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

Patty Gowland RN, BSN, OCN, CCRC,
Joy Vlamakis RN, OCN, Julie Koch RN, BSN,
Ingalls Memorial Hospital , Cancer Research Center, Harvey, IL
Kimberly Lloyd, M.Sc. MPM Medical Inc., Irving, Tx.
J.B. Spalding, PhD, University of North Texas, Denton Tx.
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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.

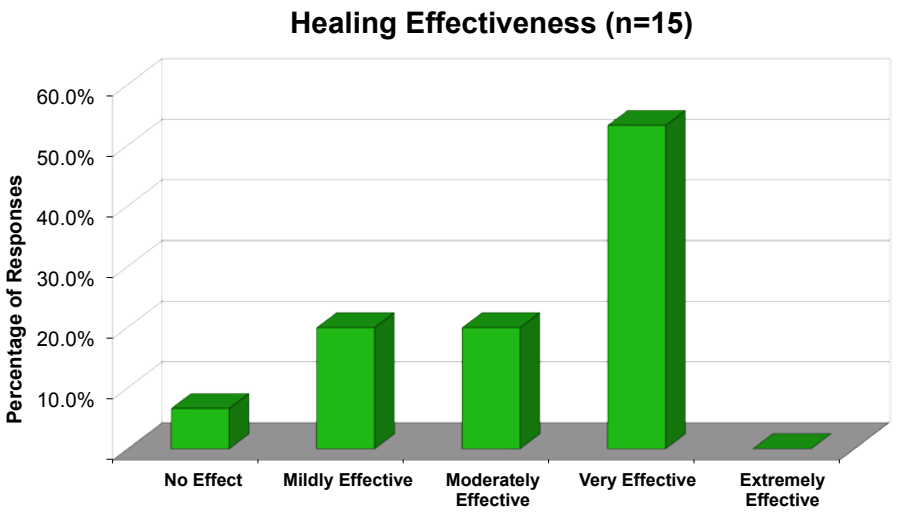
Ingalls Health System

Introduction

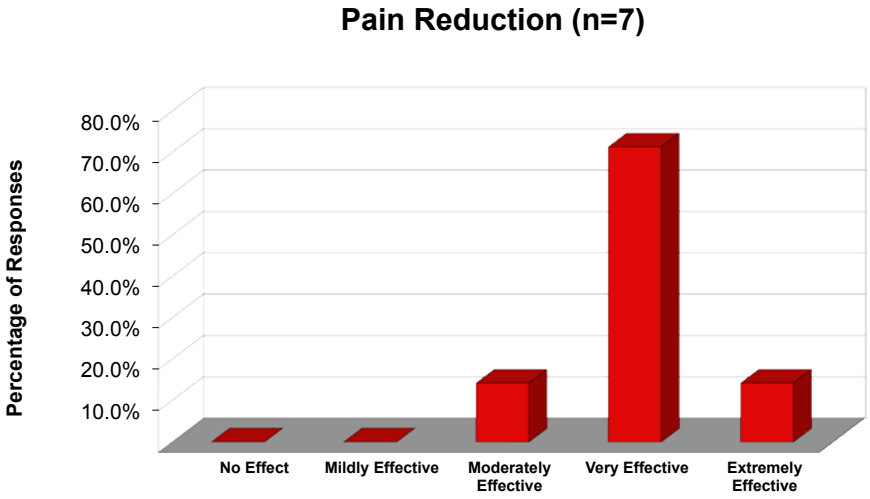
The clinical use of Epidermal Growth Factor Receptor (EGFR) inhibitor drugs are now commonly used to treat numerous malignancies including colon, lung, breast, and head and neck. EGFR inhibitor drugs target epidermal derived tissues including capillaries, sebaceous cells, hair shaft, and hair follicles 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: Healing



Regenecare® Gel Applied 4 x Daily to EGFR Rash for 4 Weeks Patients' Responses re: Pain Relief



Clinical Study

The trial was a single center, prospective pilot study. Twenty EGFR subjects were eligible for participation. Selection criteria included being over 18 years and having no concomitant skin disorders. Patients likely to comply and be available for follow-up, signed informed consent and were enrolled. Patients were instructed to apply Regenecare, the topical gel, 4x daily to rash beginning at the initial appearance of rash.

Regenecare wound gel (MPM Medical Inc., Irving, TX) is an FDA prescription Medical Device approved for the management of pressure ulcers, superficial wounds and scrapes, and 1st and 2nd degree burns. It contains 2% lidocaine-HCl in a base of aloe vera extract (medium molecular weight polysaccharides), marine collagen and other moisturizers. Collagen is a natural humectant and plays a role in wound healing.[6,7] Aloe vera has shown effectiveness in stimulating fibroblast formation, wound healing and as an anti-inflammatory.[8,9,10]

Before applying Regenecare gel, patients were instructed to gently wash rash area with soap and water or to apply immediately after bath or shower. Patients were instructed to apply gel generously in a circular motion covering affected areas.

Clinical nurses assessed patients weekly for rash severity using the NCI CTCAE Version 3 and took digital pictures. Patients provided quality of life questionnaires to evaluate gel effectiveness towards: reducing itching, reducing pain, reducing appearance of rash, moisturizing, healing and soothing the skin. Subjects graded Regenecare® topical gel as extremely effective, very effective, moderately effective, mildly effective or no effect for each rash symptom. Ordinal data was statistically evaluated as percentage outcome and reported.

Results

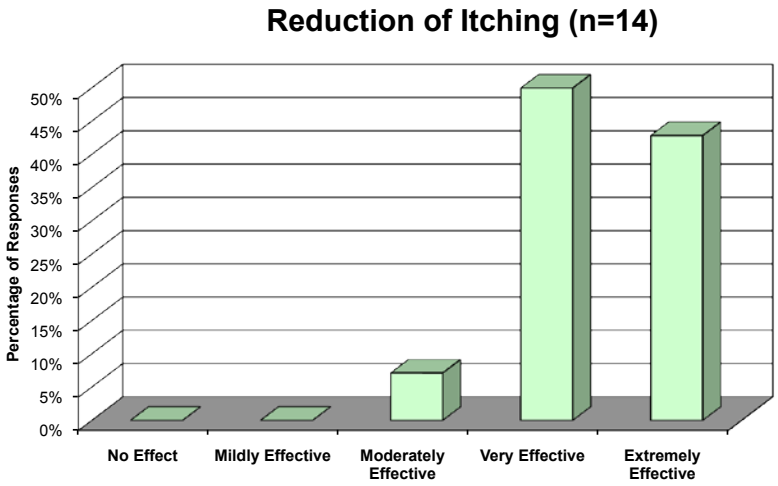
Table 1 shows the outcome of responses for each category for the overall 4 week evaluation criteria. Three study patients experienced grade 3 or worse rash symptoms and were eliminated from study due to use of other intervention

therapies. One study subject was transferred to hospital during treatment therapy. Each graph shows outcome of patient evaluation results and response to question "Would you recommend this product to others?" Table 2 shows several patient response comments. All patients indicated relief within 30 minutes of application with the majority (60%) experiencing symptom relief of pain and itching within 15 minutes after application.

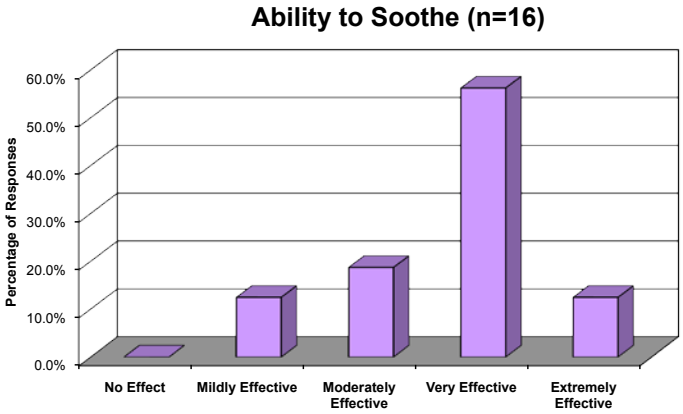
Discussion

Current practice considerations have indicated that topical steroids should not be considered as maintenance medications, due to their long term side effects.[5] EGFR inhibitors rash is not bacterial acne in origin and therefore antibiotics are not usually indicated in Grade 1 and 2 rash unless scratching the areas produces secondary infection.

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



Regenecare® Gel Applied 4 x Daily to EGFR Rash for 4 Weeks Patients' Responses re: Ability to Soothe

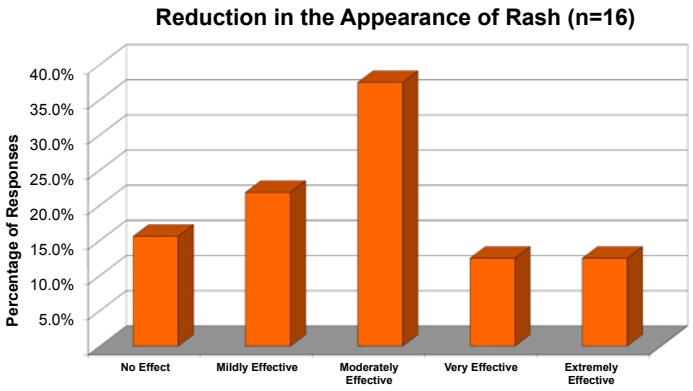


Patients need more than temporary moisturizers for EGFR rash symptoms. Lotions used to treat dry skin have not been clinically investigated for reducing EGFR rash symptoms or for safety. Because Regenecare contains ingredients that act as buffering agents when topically applied to open wounds or abraded skin, it appears to prevent pain or sting which is often associated with the use of pharmaceutical 2-4% lidocaine jelly.[12] 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).[13]

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."[5]

EGFR inhibitors function as monoclonal antibodies to block the growth

Regenecare® Gel Applied 4 x Daily to EGFR Rash for 4 Weeks Patients' Responses re: Reduced Appearance of Rash



Statistical Evaluation of Results Overall Rating of Topical Gel (at 4 weeks) – TABLE 1

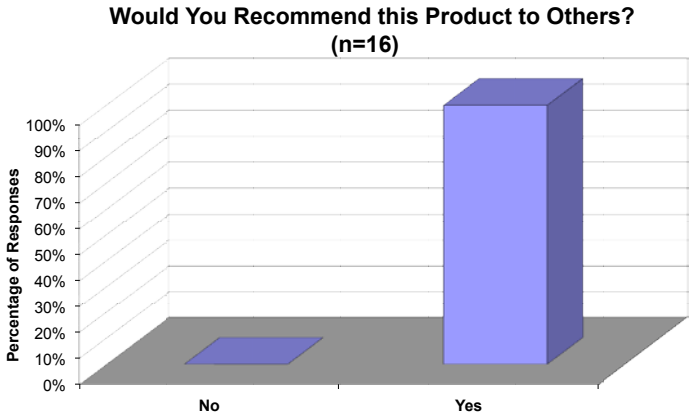
	Appearance	Reduce Itching	Reduce Pain	Moisturizing	Healing	Sooth Skin
No Effect	15.63%	0.00%	0.00%	37.50%	6.67%	0.00%
Mildly Effective	21.87%	0.00%	0.00%	18.75%	20.00%	12.50%
Moderately Effective	37.50%	7.14%	14.29%	6.25%	20.00%	18.75%
Very Effective	12.50%	50.00%	71.42%	37.50%	53.33%	56.25%
Extremely Effective	12.50%	42.86%	14.29%	0.00%	0.00%	12.50%
	100%	100%	100%	100%	100%	100%

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

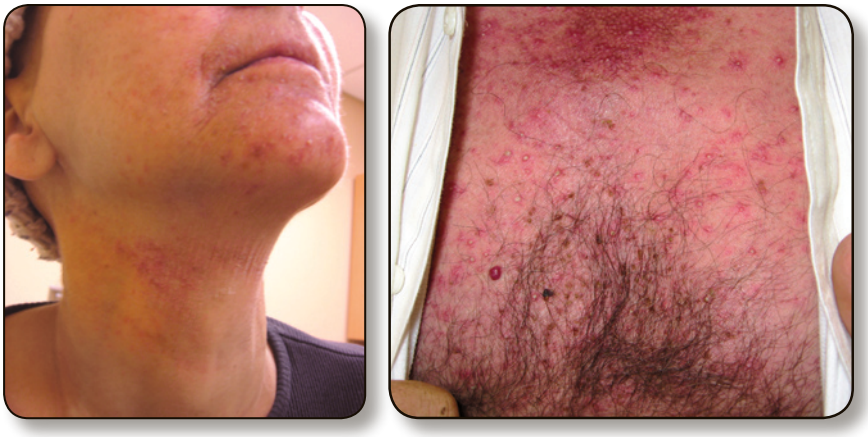
The pilot study trial showed that 100% of patients reported effectiveness of Regenecare® in reducing itching and pain. Patients' total response was 92.9% (cumulative "very" and "extremely" effective) for relieving itching. Patients' total response was 85.7% (cumulative "very" and "extremely" effective) 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.

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



Why would you recommend this product to others for skin rash?	CTC Rash Grade (Rash Eruption Areas)
"It provides relief."	Grade 1 Cetuximab subject. (Face, upper chest, scalp)
"It worked well for me."	Grade 2 Erlotinab subject. (Face, upper chest)
"It helped."	Grade 2 Erlotinab subject. (Face, upper chest, back, arms, legs, fingers)
"It relieved the redness."	Grade 2 Erlotinab subject. (Face, upper chest, back, arms, legs)

Erbitux® Study Patients Rate Regenecare® Gel "*Extremely Effective* for Reducing Pain and Itching and *Very Effective* for Skin Healing"



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