Evaluation of Regenecare® Topical Gel for Treatment of Adverse Rash Symptoms Associated with EGFR Inhibitors

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ABSTRACT

Significance & Background: Targeted cancer therapies that inhibit the epidermal growth factor receptor (EGFR) have emerged as a novel and effective therapy against various malignancies such as breast, lung, head and neck, and colorectal cancers. EGFR inhibitor drugs are attractive treatment options because they are more tumor-specific and have a more manageable toxicity profile compared to traditional chemotherapy. Unlike standard chemotherapy, which affects most replicating cells, EGFR inhibitors target pathways that are crucial for cancer cell growth and survival. Despite these benefits, the increasing clinical use of EGFR inhibitors have led to the identification of a commonly occurring side effect of an acneform rash in about 88% of treated patients. This adverse event can result in treatment dose reduction, interruption, or cessation. Clinicians need new insights into managing this common adverse side effect.

Purpose: The purpose is to provide evidence based adjunct therapy to treat rash symptoms at its earliest onset for optimum patient management.

Interventions: A single center, prospective pilot study of 20 EGFR-inhibitor treated patients were enrolled to evaluate Regenecare topical gel in reducing itching and pain associated with EGFR rash. Participants were instructed to apply gel four times daily to rash areas during treatment cycle. Nurses assessed rash severity weekly using NCI CTCAE version 3. Patients responded weekly and at end of treatment cycle to questionnaires. A statistician evaluated original data and reported results.

Evaluation: The topical aloe, collagen and lidocaine gel showed 92.9% and 85.7% affectivity in reducing itching and pain respectively, the most commonly reported adverse symptoms of patients with grade 1-3 rash. The gel was reported to reduce these symptoms within 15-30 minutes after application.

Discussion: Evidence-based symptom management is important for clinicians to offer patients with EGFR-inhibitor induced rash. The clinical results indicated the gel is a safe and effective adjunct therapy for managing Grade 1-2 rash symptoms for out-patient care.
Introduction

The clinical use of Epidermal Growth Factor Receptor (EGFR) inhibitor drugs are now commonly used to treat numerous malignancies including colon, lung, breast, and head and neck. EGFR inhibitor drugs target epidermal derived tissues including capillaries, sebaceous cells, hair shaft, and hair follicles causing a severe side effect of an acneform skin rash. This is described as a severe macular or papular eruptive rash with associated pain, itching and redness and can occur on face, neck, scalp, arms, legs and hands.1 Rash appearance has been associated with a positive treatment outcome and these areas are under further investigation.2 Severe and uncomfortable symptoms, however, can result in treatment dose reduction, interruption, or cessation. To date, there have been no evidence-based therapies for practitioners to use to treat these symptoms.

One study showed patients that identified the physical discomfort of the rash on their HRQL (Health Related Quality of Life Questionnaire), specifically the sensations of pain, burning, and skin sensitivity. Patients also experienced worry, frustration, depression and withdrawal from socializing because of the dermatologic symptoms.4 Oncology nurses play an important role in providing patient education, instituting preventive measures, and assuring early detection and intervention for patients on targeted therapies.5

Regenecare® Gel Applied 4 x Daily to EGFR Rash for 4 Weeks

Patients’ Responses re: Pain Relief

Pain Reduction (n=7)

<table>
<thead>
<tr>
<th>Percentage of Responses</th>
<th>No Effect</th>
<th>Mildly Effective</th>
<th>Moderately Effective</th>
<th>Very Effective</th>
<th>Extremely Effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Reduction</td>
<td>80.0%</td>
<td>70.0%</td>
<td>60.0%</td>
<td>50.0%</td>
<td>40.0%</td>
</tr>
</tbody>
</table>

Results

Table 1 shows the outcome of responses for each category for the overall 4 week evaluation criteria. Three study patients experienced grade 3 or worse rash symptoms and were eliminated from study due to use of other intervention
Statistical Evaluation of Results Overall Rating of Topical Gel (at 4 weeks) – TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>Appearance</th>
<th>Reduce Itching</th>
<th>Reduce Pain</th>
<th>Moisturizing</th>
<th>Healing</th>
<th>Sooth Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Effect</td>
<td>15.63%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>37.50%</td>
<td>6.67%</td>
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</tr>
<tr>
<td>Mildly Effective</td>
<td>21.87%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>18.75%</td>
<td>20.00%</td>
<td>12.50%</td>
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<tr>
<td>Moderately Effective</td>
<td>37.50%</td>
<td>7.14%</td>
<td>14.29%</td>
<td>6.25%</td>
<td>20.00%</td>
<td>18.75%</td>
</tr>
<tr>
<td>Very Effective</td>
<td>12.50%</td>
<td>50.00%</td>
<td>71.42%</td>
<td>37.50%</td>
<td>53.33%</td>
<td>56.25%</td>
</tr>
<tr>
<td>Extremely Effective</td>
<td>12.50%</td>
<td>42.86%</td>
<td>14.29%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>12.50%</td>
</tr>
<tr>
<td>Overall</td>
<td>100%</td>
<td>100%</td>
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<td>100%</td>
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</tbody>
</table>

Regenecare® Gel Applied 4 x Daily to EGFR Rash for 4 Weeks
Patients’ Responses re: Itching

Patients need more than temporary moisturizers for EGFR rash symptoms. Lotions used to treat dry skin have not been clinically investigated for reducing EGFR rash symptoms or for safety. Because Regenecare contains ingredients that act as buffering agents when topically applied to open wounds or abraded skin, it appears to prevent pain or sting which is often associated with the use of pharmaceutical 2-4% lidocaine jelly. Brad Pontani, M.D. of Southeast Texas Hyperbaric Medicine Center, Conroe, Texas has also shown that Regenecare effectively relieves pain for up to 4 hours reducing the need for narcotic pain control (Pontani, unpublished data). Mario E. Lacouture, M.D. (SERIES Dermatology Clinic, Northwestern University Feinberg School of Medicine, Chicago Ill.) specializes in EGFR inhibitors induced rash treatment methods. He has stated that “Regenecare® is a prescription topical gel…which soothes inflamed rash and provides symptomatic relief from itching, burning and tenderness.” EGFR inhibitors function as monoclonal antibodies to block the growth
factor receptor site on the epidermal derived cells to thus inhibit cell replication. It is acknowledged that the rash will remain during the course of the treatment. It was of interest to observe that 62% of patients’ response noticed a perceived reduction in rash appearance (cumulative “moderately”, “very,” and “extremely” effective scores). Because of the benefits of ingredients in the Regenecare formulation it may be noteworthy to assume a possible reduction in inflammation and the resulting redness.

Conclusion

The pilot study trial showed that 100% of patients reported effectiveness of Regenecare® in reducing itching and pain. Patients’ total response was 92.9% (cumulative “very” and “extremely” effective) for relieving itching. Patients’ total response was 85.7% (cumulative “very” and “extremely” effective) for relieving pain. Fewer patients responded to the pain question than to the itching question. Although the rash can be painful, sensations such as burning, itching and tenderness have been used to describe the discomfort of EGFR inhibitors induced rash. Pruritis (itching) is the most common uncomfortable symptom reported. Application of Regenecare showed benefit in alleviating this symptom. Patients reported healing and soothing benefits during 4 weeks of gel application. No untoward clinical side effects were observed during 4 weeks of continued gel application. Regenecare® appears to be a safe and effective adjunct therapy for managing symptoms of EGFR inhibitors-induced Grade 1 and 2 rash.

References

12. Brad Pontani M.D. Regenecare® wound care gel with 2% lidocaine-HCl was evaluated in a cross over design of 55 patients with deep wounds for pain management and healing associated with dressing changes. Southeast Texas Hyperbaric Medicine Center, 2008.
13. Brad Pontani, M.D. Regenecare® topical gel with 2% lidocaine HCl was compared to 2% Lidocaine Jelly for managing pain associated with deep wound dressing changes. Southeast Texas Hyperbaric Medicine Center, 2007.

Why would you recommend this product to others for skin rash?

CTC Rash Grade (Rash Eruption Areas)

- Grade 1
  - Cetuximab subject.
  - (Face, upper chest, scalp)

- Grade 2
  - Erlotinab subject.
  - (Face, upper chest)

- Grade 2
  - Erlotinib subject.
  - (Face, upper chest, back, arms, legs, fingers)

Erbitux® Study Patients Rate Regenecare® Gel

“Extremely Effective for Reducing Pain and Itching and Very Effective for Skin Healing”

Regenecare® Gel Applied 4 x Daily to EGFR Rash for 4 Weeks

Patients’ Responses re: Recommending Gel

Would You Recommend this Product to Others? (n=16)

<table>
<thead>
<tr>
<th>Percentage of Responses</th>
<th>No</th>
<th>Yes</th>
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<tbody>
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<td>0%</td>
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<td>10%</td>
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References supported by a grant from MPM Medical Inc., Irving, Texas

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