WHAT'S NEW
IN THE
MEDICINE CHEST? PART 1
SUNDAY, JANUARY 15, 2017 – 9:40AM

JAMES Q. DEL ROSSO, DO
ADJUNCT CLINICAL PROFESSOR (DERMATOLOGY)
TOURO UNIVERSITY NEVADA
HENDERSON, NEVADA
JDR DERMATOLOGY RESEARCH
THOMAS DERMATOLOGY
LAS VEGAS, NEVADA

Disclosures

Allergan #
Anacor/Pfizer #
Aqua/Almirall #
Bayer Dermatology #
BioPharmX #
Celgene #
Cutanea #
Dermira #
Ferndale #
Galderma #
Genentech #
LeoPharma #
Novartis #
Novan #
Valeant #
Pharmaderm #
Promius #
Sebacia #
Sun Pharma #
Unilever #
Viamet #
Consultant / Speaker / Researcher #
(Updated as of 9-29-16)

POLYPODIUM LEUCOTOMAS

ACNE VULGARIS
TIME TO ONSET OF ACTION (25% Reduction)
Non-Inflammatory Lesion Count Reduction with Clindamycin-BP 3.75% Gel and Vehicle from Baseline to Week 12 (ITT Population)

FMX101 (Topical Minocycline Foam) Phase 2 Dose-Ranging Trial
Mean % Reduction in Lesion Counts Over Study Duration

New Modalities Under Evaluation for Acne
What Is On The Horizon?

Topical Minocycline Formulations
GAMMA-SPECIFIC TOPICAL RETINOID (TRIFAROTENE)

Topical Nitric Oxide

Plasma Minocycline Concentration After Once-Daily Topical Minocycline 4% Foam (FMX101) vs Single-Dose Oral Minocycline-ER*

Phase 2 Efficacy and Safety Dose-Ranging Study of Nitric Oxide (NO)-Releasing Topical Gel in Acne (N=153)*
Percent Change in Lesion Counts From Baseline to Week 12

**Active vs. vehicle at week 4, p=0.020
**Multiple Pathophysiologic Mechanisms of Rosacea and Diffuse Facial Erythema**

Augmented Immune Response
- Th2-bias
- Cathelicidin (ll-37)
- IL-12

Altered Vascular Response
- Inflammatory cell infiltration
- Angiogenesis

Angiogenesis
- Inflammatory cytokine induction
- 

Dermal Matrix Degradation
- 

Rosacea Dermatitis
- 

**Results from the DRM01-ACN02 Phase 2b Randomized Controlled Trial**

Baseline Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>Combined QD/QD</th>
<th>4% QD</th>
<th>7.5% QD</th>
<th>7.5% BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD) years</td>
<td>31.0 (12.0)</td>
<td>31.6 (12.7)</td>
<td>29.8 (11.9)</td>
<td>31.9 (13.1)</td>
</tr>
<tr>
<td>Sex, % male</td>
<td>59.8%</td>
<td>62.5%</td>
<td>59.4%</td>
<td>61.8%</td>
</tr>
<tr>
<td>Race, % white</td>
<td>78.2%</td>
<td>75.5%</td>
<td>76.6%</td>
<td>76.5%</td>
</tr>
<tr>
<td>Lesion Type, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory</td>
<td>27.4 (18.8)</td>
<td>26.3 (18.0)</td>
<td>27.6 (16.9)</td>
<td>27.2 (18.3)</td>
</tr>
<tr>
<td>Non-inflammatory</td>
<td>36.1 (24.7)</td>
<td>36.3 (20.4)</td>
<td>36.3 (18.6)</td>
<td>36.3 (17.0)</td>
</tr>
<tr>
<td>IGA, %</td>
<td>3 moderate</td>
<td>4 low</td>
<td>3 moderate</td>
<td>3 moderate</td>
</tr>
<tr>
<td></td>
<td>9 (0.4%)</td>
<td>10 (0.5%)</td>
<td>10 (0.4%)</td>
<td>10 (0.4%)</td>
</tr>
<tr>
<td>Response type, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burns easily, slowly</td>
<td>32.3%</td>
<td>32.3%</td>
<td>32.3%</td>
<td>32.3%</td>
</tr>
<tr>
<td>Burns mildly, fast</td>
<td>18.5%</td>
<td>18.5%</td>
<td>18.5%</td>
<td>18.5%</td>
</tr>
<tr>
<td>Burns moderately, fast</td>
<td>30.5%</td>
<td>30.5%</td>
<td>30.5%</td>
<td>30.5%</td>
</tr>
<tr>
<td>Burns with no response</td>
<td>28.7%</td>
<td>28.7%</td>
<td>28.7%</td>
<td>28.7%</td>
</tr>
<tr>
<td>Skin sensitivity</td>
<td>26.3%</td>
<td>26.3%</td>
<td>26.3%</td>
<td>26.3%</td>
</tr>
<tr>
<td>Sticky burns, low prof</td>
<td>12.3%</td>
<td>12.3%</td>
<td>12.3%</td>
<td>12.3%</td>
</tr>
<tr>
<td>Sticky burns, high prof</td>
<td>19.8%</td>
<td>19.8%</td>
<td>19.8%</td>
<td>19.8%</td>
</tr>
</tbody>
</table>

**Ivermectin (IVM) 1% Cream Once Daily**

*Case Series on Rosacea Treatment (N=34)*

47 Year Old Woman with Severe Papulopustular Rosacea, Thrombosed With Ivermectin 1% cream and Azelaic Acid 15%. 75-80% Improvement Over 6 Weeks.

*Old Woman with Moderate Papulopustular Rosacea, Previous Therapy with Topical Erythromycin, Tretinoin, Metronidazole, and Oral Antibiotics. 75-100% Improvement Over 8 Weeks.*
Azelaic Acid 15% Foam Twice Daily
Phase 3 Clinical Studies in Papulopustular Rosacea

<table>
<thead>
<tr>
<th>STUDY 1</th>
<th>Finacea Foam (n=483)</th>
<th>Vehicle (n=478)</th>
<th>STUDY 2</th>
<th>Finacea Foam (n=198)</th>
<th>Vehicle (n=203)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) [mean, SD]</td>
<td>51.2 (13.3)</td>
<td>51.9 (13.2)</td>
<td>Age (years) [mean, SD]</td>
<td>48.1 (10.6)</td>
<td>48.0 (20.6)</td>
</tr>
<tr>
<td>Sex (%)</td>
<td>Male Female</td>
<td>Male Female</td>
<td>Race (%)</td>
<td>White Nonwhite* Not reported</td>
<td>White Other</td>
</tr>
<tr>
<td>129 (27.7) 354 (73.3)</td>
<td>110 (27.2) 344 (72.8)</td>
<td>43 (21.7) 155 (78.3)</td>
<td>60 (29.6) 143 (70.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race (%)</td>
<td>White Nonwhite* Not reported</td>
<td>White Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>463 (95.9) 12 (2.5) 6 (1.2)</td>
<td>455 (95.2) 14 (2.9) 9 (1.9)</td>
<td>190 (96.0) 8 (4.0)</td>
<td>197 (97.0) 7 (3.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline lesion count [mean, SD]</td>
<td>21.7 (9.1)</td>
<td>21.2 (8.7)</td>
<td>Baseline lesion count [mean, SD]</td>
<td>21.6 (9.9)</td>
<td>26.4 (8.8)</td>
</tr>
</tbody>
</table>

Azelaic Acid 15% Foam
Formulation Characteristics

- Azelaic Acid 15% Foam
  - 15% (w/w) azelaic acid
  - Suspended in an oil-in-water emulsion vehicle
  - Hydrophilic
  - Non-white* Propellant foam formulation
  - Not metered

Azelaic Acid 15% Foam
Skin Tolerability Characteristics from Pivotal Studies

<table>
<thead>
<tr>
<th>System/Organ-Class Preferred Term</th>
<th>Finacea® Foam, 15% (n=681)</th>
<th>Vehicle (n=681)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General disorders and application site conditions</td>
<td>42 (6.2%)</td>
<td>16 (1.5%)</td>
</tr>
<tr>
<td>Application site pain*</td>
<td>42 (6.2%)</td>
<td>16 (1.5%)</td>
</tr>
<tr>
<td>Application site pruritus</td>
<td>17 (2.5%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Application site dryness</td>
<td>5 (0.7%)</td>
<td>5 (0.7%)</td>
</tr>
<tr>
<td>Application site erythema</td>
<td>5 (0.7%)</td>
<td>6 (0.9%)</td>
</tr>
</tbody>
</table>

**Application site pain* is a Medical Dictionary for Regulatory Activities (MedDRA) Preferred Term used to describe disagreeable skin sensations, including burning, stinging, pain, numbness, and tenderness

Topical Minocycline Foam (FMX103) for Papulopustular Rosacea
Phase 2 Dose-Ranging Study (N=213)

- Both the 1.5% and 3% doses of FMX103 were effective in reducing the number of inflammatory lesions (P < 0.05 for both FMX103 1.5% and 3%)
- 64.6% and 55.9% reduction, respectively, vs. 29.7% reduction in the Vehicle-controlled group (P < 0.05 for both FMX103 1.5% and 3%)

Persistent vs Perilesional Erythema of Rosacea

- Diffuse persistent (non-transient) facial erythema
- Almost always persistent after resolution of inflammatory lesions
- Presents with or without previous or concurrent inflammatory lesions

- Flare of erythema presents around papulopustular lesions
- Develops as the inflammatory lesion emerges and resolves as the inflammatory lesion resolves

- Multiple closely involved face: Face due to proximity
- Appears similar to diffuse persistent facial erythema

**α-Adrenergic Receptors in Superficial Cutaneous Vasculature**

Application for Facial Erythema of Rosacea

- Diffused facial erythema is associated with increased cutaneous circulation
- Enlarged vasculature in rosacea remains responsive to vascular tone regulation primarily by sympathetic nervous system
- Complex family of related receptors
  - 6 α-subtypes and 3 β-subtypes
  - Subtypes differ in distribution and function
- α-adrenergic agonists stimulate smooth muscle layer in the dermal vascular plexus → **VASOCONSTRICTION** → shunting of blood from dermal vessels
  - Does not alter telangiectasias (no smooth muscle layer)
  - Inflammatory lesions are not affected

References:

**THANK YOU**

The real problem is not whether machines think but whether men do.

B. F. Skinner