# A pilot cross-over study to evaluate the use of Regenecare® topical gel in patients with cutaneous toxicity caused by epidermal growth factor receptor (HER1/EGFR) inhibitors

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## Background

Acneform rash presents as a dose-limiting side effect when anti-cancer agents known as HER1/EGFR (epidermal growth factor receptor) inhibitors (cetuximab, erlotinib, and panitumumab) are administered to cancer patients.[1,2] Patients report pain and itching that led to discontinuation or reduction of the EGFR inhibitors. Secondary skin infection can occur from scratching. The appearance of the rash can affect patients' quality of life.[3,4] Recent studies suggested that the papulopustular eruption might be a surrogate marker for HER1/EGFR inhibitor efficacy; therefore better rash management is of critical importance to promote optimal use of these agents.[5,6] Antibiotics, corticosteroids, and retinoids are treatment options for rash management with minimal or moderate success.[2,4,6] Regenecare® Gel (MPM Medical, Inc., Irving, TX) contains 2% lidocaine for local pain management, marine collagen to promote tissue formation, aloe vera to enhance circulation and promote emollient effect, and sodium alginate to absorb exudates, which can be optimal for managing the symptoms of HER1/EGFR inhibitor-induced acneform rash.

## Purpose

This study evaluates the effectiveness of Regenecare® Gel in relieving the clinical symptoms of HER1/EGFR inhibitors-induced skin rash, pain and itching. The secondary objective assesses patient tolerability and satisfaction.

## Methods

A single center, randomized, prospective pilot cross-over study is being conducted with 20 cancer patients treated with cetuximab-, erlotinib-, or panitumumab-based regimen. Baseline photographs of both sides of the face were obtained after subjects signed an Institutional Review Board approved informed consent. Rash was graded using NCI CTC version 3 Grading of Acneform rash/desquamation. At the first sign of grade 2 (symptomatic) skin rash, subjects were instructed to start applying Regenecare® on the right side of the face following standardized training. After at least one week of treatment, subjects are permitted to cross-over to apply Regenecare® gel to both sides of the face. Subjects were asked to self-report the severity of the rash-related clinical symptoms (pain, itch, redness, and swelling) in a study diary at home or at the office. Subjects were examined weekly for facial evaluations and photographs. Scoring of rash pain and itching was rated as none, mild, moderate or severe. The study continued for a total of six weeks.

**Results:**

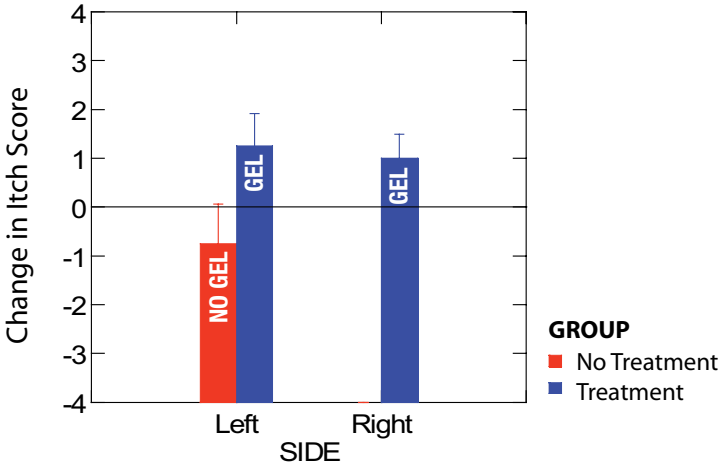
Eight patients were enrolled with 6 meeting criteria (3 cetuximab, 2 panitumumab, 1 erlotinib). The summary table includes the number of patients who reported improvement, same, or worsening of their itch and pain from baseline to week 1, week 1 to week 2, and baseline to week 2. The graphs capture the changes in no gel vs. gel treatment, as well as, right vs. left side. Itch and pain scoring are subjective and depend on individual patient assessment therefore a change in scoring (mean differences) is reported and statistically evaluated.

## Number of Patients Reporting Regenecare® Effectiveness on Pain and Itch on EGFR Inhibitors Rash

| | ITCH | | | | | |
|---|---|---|---|---|---|---|
| | Baseline vs Wk #1 | | Baseline vs Wk #2 | | Wk #1 vs Wk #2 | |
| | Right | Left | Right | Left | Right | Left |
| Improved | 5 | 1 | 3 | 2 | 0 | 3 |
| Same | 0 | 2 | 2 | 3 | 4 | 3 |
| Worse | 1 | 3 | 1 | 1 | 2 | 0 |

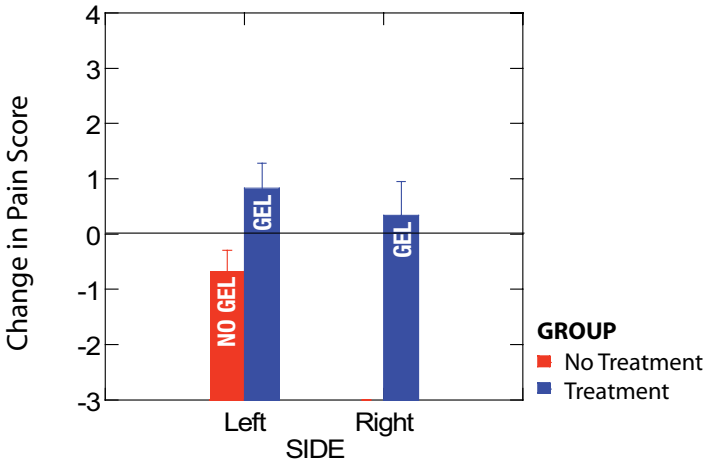
| | PAIN | | | | | |
|---|---|---|---|---|---|---|
| | Baseline vs Wk #1 | | Baseline vs Wk #2 | | Wk #1 vs Wk #2 | |
| | Right | Left | Right | Left | Right | Left |
| Improved | 1 | 0 | 2 | 2 | 3 | 1 |
| Same | 4 | 3 | 3 | 2 | 3 | 4 |
| Worse | 1 | 3 | 1 | 2 | 0 | 1 |

**Mean Difference of Scores (N=6) for Itching Relief Regenecare® Treatment Compared to Baseline (P ≤ 0.05)**




Difference in means = -1.875; 95.00% CI = -3.396 to -0.354
t = -2.614; f = 16; p-value= 0.019

**Mean Difference of Scores (N=6) for Pain Relief Regenecare® Treatment Compared to Baseline (P ≤ 0.05)**




Difference in means = -1.250; 95.00% CI=-2.382 to -0.118
t = -2.341; df = 16; p-value = 0.033

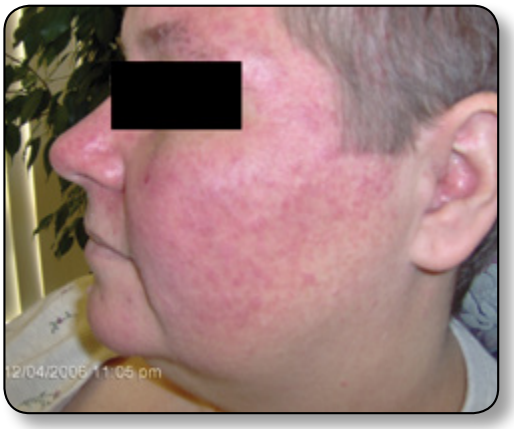
## Product Satisfaction Patient Questionnaire Survey Summary

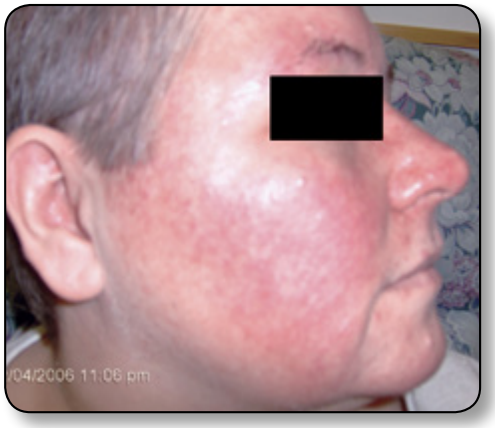
- Five out of 5 patients rated gel “very” or “extremely” effective in reducing itching.
- Five out of 5 patients rated gel “very” or “extremely” effective in reducing pain.
- Four out of 5 patients rated gel “moderate” to “very” effective in skin healing properties.
- Three out of 5 patients rated gel “moderate” to “very” effective in improving appearance of rash.
- Five out of 5 patients rated gel “very” to “extremely” effective as to ease of use (easy to apply, messiness, etc.).
- The onset of pain relief was immediate to 30 minutes and lasted 2-4 hours.
- The onset of itch relief was 15-30 minutes.

**Left Side**
**1 Week No Gel Treatment**
**Mild Itching, Moderate Pain**

**Vectibix® Treated Patient**

**Right Side**
**1 Week Regenecare® Gel Treatment**
**No Itching, Mild Pain**

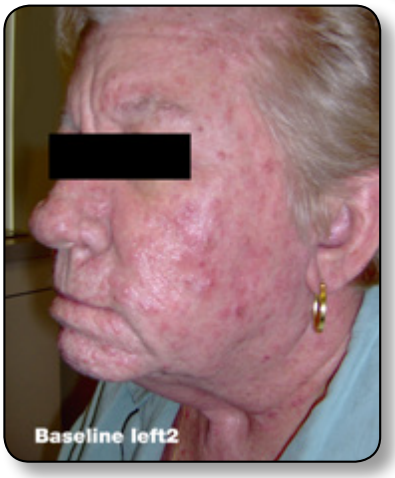


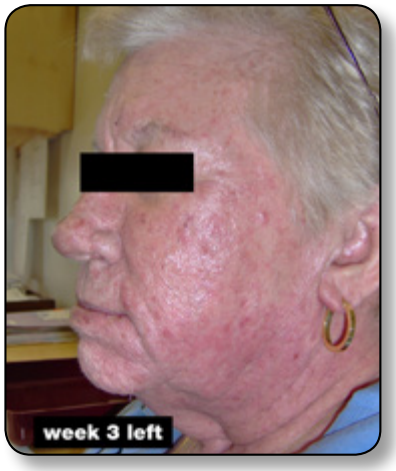


**Left Side**
**Baseline No Gel Treatment**
**Mild Itching, Severe Pain**

**Erbitux® Treated Patient**

**Left Side**
**1 Week Regenecare® Gel Treatment**
**Mild Itching, Mild Pain**




## Conclusion

Comparative analysis for Treatment vs. No Treatment showed significant improvement with respect to self-reported level of itch (p=0.019) and pain (p=0.033). All patients tolerated the study gel without any adverse effect and all patients were very satisfied with the effectiveness of the gel. In some patients the gel may help in reducing the redness. None of the subjects developed secondary skin infection during the study period. Regenecare® Gel appears effective in relieving EGFR inhibitors rash-associated pruritus and pain based on these preliminary analyses. Study is ongoing for further assessment.

**REFERENCES:**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