Progressive Treatments for Rosacea

Joshua Harper
Biomedical Engineering
September 29th, 2015
What is Rosacea?

- erythematotelangiectatic (ET),
- papulopustular (PP)
- phymatous (PH)
- ocular

http://theherbalfacefood.com/rosy-or-rosacea/
What Triggers Flares?

<table>
<thead>
<tr>
<th>Rosacea presentation</th>
<th>Current and emerging drug treatment options</th>
</tr>
</thead>
</table>
| Episodic erythema or flushing | Topicals (oxymetazoline)  
Oral (nadolol and clonidine) |
| Persistent erythema | Topical α-adrenoreceptor agonists (brimonidine tartrate and oxymetazoline)  
Topical azelaic acid or sulacetamide |
| Papulopustular | Mild: topical antimicrobials (metronidazole, clindamycin, and sulacetamide-sulfur, and ivermectin), azelaic acid, or retinoids  
Moderate: topicals plus oral antimicrobials [tetracyclines (low-dose doxycycline 40 mg/day), macrolides, or ivermectin]  
Severe: topicals plus high-dose tetracyclines or low-dose isotretinoin |

Recommendations based on the Rosacea International Expert Group, the Consensus Recommendations from the American Acne and Rosacea Society on the management of rosacea, and the current literature [5, 14, 18, 20, 21, 33, 34, 41–43, 46, 47]
Brimonidine Tartrate

- \(\alpha_2\)-adrenergic receptor agonist
- vasoconstriction action
- anti-inflammatory
<table>
<thead>
<tr>
<th>Study</th>
<th>No. of subjects</th>
<th>Methods</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase II(a)</td>
<td>122</td>
<td>Subjects were randomized in a 1:1:1 to receive BT 0.5 %:BT 0.18 %:BT 0.07 %:vehicle</td>
<td>One-grade improvement in CEA and PSA scores</td>
<td>BT topical gel was effective in a dose-dependent fashion in reduction of erythema for up to 12 h after one application</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Percentage of subjects with one-grade improvement in CEA and PSA was 84, 81, 75, and 28 % (BT 0.5, 0.18, 0.07 %, vehicle, respectively)</td>
</tr>
<tr>
<td>Phase II(b)</td>
<td>269</td>
<td>Patients were randomized in a 1:1:1:1 to receive BT 0.5 % once daily:BT 0.18 % once daily:vehicle once daily:BT 0.18 % twice daily:vehicle twice daily for 4 weeks</td>
<td>Two-grade improvement in CEA and PSA (primary) One-grade improvement in CEA and PSA (secondary)</td>
<td>Largest effect was observed in the BT 0.5 % group</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Percentage of subjects using BT 0.5 % gel who had a two-grade improvement on CEA and PSA scores on day 29 at hours 3, 6, 9, and 12 after application was 30, 28, 32, and 19 %, respectively (vs. 4, 7, 4, and 4 % for vehicle once daily) (( p &lt; 0.001 ))</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Percentage of subjects using BT 0.5 % gel who had a one-grade improvement on CEA and PSA scores on day 29 at hours 3, 6, 9, and 12 after application ranged from 60 to 76 % (vs. 31–42 % for vehicle once daily) (( p &lt; 0.001 ))</td>
</tr>
<tr>
<td>Phase III(a)</td>
<td>254</td>
<td>Patients were randomized in a 1:1 fashion to apply BT gel 0.5 %:vehicle for 4 weeks. Six visits (screening visit, days 1, 15, 29 of treatment phase, and weeks 6 and 8 of the follow-up phase). During the treatment phase (days 1, 15, 29), subjects remained in the clinic for 12 h and were assessed prior to study drug application, then again at 30 min, and 1, 3, 6, 9, and 12 h after application</td>
<td>Two-grade improvement in CEA and PSA One-grade improvement in CEA and PSA (secondary)</td>
<td>Percentage of subjects using BT 0.5 % gel who had a two-grade improvement on CEA and PSA scores on day 29 at hours 3, 6, 9, and 12 after application was 31.5, 30.7, 26.0, and 22.8 %, respectively (vs. 10.9, 9.4, 10.2, and 8.6 % for vehicle once daily) (( p &lt; 0.05 ))</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Percentage of subjects using BT 0.5 % gel who had a one-grade improvement on CEA and PSA scores on day 29 at hours 3, 6, 9, and 12 after application was 70.9, 69.3, 63.8, and 56.7 %, respectively (vs. 32.8, 32.0, 29.7, and 30.5 % for vehicle) (( p &lt; 0.001 ))</td>
</tr>
<tr>
<td>Phase III(b)</td>
<td>283</td>
<td>Same as phase IIIa</td>
<td>Two-grade improvement in CEA and PSA One-grade improvement in CEA and PSA (secondary)</td>
<td>Percentage of subjects using BT 0.5 % gel who had a two-grade improvement on CEA and PSA scores on day 29 at hours 3, 6, 9, and 12 after application was 25.4, 25.4, 17.6, and 21.1 %, respectively (vs. 9.2, 9.2, 10.6, and 9.9 % for vehicle once daily) (( p &lt; 0.05 ))</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Percentage of subjects using BT 0.5 % gel who had a one-grade improvement on CEA and PSA scores on day 29 at hours 3, 6, 9, and 12 after application was 71.1, 64.8, 66.9, and 53.5 %, respectively (vs. 40.1, 43.0, 29.4, and 40.1 % for vehicle) (( p &lt; 0.001 ))</td>
</tr>
</tbody>
</table>

\( BT \) brimonidine tartrate, \( CEA \) Clinician’s Erythema Assessment, \( PSA \) Patient’s Self-Assessment

Oxymetazoline

• selective adrenoreceptor agonist (a1 and partial a2)

• present in over-the-counter decongestants
Mechanism of action of intense pulsed light in vascular lesions:

1. Hemoglobin captures energy
2. Leading to coagulation in the vessel
3. Which is subsequently destroyed
Sources

• A.J. González-Rodríguez, R. Lorente-Gualb, a Instituto Dermatológico Dr. Alonso, Hospital Nisa 9 de Octubre, Valencia, Spain b Facultad de Fisioterapia y Podología, Universidad Católica de Valencia San Vicente Mártir, Torrente, Valencia, Spain. Received 15 May 2014; accepted 3 October 2014. Available online 2 May 2015
• National Institutes of Health. Oxymetazoline drug information. 2014.
• Jancin B. Novel topical rosacea drug sails through phase III: expert analysis from SDEF Hawaii Dermatology Seminar. Skin and Allergy News. 2-19-2014