New Medications for Preteen Acne

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Disclosures

Vyne pharmaceuticals (Speaker Bureau)
Almirall – A[H]
Learning Objective:

Review New Therapies for Preteen Acne

Outline

- New Oral Agents
- New Topical Agents
- Future
Sarecycline

- New tetracycline class oral antibiotic
- Only narrow spectrum tetracycline antibiotic
- Daily dosing
- Weight based dosing
- 1.5mg/kg/day
- FDA Approved ages 9 years and up
- Cutibacterium acnes has a low propensity to develop resistance

Sarecycline

- Initial studies from age 9-45 years of age
- Lesions
  - 20-50 inflammatory
  - ≤ noninflammatory
- Nodules ≤ 2
- IGA score of 3 (moderate) or 4 (severe)
Sarecycline

- 2 studies done and presented in one paper
- Both had similar statistically significant results
- Side effect profile was low

Sarecycline side effect profile

Moore A, Green LJ, Bruce S, et al. Once-Daily Oral Sarecycline 1.5 mg/kg/day Is Effective for Moderate to Severe Acne Vulgaris: Results from Two Identically Designed, Phase 3, Randomized, Double-Blind Clinical Trials. J Drugs Dermatol. 2018 Sep;17(9):987-996

TABLE 3. Treatment-Emergent Adverse Events Common to Tetracycline-Class Antibiotics (Safety Population)

<table>
<thead>
<tr>
<th>Event</th>
<th>Sarecycline (n=461)</th>
<th>Placebo (n=462)</th>
<th>Sarecycline (n=462)</th>
<th>Placebo (n=463)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal effects in &gt;1% of patients in any group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>22 (4.8)</td>
<td>12 (2.6)</td>
<td>18 (3.9)</td>
<td>13 (2.8)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10 (2.1)</td>
<td>7 (1.5)</td>
<td>9 (1.9)</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>6 (1.3)</td>
<td>6 (1.3)</td>
<td>3 (0.6)</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>6 (1.3)</td>
<td>6 (1.3)</td>
<td>2 (0.4)</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5 (1.1)</td>
<td>8 (1.7)</td>
<td>6 (1.3)</td>
<td>6 (1.3)</td>
</tr>
<tr>
<td>Vestibular effects</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>9 (1.9)</td>
<td>7 (1.5)</td>
<td>2 (0.4)</td>
<td>4 (0.9)</td>
</tr>
<tr>
<td>Motion sickness</td>
<td>0</td>
<td>0</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vertigo</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Phototoxic effects</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Photodermatitis</td>
<td>0</td>
<td>0</td>
<td>1 (0.2)</td>
<td>0</td>
</tr>
<tr>
<td>Sunburn</td>
<td>3 (0.6)</td>
<td>2 (0.4)</td>
<td>4 (0.8)</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Genital yeast infections</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vulvovaginal candidiasis</td>
<td>3 (0.6)</td>
<td>0</td>
<td>1 (0.2)</td>
<td>0</td>
</tr>
<tr>
<td>Vulvovaginal mycotic infection</td>
<td>2 (0.4)</td>
<td>0</td>
<td>3 (0.6)</td>
<td>0</td>
</tr>
</tbody>
</table>

Sarecycline treating **truncal** acne

Moore A, Green LJ, Bruce S, et al. Once-Daily Oral Sarecycline 1.5 mg/kg/day Is Effective for Moderate to Severe Acne Vulgaris: Results from Two Identically Designed, Phase 3, Randomized, Double-Blind Clinical Trials. J Drugs Dermatol. 2018 Sep;17(9):987-996

FIGURES: Percentage of patients with nodular/IGA acne at each site (ITT population). Nodular/IGA acne was defined as a ≥3 point decrease in nodular/IGA acne score from baseline and a score of 0 or A1 at follow-up. In SC1481, 36.0% and 35.6% of the ITT population had baseline IGA scores ≥2 for chest and back acne, respectively; in SC1482, 47.2% and 62.3% of the ITT population had baseline IGA scores ≥2 for chest and back acne, respectively. IGA, Investigator’s Global Assessment; ITT, intention-to-treat. *P<0.001 vs placebo; †P<0.05 vs placebo.
New Topicals

New retinoid – Trifarotene

- Trifarotene .0005% cream
- Trifarotene 50 μg/g cream is for the treatment of moderate acne on the face and trunk.
- Approved from age 9 years and up

New retinoid – Trifarotene

- Trifarotene .0005% cream

- The onset of effect was rapid versus vehicle:
  - significant reductions in both inflammatory and noninflammatory lesion counts seen as early as 1 week after treatment on the **face**
  - as early as 2 weeks after treatment on the **trunk**

- Side effect profile was mostly mild to moderate when applied not only to the face but the trunk which is a large surface area.
  - skin dryness, erythema, scaling, stinging, and burning


Trifarotene treatment responses
New Retinoid formulations.... old retinoid

- Tazarotene 0.045% lotion with polymeric emulsion technology
- Tretinoin 0.05% lotion with polymeric emulsions technology

Similar efficacies with respect to inflammatory and noninflammatory lesions in moderate to severe acne

Take home: As effective as the Tazarotene 0.1% cream but with less adverse effects

- Tanghetti EA, Kirick L, Green L, Guenin E, Harris S, Martin G, Pillai R. A Phase 2, Multicenter, Double-Blind, Randomized, Vehicle-Controlled Clinical Study to Compare the Safety and Efficacy of a Novel Tazarotene 0.045% Lotion and Tazarotene 0.1% Cream in the Treatment of Moderate-to-Severe Acne Vulgaris. J Drugs Dermatol. 2019 Jun 1;18(6):542.
Tazarotene lotion 0.045%

Preadolescents (aged 9-13 years)

- Randomized Patients (n=136)
  - Tazarotene 0.045% Lotion (n=66)
  - Vehicle (n=70)
- Reasons for Discontinuation
  - Lost to Follow-up (n=5 [7.6%])
  - Adverse Event (n=2 [3.0%])

- Completed
  - Tazarotene (n=59 [89.4%])
  - Vehicle (n=65 [92.9%])

- Reasons for Discontinuation
  - Lost to Follow-up (n=3 [4.3%])
  - Parent/Guardian Withdrawal (n=1 [1.4%])
  - Patient Request (n=1 [1.4%])

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Tazarotene lotion 0.045%

- Percentage of Participants
  - 9-13 years: 22.9% (TAZ), 7.1% (Vehicle)
  - 14-17 years: 24.4% (TAZ), 11.3% (Vehicle)

*P<0.05 versus vehicle; ***P<0.001 versus vehicle
There was no significance difference between TAZ-treated age groups for treatment success.
Weeks 4 and 8 also assessed; no significant differences between treatment and vehicle for any age group at those weeks.
At least a 2-grade improvement from baseline in EGSS and ‘clear’ or ‘almost clear’.
EGSS, Evaluator’s Global Severity Score.
Figure 3. Percent Reduction in Inflammatory Lesion Count in Tazarotene lotion 0.045%

Figure 4. Percent Reduction in Noninflammatory Lesion Count in Tazarotene 0.045% lotion
Before and After Pictures

12-year-old TAZ 0.045%-treated female

Baseline EGSS 3 (Moderate)
Week 12 EGSS 1 (Almost Clear)

14-year-old TAZ 0.045%-treated male

Baseline EGSS 3 (Moderate)
Week 12 EGSS 1 (Almost Clear)

Figure 6. Change from Baseline at Week 12 in QoL Domains

9-13 years

<table>
<thead>
<tr>
<th>Domain</th>
<th>TAZ 0.045% Lotion (n=59)</th>
<th>Vehicle Lotion (n=65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-perception</td>
<td>4.2</td>
<td>2.5</td>
</tr>
<tr>
<td>Role-emotional</td>
<td>3.2</td>
<td>2.5</td>
</tr>
<tr>
<td>Role-social</td>
<td>1.8</td>
<td>2.2</td>
</tr>
<tr>
<td>Acne symptoms</td>
<td>4.5</td>
<td>2.4</td>
</tr>
</tbody>
</table>

14-17 years

<table>
<thead>
<tr>
<th>Domain</th>
<th>TAZ 0.045% Lotion (n=258)</th>
<th>Vehicle Lotion (n=256)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-perception</td>
<td>4.3</td>
<td>4.4</td>
</tr>
<tr>
<td>Role-emotional</td>
<td>3.4</td>
<td>3.7</td>
</tr>
<tr>
<td>Role-social</td>
<td>2.7</td>
<td>2.2</td>
</tr>
<tr>
<td>Acne symptoms</td>
<td>4.3</td>
<td>3.9</td>
</tr>
</tbody>
</table>

Significant differences between treatment and vehicle were not assessed.
QoL, quality of life.
Figure 7. Cutaneous Safety and Tolerability

9-13 years

- Scaling: Baseline Week 12
- Erythema: Baseline Week 12
- Hyperpigmentation: Baseline Week 12
- Hyperpigmentation: Baseline Week 12
- Itching: Baseline Week 12
- Burning: Baseline Week 12
- Stinging: Baseline Week 12

14-17 years

- Scaling: Baseline Week 12
- Erythema: Baseline Week 12
- Hyperpigmentation: Baseline Week 12
- Hyperpigmentation: Baseline Week 12
- Itching: Baseline Week 12
- Burning: Baseline Week 12
- Stinging: Baseline Week 12

Tretinoin 0.05% Lotion

- Tretinoin 0.05% lotion with polymeric emulsions technology
- Low side effect profile
**Figure 1: Patient Disposition Showing Percent Completion and Reasons for Discontinuation (ITT population pooled data): Comparison of Preadolescent and Adolescent Populations**

### Preadolescent Population (9-13 years)  
Randomized Subjects (N=154)
- Tretinoin 0.05% lotion (N=74)
  - Reasons for Study Discontinuation
- Vehicle (N=80)
  - Reasons for Study Discontinuation

### Adolescent Population (14-17 years)  
Randomized Subjects (N=575)
- Vehicle (N=281)
  - Reasons for Study Discontinuation

<table>
<thead>
<tr>
<th>Reasons for Study Discontinuation</th>
<th>Preadolescent Population</th>
<th>Adolescent Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject Request (N=3 [4.1%])</td>
<td>1.4%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Subject Request (N=1 [0.7%])</td>
<td>0.4%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Lost to Follow-up (N=1 [1.3%])</td>
<td>0.7%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Withdrawal by parent/guardian (N=1 [1.3%])</td>
<td>0.7%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Other (N=1 [0.4%])</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Follow-up (N=1 [1.3%])</td>
<td>0.7%</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

**Table 1: Demographics and Baseline Characteristics (ITT adolescent population, pooled data)**

<table>
<thead>
<tr>
<th></th>
<th>Pooled data preadolescent population</th>
<th>Pooled data adolescent population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tretinoin 0.05% lotion (N=74)</td>
<td>Total (N=154)</td>
<td>Total (N=154)</td>
</tr>
<tr>
<td>Age- Mean years (SD)</td>
<td>12.4 (0.97)</td>
<td>12.4 (0.94)</td>
</tr>
<tr>
<td>Range</td>
<td>9-13</td>
<td>9-13</td>
</tr>
<tr>
<td>Sex N (%)</td>
<td>Male</td>
<td>31 (41.9%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>43 (58.1%)</td>
</tr>
<tr>
<td>Ethnicity N (%)</td>
<td>Hispanic or Latino</td>
<td>17 (23.0%)</td>
</tr>
<tr>
<td></td>
<td>Non Hispanic or Latino</td>
<td>57 (77.0%)</td>
</tr>
<tr>
<td>Race N (%)</td>
<td>American Indian or Alaska Native</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>3 (4.1%)</td>
</tr>
<tr>
<td></td>
<td>Black or African American</td>
<td>14 (18.9%)</td>
</tr>
<tr>
<td></td>
<td>Native Hawaiian or Other Pacific Islander</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td></td>
<td>Caucasian</td>
<td>55 (74.3%)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>2 (2.7%)</td>
</tr>
<tr>
<td>Evaluator’s Global Severity Score N (%)</td>
<td>3 – Moderate</td>
<td>72 (97.3%)</td>
</tr>
<tr>
<td></td>
<td>4 - Severe</td>
<td>2 (2.7%)</td>
</tr>
<tr>
<td>Inflammatory Lesion Count- Mean (SD)</td>
<td>26.2 (5.50)</td>
<td>27.2 (6.49)</td>
</tr>
<tr>
<td>Noninflammatory Lesion Count- Mean (SD)</td>
<td>48.3 (22.01)</td>
<td>52.1 (21.78)</td>
</tr>
</tbody>
</table>
Figure 2: Percent Change in Inflammatory Lesions from Baseline to Week 12 (ITT population, pooled data, LS Mean)

Preadolescent Population (9-13 years)

Baseline                      Week 4                     Week 8                   Week 12
*P=0.029 versus vehicle
**P=0.001 versus vehicle

Adolescent Population (14-17 years)

Baseline                      Week 4                     Week 8                   Week 12
*P=0.010 versus vehicle
**P=0.001 versus vehicle

Figure 3: Percent Change in Noninflammatory Lesions from Baseline to Week 12 (ITT population pooled data, LS Mean)

Preadolescent Population (9-13 years)

Baseline                      Week 4                     Week 8                   Week 12
*P=0.012 versus vehicle
**P=0.001 versus vehicle

Adolescent Population (14-17 years)

Baseline                      Week 4                     Week 8                   Week 12
*P=0.05 versus vehicle
**P<0.001 versus vehicle
Figure 4: Treatment Success. Subjects with at least a 2-grade improvement and ‘clear’ or ‘almost clear at each study visit (ITT population pooled data)

Table 2: Treatment-Emergent and Related Adverse Event (AE) Characteristics through Week 12 (Safety population, pooled data)
Figure 5a: Cutaneous Safety and Tolerability Assessment from Baseline to Week 12 (Safety preadolescent population, pooled data)

Figure 5b: Cutaneous Safety and Tolerability Assessment from Baseline to Week 12 (Safety adolescent population, pooled data)
Tretinoin 0.05% Lotion

- Hispanics
- Asian
- Showed it worked well in specific populations


Minocycline foam 4%

- Once daily minocycline foam 4%
- Minimal systemic minocycline exposure
- 730 to 765 times LOWER that what is seen in oral minocycline \(^1\)
- Approved for ages 9 and up
- Watch the foam can be flammable

New topical antiandrogen - clascoterone

- To what age?
  - 12 years and above
- Suppression of HPA axis?
  - By lab analysis there is suggestion this could happen
  - But clinically tolerated well
  - Should avoid using over large areas
Clascoterone Efficacy in 2 Phase 3 trials

- Both trials met the primary efficacy end points.
- Considerably more patients receiving clascoterone cream, 1%, vs vehicle achieved treatment success at week 12
- Clascoterone 18.4% (patients improved) vs Placebo 9.0%
- Clascoterone 20.3% vs Placebo 6.5%
- The absolute change from baseline in NILC and ILC at week 12 were also substantially greater with use of clascoterone cream, 1% vs vehicle.


Clascoterone cream

- No systemic adverse effects were observed, which is consistent with the results of in vivo studies showing clascoterone has only local, not systemic, antiandrogenic activity.
- Side effect profile similar to placebo

New combination products in the pipeline

- Encapsulated benzoyl peroxide 3% / encapsulated tretinoin 0.1%
- Encapsulated benzoyl peroxide 5%

Remember the oldies but goodies, especially washes as these are easy to use.

- Benzoyl Peroxide
- Glycolic Acid
- Salicylic Acid
Thank you!