ACNE BOOT CAMP
TOPICAL THERAPY BASICS

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Relevant Disclosures

• Investigator
  - Allergan, Dermira, Foamix, Valeant
• Speaker
  - Valeant
• Consultant
  - Allergan, Dermira, Valeant
Overview

• Acne is a common condition, but can be confused with other facial skin conditions
• Proper diagnosis is key to successful acne treatment
• Recognizing unique acne signs can prevent misdiagnosis

Acne Pathophysiology

- Acne is caused by 4 interrelated processes affecting the pilosebaceous unit\textsuperscript{1,2}
  - Altered follicular hyperkeratinization
  - Sebaceous gland hyperactivity
  - Propionibacterium acnes (\textit{P acnes}) proliferation
  - Inflammation/immune hypersensitivity to \textit{P acnes}

Comedonal Acne
Mild Inflammatory Acne
Acne
Treatment Goals

• Reduce/eliminate comedones/inflammatory lesions\(^1\)
  • Reduce \textit{P acnes}
  • Reduce dilated pores
  • Reduce inflammatory response

• Prevent sequelae\(^2\)
  • Minimize psychological effects
  • Minimize scarring

# Mechanisms of Topical Acne Therapy

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Comedogenesis</th>
<th>↓ <em>P. acnes</em></th>
<th>↓ Inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPO</td>
<td>√</td>
<td>√</td>
<td></td>
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<tr>
<td>Retinoids</td>
<td>√</td>
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<tr>
<td>Antibiotics</td>
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</tbody>
</table>

Benzoyl Peroxide (BPO)

• Mechanism$^1$
  • ↓ P acnes (bactericidal)
  • Comedolysis$^2$

• Preparations$^1$
  • OTC/Rx (2.5%–10%)

• Safety$^1$
  • Irritation, dry skin
  • Bleaching of fabric
  • Rare allergic contact dermatitis

Topical Retinoids

- **Mechanisms**\(^1\)
  - Normalizes follicular keratinization
  - ↓ Inflammation

- **Clinical utility**\(^2\)
  - Treatment of comedonal and inflammatory lesions
  - Available in 3 forms: tretinoin, adapalene, tazarotene

- **Safety**\(^1,2\)
  - Skin irritation
  - Photosensitivity
  - Acne flare prior to perceived improvement

Topical Antibiotics/Anti-Inflammatory (besides BPO)

• Clindamycin
• Erythromycin
• Dapsone 5% and 7.5%
• Azaleic acid
• Minocycline (coming soon)
• Sebum inhibitors (coming soon)

Mechanisms
• Antibacterial
  • Anti-inflammatory

  • Risk of resistant strains of *P. acnes* with antibiotics alone

References:
ACZONE® (dapsone) 7.5% w/w Topical gel:
A Product for the Topical Treatment of Acne

- Once-daily dosing\(^1\)
- Proven efficacy and tolerability\(^1,2\)
- Studied in large pivotal trials
  used for a topical acne drug\(^2\)
  - 4340 acne patients studied\(^2\)
  - 100% had moderate acne\(^1,3\)
- Features a pump design\(^1\)

Inflammatory Lesion Count Reduction
At Week 12

Study design: Pooled analysis of 4,340 patients in 2 identical, 12-week, multicenter, randomized, double-blind, vehicle-controlled, parallel-group studies.

Adapted from Thiboutot 2016

<table>
<thead>
<tr>
<th>Week</th>
<th>ACZONE® (dapsone) 7.5% w/w gel (n = 2162)</th>
<th>Vehicle (n = 2178)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-48.1% (-13.9)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-54.6% (-15.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P &lt; .001</td>
<td></td>
</tr>
</tbody>
</table>

Note: Values in parentheses indicate baseline values.
Comedonal (Noninflammatory) Lesion Count Reduction at Week 12<sup>1,*</sup>

**Study design:** Pooled analysis of 4,340 patients in 2 identical, 12-week, multicenter, randomized, double-blind, vehicle-controlled, parallel-group studies.
Local Dermal Tolerability Assessments

Pooled Tolerability:

- Erythema
- Scaling
- Dryness
- Stinging/Burning

Mean Severity Score
0 = none
1 = mild
2 = moderate
3 = severe

\[ \text{Mean Severity Score} = \frac{\text{Sum of Ratings}}{\text{Number of Assessments}} \]
Use of Aczone® 5% Gel as Maintenance Treatment of Acne Vulgaris Following Completion of Oral Doxycycline and Aczone® 5% Gel Treatment
Results

Mean % decrease in inflammatory lesion counts

Decrease Compared to Baseline

All results are statistically significant (p<.0001)
Combination Topical Antibiotic/BPO Products

• Topical antibiotic/BPO combinations
  • Reduce *P. acnes* proliferation and associated inflammation
  • Have mild direct and indirect comedolytic activity
  • Provide improved efficacy and reduced risk for resistance
  • Appear to be most beneficial in patients with mild-to-moderate inflammatory acne
Combination Therapy Is Standard of Care

Global Alliance Acne Treatment Algorithm

- **Acne Severity**
  - MILD
  - MODERATE
  - SEVERE

- **Comedonal**
  - Topical Retinoid
  - Topical Retinoid + Topical Antimicrobial
  - Oral Antibiotic + Topical Retinoid +/- BPO

- **Mixed and Papular/pustular**
  - Topical Retinoid + Topical Antimicrobial
  - Oral Antibiotic + Topical Retinoid + BPO

- **Mixed and Papular/pustular**
  - Oral Antibiotic + Topical Retinoid + BPO

- **Nodular[2]**
  - Oral Isotretinoin

- **Nodular/Conglobate**
  - Oral Isotretinoin

**1st Choice**
- Topical Retinoid

**Alternatives (1)**
- Alr. Topical Retinoid or Azelaic acid or Salicylic acid

**Alternatives for Females (1,4)**
- Oral Antandrogen

**Maintenance Therapy**
- Topical Retinoid +/- BPO

**Notes**
1. Consider physical removal of comedones.
2. With small nodules (<0.5 cm).
3. Second course in case of relapse.
4. For pregnancy, options are limited.
Adapalene 0.1%/BPO 2.5% Gel: Long Term Study

Efficacy: Lesion Count Reduction (Per protocol population [N=327])

- Total: 70.8%
- Inflammatory: 76%
- Non-inflammatory: 70%

Median Change in Lesion Counts (%)

- n=397 (88%) 3+ mos
- n=366 (81%) 6+mos
- n=334 (73.9%) 9+mos
- n=327 (72.3%) 12 mos

Inflammatory Lesion Reduction With Topical Combination Product

-70 -60 -50 -40 -30 -20 -10 0 10 20 30 40 50
Mean Change From Baseline (%)

Clindamycin 1%-BPO 5% gel
BPO 5% gel
Clindamycin 1% gel
Vehicle

-65% *
-36%
-34%
-19%

* $P < 0.05$ versus other treatments.

Reduction of *P. acnes*: Topical Combinations Versus Antibiotics Alone

BPO 3.75 / CP 1.2 Long Term Lesion Count Reductions

**Figure 1.** Mean percent reduction (SD) in inflammatory and noninflammatory lesion counts from baseline (N=20 baseline to week 12; N=18 week 12-24)*

*All results P<0.001 versus baseline from Week 4.*
Greater Efficacy When Combined With a Retinoid

- 90% of patients achieved ≥50% global improvement with Duac Topical Gel (clindamycin 1%, benzoyl peroxide 5%) + retinoid (tazarotene), more than with tazarotene alone in 12-week study.

Tazarotene 0.1% cream + Duac® Topical Gel (clindamycin 1%, benzoyl peroxide 5%)

Median Change in Papule and Pustule Count (%)

<table>
<thead>
<tr>
<th>Week</th>
<th>17%</th>
<th>42%</th>
<th>52%</th>
<th>30%</th>
<th>52%</th>
<th>63%</th>
</tr>
</thead>
</table>

* $P \leq 0.01$ versus tazarotene alone.

- Significant reduction with combination regimen from baseline inflammatory lesion count $\geq 25$

The Effect of 24 Weeks of Adapalene 0.3% and Benzoyl Peroxide 2.5% Gel Versus Vehicle Gel on the Risk of Formation of Atrophic Acne Scars in Moderate to Severe Acne Subjects

RESULTS
A/BPO 0.3%/2.5% vs Vehicle and Scar Formation Risk in Moderate to Severe Acne: Total Atrophic Acne Scar Count at Week 24

- After 24 weeks:
  - There was a mean of about 4 fewer acne scars (total scars) on the A/BPO 0.3%/2.5% Gel treated half-face
  - Fewer scars of both scar sizes assessed were observed in the A/BPO 0.3%/2.5% Gel treated half-face

Clinical Study RD.03.SPR.105061, Galderma R&D
A/BPO 0.3%/2.5% vs Vehicle and Scar Formation Risk in Moderate to Severe Acne: Total Atrophic Acne Scar Count by Visit

- A/BPO 0.3%/2.5% was significantly superior to its vehicle at all study visits and as early as week 1
- Mean scar counts decreased over time with A/BPO 0.3%/2.5%

Clinical Study RD.03.SPR.105061, Galderma R&D.
A/BPO 0.3%/2.5% vs Vehicle and Scar Formation Risk in Moderate to Severe Acne: Percent Change From Baseline - Total Atrophic Scar Count

- A/BPO 0.3%/2.5% was significantly superior to vehicle at all study visits and as early as week 1
- The mean number of scars decreased over time with A/BPO 0.3%/2.5%
- The mean number of scars increased over time with the vehicle
- The difference in the mean percent change in scars (A/BPO 0.3%/2.5% vs vehicle) after 24 weeks was 29.9%

Clinical Study RD.03.SPR.105061, Galderma R&D
Take away for your practice…

• New topical drugs are coming over the next few years

• For now, combination therapy is standard of care
  • continued improvements over time in the real world

• Non-BPO combos exist
  • Combine with BPO cleansers to prevent antibiotic resistance
THANK YOU!

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