AARS HOT TOPICS MEMBER NEWSLETTER

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American Acne and Rosacea Society
201 Claremont Avenue • Montclair, NJ 07042
(888) 744-DERM (3376) • info@aarsmember.org
www.acneandrosacea.org

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AARS Event

Save the Date: 14th Annual AARS Reception, Friday, March 1, 2019 6P – 9PM, Washington, DC

Join your AARS colleagues and President Julie Harper and President-Elect Mark Jackson for a wonderful evening! All members are welcome!

Industry News

Almirall and X-Chem team up to develop oral compounds for dermatological diseases. Practical Dermatology, DermWire. Wednesday, December 12, 2018. http://practicaldermatology.com/dermwire/2018/12/12/almirall-and-x-chem-team-up-to-develop-oral-compounds-for-dermatological-diseases

Almirall, S.A. signed a collaborative research and license agreement with the X-Chem, Inc. for the development of oral compounds for patients suffering from dermatological diseases, a strategic area for Almirall. X-Chem, Inc. is a privately held biotechnology company focused on applying its industry-leading DNA-encoded library (DEX) drug discovery engine to the generation of novel small molecule therapeutics. This collaboration will enrich Almirall's R&D pipeline with the development of new solutions for patients with dermatological unmet medical needs. Under the terms of the agreement, X-Chem will screen its proprietary DEX libraries, which contain >120 billion individually DNA-encoded small molecules, toward the discovery of novel, high-value therapeutic leads for dermatological diseases. Almirall will subsequently assess the biochemical and/or cellular activity, novelty of the structures, and in some cases advanced properties. Almirall has the option to license drug leads discovered under the collaboration, and will be responsible for further development and commercialization of the resulting programs. Bhushan Hardas, MD, MBA, Chief Scientific Officer of Almirall,says, "This agreement takes us one step further in our goal of becoming a leading medical dermatology company. With the cutting edge technology offered by X-Chem and our strong knowledge of the area of dermatology, we will be able to broaden our pipeline and provide further medical solutions for the physicians and patients, specially designed for dermatological diseases with unmet medical needs". Rick Wagner, Ph.D., President and Chief Executive Officer of X-Chem, adds, "The treatment of skin disease is an important field of research with unmet medical needs. We are delighted to align with Almirall, a leader in dermatology, to apply our DEX platform to the discovery of new treatments for patients worldwide".

Crown Laboratories acquires select healthcare brands from GlaxoSmithKline. Practical Dermatology, DermWire. Friday, November 30, 2018. http://practicaldermatology.com/dermwire/2018/11/30/crown-laboratories-acquires-select-healthcare-brands-from-glaxosmithkline/?c=&t=

Crown Laboratories, Inc. has acquired North American distribution rights of five OTC consumer brands from GlaxoSmithKline (GSK). The acquired portfolio includes: PanOxyl® daily acne wash, Sarna® anti-itch lotion, Zeasorb® anti-fungal and prevention product, Desenex® anti-fungal powder for athlete's foot, and Mineral Ice® pain-relieving gel. The brands all have a strong heritage and lengthy history in the market. PanOxyl, Sarna, and Zeasorb are three former Stiefel Laboratories brands that have earned #1 Dermatologist Recommended status through decades of strong support from dermatologists. "Acquiring these strong heritage brands strengthens Crown's OTC portfolio and adds significant value across multiple categories," says Jeff Bedard, Crown Laboratories

President and CEO. “I am especially excited to bring the Stiefel brands to Crown as I personally enjoyed tremendous success in marketing them as a field sales representative for Stiefel in the 80s and 90s.” Crown Laboratories has chosen the Emerson Group to manage the sales activity and all logistics for the PanOxyl, Sarna, Zeasorb, Desenex, and Mineral Ice brands across all retailers. Financial terms of the transaction were not disclosed.

New Medical News

The IL-1 pathway is hyperactive in hidradenitis suppurativa and contributes to skin infiltration and destruction. Witte-Händel E, Wolk K, Tsaousi A, et al. J Invest Dermatol. 2018 Dec 5. pii: S0022-202X(18)32909-9. doi: 10.1016/j.jid.2018.11.018. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30528824

Hidradenitis suppurativa (HS; also designated as acne inversa) is a chronic inflammatory disease characterized by painful purulent skin lesions and progressive destruction of skin architecture. Despite the high burden for the patients, pathogenetic pathways underlying HS alterations remain obscure. Investigating the lesional HS cytokine pattern, IL-1β turned out as a highly prominent cytokine, being overexpressed even compared to psoriatic lesions. Analyses of IL-1β-induced transcriptome in various cell types disclosed an overlap of upregulated molecules causing immune cell infiltration and extracellular matrix degradation, as well as of specific cytokines including IL-6, IL-32, and IL-36. Matching cellular IL-1 receptor levels, dermal fibroblasts showed both the strongest and broadest IL-1β response, which was not clearly shared or strengthened by other cytokines. The IL-1β signature was specifically present in HS lesions and could be reversed by application of IL-1 receptor antagonist. Search for blood parameters associated with IL-1β pathway activity in HS identified SAA, which was synergistically induced by IL-1β and IL-6 in hepatocytes. Consequently, strongly elevated blood SAA levels in HS correlated positively with the extent of inflammatory skin alterations. In summary, the IL-1β pathway represents a pathogenetic cascade, whose activity may be therapeutically influenced and monitored by blood SAA levels.

Does isotretinoin cause depression and anxiety in acne patients? Metekoglu S, Oral T, Ucar Psy C, Akalin MA. Dermatol Ther. 2018 Dec 5:e12795. doi: 10.1111/dth.12795. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30515924

Background: Acne is the most common skin disease, and isotretinoin is the most powerful drug amongst the various drugs used for its treatment. A causal relationship has not yet been established between isotretinoin use and depression. Objectives: The aim of this study is to research the effect of isotretinoin treatment on depression in a group of patients undergoing isotretinoin therapy. Methods: Behavioral tests measuring anxiety and depression, and the measures assessing acne severity and quality of life were applied to 112 acne patients consulted at Dermatology Clinic of Beyazit Medico Social Center of Istanbul University. Results: In this study, 72 acne patients (61 female and 11 male) were evaluated. A significant decrease was observed in HAD-D, GAGS and CADI scores at the end of the therapy. There was no significant relationship between patients' depression history and HAD-D scores at the end of first month of therapy and at the end of treatment. Conclusion: Although the psychiatrists are concerned about the potential psychiatric side effects of isotretinoin, our data support no causal relationship between isotretinoin use and depression in acne patients.

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Anti-acne properties of hydrophobic fraction of red ginseng (Panax ginseng C.A. Meyer) and its active components. Hou JH, Shin H, Jang KH, et al. Phytother Res. 2018 Dec 3. doi: 10.1002/ptr.6243. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30506753

Acne is a chronic inflammatory disease of the skin that occurs when bacteria abnormally grow in hair follicles. The most common treatment is antibiotics, but they are limited due to antibiotic resistance. The purpose of this study was to identify the active ingredients of the antimicrobial effects of red ginseng (Panax ginseng C.A. Meyer), compare it to existing antibacterial substances, and determine its potential efficacy as a natural drug product. The hydrophobic fraction in red ginseng ethanol extract (RGEF) showed the same or better antimicrobial activity against Propionibacterium acnes than benzoyl peroxide or azelaic acid. In addition, the antimicrobial component derived from red ginseng selectively showed a high antimicrobial effect on P. acnes. Nuclear magnetic resonance spectroscopic analysis showed that the active antimicrobial substance in this fraction was panaxynol and panaxydol. Twenty subjects who had acne symptoms were treated with cream containing 3 mg/g of RGEF for 4 weeks. It was found that oxidized sebum contents and redness of the skin were reduced, and symptoms of the early to middle stage of acne were effectively improved. This study showed that red ginseng extract containing panaxynol and panaxydol can effectively control the symptoms of acne.

Standardized laboratory monitoring with use of isotretinoin in acne. Lake E. J Am Acad Dermatol. 2018 Dec 3. pii: S0190-9622(18)32971-2. doi: 10.1016/j.jaad.2018.10.074. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30521826

The optimal timing of laboratory tests for patients on isotretinoin treatment for acne is uncertain.-In this series, although abnormalities in serum lipids in patients receiving isotretinoin were not infrequent, they were mild to moderate, and were generally noted around the second month of treatment.-For healthy patients on isotretinoin, we recommend that a lipid panel and liver function test be performed at baseline and at month 2, when peak dosing is achieved. Further testing should be considered if a significant abnormal value is noted.

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Enhanced skin targeting of retinoic acid spanlastics: In-vitro characterization and clinical evaluation in acne patients. Nabil Shamma R, Sayed S, Ahmed Sabry N, Ibrahim El-Samanoudy S. J Liposome Res. 2018 Dec 2:1-23. doi: 10.1080/08982104.2018.1552706. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30501429

Acne vulgaris is the most common dermatological disorder affecting millions of individuals. Acne therapeutic solutions include topical treatment with retinoic acid (RA) which showed a god efficacy in treatment of mild and moderate cases. However, the high prevalence of adverse events, such as skin dryness, shedding and skin irritation affects the patient convenience and obstructs the acne treatment. Thus, the objective of this paper was to produce Span 60 based elastic vesicles enriched with penetration enhancers, and study their influence on the delivery of RA and its skin irritation. RA-loaded nanovesicles, enriched with Transcutol®/Labrasol®, were made using the thin film hydration technique, and assessed for entrapment efficiency, particle size and zeta potential. The optimized RA-loaded nanovesicles (composed of Span 60-Tween 20, and Transcutol ®) were morphologically assessed via transmission electron microscopy. Moreover, RA deposition into newborn mice skin was assessed in vitro under non-occlusive conditions, where the optimized RA-loaded nanovesicles showed 2-fold higher RA deposition in the skin compared to the corresponding one lacking Transcutol. The optimized RA-loaded

nanovesicles incorporated into 1% carbopol gel was evaluated for in-vivo clinical performance in acne patients, and showed appreciable advantages over the marketed formulation (Acretin®) in the treatment of acne regarding skin tolerability and patient's compliance.

Enhancement of lipid content and inflammatory cytokine secretion in SZ95 sebocytes by palmitic acid suggests a potential link between free fatty acids and acne aggravation. Choi CW, Kim Y, Kim JE, et al. Exp Dermatol. 2018 Dec 2. doi: 10.1111/exd.13855. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30506807

A relationship between acne and free fatty acids (FFAs) has been suggested recently. However, the effects of FFAs on sebaceous glands are still largely unknown. At the same time, the role of FFAs during chronic inflammation is well established. Considering that FFAs are also a major component of sebum, it is likely that changes in FFA affect both the synthesis of sebum and the inflammatory response in sebaceous glands. In this study, we examined a hypothesis that FFAs increase the production of sebum and induce inflammation in the sebaceous glands. We found that treatment of SZ95 sebocytes with exogenously applied palmitic acid (PA), a major saturated FFA, induced a significant increase in intracellular lipid levels. Moreover, PA treatment also increased the expression and secretion of the proinflammatory cytokines in SZ95 sebocytes. We also found that Toll-like receptors were required for the inflammatory response triggered by PA. The results of our study strengthen the notion about the link between acne and FFAs and suggest the mechanism underlying this relationship. Our results serve as a foundation for future work that will explore the association between FFA and acne and pave way to the development of novel treatment options for acne.

Use of an alternative method to evaluate erythema severity in a clinical trial: Difference in vehicle response with evaluation of baseline and postdose photographs for effect of oxymetazoline cream 1.0% for persistent erythema of rosacea in a phase 4 study. Eichenfield LF, Del Rosso JQ, Tan JKL, et al. Br J Dermatol. 2018 Nov 30. doi: 10.1111/bjd.17462. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30500065

Background: Once-daily topical oxymetazoline cream 1.0% significantly reduced persistent facial erythema of rosacea in trials requiring live, static patient assessments. Objective: To critically evaluate the methodology of clinical trials that require live, static patient assessments by determining whether assessment of erythema is different when reference to the baseline photograph is allowed. Methods: In two identically designed, randomised, phase 3 trials, adults with persistent facial erythema of rosacea applied oxymetazoline or vehicle once daily. This phase 4 study evaluated standardised digital facial photographs from the phase 3 trials to record ≥1-grade Clinician Erythema Assessment (CEA) improvement at 1, 3, 6, 9, and 12 hours postdose. Results: Among 835 patients (oxymetazoline n=415, vehicle n=420), significantly greater proportions of patients treated with oxymetazoline versus vehicle (P<0.0001) achieved ≥1-grade CEA improvement (up to 85.3% vs 29.8%). When reference to baseline photographs was allowed while evaluating posttreatment photographs, the results for oxymetazoline were similar to results of the phase 3 trials, but a significantly lower proportion of vehicle recipients achieved ≥1-grade CEA improvement (up to 52.3% vs 29.7%; P<0.001). Up to 80.2% of oxymetazoline patients achieved at least moderate erythema improvement, versus up to 22.9% of vehicle patients. The association between patients' satisfaction with facial skin redness and percentage of erythema improvement was statistically significant (Spearman rank correlation, 0.1824; P<0.0001 [oxymetazoline]; 0.0623; P=0.01 [vehicle]). Conclusions: Assessment of study photographs, with comparison to baseline, confirmed significant erythema reduction with oxymetazoline on the first day of application. Compared to the phase 3 trials results, significantly fewer vehicle

recipients attained ≥1-grade CEA improvement, inferring a mitigated vehicle effect. This methodology may improve the accuracy of clinical trials evaluating erythema severity.

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Clindamycin versus clindamycin plus rifampicin in hidradenitis suppurativa treatment: Clinical and ultrasound observations. Caposiena Caro RD, Cannizzaro MV, Botti E, et al. J Am Acad Dermatol. 2018 Nov 28. pii: S0190-9622(18)32961-X. doi: 10.1016/j.jaad.2018.11.035. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30502416

Background: Antibiotics are recognized as first-line treatments for Hidradenitis Suppurativa (HS), but there is limited data on their efficacy. Objective: Evaluate the efficacy of oral clindamycin versus clindamycin plus rifampicin in HS patients. Methods: Sixty mild to moderate-severe HS patients classified according IHS4 and Hurley scores, were subdivided into two groups of 30 patients each (Group A receiving clindamycin+rifampicin and Group B treated with clindamycin alone), and retrospectively studied. The main outcome was to evaluate and compare the clinical and ultrasound response between groups after 8 weeks of treatment according to Hidradenitis Suppurativa Clinical Response (HiSCR). Results: After the treatment, 17/30 patients in Group A and 19/30 in Group B met the primary outcome. Both groups showed a similar improvement of IHS4, while DLQI and Pain VAS improved more in Group B. In particular, nodules and abscesses count reduction was similar between the two groups. Whereas, the number of draining tunnels decreased more in Group B. The factors significantly associated with HiSCR were age, BMI, IHS4 and absence of axillary involvement. The disease free survival was similar between the two groups. Limitations: The study was not randomized or placebo-controlled. Conclusion: Clindamycin may be a useful treatment alternative to antibiotic combination regardless of HS clinical stage.

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Topical nano-emulgel for skin disorders: Formulation approach and characterization. Ahmad J, Gautam A, Komath S, et al. Recent Pat Antiinfect Drug Discov. 2018 Nov 28. doi: 10.2174/1574891X14666181129115213. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30488798

Backgrounds: Acne vulgaris is a common chronic skin disease that affects approximately 650 million people or about 9.4% of the population globally. Growing research in the area of nanotechnology over the years has now been exploited in management of various human disorders by their application in drug delivery. These approaches have an enormous opportunity for the designing of a novel, low-dose and effective treatment systems to control acne disease. Topical nanoemulsion-based gel preparations are said to have various benefits over the conventional formulations. The recent patents on topical anti-acne formulation (US 7241456B2; US 6897238B2; US 6284234B1) provided the concept to design thymol loaded nano-emulgel for topical application in acne. Methods: The aim of the present study was to design a thymol loaded nano-emulgel preparation by exploiting low-energy emulsification method for topical application in acne. Furthermore, developed formulation was characterize for thermodynamic stability, mean droplet size, zeta potential, drug content and in-vitro drug diffusion study. Results: The optimized thymol loaded nanoemulsion was found to be 13.60±0.117 nm with PdI 0.197±0.008. Nanoemulsions will provide enormous surface area for better penetration of therapeutic agent into the pilosebaceous region, resulting better efficacy. Conclusions: From the above studies, it concluded that aqueous-based gel vehicle of the developed formulation system exploited for topical delivery has moisturising properties which can improve local tolerability also.

Topical oxymetazoline cream 1.0% for persistent facial erythema associated with rosacea: Pooled analysis of the two phase 3, 29-day, randomized, controlled REVEAL trials. Stein-Gold L, Kircik L, Draelos ZD, et al. J Drugs Dermatol. 2018 Nov 1;17(11):1201-1208. https://www.ncbi.nlm.nih.gov/pubmed/30500142

Background: Rosacea is a chronic dermatologic condition with limited treatment options. Methods: Data were pooled from two identically designed phase 3 trials. Patients with moderate to severe persistent erythema of rosacea were randomized to receive oxymetazoline cream 1.0% or vehicle once daily for 29 days and were followed for 28 days posttreatment. The primary efficacy outcome was the proportion of patients with ≥2-grade improvement from baseline on both Clinician Erythema Assessment (CEA) and Subject Self-Assessment (SSA) at 3, 6, 9, and 12 hours postdose, day 29. Results: The pooled population included 885 patients (78.8% female); 85.8% and 91.2% had moderate erythema based on CEA and SSA, respectively. The primary outcome was achieved by significantly more patients in the oxymetazoline than vehicle group (P<0.001). Individual CEA and SSA scores and reduction in facial erythema (digital image analysis) favored oxymetazoline over vehicle (P<0.001). The incidence of treatment-emergent adverse events was low (oxymetazoline, 16.4%; vehicle, 11.8%). No clinically relevant erythema worsening (based on CEA and SSA) was observed during the 28-day posttreatment follow-up period (oxymetazoline, 1.7%; vehicle, 0.6%). Conclusion: Oxymetazoline effectively reduced moderate to severe persistent facial erythema of rosacea and was well tolerated.

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Once-daily topical dapsone gel, 7.5%: Effective for acne vulgaris regardless of baseline lesion count, with superior efficacy in females. Tanghetti E, Harper J, Baldwin H, et al. J Drugs Dermatol. 2018 Nov 1;17(11):1192-1198. https://www.ncbi.nlm.nih.gov/pubmed/30500140

Introduction: Acne vulgaris is more common in females than males and is challenging to treat. A post hoc analysis of 2 clinical trials evaluated the effect of dapsone gel, 7.5% based on sex and baseline acne lesion count. Methods: Two identically designed, randomized, double-blind, vehicle-controlled, multicenter, 12-week, phase 3 trials enrolled patients aged ≥12 years with facial acne and 20 to 50 inflammatory and 30 to 100 comedonal lesions. Patients applied dapsone gel, 7.5% or vehicle topically once daily for 12 weeks. Baseline to week 12 reductions were evaluated for total, inflammatory, and comedonal lesions in the pooled dapsone population by sex and total baseline acne lesion count (low: 50–74, medium: 75–99, and high: ≥100). Results: The analysis included 2160 patients (56% female, 44% male). Males and females had similar average baseline total, inflammatory, and comedonal lesion counts. Low, medium, and high subgroups experienced efficacy with dapsone gel, 7.5%. Females in each subgroup experienced superior efficacy to males. In females, total lesion counts in the low, medium, and high subgroups decreased by 56.07%, 50.22%, and 47.63%, respectively, compared with 47.95%, 42.30%, and 34.68% in males (P<0.001 for each male-female comparison). Females' respective inflammatory lesion count percentage reductions were 60.96%, 57.91%, and 55.83%, versus 52.75% (P<0.001), 46.85% (P<0.001), and 44.70% (P=0.008) in males. Females' respective comedonal lesion count percentage reductions were 52.96%, 45.40%, and 44.22%, versus 44.67% (P<0.001), 39.38% (P=0.030), and 29.89% (P=0.001) in males. The TEAE rate was low for the overall population (18.3%) and similar for females (19.0%) and males (17.4%). Males and females had similarly favorable dermal tolerability. Conclusion: Once-daily dapsone gel, 7.5% was efficacious for acne regardless of baseline total lesion count, with superior efficacy in females and similar tolerability in males and females. Registration identifier: Clinicaltrials.gov: NCT01974141 and NCT01974323.

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Integrated cooling-vacuum-assisted non-fractional 1540-nm Erbium:Glass laser: A new modality for the simultaneous effective treatment of acne lesions and scars. Politi Y, Levi A, Snast I, et al. J Drugs Dermatol. 2018 Nov 1;17(11):1173 - 1176. https://www.ncbi.nlm.nih.gov/pubmed/30500135

Introduction: Acne vulgaris is a common skin disorder with a significant impact on patients' quality of life. There is currently no treatment designated to treat acne lesions and scars concurrently. However, mid-infrared lasers may promote neocollagenesis within atrophic scars, while exerting a beneficial effect on acne lesions. Objectives: To determine the safety and efficacy of an integrated cooling-vacuum-assisted non-fractional 1540-nm Erbium:Glass laser for the treatment of acne lesions and scars. Patients and methods: Twenty-two patients (8 male, 14 female) with mild-to-moderate acne and moderate-to-severe acne scars were included. Patients were treated using a non-fractional 1540-nm Er:Glass laser (Harmony XL™, Alma Lasers Ltd.). Acne lesions and scars were exposed to 3-4 stacked pulses emitted at a rate of 3Hz for up to two passes per treatment session (spot size, 4 mm; fluence, 400-600 mJ/pulse), receiving overall 3-7 treatments with 2-3-week intervals. Patients were followed-up one and three months following their last treatment. Clinical evaluation including (i) overall aesthetic appearance, (ii) acne lesions, and (iii) acne scars, assessed independently by two dermatologists and graded on a scale of 0 (exacerbation) to 4 (76-100 percent improvement); and (iv) pain perception, adverse effects and patients' satisfaction. Results: All but one patient completed treatment and follow-up and had moderate-to-significant improvement in all outcomes (overall aesthetic appearance, mean 3.9 [1 month] and 3.75 [3 month] improvement; acne lesions, 3.5 [1 month] and 2.3 [3 month] improvement; scarring 4 [1 month] and 4.2 [3 month] improvement). Pain and adverse effects were mild and transient. Patients' mean satisfaction was 4.2. Conclusion: Cooling-vacuum-assisted 1540 nm laser is a safe and effective modality for the simultaneous treatment of acne lesions and scars.

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Clinical evaluation of safety and efficacy of fractional radiofrequency facial treatment of skin type vi patients. Battle F, Battle S. J Drugs Dermatol. 2018 Nov 1;17(11):1169 - 1172. https://www.ncbi.nlm.nih.gov/pubmed/30481955

Introduction: It has been well established that patients with darker skin types (Fitzpatrick skin types IV-VI) have an increased incidence of thermal induced side effects from laser and radio frequency (RF) treatments. Complications include a higher risk of post-inflammatory hyperpigmentation, hypopigmentation, and scarring, leading to unsatisfactory clinical outcomes. Fractional technologies improve the safety when treating patients with skin of color by treating only fractions of the skin while leaving a healing reservoir of untreated skin that improves the healing process. Fractional RF tips with coated pins may offer a more advantageous safety profile, particularly in the skin-of-color population (Fitzpatrick skin types IV-VI) by increasing the protection of the epidermal layer by minimizing epidermal heating the current study was intended to evaluate the safety and efficacy of fractional RF technology for the treatment of patients with Fitzpatrick skin type VI. Methods: 35 subjects with skin type VI received 3 sessions of facial treatments, 4 weeks apart using a fractional RF device with 24 pin coated tip. The treatment's safety and efficacy were evaluated at 2 follow-up visits, 6 and 12 weeks after the last treatment. Results: Skin characteristics evaluations, including Fitzpatrick Wrinkles Classification, acne scars, and overall facial appearance demonstrated improvement in follow-up visits comparing to baseline. No significant unexpected adverse events were detected. Conclusion: The current study proves the safety and efficacy of the fractional RF treatment modality with coated pins tips for skin rejuvenation treatments resulting in improved wrinkles, acne scars, and overall skin appearance, in patients with skin type VI. J Drugs Dermatol. 2018;17(11):1169-1172.

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Clinical Reviews

Clindamycin as unique antibiotic choice in hidradenitis suppurativa. Rosi E, Pescitelli L, Ricceri F, et al. Dermatol Ther. 2018 Dec 5:e12792. doi: 10.1111/dth.12792. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30515931

Background and objective: The Rifampicin (RF) - Clindamycin (CL) combination is recommended as first line therapy in moderate to severe Hidradenitis Suppurativa (HS) by European S1 guidelines. Although prolonged use of RF should be discouraged, there are currently few alternatives to this combination therapy. The aim of this study was to assess retrospectively the efficacy of oral CL monotherapy in patients diagnosed with HS. Methods: In the period January 2017 - May 2018 31 HS patients who received a 300 mg b.i.d. oral dose of CL were studied retrospectively. Efficacy of the treatment was evaluated by comparing the main HS severity scores (Sartorius score modified by J.E. Revuz, Hidradenitis Suppurativa Physician Global Assessment/HS-PGA and International Hidradenitis Suppurativa Severity Score System/IHS4) before (W0) and after (W12) CL oral therapy. Results: CL efficacy was demonstrated by the extreme and significant reduction of all three disease severity parameters during the 12-week period ($p \leq 0.01$). There was also a statistically significant change in the mean VAS for pain. Conclusions: This study demonstrates the efficacy of oral CL monotherapy as RF-sparing regimen alternative to RF-CL combination in a selected group of patients.

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Correlation of the refined Hurley classification for hidradenitis suppurativa with patient reported quality of life and objective disease severity assessment. Rondags A, van Straalen KR, van Hasselt JR, et al. Br J Dermatol. 2018 Dec 4. doi: 10.1111/bjd.17508. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30512186

Background: Hidradenitis suppurativa (HS) is a chronic, debilitating, heterogeneous disease requiring different treatment approaches. Recently, we refined the classic Hurley classification into a seven-stage classification in order to guide these treatment choices. This new classification subdivides Hurley stage I and II into three sub-stages namely mild (A), moderate (B), and severe (C) HS disease. Hurley stage III is not sub-categorised and always severe. Aim: To investigate the correlation between the given severity grades of Hurley I and Hurley II in the refined Hurley classification, and the patient reported quality of life and physician-assessed objective severity score. Methods: In this cross-sectional study, HS patients participating in the observational cohorts of two Dutch tertiary referral centres were included before June 2017. The patient reported Dermatology Life Quality Index (DLQI) and physician-assessed International HS Severity Score System (IHS4) scores were compared between the refined Hurley stages. Results: In total, 433 patients were analysed. DLQI and IHS4 scores increased within Hurley stage I and II from A through C. There was a significant positive correlation of DLQI and IHS4 with increasing refined Hurley sub-stages (refined Hurley stage I (A, B, and C) to DLQI: $r_s = 0.259$, $p < 0.001$ and refined Hurley stage II (A, B, and C) to DLQI $r_s = 0.185$, $p = 0.010$; refined Hurley stage I (A, B, and C) to IHS4 $r_s = 0.603$, $p < 0.001$ and refined Hurley stage II (A, B, and C) to IHS4 $r_s = 0.532$, $p < 0.001$). Conclusion: The refined Hurley classification accurately correlates with HS severity assessed by both patients and clinicians. Therefore, the refined Hurley classification is a useful tool for the quick assessment of severity in HS.

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Knowledge, attitudes, and perceptions of cannabinoids in the dermatology community. Robinson E, Murphy E, Friedman A. J Drugs Dermatol. 2018 Dec;17(12):1273 - 1278. http://jddonline.com/articles/dermatology/S1545961618P1273X/1

Background: Recent research has identified potential uses of cannabinoids in dermatology, including psoriasis, atopic dermatitis, and wound healing. Objective: The extent of dermatologists' familiarity with and interest in cannabinoids as therapeutics is unknown. Methods: This study examined dermatology providers' knowledge, attitudes, and perceptions on therapeutic cannabinoids using a 20-question online survey. Results: The response rate was 21% (n=531). Most responders thought cannabinoids should be legal for medical treatment (86%). Nearly all (94%) believed it is worthwhile to research dermatologic uses of cannabinoids. 55% reported at least one patient-initiated discussion about cannabinoids in the last year. Yet, 48% were concerned about a negative stigma when proposing cannabinoid therapies to patients. While most responders (86%) were willing to prescribe an FDA-approved cannabinoid as a topical treatment, fewer (71%) were willing to prescribe an oral form. 64% of respondents did not know that cannabidiol is not psychoactive and 29% did not know that tetrahydrocannabinol is psychoactive. Limitations: Limited survey population. Conclusions: Dermatology providers are interested in prescribing cannabinoids and patients are speaking about cannabinoids with their dermatologists. However, providers' fund of knowledge on this subject is lacking. These results highlight the need for further education and research to detangle the dermatologic benefits and risks of cannabinoids.

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Oral isotretinoin for acne. Costa CS, Bagatin E, Martimbianco ALC, et al. Cochrane Database Syst Rev. 2018 Nov 24;11:CD009435. doi: 10.1002/14651858.CD009435.pub2. https://www.ncbi.nlm.nih.gov/pubmed/30484286

Background: Acne vulgaris, a chronic inflammatory disease of the pilosebaceous unit associated with socialization and mental health problems, may affect more than 80% of teenagers. Isotretinoin is the only drug that targets all primary causal factors of acne; however, it may cause adverse effects. Objectives: To assess efficacy and safety of oral isotretinoin for acne vulgaris. Search methods: We searched the following databases up to July 2017: the Cochrane Skin Group Specialized Register, CENTRAL, MEDLINE, Embase, PsycINFO and LILACS. We updated this search in March 2018, but these results have not yet been incorporated in the review. We also searched five trial registries, checked the reference lists of retrieved studies for further references to relevant trials, and hand searched dermatology conference proceedings. A separate search for adverse effects of oral isotretinoin was undertaken in MEDLINE and Embase up to September 2013. Selection criteria: Randomized clinical trials (RCTs) of oral isotretinoin in participants with clinically diagnosed acne compared against placebo, any other systemic or topical active therapy, and itself in different formulation, doses, regimens, or course duration. Data collection and analysis: We used standard methodological procedures expected by Cochrane. Main results: We included 31 RCTs, involving 3836 participants (12 to 55 years) with mild to severe acne. There were twice as many male participants as females. Most studies were undertaken in Asia, Europe, and North America. Outcomes were generally measured between eight to 32 weeks (mean 19.7 weeks) of therapy. Assessed comparisons included oral isotretinoin versus placebo or other treatments such as antibiotics. In addition, different doses, regimens, or formulations of oral isotretinoin were assessed, as well as oral isotretinoin with the addition of topical agents. Pharmaceutical companies funded 12 included trials. All, except three studies, had high risk of bias in at least one domain. Oral isotretinoin compared with oral antibiotics plus topical agents. These studies included participants with moderate or severe acne and assessed outcomes immediately after 20 to 24 weeks of treatment (short-term). Three studies (400 participants) showed isotretinoin makes no difference in terms of decreasing trial investigator-

assessed inflammatory lesion count (RR 1.01 95% CI 0.96 to 1.06), with only one serious adverse effect found, which was Stevens-Johnson syndrome in the isotretinoin group (RR 3.00, 95% CI 0.12 to 72.98). However, we are uncertain about these results as they were based on very low-quality evidence. Isotretinoin may slightly improve (by 15%) acne severity, assessed by physician's global evaluation (RR 1.15, 95% CI 1.00 to 1.32; 351 participants; 2 studies), but resulted in more less serious adverse effects (67% higher risk) (RR 1.67, 95% CI 1.42 to 1.98; 351 participants; 2 studies), such as dry lips/skin, cheilitis, vomiting, nausea (both outcomes, low-quality evidence).Different doses/therapeutic regimens of oral isotretinoin For our primary efficacy outcome, we found three RCTs, but heterogeneity precluded meta-analysis. One study (154 participants) reported 79%, 80% and 84% decrease in total inflammatory lesion count after 20 weeks of 0.05, 0.1, or 0.2 mg/kg/d of oral isotretinoin for severe acne (low-quality evidence). Another trial (150 participants, severe acne) compared 0.1, 0.5, and 1 mg/kg/d oral isotretinoin for 20 weeks and, respectively, 58%, 80% and 90% of participants achieved 95% decrease in total inflammatory lesion count. One RCT, of participants with moderate acne, compared isotretinoin for 24 weeks at (a) continuous low dose (0.25 to 0.4 mg/kg/day), (b) continuous conventional dose (0.5 to 0.7 mg/kg/day), and (c) intermittent regimen (0.5 to 0.7 mg/kg/day, for one week in a month). Continuous low dose (MD 3.72 lesions; 95% CI 2.13 to 5.31; 40 participants; one study) and conventional dose (MD 3.87 lesions; 95% CI 2.31 to 5.43; 40 participants; one study) had a greater decrease in inflammatory lesion counts compared to intermittent treatment (all outcomes, low-quality evidence).Fourteen RCTs (906 participants, severe and moderate acne) reported that no serious adverse events were observed when comparing different doses/therapeutic regimens of oral isotretinoin during treatment (from 12 to 32 weeks) or follow-up after end of treatment (up to 48 weeks). Thirteen RCTs (858 participants) analyzed frequency of less serious adverse effects, which included skin dryness, hair loss, and itching, but heterogeneity regarding the assessment of the outcome precluded data pooling; hence, there is uncertainty about the results (low- to very-low quality evidence, where assessed).Improvement in acne severity, assessed by physician's global evaluation, was not measured for this comparison. None of the included RCTs reported birth defects. Authors' conclusions: Evidence was low-quality for most assessed outcomes. We are unsure if isotretinoin improves acne severity compared with standard oral antibiotic and topical treatment when assessed by a decrease in total inflammatory lesion count, but it may slightly improve physician-assessed acne severity. Only one serious adverse event was reported in the isotretinoin group, which means we are uncertain of the risk of serious adverse effects; however, isotretinoin may result in more minor adverse effects. Heterogeneity in the studies comparing different regimens, doses, or formulations of oral isotretinoin meant we were unable to undertake meta-analysis. Daily treatment may be more effective than treatment for one week each month. None of the studies in this comparison reported serious adverse effects, or measured improvement in acne severity assessed by physician's global evaluation. We are uncertain if there is a difference in number of minor adverse effects, such as skin dryness, between doses/regimens. Evidence quality was lessened due to imprecision and attrition bias. Further studies should ensure clearly reported long- and short-term standardized assessment of improvement in total inflammatory lesion counts, participant-reported outcomes, and full safety accounts. Oral isotretinoin for acne that has not responded to oral antibiotics plus topical agents needs further assessment, as well as different dose/regimens of oral isotretinoin in acne of all severities.

Hidradenitis Suppurativa. Ballard K, Shuman VL. SourceStatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018-.2018 Nov 21. https://www.ncbi.nlm.nih.gov/pubmed/30521288

Excerpt: Hidradenitis suppurativa (HS), also called acne inversus, is a chronic inflammatory skin condition with lesions including deep-seated nodules and abscesses, draining tracts, and fibrotic scars. These lesions most commonly occur in intertriginous areas and areas rich in apocrine glands. Among the most common are axillary,

groin, perianal, perineal, and inframammary locations. Treatment varies based on severity and can include topical and systemic antibiotics, hormone therapy, immune modulators, and surgery. Due to the associated pain, sensitive locations, drainage, odor and scarring, this condition may have a negative psychosocial impact.

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Acne vulgaris in patients with hidradenitis suppurativa. Ravn Jørgensen AH, Ring HC, Thomsen SF. J Am Acad Dermatol. 2018 Nov 17. pii: S0190-9622(18)32911-6. doi: 10.1016/j.jaad.2018.11.021. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30458210

We read with great interest the article by Wertenteil et al., in which the prevalence of acne vulgaris (AV) among patients with hidradenitis suppurativa (HS) and non-HS patients in a population-based sample from the U.S. is determined. They found a prevalence of AV among adults with HS of 15.2 %, compared to 2.9% for adults without HS. Furthermore, prevalence was greatest among females aged 18-44 years, non-whites, obese, and patients who had polycystic ovarian syndrome (PCOS). To expand upon these results, we explored the prevalence of AV in consecutive newly referred patients with HS attending a tertiary dermatological referral center (Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark). Age at onset of HS, family history of HS, smoking status, diagnosis of PCOS and race was noted. Furthermore, body mass index (BMI), Hurley score, Dermatology Life Quality Index (DLQI), anatomic region of HS, number of boils in the past month, and plasma inflammatory markers were examined. A total of 302 patients (191 women and 111 men) with a mean age of 39.4 years referred between January 1st 2016 and October 8th 2018 were included. The overall prevalence of AV was 21.2%: 19 (29.7%) with Hurley stage I, and 39 (60.9%) and 6 (9.4%) with Hurley stages II and III, respectively. No statistical significance between Hurley stage in HS patients with and without AV was observed. Further characteristics of the patients are presented in table 1. In subgroup analysis, HS patients with AV had a significantly lower mean age (33.8 vs. 40.8 years, $p<0.001$) and age at onset of HS (21.4 vs. 27.2 years, $p<0.001$) compared to non-AV HS patients. Additionally, we found that HS patients with AV had lower levels of plasma inflammatory markers (CRP, neutrophils, and neutrophil/lymphocyte ratio (NLR)) compared to HS patients without AV. The prevalence of AV was similar among male and female patients, smokers and non-smokers, patients with a diagnosis of PCOS, and obese and non-obese patients. Also, no difference in DLQI score, and localization of HS between the two groups was observed. We substantiate Wertenteil et al.'s registry-based findings by showing that patients with HS referred for specialized hospital care have a high prevalence of AV. Furthermore, HS patients with AV have a significantly lower mean age and age at onset of HS compared to HS patients without AV. These findings call for greater awareness of this association and for optimization of comanagement approaches.

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Afamelanotide in the treatment of dermatologic disease. McNeil MM, Nahhas AF, Braunberger TL, Hamzavi IH. Skin Therapy Lett. 2018 Nov;23(6):6-10. https://www.ncbi.nlm.nih.gov/pubmed/30517779

Afamelanotide, an α-melanocyte stimulating hormone analogue, has become an emerging therapeutic option for a variety of skin conditions previously refractory to other treatments. Its efficacy has been demonstrated in several dermatologic conditions, including erythropoietic protoporphyria (EPP), solar urticaria, polymorphic light eruption (PMLE), vitiligo, acne, and Hailey-Hailey disease. Its relatively low risk side effect profile makes it an attractive treatment option and also paves the way for innovative use in other disorders.

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The therapeutic potential of cannabinoids in dermatology. Marks DH, Friedman A. Skin Therapy Lett. 2018 Nov;23(6):1-5. https://www.ncbi.nlm.nih.gov/pubmed/30517778

Cannabinoids have demonstrated utility in the management of cancer, obesity, and neurologic disease. More recently, their immunosuppressive and anti-inflammatory properties have been identified for the treatment of several dermatologic conditions. This review thus assesses the therapeutic potential of phytocannabinoids, endoocannabinoids, and chemically synthetic cannabinoids in the management of cutaneous disease. The PubMed® and Scopus® databases were subsequently reviewed in December 2017 using MeSH and keywords, such as cannabinoid, THC, dermatitis, pruritus, and skin cancer. The search yielded reports on the therapeutic role of cannabinoids in the management of skin cancer, acne vulgaris, pruritus, atopic and allergic contact dermatitis, and systemic sclerosis. While cannabinoids have exhibited efficacy in the treatment of inflammatory and neoplastic skin conditions, several reports suggest pro-inflammatory and pro-neoplastic properties. Further investigation is necessary to understand the complexities of cannabinoids and their therapeutic potential in dermatology.

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