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Industry News

Ortho Dermatologics launches Arazlo lotion in the US. DermWire. Practical Dermatology. June 29, 2020. <https://practicaldermatology.com/news/ortho-dermatologics-launches-arazlo-lotion-in-the-us?c4src=news-landing:feed>

Bausch Health Companies Inc. and its dermatology business, Ortho Dermatologics launched Arazlo (tazarotene) Lotion, 0.045%. Now available commercially to health care professionals in the US, it was FDA approved in December 2019 as the first tazarotene acne treatment available in lotion formulation. Arazlo is Indicated for the topical treatment of acne vulgaris in patients nine years of age and older. "Retinoids like tazarotene are highly effective in treating acne and considered a cornerstone of acne treatment, but often are perceived to be associated with skin irritation. Clinical studies have demonstrated that Arazlo's proprietary formulation provides the proven efficacy of a retinoid in a lotion that is more tolerable to patients than a higher concentration tazarotene," said Bill Humphries, president, Ortho Dermatologics. "Ortho Dermatologics remains committed to bringing forward new treatment options like Arazlo to help the millions of Americans who suffer from acne." In a Phase 2, head-to-head study, Arazlo and Tazorac (tazarotene) Cream 0.1% showed similar treatment success rates and similar reductions in both inflammatory and non-inflammatory lesions over 12 weeks and Arazlo was associated with about half the number of adverse events and fewer treatment-related adverse events. "The novel lotion formulation of Arazlo has been shown to be generally well-tolerated, allowing more patients with multiple types of acne to take advantage of its efficacy," said Emil Tanghetti, M.D., lead Arazlo study investigator and founder of the Center for Dermatology and Laser Surgery, Sacramento, CA. "I am excited to offer Arazlo to my patients and anticipate they will be pleased with their results." Arazlo is priced comparable to many other branded acne products indicated to treat moderate-to-severe acne vulgaris. For most eligible patients whose commercial insurance covers the product, they should have no co-pay (or \$0 co-pay) when utilizing the Arazlo coupon at participating pharmacies. Most other eligible, commercially insured patients will have a co-pay of as little as \$65 through our access program.

Acne news: Clascoterone cream 1% exhibits long-term safety for treatment of acne. Linda Stein Gold, MD. DermWire. Practical Dermatology. June 23, 2020. <https://practicaldermatology.com/news/acne-news-clascoterone-cream-1-exhibits-long-term-safety-for-treatment-of-acne?c4src=news-landing:feed>

Cassiopea SpA's Clascoterone cream 1% is safe for the treatment of acne with low rates of treatment-related adverse events, according to a study in the online issue of Journal of the American Academy of Dermatology (JAAD). Clascoterone is a topical androgen receptor inhibitor that fights acne by limiting dihydrotestosterone binding to the androgen receptors in the sebaceous gland. The US Food and Drug Administration is reviewing a New Drug Application for Clascoterone cream 1% with an expected PDUFA date of August 27, 2020. "These results underscore the promise of Clascoterone cream 1% as a first in class topical acne treatment with a favorable safety profile that targets the androgen receptor in both males and females 9 years of age and older," says Dr. Linda Stein Gold, Director of Dermatology Clinical Research at Henry Ford Health System in Detroit, Michigan, in a news release. "Safety data published in JAAD showed that Clascoterone has a consistent and favorable safety profile." The multi-center, open-label, long-term extension study, CB-03-01/27, enrolled a total of 609 subjects from the pivotal studies /25 and /26, with 347 completing the study (n = 179 Clascoterone cream, n = 168 vehicle cream, original group assignment). Eligible patients for CB-03-01/27 must have completed one of the 12-week Phase III pivotal studies. The two Phase III vehicle-controlled studies (CB-03-01/25 and CB-03-01/26) published in JAMA Dermatology showed Clascoterone cream significantly improved Investigator's Global Assessment (IGA) scores and lesion counts in subjects greater than 9 years of age with moderate to severe acne. Clascoterone and vehicle-treated subjects from these pivotal Phase III trials participated in this study, CB-03-01/27; the extent of drug exposure and adverse events were

assessed, evaluating long-term safety of Clascoterone cream. All subjects applied Clascoterone cream 1% twice daily to the face for up to twelve months and/or trunk for up to nine months. Patient visits occurred at months 1, 3, 6, and 9 where disease severity (IGA score), medication use, vital signs, AEs, treatment-emergent adverse events (TEAEs), and serious adverse events (SAEs) were assessed in all patients. Subjects were assessed on the IGA 5-point scale from clear to severe; if subject was more than mild at an evaluation visit, the treatment regimen continued. Key safety findings showed that Clascoterone cream 1% had a low frequency of TEAE's over long-term observed treatment. Local skin reactions were mostly mild. Long-term efficacy was not a primary endpoint of this study.

Proactiv works to change the conversation about acne with new initiatives. DermWire. Practical Dermatology. June 19, 2020. <https://practicaldermatology.com/news/proactiv-works-to-change-the-conversation-about-acne-with-new-initiatives>

The brand will collaborate with Teen Vogue for "Paint Positivity: Because Words Matter" event and social media campaign. Proactiv is taking on the acne positivity movement with new initiatives aimed to help validate the emotional journey of people with acne and inspire compassion for others. As part of these initiatives, Brand Ambassador Kendall Jenner will continue to talk about acne and share her Proactiv journey and the brand will collaborate with Teen Vogue for "Paint Positivity: Because Words Matter" event and social media campaign. "#PaintPositivity #BecauseWordsMatter" kicks off with a series of exclusive content across Teen Vogue's social platforms. Coverage will showcase the effects of hateful words on the self-esteem of young acne sufferers, and emphasize how advocating for them can help restore their confidence. The movement will be brought to life through the work of interdisciplinary artist and Brooklyn native, Alice Mizrachi, who has designed a "#PaintPositivity #BecauseWordsMatter"-themed mural in Williamsburg, Brooklyn that will be finished with the help of the public. To celebrate, consumers can attend an event at the mural site, where they will be invited to participate by physically removing hateful comments by painting over them. Additionally, acne sufferers and advocates will be able to pledge their support by recording and sharing their stories at the pledge booth and enjoy Van Leeuwen ice cream. "At Proactiv we recognize that everyone's acne experience is different," says Megan MacDonald Brand Representative at The Proactiv Company, in a news release. "As a brand that has owned the acne space for over 20 years, it is our responsibility to not only help educate people on the emotional effects of acne but also to help others to understand that acne is a skin disease that should no longer be trivialized. Paint Positivity will help give us that platform and this NYC event will be one of the many initiatives we have for the rest of the year." "Teen Vogue is committed to building a community of young people who are passionate about leading cultural conversations and making change," says Lindsay Peoples Wagner, editor in chief of Teen Vogue. "Acne is something that has impacted our readers and editors alike, so we're excited to team with Proactiv for the launch of this initiative that will inspire a more positive dialogue around acne."

For more information on current or future initiatives from Proactiv follow:

Facebook: [facebook.com/proactiv](https://www.facebook.com/proactiv)

Twitter: [@proactiv](https://twitter.com/proactiv)

Instagram: [@proactiv](https://www.instagram.com/proactiv)

YouTube: [youtube.com/proactive](https://www.youtube.com/proactive)

Almirall announces FDA approval of updated label for Seysara® (sarecycline) tablets. BioSpace. Published: Jun 18, 2020. <https://www.biospace.com/article/releases/almirall-announces-fda-approval-of-updated-label-for-seysara-sarecycline-tablets/>

Almirall LLC today announced that the FDA approved an important update to the Seysara® label stating that P. acnes strains displayed a low propensity for the development of resistance to sarecycline. This information is included in the Microbiology Section (12.4) of the prescribing information. Seysara® is a novel tetracycline-derived oral antibiotic

developed specifically for the treatment of acne and was approved by the FDA in October 2018. Since its launch in January 2019, Seysara® has been prescribed for close to 100,000 patients. "The data demonstrated that *P. acnes* strains display low propensity for the development of resistance to sarecycline, with spontaneous mutation frequencies being 10-10⁻¹⁰ (or 1 in 10 billion) at 4 to 8 times the minimum inhibitory concentration (MIC). What this means in practice is that the main bacterium associated with acne (*P. acnes*) has shown very low potential of developing resistance to sarecycline," stated Ayman Grada, MD, Head of R&D and Medical Affairs for Almirall US. According to the most recent American Academy of Dermatology (AAD) guidelines on the management of acne, oral antibiotics are a first-line treatment for moderate to severe acne, however Seysara® is the only one specifically designed and studied for this indication. Due to concerns regarding antimicrobial resistance, the Centers for Disease Control and Prevention (CDC) has stressed antibiotic stewardship. This is an initiative to promote the appropriate use of antibiotics where patients receive the right dose of the right antibiotic at the right time for the right duration. Dr Grada added "We support antibiotic stewardship and the appropriate use of antibiotics in general, including when used to treat dermatologic conditions." "When considering the importance of antibiotic stewardship, this new data for sarecycline provides another reason to consider it as a viable treatment option for inflammatory lesions of non-nodular moderate to severe acne," commented Dr. Lawrence Eichenfield, Professor of Dermatology and Pediatrics at the University of California, San Diego and Rady Children's Hospital, San Diego. Seysara® is one of thirteen branded products marketed in the US by Almirall, a global family-owned company focused on medical dermatology and skin health. Ron Menezes, President and General Manager at Almirall, LLC, underscores "We are delighted that the FDA recognized the importance of this data and approved the update to our label. This highlights Seysara® as a distinct option for the treatment of the appropriate acne patient." Seysara® (sarecycline) is a once-daily, oral tetracycline-class antibiotic for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 9 years of age and older. Seysara® has demonstrated to be a safe and effective treatment in two adequate and identical 12-week multicenter, randomized, double-blind, placebo-controlled studies (Study 1 [NCT02320149] and Study 2 [NCT02322866]). Efficacy was assessed in a total of 2,002 subjects 9 years of age and older. Limitations of Use - Efficacy of SEYSARA beyond 12 weeks and safety beyond 12 months have not been established. SEYSARA has not been evaluated in the treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, SEYSARA should be used only as indicated.

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New Medical Research

Platelet rich plasma injection versus topical erythromycin 2% in treatment of acne vulgaris. Ibrahim ZA, Gheida SF, El-Halaby AR, et al. *J Dermatolog Treat.* 2020 Jul 9;1-26. doi: 10.1080/09546634.2020.1793884. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32643473/>

Background: Acne vulgaris is a common inflammatory skin disease that affects the pilosebaceous glands. There are different modalities of treatment of acne but there is no standard treatment free of side effects. Platelet rich plasma (PRP) is an autologous concentration of platelets in a small volume of plasma. When platelets are activated, multiple growth factors are released. They play an important role in angiogenesis, inflammatory process and wound healing. Aim: was to evaluate and compare the therapeutic efficacy of platelet rich plasma versus topical erythromycin 2% in treatment of acne vulgaris. Methods: 40 patients with inflammatory acne lesions were included. All patients received PRP injection sessions in one side of the face (group A) every 2 weeks for 6 sessions and topical erythromycin 2% in the other side (group B). Results: There was significant difference between both groups in which better improvement was reported in group A (55% of patients showed good to excellent improvement and 35% showed moderate improvement, especially the inflammatory lesions). Group A showed better patients' satisfaction and lower rate of

recurrence than group B. Conclusion: PRP is effective and safe treatment option for inflammatory acne and alternative to other systemic modalities especially if they are contraindicated.

Searching predictive factors of efficacy and safety in a fractional CO2 laser. Josiane H, Joelle K, Farid S, Boutros S. *Dermatol Ther.* 2020 Jul 8. doi: 10.1111/dth.13985. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32639071/>

Background: A few studies discussed short outcomes in fractional CO2 laser. Objective: This study aimed to seek factors of medium-term efficacy and safety in patients treated for facial rejuvenation or acne scars. Methods: This single-center, prospective, single-arm, evaluator-blinded cohort study included patients of 18 years and older undergoing a fractional CO2 laser for facial skin rejuvenation or atrophic acne scars. One session of ultrapulsed fractional 10600 nm CO2 laser was performed with the Deep FX TM mode in acne scars and the Active FX TM mode in facial rejuvenation and acne scars. Follow-up was carried out for six months. In the end, a patient self-satisfaction assessment was obtained. A blinded physician graded improvement based on pretreatment and 6-month photography. Results: The study included seventy-five patients, of whom 88% were women. Forty-five had facial rejuvenation, and 30 had atrophic acne scars treatment. Half of the patients were satisfied. The physician-blinded evaluation indicated "good to very good" improvement in 46.7% of facial rejuvenation patients, and 30% of acne scars patients. Hyperpigmentation and folliculitis were recorded in 15 and 3 patients, respectively. Conclusions: This study did not find statistically significant factors to predict outcomes in a fractional CO2 laser. We could however note better results in acne scar patients of thicker skin, and facial rejuvenation patients of younger age and thinner skin. We counted more hyperpigmentation events in phototypes III and IV, and it was reversible in all cases.

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Quality of life assessed using Skindex-16 scores among patients with acne receiving isotretinoin treatment. Secrest AM, Hopkins ZH, Frost ZE, et al. *JAMA Dermatol.* 2020 Jul 8;e202330. doi: 10.1001/jamadermatol.2020.2330. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32639529/>

Importance: Acne is a common dermatologic condition and significantly affects psychosocial health and quality of life. An international task force recommended routine use of quality-of-life measures for clinic visits associated with acne management, but this has yet to translate into clinical practice. Objective: To assess mean Skindex-16 scores over time among patients with moderate to severe acne receiving isotretinoin treatment. Design, setting, and participants: A longitudinal, retrospective case series study of Skindex-16 data collected at monthly visits from 57 consecutive patients with acne receiving isotretinoin; data were collected and evaluated between November 23, 2016, and January 22, 2019. Continuous variables were compared using quantile regression. Multivariable linear mixed models evaluated mean (95% CI) score trajectory over time. Main outcomes and measure: Skindex-16 scores, including normalized scores for the emotional, symptomatic, and functional aspects of having skin disease as well as an overall score. Results: Fifty-seven patients (31 [54.4 %] males, with median [interquartile range] age of 17.2 [15.9-18.1] years) in this case series study completed the Skindex-16 at baseline and at least once during follow-up. Baseline Skindex-16 scores were similar by sex but worse with increasing age. Emotional impact was more bothersome to patients with acne requiring isotretinoin treatment than either symptoms or functioning. Improvements of greater than 50% in overall and Emotional domain scores were seen by month 2 of receiving isotretinoin treatment (eg, overall scores decreased from 39.4 to 17.5 by month 2; a decrease of 22.0; $P < .001$). Qualitatively, Skindex-16 scores reached their nadir between months 3 and 5; at month 4, overall Skindex-16 scores showed a 4.4-fold improvement (from 39.4 at baseline to 8.9; $P < .001$) and Emotional domain scores showed a 4.8-fold improvement (from 57.7 at baseline to 11.9; $P < .001$). Conclusions and relevance: The findings of this case series suggest that patients receiving isotretinoin treatment achieve greater than a 50% improvement in quality of life by month 2 and can expect approximately 4-fold

to 5-fold improvements from baseline with a full course of isotretinoin. This study shows the potential of routine administration of quality of life measures to assess patient care in dermatology.

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Successful treatment of the face post acne erythema using a topically applied selective alpha 1-Adrenergic receptor agonist, oxymetazoline 1.5%, a controlled left to right face comparative trial. Agamia N, Essawy M, Kassem A. *J Dermatolog Treat.* 2020 Jul 7;1-6. doi: 10.1080/09546634.2020.1789045. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32602755/>

Background: Post-inflammatory erythema (PIE) is a common sequelae of acne inflammation, persistent post acne erythema (PAE) is cosmetically unacceptable and sometimes its complete clearance could not be achieved. Oxymetazoline (OXZ) is a synthetic, direct-acting, sympathomimetic agonist that is highly selective for the 1 α -adrenoceptor. It is a potent vasoconstrictor and well known for its ability to clinically 'get the red out'. Aim: The aim of this study was to evaluate the efficacy and safety of topical oxymetazoline (OXZ) 1.5% in treatment of post acne erythema (PAE) in a left to right face comparative study. Methods: This study was conducted on 40 patients diagnosed with post acne erythema for at least 3 months, the left side of the face was treated with topical OXZ 1.5% in liposomal base and was compared to the right side to which topical lipogel was applied as a control. Results: According to the investigator's global assessment of photographs and the analysis of erythema with image analysis software, topical OXZ was significantly effective in diminishing PAE when compared to topical placebo lipogel. Conclusion: Topical OXZ is a safe and effective treatment for post-acne erythema.

Efficacy of IPL therapy for the treatment of acne vulgaris: A meta-analysis. Lu L, Shi M, Chen Z. *J Cosmet Dermatol.* 2020 Jul 5. doi: 10.1111/jocd.13586. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32623823/>

Background: Intense pulse light (IPL) has been adopted by numerous patients. However, no existing study has analyzed the efficiency and safety of IPL in the treatment of acne vulgaris. Objective: To assess the efficiency and safety of IPL in the treatment of acne vulgaris. Methods: Electronic databases, including EMBASE, Cochrane Library, and MEDLINE, were retrieved to identify related studies. In this study, the primary and secondary outcomes were the mean percentage reduction of inflammatory acne lesion improvement (MPRI) and the mean percentage reduction of noninflammatory acne lesion improvement (NMPRI), respectively. Between-study heterogeneities were assessed using the I² statistic. Results: Eight randomized controlled trials (RCTs) including 450 patients were enrolled into the present analysis. With regard to MPRI, the result of IPL group was poorer than that of control group [mean deviation (MD)= -4.37 (95% confidence interval CI: -7.83, -0.91), P =0.01]. In addition, the efficiency of IPL was poor among African and Asian populations [MD= -3.87 (95% CI: -7.36, -0.37), P= 0.03; MD=-28.37 (95% CI: -52.26, -4.18), P=0.02]. Meanwhile, difference in the efficiency between IPL and 1064 nm Nd: YAG was not statistically significant [MD= -3.25 (95% CI: -7.01, -0.51). P =0.09]. Besides, the efficiency of IPL was lower than that of PDL [MD=-28.37 (95% CI: -52.26, -4.18), P=0.02]. There was no statistically significant difference in the efficiency between IPL and other treatments for NMPRI. With regard to adverse effects, erythema (46.73%) and pain (39.13%) were the most common. Conclusions: IPL is not so efficiency as other supplementary therapies. For inflammatory acne lesions, the efficiency of IPL is poorer than that of PDT. Difference in geographic regions may affect the IPL efficiency. However, the results obtained in this study should be cautiously interpreted due to the heterogeneities and the lack of studies with a large sample size.

Comparison of dermatologists and family physicians in terms of prescribing antibiotics for the treatment of acne vulgaris. Aslan Kayıran M, Karadağ AS, Mutlu HH, Goldust M, Sarıcaoğlu H. *Dermatol Ther.* 2020 Jul 4;e13973. doi: 10.1111/dth.13973. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32621767/>

Background: Acne Vulgaris (AV) is a common skin disease that is treated both with dermatologists and family physicians (FPs) with different strategies. Objective: To assess the antibiotics that are frequently preferred in AV treatment, and the differences between the FPs and dermatologists in treatment were investigated. Material-method: The physicians were informed about the study and sent over the internet a multiple-choice questionnaire that consists of 29 questions in total. Afterwards the answers provided were compared. Results: 201 dermatologists and 147 FPs participated in the study. Dermatologists were found to have preferred topical erythromycin, nadifloxacin, clindamycin and tetracycline, and systematically doxycycline and azithromycin in adult patients, whereas the FPs were found to have preferred mupirocin, fusidic acid (FA) and oxytetracycline, and systematically tetracycline. Dermatologists were found to have recommended topical clindamycin and erythromycin in pregnant/breastfeeding AV patients, whereas the FPs were found to have recommended FA. Dermatologists were found to have continued the antibiotics for 8-12 weeks, whereas the FPs were found to have continued for 1-4 weeks. The dermatologists preferred systemic antibiotics in cases with back involvement, moderate to severe AV, and that the FPs preferred them in severe AV. The dermatologists considered that the use of antibiotics alone or long-term were important factors causing antibiotic resistance. Conclusion: There were significant differences between the approaches of dermatologists and FPs to AV treatment. FPs were found to have insufficient information about prevention of antibiotic resistance. Therefore, we think that the continuous training of FPs on dermatology will be beneficial.

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Autologous plasma gel injection combined with scar subcision is a successful technique for atrophic post-acne scars: A split-face study. Nassar A, El-Shaarawy W, Salah E. *J Dermatolog Treat.* 2020 Jun 30;1-7. doi: 10.1080/09546634.2020.1782322. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32530334/>

Background: Different therapeutic options can be used for post-acne scarring. Scar subcision alone or in combination with other treatments have been used by many dermatologists to treat post-acne scarring. Objectives: We thought to study and compare the efficacy and safety of scar subcision combined with platelet gel injection versus scar subcision combined with PRP injection for atrophic post-acne scarring. Patients and methods: Scar subcision was done 1st on both sides of the face. Plasma gel injection was done on the right side and PRP injection was done on the left side. The sessions were done monthly for 4 months followed by a 6-month follow-up period. Evaluation of the results and any complications were recorded. Results: There was a significant improvement ($p = .035$) of the scars on the subcision-gel-side at one month following the 1st treatment session. However, along with the following sessions, there were no significant differences between both sides. Finally, at the follow-up visit after 6 months following the end of the treatment course there was a significant difference between the two sides of the face in favor of the subcision-gel-side. Conclusions: Subcision combined with autologous plasma gel injection is a successful technique for atrophic post-acne scars.

Putative genes and pathways involved in the acne treatment of isotretinoin via microarray data analyses.

Chen B, Li P, Li J, Chen J. *Biomed Res Int.* 2020 Jun 29;2020:5842795. doi: 10.1155/2020/5842795. eCollection 2020. <https://pubmed.ncbi.nlm.nih.gov/32685503/>

Acne is the eighth most common disease worldwide. Disease burden of acne such as anxiety, reduced self-esteem, and facial scarring lowers the life quality of acne patients. Isotretinoin is the most potent treatment for moderate-severe acne. However, the adverse events of isotretinoin especially teratogenicity limit its use. This study aims at investigating the therapeutical mechanisms of isotretinoin using bioinformatics analysis. Differentially expressed genes (DEGs) were filtered from microarray datasets GSE10432, GSE10433, and GSE11792. Functional and pathway enrichment analyses of DEGs were performed. Protein-protein interaction (PPI) network and module analyses were also conducted based on DEGs. Using isotretinoin for 1 week, LCN2, PTGES, and GDF15 were

upregulated and might mediate sebocytes apoptosis and thus decreased sebum production; CCL2 originated from activated TNF signaling pathway and S100A7 could be related with "acne-flare". While treating with isotretinoin for 8 weeks, key genes were downregulated, including HMGCS1, HMGCRCR, FDFT1, MVD, IDI1, and FDPS, which may be associated with decreased sebum synthesis; HMGCS1, HMGCRCR, and FDFT1 also probably associated with apoptosis of sebocytes. There were only two common genes including ACSBG1 and BCAT2 which worked in both 1 week and 8 weeks and could associate with decreased sebum synthesis and apoptosis of sebocytes, respectively. These results indicate potential therapeutics and side effect mechanisms of isotretinoin in the acne treatment and provide a research direction to further investigate the therapeutic mechanism of isotretinoin and thus develop retinoid-like compounds with similar curative effect and without teratogenicity.

Self-contrast study of pinprick therapy combined with super pulse fractional CO 2 laser for the treatment of atrophic acne scars. Yang Z, Jiang S, Zhang Y, et al. *J Cosmet Dermatol*. 2020 Jun 25. doi: 10.1111/jocd.13568. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32585741/>

Aims: This study is to evaluate the clinical efficacy and safety of a "double-layer" mode of super pulse fractional CO2 laser and a combined treatment of pinprick therapy with fractional CO2 laser for the treatment of atrophic acne scars. **Methods:** A split-face and self-contrast method was applied. A total of 20 patients with atrophic acne scars randomly received the above mentioned therapy on the left or right side of the cheek for 3 times with an interval of 3 months. ECCA scores, IVA scores, patients' satisfaction, VAS scores, and adverse reactions were evaluated. **Results:** Atrophic acne scars on both sides of the cheek were improved obviously. The ECCA scores showed a significant decrease, while IVA scores significantly increased. Compared with the super pulse fractional CO2 laser group, the decrease of ECCA scores, the increase of IVA scores and the patients' satisfaction were significantly higher and improvement on V-shaped and U-shaped acne scars was significantly better in the combined treatment group. No patients had severe adverse reactions such as blister, infection or hypertrophic scars. **Conclusions:** Super pulse fractional CO2 laser and pinprick treatment combined with fractional CO2 laser are both safe and effective therapy for the treatment of atrophic acne scars.

Clinical Reviews

Isotretinoin and the eye: A review for the dermatologist. Ruiz-Lozano RE, Hernández-Camarena JC, Garza-Garza LA, et al. *Dermatol Ther*. 2020 Jul 19;e14029. doi: 10.1111/dth.14029. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32683764/>

Due to the prevalence of acne vulgaris, isotretinoin is one of the most prescribed drugs among physicians and dermatologists. Although exhibiting an adequate safety profile, adverse events secondary to isotretinoin use are common. Before prescribing isotretinoin, physicians usually inquire about pregnancy and perform serologic tests including cholesterol, triglycerides, and liver enzymes. Ocular manifestations are commonly neglected. Despite being generally mild, ocular manifestations related to either topical or systemic isotretinoin may cause important ocular morbidity. The ocular surface is the most affected site within the eye; however, retinal, and optic nerve disease also have been documented. Evaporative dry eye disease, which may range from mild to severe, is the most common adverse ocular effect associated with isotretinoin use. The aim of this review is to present an up-to-date overview for the dermatologist about the prevention, diagnosis, and treatment of the ocular side effects of isotretinoin, and when to refer to the eye specialist.

Pulsed dye laser followed by intradermal botulinum toxin type-A in the treatment of rosacea-associated erythema and flushing. Al-Niaini F, Glagoleva E, Araviiskaia E. *Dermatol Ther.* 2020 Jul 7. doi: 10.1111/dth.13976. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32633449/>

Rosacea is a common inflammatory skin disease characterized by erythema, episodes of flushing and inflammatory lesions. It typically affects the face and is more prevalent among fair skin individuals affecting women more than men. Various treatments are available for rosacea with light-based therapies commonly used in the management of erythema. The use of intradermal botulinum toxin type-A has been reported to be beneficial in the treatment of rosacea-associated erythema and flushing with good results and a low side-effect profile. In this article we present our experience on the successful combination of both pulsed dye laser and intradermal botulinum toxin type-A in erythema and flushing in 20 rosacea patients. In addition to subjective improvement we measured the degree of erythema using a 3D Antera™ camera in order to quantify our results. We demonstrated high efficacy and satisfaction rate with this combined approach and a low side-effect profile. To our knowledge the combination of laser and intradermal botulinum toxin in the management of rosacea has not been previously reported.

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Subject satisfaction with Trifarotene 50 µg/g cream in the treatment of facial and truncal acne vulgaris: A case series. Johnson SM, Chavda R, DuBois JC. *Dermatol Ther (Heidelb).* 2020 Jul 4. doi: 10.1007/s13555-020-00417-4. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32623660/>

There is a paucity of literature covering patient-reported outcomes of treatments for truncal acne. Trifarotene 50 µg/g cream is a novel retinoid molecule approved for once-daily topical treatment of facial and truncal acne vulgaris. As physicians are starting to gain real-world experience with this retinoid treatment, their access to reporting from the patient's perspective provides a valuable adjunct to the pivotal studies. We report a case series of three subjects with moderate facial and truncal acne treated with trifarotene 50 µg/g cream on the face, shoulders, upper back and upper anterior chest for 12 weeks and evaluated by satisfaction questionnaires. This case series illustrating the treatment of facial and truncal acne with trifarotene 50 µg/g cream, in the form of real-world data, describes high overall satisfaction and excellent tolerability to support the use of this new retinoid molecule in the treatment of acne vulgaris on both the face and trunk.

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Amzeeq (minocycline topical foam): A new drug for the treatment of acne. St Onge E, Mobley WC. *Ann Pharmacother.* 2020 Jul 3;1060028020939926. doi: 10.1177/1060028020939926. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32618475/>

Objective: To review the safety and efficacy of minocycline 4% topical foam for the treatment of moderate to severe acne vulgaris in adults and pediatric patients aged 9 years and older. Data Sources: A literature search through PubMed and EMBASE was conducted using the following keywords: FMX101, minocycline, foam, and acne. Study Selection and Data Extraction: Articles selected included those describing preclinical and clinical studies of pharmacokinetics, efficacy, or safety of topical minocycline foam. Data Synthesis: Minocycline 4% topical foam was shown in a preclinical study to effectively deliver minocycline to the pilosebaceous unit, with little penetration beyond the stratum corneum. This was consistent with a phase 1 pharmacokinetic study of the foam, which yielded a significantly reduced systemic exposure of minocycline compared with oral minocycline. In phase 2 and phase 3 clinical trials, the foam significantly reduced acne lesion counts and Investigator's Global Assessment scores of acne severity compared with placebo. The foam has a good safety profile, with headache, mild erythema, hyperpigmentation, and mild dryness among the most common adverse effects. Relevance to Patient Care and Clinical Practice: Topical antibiotics have been a mainstay of acne therapy with the benefit of less systemic exposure

compared with oral antibiotics. However, the development of bacterial resistance has reduced their use, thereby reducing options for many patients with acne. Minocycline 4% topical foam is a safe and effective alternative, which may help restore this important therapeutic approach for treating acne vulgaris.

Demodex-induced Lupus miliaris disseminatus faciei: A case report. Luo Y, Wu LX, Zhang JH, et al. Case Reports Medicine (Baltimore). 2020 Jul 2;99(27):e21112. doi: 10.1097/MD.00000000000021112. <https://pubmed.ncbi.nlm.nih.gov/32629745/>

Rationale: Lupus miliaris disseminatus faciei (LMDF) is an inflammatory granulomatous skin disease without a clear etiology that frequently involves the middle area of the face and the upper eyelids. Pathological features of the disease include caseation necrosis and epithelioid granuloma. Consensus treatment for LMDF is currently unavailable. **Patient concerns:** A 47-year-old Chinese female patient who presented with facial pruritic, erythematous papules 8 months before this study. She was diagnosed with skin tuberculosis at another hospital and given antituberculosis medication. However, the treatment was not efficacious. **Diagnoses:** In this study, the diagnosis of Demodex-induced LMDF was made by a dermatologist according to physical examination, skin biopsy pathology, and microscopic examination. **Interventions:** The patient was given ornidazole tablets (500 mg twice a day) and recombinant bovine basic fibroblast growth factor gel (0.2 g/cm twice a day) for an 8-week period. **Outcomes:** Eight weeks after the treatment, the facial erythematous papules were improved, and no new skin lesions were observed. The patient showed no signs of recurrence during the 6-month follow-up. **Lessons subsections:** This case showed that ornidazole combined with recombinant bovine basic fibroblast growth factor gel might be useful in treatment of Demodex-induced LMDF. In addition, the results suggested that pathological caseation necrosis was caused by a series of inflammatory and immune responses to Demodex infection.

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Is there an association between long-term antibiotics for acne and subsequent infection sequelae and antimicrobial resistance? A systematic review protocol. Bhate K, Lin LY, Barbieri J, et al. BMJ Open. 2020 Jul 2;10(7):e033662. doi: 10.1136/bmjopen-2019-033662. <https://pubmed.ncbi.nlm.nih.gov/32616485/>

Introduction: Antimicrobial resistance (AMR) is a global health emergency. Acne vulgaris is a highly prevalent condition and the dominant role antibiotics play in its treatment is a major concern. Antibiotics are widely used in the treatment of acne predominantly for their anti-inflammatory effect, hence their use in acne may not be optimal. Tetracyclines and macrolides are the two most common oral antibiotic classes prescribed, and their average use can extend from a few months to several years of intermittent or continuous use. The overall aim of this systematic review is to elucidate what is known about oral antibiotics for acne contributing to antibiotic treatment failure and AMR. **Methods and analysis:** A systematic review will be conducted to address the question: What is the existing evidence that long-term oral antibiotics used to treat acne in those over 8 years of age contribute towards antibiotic treatment failure or other outcomes suggestive of the impact of AMR? We will search the following databases: Embase, MEDLINE, the Cochrane Library and Web of Science. Search terms will be developed in collaboration with a librarian by identifying keywords from relevant articles and by undertaking pilot searches. Randomized controlled trials, cohort and case-controlled studies conducted in any healthcare setting and published in any language will be included. The searches will be re-run prior to final analyses to capture the recent literature. The Cochrane tool for bias assessment in randomized trials and ROBINS-I for the assessment of bias in non-randomized studies will be used to assess the risk of bias of included studies. GRADE will be used to make an overall assessment of the quality of evidence. A meta-analysis will be undertaken of the outcome measures if the individual studies are sufficiently homogeneous. If a meta-analysis is not possible, a qualitative assessment will be presented as a narrative review.

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Skin needling for the treatment of acne scarring: A comprehensive review. Villani A, Carmela Annunziata M, Antonietta Luciano M, Fabbrocini G. *J Cosmet Dermatol.* 2020 Jun 29. doi: 10.1111/jocd.13577. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32598509/>

Background: Skin needling, also called "collagen induction therapy," is a nonpharmacological treatment modality that has been increasingly utilized for the treatment of acne scars. Aims: To review the medical literature and to select the most significant and recent studies regarding skin needling as a treatment for acne scarring, used alone or combined with other treatments. Methods: A literature search was performed using the PubMed, Medline, and Embase databases, in addition to reviewing the bibliographies of relevant articles. Results: Almost all the articles evaluated showed improvement of acne scars severity after microneedling treatment. When combined with other treatments such as autologous platelet-rich plasma (PRP), chemical peels, filler injections, or laser treatment, a greater improvement was reported. Needling technique is well-tolerated with erythema and dryness representing the most frequent adverse events. Conclusions: Microneedling is a useful treatment for acne scarring. Further studies are needed to evaluate its efficacy and safety and to create a standardized protocol to adopt for each patient according to the severity of acne scars.

Esc-1GN shows therapeutic potentials for acne vulgaris and inflammatory pain. Ye T, Wu J, Xu Z, et al. *J Pept Sci.* 2020 Aug;26(8):e3269. doi: 10.1002/psc.3269. Epub 2020 Jun 18. <https://pubmed.ncbi.nlm.nih.gov/32558003/>

The inflammatory response plays important roles in acne vulgaris and pain pathogenesis. In previous study, Esc-1GN with anti-inflammatory, antimicrobial, and lipopolysaccharide (LPS) binding activity was identified from the skin of the frog *Hylarana guentheri*. Here, we report its therapeutic potentials for acne vulgaris and inflammatory pain. Esc-1GN destroyed the cell membrane of *Propionibacteria acnes* in the membrane permeability assays. In addition, bacterial agglutination test suggested that Esc-1GN triggered the agglutination of *P. acnes*, which was affected by LPS and Ca^{2+} . Meanwhile, in vivo anti-*P. acnes* and anti-inflammatory effects of Esc-1GN were confirmed by reducing the counts of *P. acnes* in mice ear, relieving *P. acnes*-induced mice ear swelling, decreasing mRNA expression and the production of pro-inflammatory cytokines, and attenuating the infiltration of inflammatory cells. Moreover, Esc-1GN also displayed antinociceptive effect in mice induced by acetic acid and formalin. Therefore, Esc-1GN is a promising candidate drug for treatment of acne vulgaris and inflammatory pain.

Butterfly effect and acne - The role of diet. Clatici VG, Voicu C, Barinova E, et al. *Dermatol Ther.* 2020 Jun 15. doi: 10.1111/dth.13832. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32537797/>

The authors aim to present the butterfly effect, a concept based on the theory that small changes might have a powerful effect, as an example of the important connection between diet and acne. Western diet is currently a well-known environmental factor which, mainly via the overstimulation of mTORC1 (mammalian target of rapamycin complex 1), is responsible for the development and aggravation of acne and other age-related diseases of civilization. From the authors' point of view, "the butterfly effect" extrapolated to Acne and Diet depicts the importance of dietary interventions in acne so as to prevent more serious mTORC1-driven diseases of civilization like obesity, diabetes and cancer.

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Laser safety in isotretinoin use: Online survey of public perception. AlKhowailed M, AlWayili S, Altalhab S, et al. *J Dermatolog Treat.* 2020 Jun 14;1-4. doi: 10.1080/09546634.2020.1775772. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32538248/>

Background: The safety of laser therapy in patients taking isotretinoin is controversial. Recent evidence suggests that laser during isotretinoin treatment is safe. Our study aims to assess public perception and willingness to undergo

laser intervention while receiving isotretinoin. Methods: An online-based cross-sectional survey was conducted between November 2019 and March 2020. Information on participants knowledge about isotretinoin precautions with laser therapy and their willingness to undergo laser intervention while on isotretinoin therapy was collected. Results: Out of 509 respondents, almost one-third used laser therapy while on isotretinoin treatment. Those who did not use laser therapy most commonly attributed to isotretinoin treatment (43%). Forty-two percent of participants thought that laser therapy while on isotretinoin is harmful. Almost half of the participants were aware that current guidelines recommend waiting for six months after isotretinoin. Nearly, half of the participants decided to postpone laser therapy for acne scars even after knowing that recent studies reported the safety of laser therapy for acne scars while on isotretinoin. Conclusion: Even with the knowledge of recent safety data of laser during isotretinoin therapy, a significant proportion of patients are still concerned about potential complications. Increasing awareness regarding the safety of laser skin therapy during isotretinoin treatment might be needed.

Topical antibiotics in the dermatological clinical practice: Indications, efficacy and adverse effects.

Bonamonte D, De Marco A, Giuffrida R, et al. *Dermatol Ther.* 2020 Jun 12;e13824. doi: 10.1111/dth.13824. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/32531105/>

Topical antibiotic therapy is a central component of patient management for several skin conditions, including acne, hidradenitis suppurativa, rosacea, impetigo or other superinfected dermatitis, prevention of wound infections. Moreover, particular situations, such as skin diseases of bacterial origin in pregnancy and infants often warrant topical therapy. However, the occurrence of local delayed hypersensitivity reactions and the rising rate of antibiotic resistance are becoming great challenges faced by many dermatologists today. This narrative review provides an overview of the main topical antibiotics used in dermatology, focusing on their clinical role in the most common dermatological indications. For this purpose, a review of MEDLINE and PubMed for pertinent, scientific, and clinical publications till March 2020 was performed. Only articles published in English language were included.

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