AARS HOT TOPICS MEMBER NEWSLETTER

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Industry News

Sebacia announces financing to advance acne treatment. July 25, 2017. Healio Dermatology News. https://www.healio.com/dermatology/acne/news/online/%7B3714b778-58e2-41e2-8ab0-bffee9111475%7D/sebacia-announces-financing-to-advance-acne-treatment

Sebacia announced that the company has completed a $20 million Series D financing and closed a $16 million debt facility with Hercules Capital to continue the development of a proprietary microparticle treatment for moderate-to-severe acne. The privately held, clinical and commercial stage dermatology and aesthetics company intends to use the proceeds from the financing to complete a U.S. pivotal trial of the treatment with expected results by mid-2018, and submission and FDA response expected by the end of 2018, according to a news release. Sebacia reported that it also intends to expand its commercial presence in the European Union, where the treatment has been CE Marked, according to the release. The microparticles are made of gold and silica and are delivered in a topical suspension specifically designed to work with hair removal or pigmented lesion treatment laser systems already owned by a dermatologist. The treatment is intended to be a physician-guided, in-office procedure that could provide an alternative to existing therapies, such as oral antibiotics and isotretinoin. The microparticles are specially designed to be activated by the light from the lasers and are placed in a suspension designed to penetrate the sebaceous follicles. When exposed to a laser pulse, they create a focused photothermal effect in the sebaceous gland and follicle to reduce the activity level of the gland and acne-causing inflammatory lesions, according to the release. The financing was led by existing investors Versant Ventures, Domain Associates, Accuitive Medical Ventures and Partners Healthcare Innovation Fund, while new investors, including Salem Partners, accounted for approximately 60% of the round, according to the release. Reference: www.sebacia.com

Sol-Gel announces positive results for combination therapy for acne. July 25, 2017. Healio Dermatology News. https://www.healio.com/dermatology/acne/news/online/%7B3714b778-58e2-41e2-8ab0-bffee9111475%7D/sebacia-announces-financing-to-advance-acne-treatment

Sol-Gel Technologies Ltd. has announced positive results from its phase 2 clinical trial of its topical drug candidate TWIN for treating acne vulgaris. TWIN is a once-daily cream containing a fixed-dose combination of tretinoin and benzoyl peroxide, separately encapsulated in a silica-based proprietary drug delivery technology, according to a news release. There were 726 patients aged 9 years and older with facial acne vulgaris enrolled at 36 sites in the U.S. for the six-arm, double-blind, placebo-controlled trial that evaluated efficacy, tolerability and safety of two concentrations of TWIN, which contained a higher or lower concentration of tretinoin and an identical concentration of benzoyl peroxide, to vehicle. Inclusion criteria included 20 to 50 inflammatory lesions, 25 to 100 non-inflammatory lesions and an investigator's global assessment score of 3 or 4 ("moderate" or "severe") on a five-point scale that ranges from a score of zero, representing "clear" skin, to a score of four, representing "severe" disease. Patients were randomized into six separate treatment cohorts and instructed to apply the investigational drug once daily before bedtime for 12 weeks, according to the release. The study also evaluated the separate active components of TWIN; both the higher and lower concentrations of encapsulated tretinoin and encapsulated benzoyl peroxide administered as a single agent. There were statistically significant improvements in all pre-defined co-primary and secondary efficacy endpoints for TWIN, as compared to vehicle. TWIN also exhibited favorable efficacy results compared to its active components, according to the release. There were no treatment-related serious adverse events with TWIN. Four patients treated with TWIN High and two patients treated with TWIN Low discontinued due to related adverse events, which were primarily mild or moderate in severity, according to the

release. "Acne is a multifactorial disorder and is better treated with drugs affecting as many components as possible that contribute to its development," Guy Webster, MD, PhD, clinical professor of dermatology at Jefferson Medical College, Thomas Jefferson University, Philadelphia, and the medical monitor of the phase 2 study, stated in the release. "TWIN is pursuing this approach by designing a fixed-dose combination of tretinoin, which is a modulator of cellular differentiation, keratinization and inflammatory processes, and benzoyl peroxide, which is an oxidizing agent with bactericidal and keratolytic effects." Based on the study results and subject to an end of phase 2 meeting to be scheduled with the FDA, Sol-Gel plans to initiate a phase 3 program to measure the efficacy, tolerability and safety of TWIN for treating acne in adults and adolescents. Sol-Gel also plans to use results from the encapsulated tretinoin arms of the study to develop its single agent, encapsulated tretinoin drug product candidate, SIRS-T, as a first-line treatment for adult and adolescent patients with acne, according to the release. Reference: www.sol-gel.com

New Medical News

Psychiatric disorders, acne and systemic retinoids: comparison of risks. Le Moigne M, Bulteau S, Grall-Bronnec M, et al. Expert Opin Drug Saf. 2017 Jul 12:1-7. doi: 10.1080/14740338.2017.1344641. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/?term=28657366

BACKGROUND: The link between isotretinoin, treatment of a severe form of acne, and psychiatric disorders remains controversial, as acneitself could explain the occurrence of psychiatric disorders. This study aims at assessing the disproportionality of psychiatric adverse events reported with isotretinoin in the French National PharmacoVigilance Database, compared with other systemic acne treatments and systemic retinoids. MATERIALS AND METHODS: Data were extracted from the French National Pharmaco Vigilance Database for systemic acne treatments, systemic retinoids and drugs used as comparators. Each report was subjected to double-blind analysis by two psychiatric experts. A disproportionality analysis was performed, calculating the number of psychiatric ADRs divided by the total number of notifications for each drug of interest. RESULTS: Concerning acne systemic treatments: all 71 reports of severe psychiatric disorders involved isotretinoin, the highest proportion of mild/moderate psychiatric adverse events was reported with isotretinoin (14.1%). Among systemic retinoids, the highest proportion of severe and mild/moderate psychiatric events occurred with isotretinoin and alitretinoin. CONCLUSION: Our study raises the hypothesis that psychiatric disorders associated with isotretinoin are related to a class effect of retinoids, as a signal emerges for alitretinoin. Complementary studies are necessary to estimate the risk and further determine at-risk populations.

Combination of benzoyl peroxide 5% gel with liquid cleanser and moisturizer SPF 30 in acne treatment results in high levels of subject satisfaction, good adherence and favorable tolerability. Kim MR, Kerrouche N. J Dermatolog Treat. 2017 Jul 5:1-6. doi: 10.1080/09546634.2017.1342758. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/?term=28678647

BACKGROUND: Skin care products (cleansers and moisturizers) to complement benzoyl peroxide (BPO) in the treatment of acne may improve treatment tolerability and adherence. OBJECTIVE: Evaluate subject satisfaction after use of BPO 5% gel in combination with liquid cleanser and moisturizer SPF 30. METHODS: Open-label study including subjects aged ≥12 years with mild-to-moderate facial acne; ClinicalTrials.gov Identifier: NCT02589405. Once daily BPO 5% gel, twice daily liquid cleanser and once daily moisturizer SPF 30 were applied for 12 weeks.

Assessments included a subject satisfaction questionnaire, investigator global assessment of improvement, lesion counts, the presence of Propionibacterium acnes, and safety. RESULTS: Fifty subjects were enrolled. Most subjects were overall satisfied with the three-part regimen (87%) and felt better about themselves (94%). Subjects indicated the skin care products helped prepare the skin for treatment (85%), relieve itchy skin (81%) and reduce irritation (87%). Most subjects considered that the liquid cleanser (80%) and moisturizer SPF 30 (84%) were a necessary part of acne treatment. BPO reduced P. acnes load by 89% at week 1. The treatment was well tolerated.

CONCLUSIONS: The combination of BPO 5% gel with liquid cleanser and moisturizer SPF 30 resulted in high levels of subject satisfaction, good tolerability and treatment adherence.

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Hidradenitis suppurativa is characterized by dysregulation of the Th17:Treg cell axis, which is corrected by anti-TNF therapy. Moran B, Sweeney CM, Hughes R, et al. J Invest Dermatol. 2017 Jun 23. pii: S0022-202X(17)31666-4. doi: 10.1016/j.jid.2017.05.033. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/28652108

Hidradenitis suppurativa (HS) is a chronic, inflammatory and debilitating disease of hair follicles with 1-4% prevalence and high morbidity. There is a dearth of information on the pathogenesis and immune dysregulation underlying HS therefore we carried out a detailed analysis of skin infiltrating T cells. Cells isolated from skin biopsies and blood from HS patients and healthy controls were analysed by 16-parameter flow cytometry to provide detailed profiles of CD4 T cell subsets. We observed substantial infiltration of inflammatory T cells with a striking Th17-skewed cytokine profile in HS skin, these cells expressed the Th17 lineage marker CD161 and IL-17, as well as other pro-inflammatory cytokines GM-CSF, IL-22, IFN-γ, and TNF. Regulatory T (Treg) cells were also enriched in HS lesional skin, however the ratio of Th17:Treg cells was nonetheless highly dysregulated in favour of Th17 cells. In contrast, lesional skin from anti-TNF treated HS patients who showed substantial clinical improvement, exhibited a significant reduction in the frequency of Th17 cells and normalisation of the Th17:Treg cell ratio. These data suggest that inhibition of pathogenic IL-17 via TNF blockade is associated with improvement in the immune dysregulation in HS and may provide a rationale for targeting IL-17 in the disease. PMID: 28652108 DOI: 10.1016/j.jid.2017.05.033

The Efficacy and Safety of Azelaic Acid 15% Foam in the Treatment of Truncal Acne Vulgaris.

Hoffman LK, Del Rosso JQ, Kircik LH. J Drugs Dermatol. 2017 Jun 1;16(6):534-538. https://www.ncbi.nlm.nih.gov/pubmed/?term=28686770

INTRODUCTION: Truncal acne is often associated with facial acne, but there are fewer options for an effective topical treatment on the trunk. Given the advent of foam formulations with enhanced percutaneous absorption and convenient application due to easy spreadability on skin, the previously held idea that effective treatment of truncal acne requires oral treatment is challenged. Azelaic acid cream has been previously approved for acne vulgaris, thus azelaic acid foam may be a viable treatment option for truncal acne. STUDY DESIGN: A single-center, open label pilot study was conducted to investigate the efficacy and safety of azelaic acid 15% foam as a treatment modality for moderate truncal acne. Use for facial acne was also allowed and monitored during the study. RESULTS: Twice-daily application of azelaic acid 15% foam to affected areas resulted in a 1-grade reduction in truncal investigator global assessment (IGA) scores in nearly all patients (16/18). Eight out of 18 patients (44%) were rated as Clear or Almost Clear in the trunk by the end of the study. There were also improvements in facial IGA scores; 9 of 18

patients (50%) exhibited a 1-grade improvement in IGA scores and 11 of 18 were Clear or Almost Clear by the end of the study. A significant reduction in lesion counts was found throughout the study and the medication was well tolerated. CONCUSION: Azelaic acid 15% foam was effective in treating moderate truncal acne and facial acne in this pilot study. Given the efficacy and convenience of the foam vehicle, azelaic acid may be considered as a viable option for treatment of acne vulgaris, including on the trunk. Further studies are suggested in a larger population of patients, including adult females with acne.

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A Randomized Controlled Study of a Novel Botanical Acne Spot Treatment. Barak-Shinar D, Draelos ZD. J Drugs Dermatol. 2017 Jun 1;16(6):599-603. https://www.ncbi.nlm.nih.gov/pubmed/?term=28686778

OBJECTIVE: The study evaluated the tolerability and efficacy of a new presented treatment for acne. The product is an OTC topical gel consisting of 2% SA, which is also enriched in botanicals that have been shown to have anti-inflammatory properties. DESIGN: The study was designed as a single-site, randomized, investigator-blinded, split-face 10-day study. SETTING: Subjects enrolled with a minimum of 2 inflammatory papular acne lesions and 2 non-inflammatory open or closed comedones on both sides of the face in symmetrical locations, to the greatest degree possible. One side of each subject's face was randomly selected to receive the study treatment product. PARTICIPANTS: 25 subjects, 15 female and 10 males, ages 12 to 43 years, suffering from mild to moderate acne. Measurements: Study duration was 10 days, with study visits occurring at baseline (day 0), day 1, day 2, day 3, day 7, and day 10. Subjects underwent investigator facial evaluation and lesion assessment by dermatologist at each of the visit days. For the inflammatory lesions, the assessed parameters were erythema, elevation, induration, and overall impression. The assessed non-inflammatory parameters were elevation and overall impression. Results: The observed difference between the treatment and the control group increased between day 1 and day 2 and reached an average of 15% to 20% with small varieties between the parameters and stayed similar across the remaining visits. Statistically significance (P less than 0.005) was achieved for all inflammatory and non-inflammatory tested parameters. Conclusion: This study was performed to determine the safety, efficacy, and ease of use of a botanical acne treatment gel in providing a reduction in inflammatory acne lesion erythema, elevation, and induration. Erythema and elevation were the most influential parameters in inflammatory lesion with improvement noted after 2 days of application.

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Treatment Response With Once-Daily Topical Dapsone Gel, 7.5% for Acne Vulgaris: Subgroup Analysis of Pooled Data from Two Randomized, Double-Blind Study. Draelos ZD, Rodriguez DA, Kempers SE, et al. J Drugs Dermatol. 2017 Jun 1;16(6):591-598. https://www.ncbi.nlm.nih.gov/pubmed/?term=28686777

BACKGROUND: Acne vulgaris has varying physical and psychological effects in men and women of different ages, races, and ethnicities. OBJECTIVE: This analysis assessed the relationship of age, sex, and race to treatment response with once-daily topical dapsone gel, 7.5%. METHODS: We conducted a pooled subgroup analysis of 2 randomized, double-blind, vehicle-controlled clinical trials conducted in the US and Canada. The studies included patients with 20 to 50 inflammatory and 30 to 100 noninflammatory facial lesions, and a Global Acne Assessment Score (GAAS) of 3 (moderate). Pooled data (N=4340) were analyzed by age (12-17 and ≥18 years), sex, and race (Caucasian and non-Caucasian) for GAAS success (score of 0 [none] or 1 [minimal]) and mean percent change from baseline in inflammatory, noninflammatory, and total lesion counts. The impact of age and sex on treatment

response was examined using multivariate analysis. Adverse events were analyzed by subgroups. RESULTS: Treatment responses with dapsone gel, 7.5% were greater overall and for all subgroups versus vehicle. GAAS success rates and mean decrease in all lesion counts with dapsone gel, 7.5% were greater in older (aged ≥18 years) versus younger patients, and for females versus males. Treatment response with dapsone gel, 7.5% in racial subgroups was similar. Multivariate analysis showed statistical significance for age group and sex as predictors of GAAS success (P less than equal to .005) and reduction in lesion counts (P less than equal to .025). Adverse events were similar across subgroups. CONCLUSIONS: Older age (≥18 years) and female sex were predictors of treatment response. These subgroups tended to have greater acne improvement in subgroup comparisons. Caucasian and non-Caucasian patients had similar responses. The safety profile of dapsone gel, 7.5% was similar across subgroups.

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Clinical Reviews

Current Treatments or Acne: Medications, Lights, Lasers, and a Novel 650-MS 1064-NM ND: YAG Laser. Gold MH, Goldberg DJ, Nestor MS. J Cosmet Dermatol. 2017 Jul 13. doi: 10.1111/jocd.12367. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/28703382

The treatment of acne, especially severe acne, remains a challenge to dermatologists. Therapies include retinoids, antibiotics, hormones, lights, lasers, and various combinations of these modalities. Acne is currently considered a chronic rather than an adolescent condition. The appropriate treatment depends on the patient and the severity of disease. The purpose of this study was to review current therapies for acne of all severities and to introduce the 650-μs 1064-nm laser for the treatment of acne.

Swiss Practice Recommendations for the Management of Hidradenitis Suppurativa/Acne Inversa.

Hunger RE, Laffitte E, Läuchli S, et al. Dermatology. 2017 Jul 7. doi: 10.1159/000477459. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/?term=28683447

Hidradenitis suppurativa (HS) is a painful, inflammatory, debilitating skin disease with a chronic intermittent course. The central pathogenetic event seems to be the occlusion of the hair follicle. HS has a 1-year prevalence of about 1%. It typically presents after puberty with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body: most commonly the axillae, inguinal, and anogenital regions. HS has a high negative impact on patients' quality of life even in patients with only limited disease burden, and the diagnosis of HS is often made with a long diagnostic delay. In this practical short version we present diagnostic and therapeutic recommendations which are based on a systematic literature search as well as an informal expert consensus of Swiss dermatologists and dermatosurgeons.

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AGREE II assessments of recent acne treatment guidelines: how well do they reveal trustworthiness as defined by the Institute of Medicine (IOM) criteria? Eady EA, Layton AM, Sprakel J, et al. Br J Dermatol. 2017 Jul 1. doi: 10.1111/bjd.15777. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/?term=28667760

BACKGROUND: Up-to-date, trustworthy guidelines are a widely relied-upon means of promoting excellent patient care. OBJECTIVES: To determine the quality of recently published acne treatment guidelines by utilizing the Appraisal of Guidelines for Research and Evaluation (AGREE) II Reporting Checklist, the US Institute of Medicine's (IOM) criteria of trustworthiness, Lenzer et al's red flags and CheckUp. METHODS: Systematic searches were conducted in bibliographic databases, guideline depositories and using Google™ to identify acne treatment guidelines published since 2013. Six assessors independently scored each guideline using the AGREE II Reporting Checklist. Guidelines were concomitantly assessed for trustworthiness using the IOM criteria and for Lenzer et al's red flags indicative of potential bias. Updates were screened using CheckUp. RESULTS: Eight guidelines were identified, two of which were updates. Lowest scoring AGREE II domains across all guidelines were rigour (6/8 poor, one fair, one average) and applicability (4/8 poor, one fair, three average). Two out of the three highest scoring guidelines were developed using AGREE II. No guideline fully met each IOM criterion and all raised at least one red flag indicative of potential bias. One updated guideline did not address seven of 16 items on CheckUp and the other did not address four. Patient involvement in guideline development was minimal. CONCLUSIONS: Use of the AGREE II Instrument during guideline development did not have as great an effect on guideline quality as might be expected. There is considerable room for improvement in acne treatment guidelines in order to satisfy the IOM trustworthiness criteria and avoid bias.

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Trends in prescribing behavior of systemic agents used in the treatment of acne among dermatologists and nondermatologists: A retrospective analysis, 2004-2013. Barbieri JS, James WD, Margolis DJ. J Am Acad Dermatol. 2017 Jul 1. pii: S0190-9622(17)30503-0. doi: 10.1016/j.jaad.2017.04.016. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/28676330

BACKGROUND: Despite recommendations to limit the use of oral antibiotics and increasing support for hormonal agents in the treatment of acne, it is unclear whether there have been any significant changes in practice patterns.

OBJECTIVE: To characterize changes in prescribing behavior for systemic agents in the treatment of acne in the United States between 2004 and 2013. METHODS: We conducted a retrospective analysis using the OptumInsight Clinformatics DataMart (Optum, Eden Prairie, MN). RESULTS: The number of courses of spironolactone prescribed per 100 female patients being managed for acne by dermatologists and nondermatologists increased from 2.08 to 8.13 and from 1.43 to 4.09, respectively. The median duration of therapy with oral antibiotics was 126 and 129 days among patients managed by dermatologists and nondermatologists, respectively, and did not change significantly over the study period. LIMITATIONS: The OptumInsight Clinformatics DataMart lacks information on acne severity and clinical outcomes. CONCLUSIONS: Additional work to identify patients who would benefit most from alternative therapies such as spironolactone, oral contraceptives, or isotretinoin represents a potential opportunity to improve the care of patients with acne.

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Isotretinoin Monitoring Trends: A National Survey of Dermatologists. Hobson JG, Cunningham MJ, Lesiak K, et al. J Drugs Dermatol. 2017 Jun 1;16(6):557-564. https://www.ncbi.nlm.nih.gov/pubmed/28652108

BACKGROUND: Isotretinoin is an effective treatment for nodulocystic acne. Outside of required pregnancy testing, laboratory monitoring suggested by the manufacturers is vague. Dermatologists, therefore, monitor a variety of tests with variable frequency. Despite intense monitoring, the majority of patients do not have gross laboratory

abnormalities that warrant changes in management. OBJECTIVE: To survey US dermatologists regarding laboratory monitoring practices while prescribing isotretinoin. METHODS: An online survey sent via e-mail to members of the American Academy of Dermatology. RESULTS: 12,396 surveys were sent with a response rate of ~19%. At baseline >60% of responders check a CBC, LFTs, and a lipid panel. 74% check a monthly lipid panel and LFTs, while 57% check a monthly CBC. 75% report stopping isotretinoin when AST or ALT values reach 3 times normal; 89% report stopping at 4 times normal. When triglycerides reach 4 times normal, 72% stop the medication. CONCLUSIONS: There is no consensus on isotretinoin monitoring tests and frequency, though the majority of dermatologists surveyed monitor a lipid panel and LFTs.

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Patient Counseling/Communication

Debunking Acne Myths: Is Itching a Symptom of Acne? Publish date: July 5, 2017. Cutis. http://www.mdedge.com/cutis/article/141860/acne/debunking-acne-myths-itching-symptom-acne?channel=171

Myth: Itching is not a symptom of acne. Acne vulgaris typically is not considered to be a pruritic disease; however, many patients experience itching, which leads them to scratch their acne lesions, causing secondary bacterial infections and subsequent scarring, hypopigmentation, or hyperpigmentation of the involved skin. Although itching rarely is mentioned as a clinical feature of acne, pruritus can be an important contributory factor to the burden of disability and impaired quality of life in acne patients of all ages, and acne itching may be an important target for therapy. In a descriptive study of 120 consecutive acne patients in Singapore, itch was found to be a common (70% of patients) and debilitating symptom of acne. The majority of patients (83%) reported itch at noon with severity that was comparable to a mosquito bite, and the most common physical descriptor was tickling (68%). Common aggravating factors included sweat (71%), heat (62%), and stress (31%). Fifty-five percent of patients said itching had a negative impact on their mood, and 52% reported that they had scratched or rubbed the affected area. A study of 108 adolescents with acne limited to the face yielded half who reported itching within acne lesions. The presence of itching was unrelated to age, gender, where they lived, positive family history, or acne severity. In most patients, pruritus appeared relatively infrequently and for a short period of time: 7.4% reported itching every day, 24.1% on a weekly basis, 29.6% at least once a month, and 37.7% even less frequently. Itch episodes lasted less than 1 minute in most participants. However, 31.5% of participants sought medical treatment to reduce itching. The most important factors aggravating the intensity of itching were sweat, stress, physical effort, heat, fatigue, and dry air, respectively. Regarding the impact of acne itching on quality of life, 29.6% of participants felt depressed and 1.8% were anxious because of their itching. Some participants also noted that itching caused difficulties in falling asleep and awakening from itching. The pathogenesis of localized itching in acne could be connected with the change in pH of the microenvironment of the acne follicle, providing an optimal environment for the production of histamine or histaminelike products by Propionibacterium acnes. Pruritus also may be a complication of certain acne therapies. Increased awareness among patients of this potential side effect may be helpful in preventing the unnecessary discontinuation of an otherwise effective acne therapy. Understanding factors that may aggravate itching in acne lesions also may be helpful to patients. References: Lim YL, Chan YH, Yosipovitch G, et al. Pruritus is a common and significant symptom of acne [published online July 8, 2008]. J Eur Acad Dermatol Venereol. 2008;22:1332-1336. Reich A, Trybucka K, Tracinska A, et al. Acne itch: do acne patients suffer from itching? Acta Derm Venereol. 2008;88:38-42.