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Industry News

Sienna Biopharmaceuticals announces financing for dermatologic therapies. April 26, 2017. Healio Dermatology News. <http://www.healio.com/dermatology/psoriasis/news/online/%7B6a6e3866-7717-4941-a4ff-318045b602b7%7D/sienna-biopharmaceuticals-announces-financing-for-dermatologic-therapies>

Sienna Biopharmaceuticals announced it has completed a \$40 million, Series B financing to advance its diversified topical biotech pipeline. The clinical stage medical dermatology and aesthetics company is developing lead assets including SNA-120 for pruritus and psoriasis, and SNA-125 for atopic dermatitis, psoriasis and pruritus, and through a photoparticle therapy platform, SNA-001 for treating acne vulgaris and permanent reduction of unwanted light-pigmented hair, according to a news release. "We believe this financing will enable us to advance our development programs, which span pivotal clinical trials to preclinical programs," Frederick C. Beddingfield III, MD, PhD, president and CEO of Sienna, stated in the release. The financing was led by existing investors ARCH Venture Partners and Venvest Capital and additional investors including Partner Fund Management, Altitude Life Science Ventures and David Pyott, MBA. New investors, accounting for approximately half of the investments, included Fidelity Management and Research Company, certain investments funds advised by Clough Capital Partners L.P., and Omega Fund Management, according to the release.

Increased alcohol consumption linked to higher risk of rosacea in women. April 20, 2017. News-Medical.net. <http://www.news-medical.net/news/20170420/Increased-alcohol-consumption-linked-to-higher-risk-of-rosacea-in-women.aspx>

According to new research published online today in the Journal of the American Academy of Dermatology, increased consumption of alcohol, particularly white wine and liquor, is associated with a higher risk of rosacea in women. "Drinking alcohol has a number of effects on your body that can impact your skin," says board-certified dermatologist and study author Abrar A. Qureshi, MD, MPH, FAAD, chair of the department of dermatology at Brown University in Providence, R.I. "While alcohol has been linked to a variety of skin disorders, including psoriasis and acne, our research suggests that it's also associated with the development of rosacea in women." Rosacea, a skin disease that causes redness and flushing on the face and neck, affects approximately 16 million Americans. To examine this condition's connection to alcohol consumption, the study authors reviewed data collected from 82,737 women via the Nurses' Health Study II. Over the 14-year period from 1991 to 2005, there were 4,945 cases of rosacea in the study population. The research, led by Wen-Qing Li, an assistant professor of dermatology at Brown University, found that women who drank alcohol had an elevated risk of developing rosacea, and that risk increased as their alcohol consumption increased. In examining the risk associated with specific types of alcohol, the researchers found that white wine and liquor were significantly associated with a higher rosacea risk. Although more research is necessary to determine why alcohol consumption may increase the risk of rosacea, the authors believe that alcohol's weakening of the immune system and widening of the blood vessels could contribute to the redness and flushing that occur when one develops the condition. The authors say further research is also needed to shed more light on the connections between specific types of alcohol and rosacea. While red wine has been identified as a rosacea trigger for those who already have the disease, this study suggests it is not significantly associated with developing rosacea in the first place. The authors note that white wine and liquor contain high concentrations of alcohol without the flavonoids and other anti-inflammatory substances found in red wine. Despite its anti-inflammatory properties, however, red wine also contains other substances, like histamine and resveratrol, that may

contribute to flushing in patients who already have rosacea, the study says. "Our research contributes to the sizable body of evidence that demonstrates alcohol's harmful effects on the body, including the skin," Dr. Qureshi says. "Science has identified many factors that may potentially cause rosacea, and our study indicates that alcohol may be one of them." Source: <https://www.aad.org/media/news-releases/alcohol-and-rosacea-in-women>

Dermata, Villani to develop natural sponge product to treat acne. April 13, 2017. Healio Dermatology News. <http://www.healio.com/dermatology/acne/news/online/%7B4f2701f6-f6a3-4728-9106-061eda7b009a%7D/dermata-villani-to-develop-natural-sponge-product-to-treat-acne>

Dermata Therapeutics and Villani announced they have entered into an exclusive global license agreement for Dermata to develop Villani's natural sponge product as a potential treatment for a variety of skin diseases, including acne. "I am very excited to begin working with the Dermata team to bring this potentially significant breakthrough to patients living with moderate to severe acne because I know firsthand how patients feel living with acne," Maria Villani, MD, CEO and founder of Villani, stated in a press release. "I look forward to collaborating with the Dermata team to further advance development of my sponge product, hopefully bringing the first natural prescription drug product to market for moderate to severe acne sufferers. Villani's patented sponge-based product will be exclusively developed and commercialized by Dermata, initially for treating moderate-to-severe acne. Villani will receive milestone and royalty payments under terms of the agreement, according to the release. "After many years of research, Dr. Villani has developed a product to harness the therapeutic effects of a natural sponge product that has the potential to address the needs of patients with moderate to severe acne," Gerald Proehl, President and CEO of Dermata, stated in the release. "We believe that developing a natural alternative to currently available prescription products will represent a major advancement in the treatment of acne." The sponge product was discovered by Villani who located a fresh water sponge with a specific variant with a unique chemical structure, according to the release. Reference: www.dermatarx.com, www.villaniskin.com.

New Medical News

Randomized, controlled trial split-faced study of 595-nm pulsed dye laser in the treatment of acne vulgaris and acne erythema in adolescents and early adulthood. Lekwuttikarn R, Tempark T, Chatproedprai S, Wanankul S. *Int J Dermatol.* 2017 Apr 26. doi: 10.1111/ijd.13631. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/28447362>

The high prevalence of acne vulgaris in teenagers has increased comorbidities. Lasers offer alternative options for acne treatment because they have rapid action, low systemic adverse effects, and do not require everyday treatment. To study the efficacy and patients' satisfaction of 595-nm pulse dye laser (PDL) treatment of acne vulgaris and acne erythema in adolescents and early adulthood, we designed a blocked-randomized, split-faced 595-nm PDL (fluence 8 J/cm² pulse duration 10 ms, spot size 7 mm, 2 session every 2 weeks) study in patients with mild to moderate acne by comparing the laser-treated and non-treated side. The acne lesion counts, acne erythema grading, and acne severity grading were evaluated at baseline and 2, 4, and 8 weeks. Thirty patients were recruited. The results showed no statistically significant difference except the papule count at week 4 which was -1.828 on the treated side and 0.103 on the non-treated side of the face, P-value 0.0018. There was no statistically significant difference of acne severity grading and acne erythema grading between both sides of the face. The mean scores of patients' satisfaction on the laser-treated side were 75, 81, and 81%, respectively. The

PDL treatment in this study reveals no significant improvement in acne therapy; however, the patients were satisfied with this laser treatment.

International inter-rater agreement in scoring acne severity utilizing cloud-based image sharing of mobile phone photographs. Foolad N, Ornelas JN, Clark AK, Ali I, et al. *Int J Dermatol.* 2017 Apr 24. doi: 10.1111/ijd.13621. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/28436531>

BACKGROUND: Cloud-based image sharing technology allows facilitated sharing of images. Cloud-based image sharing technology has not been well-studied for acne assessments or treatment preferences, among international evaluators. We evaluated inter-rater variability of acne grading and treatment recommendations among an international group of dermatologists that assessed photographs. **METHODS:** This is a prospective, single visit photographic study to assess inter-rater agreement of acne photographs shared through an integrated mobile device, cloud-based, and HIPAA-compliant platform. Inter-rater agreements for global acne assessment and acne lesion counts were evaluated by the Kendall's coefficient of concordance while correlations between treatment recommendations and acne severity were calculated by Spearman's rank correlation coefficient. **RESULTS:** There was good agreement for the evaluation of inflammatory lesions (KCC = 0.62, $P < 0.0001$), noninflammatory lesions (KCC = 0.62, $P < 0.0001$), and the global acne grading system score (KCC = 0.69, $P < 0.0001$). Topical retinoid, oral antibiotic, and isotretinoin treatment preferences correlated with photographic based acne severity. **CONCLUSIONS:** Our study supports the use of mobile phone based photography and cloud-based image sharing for acne assessment. Cloud-based sharing may facilitate acne care and research among international collaborators.

Efficacy of fractionated microneedle radiofrequency with and without adding subcision for the treatment of atrophic facial acne scars: A randomized split-face clinical study. Faghihi G, Poostiyan N, Asilian A, Abtahi-Naeini B, et al. *J Cosmet Dermatol.* 2017 Apr 22. doi: 10.1111/jocd.12346. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/28432727>

BACKGROUND: There is no gold standard treatment for facial acne scars, and overall, little literature exists about the combination therapy for treatment of acne scar. **AIMS:** The aim of this study was to evaluate the efficacy of fractionated microneedle radiofrequency (FMR) vs FMR combined with subcision for the treatment of atrophic acne scars. **PATIENTS/METHODS:** This was a randomized, split-face clinical study of 25 patients with II-IV Fitzpatrick skin types with moderate to severe facial atrophic acne scars. Initially, standard subcision by Nokor needle was performed on one side. Two weeks after subcision, FMR treatment was performed on both cheeks of each participant. Second and third FMR treatment sessions were performed within 4-week intervals. Two-blinded dermatologists performed clinical assessments using a quartile grading scale, and patients were also asked to judge their satisfaction using a visual analog scale (VAS) scoring system. **RESULTS:** The age of the patients varied from 24 to 40 years (mean: 30.08 ± 4.94 years). Only nine patients (36%) were males. Clinical assessment by two-blinded dermatologists showed statistically significant improvement in the combination (FMR+subcision) group ($P=.009$). Patient satisfaction was statistically significantly better in the combination group ($P=.001$). A darkening of skin phototype was associated with a decrease in patient's satisfaction VAS score ($P=.07$). **CONCLUSION:** The combination of subcision and FMR is a safe and effective modality for mixed type acne scars. Additional randomized clinical study with long-term follow-up is necessary for further evaluation of FMR in combination with other procedures. The full trial protocol can be accessed in: <http://www.irct.ir/searchresult.php?keyword=%20IRCT2016103130597N1&id=30597&number=1&field=a&prt=1&total=1&m=1>. The clinical trial registration number is IRCT2016103130597N1.

Alcohol intake and risk of rosacea in US women. Li S, Cho E, Drucker AM, et al. J Am Acad Dermatol. Article in Press. Published online: April 20, 2017. [http://www.jaad.org/article/S0190-9622\(17\)30292-X/abstract](http://www.jaad.org/article/S0190-9622(17)30292-X/abstract)

Background: The epidemiologic association between alcohol and rosacea is unclear and inconsistent based on the previous cross-sectional or case-control studies. Objective: We conducted a cohort study to determine the association between alcohol intake and the risk of rosacea in women. Methods: A total of 82,737 women were included from the Nurses' Health Study II (1991-2005). Information on alcohol intake was collected every 4 years during follow-up. Information on history of clinician-diagnosed rosacea and year of diagnosis was collected in 2005. Results: Over 14 years of follow-up, we identified 4945 cases of rosacea. Compared with never drinkers, increased alcohol intake was associated with a significantly increased risk of rosacea (Ptrend <.0001). The multivariate-adjusted hazard ratios (HRs) and confidence intervals (CIs) were 1.12 (95% CI 1.05-1.20) for alcohol intake of 1-4 g/day and 1.53 (1.26-1.84) for ≥30 g/day. The associations remained consistent across categories of smoking status. Further examination of types of alcoholic beverage consumed revealed that white wine (Ptrend <.0001) and liquor intake (Ptrend = .0006) were significantly associated with a higher risk of rosacea. Limitations: This was an epidemiologic study without examination into etiologic mechanisms. Conclusions: Alcohol intake was significantly associated with an increased risk of rosacea in women.

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A comparative study of Cutibacterium (Propionibacterium) acnes clones from acne patients and healthy controls. Lomholt HB, Scholz CFP, Brüggemann H, et al. Anaerobe. 2017 Apr 19;47:57-63. doi: 10.1016/j.anaerobe.2017.04.006. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/28434779>

BACKGROUND: Cutibacterium (Propionibacterium) acnes is assumed to play an important role in the pathogenesis of acne. OBJECTIVES: To examine if clones with distinct virulence properties are associated with acne. METHODS: Multiple C. acnes isolates from follicles and surface skin of patients with moderate to severe acne and healthy controls were characterized by multilocus sequence typing. To determine if CC18 isolates from acne patients differ from those of controls in the possession of virulence genes or lack of genes conducive to a harmonious coexistence the full genomes of dominating CC18 follicular clones from six patients and five controls were sequenced. RESULTS: Individuals carried one to ten clones simultaneously. The dominating C. acnes clones in follicles from acne patients were exclusively from the phylogenetic clade I-1a and all belonged to clonal complex CC18 with the exception of one patient dominated by the worldwide-disseminated and often antibiotic resistant clone ST3. The clonal composition of healthy follicles showed a more heterogeneous pattern with follicles dominated by clones representing the phylogenetic clades I-1a, I-1b, I-2 and II. Comparison of follicular CC18 gene contents, allelic versions of putative virulence genes and their promoter regions, and 54 variable-length intragenic and inter-genic homopolymeric tracts showed extensive conservation and no difference associated with the clinical origin of isolates. CONCLUSIONS: The study supports that C. acnes strains from clonal complex CC18 and the often antibiotic resistant clone ST3 are associated with acne and suggests that susceptibility of the host rather than differences within these clones may determine the clinical outcome of colonization.

Propionibacterium Acnes Incubation in the Discs Can Result in Time-Dependent Modic Changes: A Long Term Rabbit Model. Shan Z, Zhang X, Li S, Yu T, Liu J, Zhao F. Spine (Phila Pa 1976). 2017 Apr 10. doi: 10.1097/BRS.0000000000002192. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/28399545>

STUDY DESIGN: A case control study of animal model of Modic changes (MCs) on Rabbits. **OBJECTIVE:** To evaluate the feasibility of inducing of MCs by injection of *Propionibacterium acne* (*P. acnes*) into the lumbar intervertebral discs of rabbits. **SUMMARY OF BACKGROUND DATA:** MCs have been widely observed, and assume to be closely associated with low back pain and *P. acnes*, but there are few animal models showing the progression of MCs. **METHODS:** Ten rabbits were used for the study. The L3-4 and L4-5 discs of all rabbits were injected with 100 μ L *P. acnes* (1.6 x 10CFU/mL) as *P. acnes* group, L2-3 disc were injected with 100 μ L normal saline as vehicle, and L5-6 disc was untreated (blank). MCs was investigated by magnetic resonance imaging (MRI) before operation and at 2 weeks, 1, 3, 4.5, 6 and 9 months postoperatively. Following sacrifice, histological analysis, blood test and micro-CT were performed. Cytokine expression in nucleus and endplate tissues was quantified using real-time polymerase chain reaction (RT-PCR). **RESULTS.:** From 3-months post-operatively, the *P. acnes* group showed significantly decreased T1-weighted signal intensity, while the T2-weighted signal was significantly higher at 3 and 4.5 months, and then decreased remarkably at 6 and 9 months. 11/20 inferior endplates were identified as type I MCs at 4.5-months, and 9/20 were identified as type II MCs at 9-months. RT-PCR showed that expression of IL-1 β , TNF- α , IFN- γ , MMP-9 and ADAMTS-5 in the NP, and IL-1 β , TNF- α and ADAMTS-5 in the endplates, were significantly up-regulated following injection of *P. acnes*. Histological slices of discs injected with *P. acnes* showed disc degeneration, endplate abnormalities and inflammatory response, with micro-CT confirming bone resorption. **CONCLUSION:** *P. acnes* incubation the disc can induce degeneration of the disc and an inflammatory response in the endplate region, presenting as MCs type I and II time-dependently.

Bacterial communities on facial skin of teenage and elderly Thai females. Somboonna N, Wilantho A, Srisuttiyakorn C, et al. Arch Microbiol. 2017 Apr 8. doi: 10.1007/s00203-017-1375-0. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/28391505>

The Human Microbiome Project was first established to understand the roles of human-associated microbes to human health and disease. This study presents preliminary findings of Thai female facial skin microbiome using three pooled samples from groups of skin microbiome profiles, namely (1) healthy and (2) acne-prone young adults (teenage.heal and teenage.acn) and (3) healthy elderly adults (elderly.heal) based on standard dermatological criteria. These samples were sequenced using 454-pyrosequencing targeting 16S rRNA (V3-V4 regions). Good's coverage index of greater than 92% shows sufficient sampling of our data for each group. Three unique OTUs for each microbiome profile (43, 258 and 59 for teenage.heal, teenage.acn and elderly.heal, respectively) were obtained with 134 shared OTUs among the three datasets. Based on Morisita-Horn similarity coefficient, age is the major factor that brings the community relationship factor closer. The comparison among the three datasets reveal majority of Gemmatimonadetes, Planctomycetes and Nitrospirae in the teenage.heal, whereas Firmicutes are more prevalent in teenage.acn and elderly.heal skin types. In addition, when comparing Thai facial microbial diversity with the 16S data from U.S. forehead female database, significant differences were found among orders of bacteria, pointing to possible differences in human ecto-flora.

Improvement of Atrophic Acne Scars in Skin of Color Using Topical Synthetic Epidermal Growth Factor (EGF) Serum: A Pilot Study. Stoddard MA, Herrmann J, Moy L, Moy R. J Drugs Dermatol. 2017 Apr 1;16(4):322-326. <https://www.ncbi.nlm.nih.gov/pubmed/28403265>

BACKGROUND: Atrophic scarring in skin of color is a common, permanent, and distressing result of uncontrolled acne vulgaris. Ablative lasers and chemical peels are frequently used to improve the appearance of atrophic scars, primarily through the stimulation of collagen and elastin; however, these treatment modalities are associated with

risks, such as dyspigmentation and hypertrophic scarring, especially in patients with darker skin. **OBJECTIVE:** We evaluated the efficacy of topically applied synthetic epidermal growth factor (EGF) serum in reducing the appearance of atrophic acne scars in skin of color. **METHODS:** A single-center clinical trial was performed on twelve healthy men and women (average age 32.5) with Fitzpatrick Type IV-V skin and evidence of facial grade II-IV atrophic acne scars. Subjects applied topical EGF serum to the full-face twice daily for 12 weeks. Scar improvement was investigated at each visit using an Investigator Global Assessment (IGA), a Goodman grade, clinical photography, and patient self-assessment. **RESULTS:** Eleven subjects completed the trial. Compared to baseline, there was an improvement in mean IGA score from 3.36 (SEM = 0.15) to 2.18 (SEM = 0.33). Mean Goodman grade was reduced from 2.73 (SEM = 0.19) to 2.55 (SEM = 0.21). Of the eleven pairs of before and after photographs, nine were correctly chosen as the post-treatment image by a blind investigator. On self-assessment, 81% reported a "good" to "excellent" improvement in their scars compared to baseline (P = 0.004). **CONCLUSION:** Topical EGF may improve the appearance of atrophic acne scars in skin of color. Additional, larger studies should be conducted to better characterize improvement.

Dose dependent treatment with isotretinoin induces more changes in the ileum than in the duodenum and jejunum in Wistar rats. Thomazini BF, Dolder MA. *Tissue Cell.* 2017 Apr;49(2 Pt B):203-208. doi: 10.1016/j.tice.2017.03.003. Epub 2017 Mar 9. <https://www.ncbi.nlm.nih.gov/pubmed/28341060>

Acne is the most common skin disorder and can directly affect the patients' self-esteem. Systemic treatment has been indicated for nodular, cystic or persistent acne rather than another type of treatment, such as a topic one. Isotretinoin is an analogue of vitamin A and by suppressing the sebaceous glands the disease can be controlled. This study was designed to mimic the treatment performed in young patients using the dosage of 1mg/kg, and a higher one of 10mg/kg, for 60days in young male Wistar rats. 24 Wistar rats were divided into four groups: control(water), D0(soybean oil, control group), D1(1mg/kg of Isotretinoin solution), D10(10mg/kg of Isotretinoin solution). Using the morphometry tool and histochemical techniques we evaluated the villus, intestinal crypts, and goblet cells to find signs of possible alterations of the duodenum, jejunum and ileum segments of the small intestine. We found no signs of changes in the jejunum mucosa after 60 days of treatment with 1mg/kg and 10mg/kg. The duodenum is also less affected, whereas significant modifications were found in the ileum. The goblet cell frequency was altered, indicating a proliferative potential for the substance. Although some patients have described intestinal symptoms, no important alterations were found with this protocol, reaffirming the security involved in the treatment with this substance.

TRPV4 Mediates Mast Cell Activation in Cathelicidin-Induced Rosacea Inflammation. Mascarenhas NL, Wang Z, Chang YL, Di Nardo A. *J Invest Dermatol.* 2017 Apr;137(4):972-975. doi: 10.1016/j.jid.2016.10.046. Epub 2016 Nov 28. [http://www.jidonline.org/article/S0022-202X\(16\)32747-6/abstract](http://www.jidonline.org/article/S0022-202X(16)32747-6/abstract)

Rosacea is a chronic skin disorder characterized by painful episodes of facial inflammation provoked by a number of sensory stimuli (Two et al., 2015). It is known that cathelicidin is highly expressed in rosacea skin and that in combination with increased serine protease activity, its cleavage product, LL37, can trigger a number of inflammatory processes, including mast cell (MC) activation (Yamasaki et al., 2007). Having previously shown that MCs are the key mediators of LL37-induced rosacea inflammation (Muto et al., 2014), we sought to determine what factors lead to the increased activation of MCs and the increased release of their mediators in rosacea skin.

TRPV4 Moves toward Center-Fold in Rosacea Pathogenesis. Chen Y, Moore CD, Zhang JY, et al. *J Invest Dermatol.* 2017 Apr;137(4):801-804. doi: 10.1016/j.jid.2016.12.013. <https://www.ncbi.nlm.nih.gov/pubmed/28340683>

Mascarenhas et al. report that TRPV4 expression is upregulated in mast cells in response to the proteolytic cathelicidin fragment LL37 in a murine rosacea model and that TRPV4 loss of function attenuates mast cell degranulation. These findings render TRPV4 a translational-medical target in rosacea. However, signaling mechanisms causing increased expression of TRPV4 await elucidation. Moreover, we ask whether TRPV4-mediated Ca⁺⁺-influx evokes mast cell degranulation.

Rosacea Subtypes Visually and Optically Distinct When Viewed with Parallel-Polarized Imaging Technique. Kwon IH, Choi JE, Seo SH, et al. *Ann Dermatol.* 2017 Apr;29(2):167-172. doi: 10.5021/ad.2017.29.2.167. Epub 2017 Mar 24. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5383741/>

BACKGROUND: Parallel-polarized light (PPL) photography evaluates skin characteristics by analyzing light reflections from the skin surface. **OBJECTIVE:** The aim of this study was to determine the significance of quantitative analysis of PPL images in rosacea patients, and to provide a new objective evaluation method for use in clinical research and practice. **METHODS:** A total of 49 rosacea patients were enrolled. PPL images using green and white light emitting diodes (LEDs) were taken of the lesion and an adjacent normal area. The values from the PPL images were converted to CIELAB coordinates: L* corresponding to the brightness, a* to the red and green intensities, and b* to the yellow and blue intensities. **RESULTS:** A standard grading system showed negative correlations with L* (r=-0.67862, p=0.0108) and b* (r=-0.67862, p=0.0108), and a positive correlation with a* (r=0.64194, p=0.0180) with the green LEDs for papulopustular rosacea (PPR) types. The xerosis severity scale showed a positive correlation with L* (r=0.36709, p=0.0276) and a negative correlation with b* (r=-0.33068, p=0.0489) with the white LEDs for erythematotelangiectatic rosacea (ETR) types. In the ETR types, there was brighter lesional and normal skin with white LEDs and a higher score on the xerosis severity scale than the PPR types. **CONCLUSION:** This technique using PPL images is applicable to the quantitative and objective assessment of rosacea in clinical settings. In addition, the two main subtypes of ETR and PPR are distinct entities visually and optically.

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Twelve-week, multicenter, placebo-controlled, randomized, double-blind, parallel-group, comparative phase II/III study of benzoyl peroxide gel in patients with acne vulgaris: A secondary publication. Kawashima M, Sato S, Furukawa F, et al. *J Dermatol.* 2017 Mar 11. doi: 10.1111/1346-8138.13798. [Epub ahead of print]

<http://onlinelibrary.wiley.com/doi/10.1111/1346-8138.13798/abstract?sessionid=B4BCD6E98B70FE2A40DC494C900C4479.f03t04>

A placebo-controlled, randomized, double-blind, parallel-group, comparative, multicenter study was conducted to investigate the efficacy and safety of benzoyl peroxide (BPO) gel, administered once daily for 12 weeks to Japanese patients with acne vulgaris. Efficacy was evaluated by counting all inflammatory and non-inflammatory lesions. Safety was evaluated based on adverse events, local skin tolerability scores and laboratory test values. All 609 subjects were randomly assigned to receive the study products (2.5% and 5% BPO and placebo), and 607 subjects were included in the full analysis set, 544 in the per protocol set and 609 in the safety analyses. The median rates of reduction from baseline to the last evaluation of the inflammatory lesion counts, the primary end-

point, in the 2.5% and 5% BPO groups were 72.7% and 75.0%, respectively, and were significantly higher than that in the placebo group (41.7%). No deaths or other serious adverse events were observed. The incidences of adverse events in the 2.5% and 5% BPO groups were 56.4% and 58.8%, respectively; a higher incidence than in the placebo group, but there was no obvious difference between the 2.5% and 5% BPO groups. All adverse events were mild or moderate in severity. Most adverse events did not lead to study product discontinuation. The results suggested that both 2.5% and 5% BPO are useful for the treatment of acne vulgaris.

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Successful Treatment of Facial Acne Fulminans: Antimicrobial Agents and Oral Prednisolone as Promising Regimes. Siadat AH, Bostakian A, Abtahi-Naeini B, Shahbazi M. *Case Rep Dermatol Med.* 2017;2017:7092910. doi: 10.1155/2017/7092910. Epub 2017 Mar 27.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5385906/pdf/CRIDM2017-7092910.pdf>

Acne fulminans (AF), also known as acne maligna, is a rare painful ulcerative form of acne with an abrupt onset and systemic symptoms. Its incidence appears to be decreasing, possibly because of earlier and better treatment of acne. This report highlights a case on a necrotizing facial wound due to AF that was successfully treated with oral prednisolone and antimicrobial medication.

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A peel-off facial mask comprising myoinositol and trehalose-loaded liposomes improves adult female acne by reducing local hyperandrogenism and activating autophagy. Fabbrocini G, Capasso C, Donnarumma M, et al. *J Cosmet Dermatol.* 2017 Mar 25. doi: 10.1111/jocd.12340. [Epub ahead of print]

<https://www.ncbi.nlm.nih.gov/pubmed/28342238>

BACKGROUND: Hyperandrogenism and reduced skin autophagy have been implicated in the pathogenesis of adult female acne (AFA). Here, we tested whether a ready-to-use peel-off facial mask containing myoinositol (an androgen inhibitor) and trehalose-loaded liposomes (as activators of cutaneous autophagy) applied overnight every other day for 60 days can improve AFA. We also sought to investigate the molecular mechanisms underlying the clinical effects. **OBJECTIVES:** We conducted an uncontrolled, open-label clinical study in 40 cases of AFA to investigate the effect of the facial mask on lesion count, sebum production (measured with the Sebutape® technique), and Global Acne Grading System (GAGS) scale. We also investigated the changes from baseline to the end of treatment in androgen and beclin-1 levels (as a marker of autophagy) in skin biopsy supernatants. **METHODS:** Forty Caucasian patients with AFA were enrolled. Changes in clinical and molecular endpoints before and after treatment were investigated. **RESULTS:** The mean counts of comedones, papules, pustules, and nodular lesions decreased significantly (all $P < .001$). The mean Sebutape® score was reduced from 3.4 ± 0.6 to 1.8 ± 0.2 ($P < .001$), whereas the mean GAGS scale score decreased from 16.8 ± 5.3 at baseline to 9.8 ± 4.6 after treatment ($P < .001$). A significant decrease in testosterone and dehydroepiandrosterone sulfate in skin biopsy supernatants was observed, whereas beclin-1 levels increased significantly ($P < .001$). **CONCLUSION:** A ready-to-use peel-off facial mask containing myoinositol and trehalose-loaded liposomes improved the cosmetic appearance of AFA by reducing cutaneous androgen content and promoting skin autophagy.

Fractional Carbon Dioxide Laser and its Combination with Subcision in Improving Atrophic Acne Scars.

Nilforoush zadeh MA, Faghihi G, Jaffary F, et al. Adv Biomed Res. 2017 Mar 1;6:20. doi: 10.4103/2277-9175.201332. eCollection 2017. <https://www.ncbi.nlm.nih.gov/pubmed/28349023>

BACKGROUND: Acne is a very common skin disease in which scars are seen in 95% of the patients. Although numerous treatments have been recommended, researchers are still searching for a single modality to treat the complication due to its variety in shape and depth. We compared the effects of fractional carbon dioxide (CO₂) laser alone and in combination with subcision in the treatment of atrophic acne scars. **MATERIALS AND METHODS:** This clinical trial study was performed in Skin Diseases and Leishmaniasis Research Center (Isfahan, Iran) during 2011-2012. Eligible patients with atrophic acne scars were treated with fractional CO₂ laser alone (five sessions with 3-week interval) on the right side of the face and fractional CO₂ laser plus subcision (one session using both with four sessions of fractional CO₂ laser, with 3-week interval) on the left side. The subjects were visited 1, 2, and 6 months after the treatment. Patient satisfaction rate was analyzed using SPSS 20 software. **RESULTS:** The average of recovery rate was 54.7% using the combination method and 43.0% using laser alone ($P < 0.001$). The mean patient satisfaction was significantly higher with the combination method than laser alone (6.6 ± 1.2 vs. 5.2 ± 1.8 ; $P < 0.001$). Bruising was only seen with the combination method and lasted for 1 week in 57.0% and for 2 weeks in 43.0%. Erythema was seen in both methods. Postinflammatory pigmentation and hyperpigmentation were associated with combination method. No persistent side effects were seen after 6 months. **CONCLUSION:** Using a combination of subcision and laser had suitable results regarding scar recovery and satisfaction rate.

Clinical Reviews

Prioritizing treatment outcomes: how people with acne vulgaris decide if their treatment is working.

Layton AM, Whitehouse H, Eady EA, et al. J Evid Based Med. 2017 Apr 26. doi: 10.1111/jebm.12249. [Epub ahead of print]

<https://www.ncbi.nlm.nih.gov/pubmed/28444879>

AIM: To collect information about how people with acne make day-to-day decisions concerning the effectiveness of their treatment. **METHODS:** Between May and August 2013, an optional question was embedded in the James Lind Alliance Acne Priority Setting Partnership's online survey to collect treatment uncertainties. The question asked people with acne to 'Tell us in your own words how you decide if your treatment has been effective'. **RESULTS:** A total of 742 respondents specified at least one outcome or means of assessing change (outcome measure). Fewer spots was the most commonly cited outcome, identified by 272 respondents (36.7%). Other frequently mentioned outcomes were, in descending order: less redness (19.4%), reduction in spot size (12.1%) and less pain/discomfort (11.4%). Signs were much more commonly used than symptoms and surrogate outcomes such as changes in aspects of life quality were infrequently mentioned. Visual inspection of the skin was the most widely adopted outcome measure (16.3%). **CONCLUSIONS:** Although the most frequently used methods map well onto the outcome measures adopted in the majority of acne trials, namely physician-assessed changes in lesion counts and global acne severity, people with acne often take into account several factors that cannot be assessed by a third party at a single point in time. The minimal use of changes in psychosocial wellbeing and mood may reflect that these are regarded as secondary consequences of improvements in appearance. The robustness of these findings now requires independent evaluation. If confirmed, they could form the basis of a new patient-reported outcome measure.

Retinoids: a journey from the molecular structures and mechanisms of action to clinical uses in dermatology and adverse effects. Khalil S, Bardawil T, Stephan C, et al. *J Dermatolog Treat.* 2017 Apr 2:1-13. doi: 10.1080/09546634.2017.1309349. [Epub ahead of print] <https://www.ncbi.nlm.nih.gov/pubmed/28318351>

Retinoids are a class of compounds derived from vitamin A or having structural and/or functional similarities with vitamin A. They are classified into three generations based on their molecular structures. Inside the body, retinoids bind to several classes of proteins including retinoid-binding proteins and retinoid nuclear receptors. This eventually leads to the activation of specific regulatory regions of DNA - called the retinoic acid response elements - involved in regulating cell growth, differentiation and apoptosis. Several clinical trials have studied the role of topical and systemic retinoids in disease, and research is still ongoing. Currently, retinoids are used in several fields of medicine. This paper aims to review the structure, mechanisms of action, and adverse effects of retinoids, as well as some of their current uses in Dermatology.

Microneedling in All Skin Types: A Review. Bonati LM, Epstein GK, Strugar TL. *J Drugs Dermatol.* 2017 Apr 1;16(4):308-313. <https://www.ncbi.nlm.nih.gov/pubmed/28403263>

INTRODUCTION: Microneedling procedures are growing in popularity for a wide variety of skin conditions. This paper comprehensively reviews the medical literature regarding skin needling efficacy and safety in all skin types and in multiple dermatologic conditions. **METHODS:** A PubMed literature search was conducted in all languages without restriction and bibliographies of relevant articles reviewed. Search terms included: "microneedling," "percutaneous collagen induction," "needling," "skin needling," and "dermaroller." **RESULTS:** Microneedling is most commonly used for acne scars and cosmetic rejuvenation, however, treatment benefit has also been seen in varicella scars, burn scars, keloids, acne, alopecia, and periorbital melanosis, and has improved flap and graft survival, and enhanced transdermal delivery of topical products. Side effects were mild and self-limited, with few reports of post-inflammatory hyperpigmentation, and isolated reports of tram tracking, facial allergic granuloma, and systemic hypersensitivity. **DISCUSS:** Microneedling represents a safe, cost-effective, and efficacious treatment option for a variety of dermatologic conditions in all skin types. More double-blinded, randomized, controlled trials are required to make more definitive conclusions.

Light therapies for acne: abridged Cochrane systematic review including GRADE assessments. Barbaric J, Abbott R, Posadzki P, et al. *Br J Dermatol.* 2017 Mar 24. doi: 10.1111/bjd.15495. [Epub ahead of print] <http://onlinelibrary.wiley.com/doi/10.1111/bjd.15495/abstract>

We undertook a Cochrane review of randomized controlled trials (RCTs) evaluating the effects of light-based interventions for acne vulgaris. We searched the Cochrane Skin Specialised Register, CENTRAL, MEDLINE, Embase, LILACS, ISI Web of Science, and grey literature sources (September 2015). We used the Grading of Recommendations Assessment, Development and Evaluation Working Group approach to assess the quality of evidence (QE). We included 71 RCTs (4211 participants, median sample size 31). Results from a single study (n = 266, low QE) showed little or no difference in effectiveness on participants' assessment of improvement between 20% aminolevulinic acid (ALA) photodynamic therapy (PDT), activated by blue light, versus vehicle plus blue light, whereas another study (n = 180) of a comparison of ALA-PDT (red light) concentrations showed 20% ALA-PDT was no more effective than 15%, but better than 10% and 5% ALA-PDT. Pooled data from three studies, (n = 360, moderate QE) showed that methyl aminolevulinate (MAL)-PDT, activated by red light, had a similar effect on changes in lesion counts, compared with placebo cream with red light. Several studies compared yellow light to

placebo or no treatment, infrared light to no treatment, gold-microparticle suspension to vehicle, and clindamycin/benzoyl peroxide (C/BPO) combined with pulsed dye laser to C/BPO alone. None of these showed any clinically significant effects. Most studies reported adverse effects, but inadequately, with scarring reported as absent, and blistering only in studies on intense pulsed light, infrared light and PDT (very low QE). Carefully planned studies, using standardised outcome measures, and common acne treatments as comparators are needed.

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Adverse effects of isotretinoin: A large, retrospective review. Brzezinski P, Borowska K, Chiriac A, Smigielski J.

Dermatol Ther. 2017 Mar 14. doi: 10.1111/dth.12483. [Epub ahead of print]

<http://onlinelibrary.wiley.com/doi/10.1111/dth.12483/abstract>

Acne is a very common and disfiguring disease that affects mostly adolescents and, to some extent, adults. The objective of our study was to estimate the adverse effects after isotretinoin by treatment of 3,525 patients due to acne vulgaris in a 5-year observation. Retrospective, comparative study was carried out in Poland and Romania from January 2012 to August 2016. Inclusion criteria into this study were moderate, severe, and nodulocystic inflammatory acne vulgaris. Exclusion criteria were mild acne, pregnant, and lactating women. Statistical analysis was carried out using T test and Chi square. All patients were treated with oral isotretinoin. Patient age ranged from 13-35 years. Dry lips was the most commonly reported adverse effect, affecting 100% of users, followed by xerosis (94.97%) and facial erythema (66.21%). Of all adverse effects, psychiatric symptoms accounted for 25.16%; eye lesions accounted for 8.96%. In lab investigations an increase in the level of total cholesterol and serum triglycerides was observed. This study documents the adverse effect profile of isotretinoin in a large number of patients collected over a period of 4 years. Side effects were mild and well tolerated and did not necessitate stopping the treatment. However, it is important to educate patients about this potential consequence.

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Patient Counseling/Communication

Acne located on the trunk, whey protein supplementation: Is there any association? Cengiz FP, Cevirgen

Cemil B, Emiroglu N, et al. Health Promot Perspect. 2017 Mar 5;7(2):106-108. doi: 10.15171/hpp.2017.19.

eCollection 2017. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5350548/pdf/hpp-7-106.pdf>

Whey protein is a source of protein that was isolated from milk. Whey proteins are composed of higher levels of essential amino acids. The role of diet in acne etiology has been investigated for several years. It was established that milk and milk products can trigger acneiform lesions, and recent evidence supports the role of whey protein supplements in acne. Herein, we report 6 healthy male adolescent patients developing acne located only to the trunk after the consumption of whey protein supplements for faster bodybuilding. This is the first observation which specified the location of acneiform lesions among bodybuilders. In our opinion, a trendy and common health problem is beginning among adolescents in the gyms.

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