat disrupts inner lining of pilosebaceous unit → selective photo thermolysis

↓ acne (inflammatory)
- Gold nanoparticles
  - absorb infrared and near – IR irradiation
  - chromophore 150 nm
- Silver microparticle suspension (SNA – 001)
  - 755 nm, 810 nm, 1064 nm
- massaged in
Mechanism of Acne Clearance
Short Pulsed 1064 nm Laser
650-Microsecond Laser Technology

1) Selective photothermolysis of blood vessels:
Coagulation of blood vessels blocks the inflammatory response and reduces pressure on the surrounding tissue, reduces pain and reduces inflammation/postinflammatory erythema.

2) Phototoxic or bactericidal effect:
Inhibition of bacterial cells or their apoptosis as a result of the light radiation absorption by endogenous porphyrins Propionibacterium acne or as a result of thermal destruction of bacteria.

3) Photothermal effect:
Deep-heating effect of lasers emitting in the mid infrared range causing thermocoagulation of collagen and sebaceous glands, reducing sebum output.
Clearance of Acne with 650-Microsecond Laser Technology

Before

3 Months After 5th Treatment

(photos courtesy of David Goldberg, MD)
Clearance of Acne with 650-Microsecond Laser Technology

Before

1 Month After 4th Treatment

(photos courtesy of David Goldberg, MD)
Microneedling

- Acne scarring, acne, pores
- Controlled dermal wounding and stimulation of wound healing cascade, release of GF’s, enhances collagen production
- 3-5 treatments every 2-4 weeks
- Microneedling with fractional RF (MFR) – acne + acne scars
  - 2 studies, ↓ inflamm lesion count + noninflamm
  - ? thermal injury to sebaceous glands → ↓ sebum excretion
- Many studies have shown success
# Overview of Blue Light Devices

<table>
<thead>
<tr>
<th></th>
<th>TRIA Skin Perfecting Blue Light</th>
<th>Omnilux Clear-U</th>
<th>Tända</th>
<th>ANSR: BLU-U</th>
<th>BLU-U</th>
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<tr>
<th>Percent Inflammatory Lesion Reduction</th>
<th>70% within 2 to 4 weeks (Reference\ 1)</th>
<th>38% by week 4 (Reference\ 2)</th>
<th>39% by week 4 (Reference\ 3)</th>
<th>No published results</th>
<th>37.5% within 3 weeks</th>
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</thead>
<tbody>
<tr>
<td>Treatment Time</td>
<td>2.5 minutes twice per day</td>
<td>20 minutes twice per week</td>
<td>6 minutes per day</td>
<td>10 minutes per day</td>
<td>17 minutes twice per week</td>
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<tr>
<td>Power Density</td>
<td>400 mW/cm(^2)</td>
<td>40 mW/cm(^2)</td>
<td>50 mW/cm(^2)</td>
<td>less than 40mW/cm(^2)</td>
<td>10 mW/cm(^2)</td>
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<tr>
<td>FDA OTC cleared</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes (Rx)</td>
</tr>
<tr>
<td>% output in therapeutic band</td>
<td>100% (412 nm)</td>
<td>100% (415 nm)</td>
<td>100% (415 nm)</td>
<td>0% (440 nm)</td>
<td>100% (417 nm)</td>
</tr>
</tbody>
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**References**

Rosacea – Links Associations

- Caffeinated coffee linked to decreased incidence rosacea
  - nurses health study II – 87,000 participants over a decade
- Consuming white wine and liquor linked with increased risk of rosacea
  - high concentrations alcohol and no flavonoids, antiinflammatories
- Rosacea associated with increased risk of cardiovascular and GI diseases, (celiac, Crohn, UC, IBD), systemic illnesses and possibly cancer
  - 33,000 patients in Taiwan - ↑ chol, ↑ CAD, HTN
  - 6,000 patients nurses Health Study II - ↑ BCC, ↑ thyroid Ca,
  - study showing ↑ dementia, alzheimers, parkinsons
  - Danish study - ↑ anxiety and depression
Rosacea – New Topicals

• Invermectin cream 1%
  – antiinflammatory and antiparasastic (demodex)
  – ↓ gene expression levels of IL-8, LL-37, HBD₃, TLR4, TNFα
  – papules and pastules
  – 83% reduction inflammatory lesions 16 weeks
  – ↓ density demodex mites 12 weeks
  – 1/3 remained clear after one year
Rosacea – New Topicals

• Oxymetazoline HCI 1% cream – α adrenergic agonist (vaso constriction)
  – phase 3 (800 patients) – statistically significant improvement in erythema (2 points on scale) 12-18% subjects
  – efficacy increased over 52 weeks
  – no rebound redness, flushing
Rosacea New Topicals

• Minocycline foam 1.5% (Fmx 103)
  - papulopustular rosacea
  - phase 3 studies (1500 patients)
  - primary endpoint: ↓ lesions, ↓ IGA (2 grades)
  - secondary endpoint: percent reduction lesions

• Minocycline gel (BPX- 04) 1%
  - Phase 2b trial

• Natural, botanical products (cannabinoids, honey)