AARS HOT TOPICS MEMBER NEWSLETTER

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TABLE OF CONTENTS

Industry News

Botanix acne phase 2 study for BTX 1503 has completed its enrollment. https://www.botanixpharma.com/clinical-trials/

LEAD PRODUCT: BTX 1503 (MODERATE TO SEVERE ACNE)

- Botanix is developing BTX 1503 as a novel treatment for moderate to severe acne
- Botanix successfully completed a Phase 1b study of BTX 1503 during 1Q CY2018
- The study achieved all the BTX 1503 program goals, indicating that it has an excellent safety profile, is very effective at reducing the number of inflammatory and non-inflammatory acne lesions, and provided an improvement in patient rated satisfaction
- BTX 1503's (on average) ~47% reduction in inflammatory lesions was greater than any other FDA-approved topical acne product for which data is available after four weeks of treatment
- The US FDA has approved commencement of Phase 2 clinical trial which will be conducted in the US and Australia
- The Phase 2 clinical trial is fully funded following the Company's successful capital raising in February 2018
- The trial, which is on track to commence in June 2018, will enroll approximately 360 patients and take about 12 months to complete
- Patients enrolling in the study will be treated with one of two high doses, a low dose or placebo (or vehicle) and have similar endpoints as the recently completed Phase 1b study
- The study is on track to commence in June 2018 and will take approximately 12 months to complete

New Medical Research

Prospective evaluation of atrophic acne scars on the face with needle-free high-pressure pneumatic injection: quantitative volumetric scar improvement. Kim BY, Chun SH, Park JH, et al. Dermatol Surg. 2019 Jun;45(6):829-835. doi: 10.1097/DSS.0000000000001708. https://www.ncbi.nlm.nih.gov/pubmed/31136357

Background: Atrophic acne facial scars still pose a treatment challenge. Needle-free high-pressure pneumatic injection has recently been introduced; however, few studies exist regarding its effectiveness. Objective: To evaluate the efficacy and safety of pneumatic injection for treating atrophic acne scars using a 3-dimensional optical profiling system. Methods and materials: A pneumatic injection device with a 0.2-mm nozzle diameter, 50% pressure power, and 85-μL injection volume was used. The degree of depression was examined and analyzed using a 3-dimensional optical profiling system and clinical photographs. The patients also evaluated any side effects. Each subject underwent a single treatment session and was followed up after 1 and 2 months. Results: A total of 13 atrophic acne scars from 10 Korean men and women aged 20 to 29 (mean age 25.8 ± 2.4) years were studied. The mean scar volume values were 0.964, 0.741, and 0.566 mm, respectively, at baseline, 1 month, and 2 months after the injection. Scar volumes after 2 months were significantly different compared with baseline volumes. However, there was no significant difference between the baseline and 1-month volumes. Conclusion: Treatment with pneumatic injection is safe and effective in reducing atrophic acne facial scars; it results in quantitative improvement in scar volumes.

Inhibitory effects of Cheongsangbangpoong-tang on both inflammatory acne lesion and facial heat in patients with acne vulgaris: a double-blinded randomized controlled trial. Kim B, Kim KI, Lee J, Kim K. Complement Ther Med. 2019 Jun;44:110-115. doi: 10.1016/j.ctim.2019.03.018. Epub 2019 Mar 28. https://www.ncbi.nlm.nih.gov/pubmed/31126542

Objectives: To investigate the inhibitory effects of an herbal formulation of Cheongsangbangpoong-tang (CBT) on inflammatory acne lesions as the control of the 'Heat' pattern. Design: A single center study. Randomized, placebo-controlled, parallel group, double-blind trial SETTING: Fifty-six subjects, who had more than 10 acne inflammatory lesions each, were randomly allocated into the CBT or placebo groups and took 5 g CBT extract (CBT group) or 5 g placebo extract (control group), respectively, three times a day for 8 weeks. Pattern identification change of the inflammatory and non-inflammatory acne lesions, temperature of the facial points, serum cortisol level, serum dehydroepiandrosterone-sulfate level, number rating scale, investigator global assessment (IGA), and severity score on the Korean acne grading system were measured. Main outcome measure: mean change of the inflammatory acne lesions. Results: After CBT/placebo administration, the percentage count of inflammatory lesions in subjects was significantly reduced in the CBT group when compared with the control group. The other outcomes showed no significant difference between the two groups. On pattern identification, subjects with the Wind-Heat pattern (, WHP) and Disharmony of the thoroughfare and conception vessels pattern (, DTCVP) tended show better effect than those with other patterns. Conclusions: CBT is a potential therapeutic agent for the treatment of acne vulgaris, linked to inhibition of inflammatory lesions and facial heat. Trial registration: CRiS (Clinical Research Information Service, Republic of Korea), KCT0001468. Registered 06 May 2015.

Topical treatment of acne vulgaris: efficiency, side effects, and adherence rate. Sevimli Dikicier B. J Int Med Res. 2019 May 24:300060519847367. doi: 10.1177/0300060519847367. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31122106

Objective: Adherence is a problem in the topical treatment of acne. This study was designed to evaluate the efficiency of current topical treatment and adherence in patients. Methods: Patients with acne vulgaris who had recently been prescribed a topical therapy were selected. A dermatologist-directed questionnaire was completed. Demographic data, acne severity, treatment and the manner of use, side effects, and reason for discontinuation were recorded. Results: A total 250 patients were included, 178 female (71.2%) and 72 male (28.8%) participants, mean age was 18.6 ± 2.8 years. Of 250 patients, 114 (45.6%) had given up therapy for two reasons: unresponsiveness in 71 (62.3%) and side effects in 43 (37.7%) patients. For antibacterial treatments, the rate of unresponsiveness was higher, but the rate of side effects was lower. Discontinuation owing to unresponsiveness was higher in patients with severe acne. Side effects were higher in patients with comedonal-type acne. The lowest rates of side effects and discontinuation were among every-other-night users. Conclusion: In this study, patients with acne gave up treatment owing to side effects and unresponsiveness, which reduced the treatment efficiency.

Skin-homing T-cell responses associated with demodex infestation and rosacea. Gazi U, Gureser AS, Oztekin A, et al. Parasite Immunol. 2019 May 24:e12658. doi: 10.1111/pim.12658. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31125450

Aims: Our aim was to investigate the skin-homing T-cell immune responses triggered in patients with Demodex infestation and/or rosacea. Methods: Collected whole blood samples were divided into four groups: control subjects; non-rosacea patients with Demodex infestation (Demodex group); papulopustular rosacea (PPR) patients without

Demodex infestation (Rosacea group); and PPR patients with Demodex infestation (Rosacea/Demodex group). Following ex vivo activation, skin-homing CLA+CD4+ T-cell subset levels were monitored by flow cytometry. Results: When compared with control subjects, among skin homing CD4+ T-cell subsets analyzed, Demodex patients had higher TH 9 and Treg cell levels; Rosacea subjects displayed elevated TH 1 cell levels; and Rosacea/Demodex patients exhibited increased frequencies of TH 9, and TH 22 cells. In contrast to Rosacea subjects, Rosacea/Demodex group members displayed higher TH 2 cell levels; and when compared with Demodex groups they had higher TH 1 and TH 2 but lower Treg cell levels. Demodex group members also exhibited higher Treg but lower TH 1 and TH 22 levels than Rosacea/Demodex group subjects. Conclusions: The skin-homing T-cell responses associated with Demodex infestation and rosacea formation seems to influence each other. The present as well as future studies could contribute to development of effective treatment strategies for demodicosis and rosacea.

Thalidomide ameliorates rosacea-like skin inflammation and suppresses NF-κB activation in keratinocytes. Chen M, Xie H, Chen Z, et al. Biomed Pharmacother. 2019 May 24;116:109011. doi: 10.1016/j.biopha.2019.109011. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31132668

Background: Rosacea is a chronic inflammatory skin disorder of uncertain etiology. Evidence suggests the underlying pathogenesis is modulated by abnormal inflammatory and vascular responses. Thalidomide is a synthetic derivative acid with anti-inflammatory and anti-angiogenic properties. However, its effects on rosacea remain unknown. Objectives: To investigate the effects of thalidomide on the lesional alterations and molecular mechanisms in rosacea. Methods: Mice were intradermally injected with LL37 to induce rosacea-like features and intraperitoneally administered with thalidomide. The severity of skin inflammation was evaluated. The mRNA levels of cytokines and chemokines associated with rosacea were assessed by qPCR. The number of CD4 positive infiltrated T helper cells and CD31 positive microvessels, and related genes were measured by immunofluorescence, qPCR and ELISA. Moreover, the effect of thalidomide on inhibiting NF-κB activation was determined by immunofluorescence and western blot. Results: Our results showed that thalidomide significantly alleviated erythema and reduced inflammatory cell infiltration in dermis of LL37-induced rosacea-like mice. The production of cytokines and chemokines induced by LL37 was decreased by thalidomide in mice skin and HaCaT keratinocytes. Particularly, we showed thalidomide reduced CD4+ T helper cell infiltration and downregulated Th1- and Th17-polarizing genes. In addition, thalidomide treatment lowered the microvessel density and vascular endothelial growth factor (VEGF) expression. We further demonstrated that thalidomide suppressed NF-κB activation in LL37-treated skin and in TNF-α-stimulated HaCaT keratinocytes in vitro. Conclusions: Our findings suggest thalidomide attenuates the inflammation and represses NF-κB activation in skin, which leads to assumptions that thalidomide may be a new therapeutic agent for rosacea.

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Alterations in IL-4, IL-10 and IFN-γ levels synergistically decrease lipid content and protein expression of FAS and mature SREBP-1 in human sebocytes. Shin J, Kim KP, Ahn HY, et al. Arch Dermatol Res. 2019 May 24. doi: 10.1007/s00403-019-01932-x. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31127384

When anti-acne alternatives from dietary and plant sources are ingested, systemic alterations of interleukin (IL)-4, IL-10, IL-12 and interferon (IFN)-γ, individually or simultaneously, are induced at a 0.1-10.0-fold (×) range of normal physiological concentrations (1×). However, little is known about the effects of these cytokines on excess sebum, a pathophysiological factor of acne development. In this study, human sebocytes were treated with 0.1-10.0× of IL-4, IL-10, IL-12 and IFN-γ for 3 or 5 days to elucidate the effects on lipid content. Treatment with individual cytokines

decreased the lipid content at specific concentrations rather than in a concentration-dependent manner. Specifically, 5.0× of IL-4, 5.0× of IFN-γ (5.0IFN), and 0.5×, 5.0× and 10.0× of IL-10 for 3 days, and 0.5× of IL-4 (0.5IL4) for 5 days decreased lipid content to 87.6-93.0% of the control. Treatment with other concentrations of IL-4, IL-10 and IFN-γ, and 0.1-10.0× of IL-12 did not alter lipid content. Combined treatment with 0.5IL4, 5.0IFN and 0.5× of IL-10 for 3 or 5 days decreased the lipid content more than each individual treatment. However, this effect was more evident after 3 days, in parallel with decreased levels of triglycerides, cholesterol esters and free fatty acids, the major lipid compositions of sebocytes, and decreased protein expression of fatty acid synthase (FAS) and mature sterol response element-binding protein-1 (SREBP-1), the lipogenesis-related factors, without altered cell proliferation. We demonstrated that suppressed IL-4 and IL-10 with enhanced IFN-γ synergistically decreased lipid content and protein expression of FAS and mature SREBP-1 in human sebocytes.

Characterizing high-burden rosacea subjects: a multivariate risk factor analysis from a global survey. Tan J, Steinhoff M, Bewley A, et al. J Dermatolog Treat. 2019 May 23:1-27. doi: 10.1080/09546634.2019.1623368. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31120382

Objective: To characterize rosacea features suitable for identification of high-burden (HB) subjects in clinical practice. Design: Global online survey with subjects recruited using an online panel from the United States, Canada, Italy, United Kingdom, Germany and France. Subjects self-reported a physician's diagnosis of rosacea. Measurements: HB subjects were defined as those with ≥3/4 domains (quality of life, lifestyle adaptation, time trade-off, willingness to pay) greater than the median. Group characteristics were analyzed, and multivariate-logistic modeling used to investigate factors most associated with HB. Results: 710 subjects completed the survey, including 158 HB subjects. HB was observed in all self-declared rosacea severities. HB subjects were more likely to spend more time daily on skin care and experienced approximately double the impact of health problems on work productivity in the past 7 days ($p < 0.01$). In the past 12 months, HB subjects were more likely to have at least one visit to the emergency room (41.8% vs 11.2%; $p < 0.01$). In the multivariate risk analysis, factors most associated with HB included rosacea severity, impact of health problems on regular daily activities and age at first symptoms. Conclusion: Rosacea has a distinct subset of HB subjects who can be successfully characterized.

Use of Raman spectroscopy in the assessment of skin after CO2 ablative fractional laser surgery on acne scars. Chiwo F, Guevara E, Ramírez-Elías MG, et al. Skin Res Technol. 2019 May 22. doi: 10.1111/srt.12722. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31115110

Background: Ablative fractional laser surgery is a common technique for treating acne scars. However, an in vivo and noninvasive analysis of the histologic variations between acne skin and the resulting resurfaced skin is needed in order to evaluate the wound healing process of the scars induced by the ablative fractional laser surgery. Materials and methods: Nine patients with acne scars underwent a single treatment with a CO2 ablative fractional laser surgery. Collagen presence on the resurfaced skin was noninvasively assessed by means of Raman spectroscopy and principal component analysis. Results: Principal component analysis shows that all the patients presented a collagen regeneration on the resurfaced skin after the laser treatment. Conclusion: Collagen plays a crucial role in the wound healing process. By assessing the collagen presence on the skin, it was possible to quantify the regenerative effects of the ablative fractional laser in a noninvasive way.

Contact sensitization to cosmetic series of allergens in patients with rosacea: a prospective controlled study. Ozbagcivan O, Akarsu S, Dolas N, Fetil E. J Cosmet Dermatol. 2019 May 20. doi: 10.1111/jocd.12989. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31106952

Background: Previous studies have documented the cosmetic allergic contact dermatitis due to common cosmetic allergens in standard series and various cosmetic products used in rosacea patients; however, the prevalence of contact sensitization to other cosmetic allergens other than those in standard series is largely unknown. Aims: To assess the prevalence of contact sensitization to a European cosmetic series of allergens (Chemotechnique Diagnostics AB, Malmö, Sweden) in rosacea patients and to compare this with the prevalence observed in general population. Methods: In this prospective monocenter study, 103 patients with rosacea and 104 control subjects were investigated for contact sensitizations via patch testing the cosmetic series including 49 allergens. Results: At least one positive allergic reaction was observed in 62 (60.2%) rosacea patients, and in 25 (24.0%) control subjects. Compared with control subjects, rosacea patients were statistically more likely to have positive patch tests. The most common allergens giving positive results were octyl gallate (10.68%), dodecyl gallate (8.74%), tert-Butylhydroquinone (7.77%), thimerosal (6.80%), euxyl K400 (6.80%), cocamidopropyl betaine (5.83%), and 2,6-Di-tert-butyl-4-cresol (4.85%). Conclusions: This study shows that rosacea patients show a strikingly high prevalence of contact sensitization to cosmetic allergens. We recommend the additional use of cosmetic series for patch testing, and the careful use of cosmetics in rosacea patients if cosmetic contact sensitivity is suspected.

Comparison of two methods of subcision Nokor and blunt blade in acne scars treatment. Asilian A, Faghihi G, Asemi Esfahani A, et al. J Cosmet Dermatol. 2019 May 18. doi: 10.1111/jocd.12981. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31102320

Context: Subcision is a simple surgical method that can be effective in treatment of acne scars. Aims: This study was conducted to evaluate and compare the two methods of Nokor needle and blunt blade (BB) subcision in treatment of acne scars. Settings and design: This clinical trial study was conducted on 28 patients with acne scars. Patients and methods: One side of the face was treated with BB subcision method, and the other side was treated with Nokor needle method. Followed up period was 6 months after treatment. Statistical analysis used: Data were analyzed by Statistical Package for the Social Sciences (version 20) software using independent sample t test, Mann-Whitney test, Friedman test, and Fisher's exact test. Results: In follow-up period, the improvement of acne scars was comparable in both groups ($P > 0.05$). Complications were lower in BB method than another method ($P < 0.05$). The patient satisfaction was higher in BB method ($P < 0.05$). Conclusions: Both of modalities offered similar improvement, but the complication rate was lower and the patient satisfaction was also higher in the BB method than another method.

Risk of suicide attempt associated with isotretinoin: a nationwide cohort and nested case-time-control study. Droitcourt C, Nowak E, Rault C, et al. Int J Epidemiol. 2019 May 16. pii: dyz093. doi: 10.1093/ije/dyz093. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31098637

Background: Isotretinoin is the only effective treatment for severe acne. An isotretinoin-related suicide risk is still debated and under scrutiny by regulatory agencies. Our objectives were: to assess the risk of suicide attempt before, during and after isotretinoin treatment; to detect any potential triggering effect of isotretinoin initiation on suicide attempt. Methods: We implemented a cohort and nested case-time-control study of subjects treated with oral isotretinoin (course or initiation) aged 10-50 years, using the Nationwide French Health Insurance data (2009-2016). The main outcome was hospitalized suicide attempt. Standardized incidence ratios for hospitalized suicide attempts

were calculated before, during and after isotretinoin treatment. The number of isotretinoin initiations was compared in risk and control periods of 2 months using a case-time-control analysis. Results: In all, 443 814 patients (median age 20.0 years; interquartile range 17.0-27.0 years) were exposed to isotretinoin, amounting to 244 154 person-years, with a marked seasonality for treatment initiation. Compared with the French general population, the occurrence of suicide attempts under isotretinoin treatment was markedly lower, with a standardized incidence ratio of 0.6 [95% confidence interval (CI) = 0.53-0.67]; the same applied, to a lesser extent, before and after isotretinoin treatment. In the case-time-control analysis, among cases of suicide attempt, 108 and 127 isotretinoin initiations were observed in the risk and control periods respectively (i.e. 0-2 months and 2-4 months before the date of suicide attempt). The comparison with the 1199 and 1253 initiations observed among matched controls in the same two periods yielded a case-time-control odds ratio of 0.89 (95% CI = 0.68-1.16). A sensitivity analysis using three-month periods and a complementary analysis adding completed suicides for case definition showed consistent results. Conclusion: Compared with the general population, a lower risk of suicide attempt was observed among patients exposed to isotretinoin and there was no evidence for a triggering effect of isotretinoin initiation on suicide attempt. A selection of patients at lower risk for suicidal behavior and appropriate treatment management could explain these findings. Risk management plans should therefore be maintained.

Human sebum requires de novo lipogenesis, which is increased in acne vulgaris and suppressed by acetyl-CoA carboxylase inhibition. Esler WP, Tesz GJ, Hellerstein MK, et al. Sci Transl Med. 2019 May 15;11(492). pii: eaau8465. doi: 10.1126/scitranslmed.aau8465. https://www.ncbi.nlm.nih.gov/pubmed/31092695

Sebum plays important physiological roles in human skin. Excess sebum production contributes to the pathogenesis of acne vulgaris, and suppression of sebum production reduces acne incidence and severity. We demonstrate that sebum production in humans depends on local flux through the de novo lipogenesis (DNL) pathway within the sebocyte. About 80 to 85% of sebum palmitate (16:0) and sapienate (16:1n10) were derived from DNL, based on stable isotope labeling, much higher than the contribution of DNL to triglyceride palmitate in circulation (~20%), indicating a minor contribution by nonskin sources to sebum lipids. This dependence on local sebocyte DNL was not recapitulated in two widely used animal models of sebum production, Syrian hamsters and Göttingen minipigs. Confirming the importance of DNL for human sebum production, an acetyl-CoA carboxylase inhibitor, ACCi-1, dose-dependently suppressed DNL and blocked synthesis of fatty acids, triglycerides, and wax esters but not free sterols in human sebocytes in vitro. ACCi-1 dose-dependently suppressed facial sebum excretion by ~50% (placebo adjusted) in human individuals dosed orally for 2 weeks. Sebum triglycerides, wax esters, and free fatty acids were suppressed by ~66%, whereas non-DNL-dependent lipid species, cholesterol, and squalene were not reduced, confirming selective modulation of DNL-dependent lipids. Last, individuals with acne vulgaris exhibited increased sebum production rates relative to individuals with normal skin, with >80% of palmitate and sapienate derived from DNL. These findings highlight the importance of local sebocyte DNL for human skin sebaceous gland biology and illuminate a potentially exploitable therapeutic target for the treatment of acne vulgaris.

Acne treatment with light absorbing gold microparticles and optical pulses: an open-label European multi-centered study in moderate to moderately severe acne vulgaris patients. Fuchs CSK, Bay C, Adatto M, et al. Lasers Surg Med. 2019 May 14. doi: 10.1002/lsm.23099. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31090089

Background and objective: Recently, a novel acne treatment based on selective photothermolysis of pilosebaceous units with follicular delivery of inert gold microparticles as an exogenous chromophore and diode laser pulses has

been developed. To evaluate the efficacy and safety of a single monotherapy treatment regimen with gold microparticles and diode laser exposure in patients with moderate and moderately severe acne. Further, to evaluate the added benefit of a second treatment regimen combined with pharmaceutical acne treatment in patients with inadequate initial response. Materials and methods: Patients with moderate and moderately severe facial acne were recruited in this open-label, pilot study. A single treatment regimen consisted of three weekly facial treatments with topically applied gold microparticles and diode laser pulses. Outcome measures were the proportion of patients with ≥40% improvement in number of acne lesions (weighted lesion count [WLC]) at 12 weeks (single treatment regimen, primary outcome measure), 24, and 36 weeks from baseline (two treatment regimens), safety, and patient satisfaction. Results: A total of 28 patients were enrolled in the study (18 males, 10 females, 19 patients with moderate acne severity, 9 with moderately severe, mean age: 19.8 years). Twenty-five patients underwent analysis for outcome measures. After a single monotherapy treatment regimen, 76% patients (19/25) achieved ≥40% reduction in WLC (mean WLC reduction: 63%; SD: 13%). Of the patients undergoing two treatment regimens (n = 9 patients), 56% experienced a reduction in acne lesion burden (WLC) ≥40% at 24 weeks and 89% 36 weeks post-baseline. Mean pain score was 4.0 (SD: 1.3), and transient erythema and perifollicular edema were commonly noted after treatment. Most patients (81%) were either "satisfied" or "very satisfied" with the treatment. Conclusion: Acne therapy based on selective photothermolysis with gold microparticles shows promise and may be used in treatment of moderate to moderately severe acne.

Clinical Reviews

Fire needle therapy for moderate-severe acne: A PRISMA systematic review and meta-analysis of randomized controlled trials. Xing M, Yan X, Sun X, et al. Complement Ther Med. 2019 Jun;44:253-260. doi: 10.1016/j.ctim.2019.04.009. Epub 2019 Apr 28. https://www.ncbi.nlm.nih.gov/pubmed/31126563

Background: Moderate-severe acne treatment involves the use of isotretinoin and antibiotics as first-line therapeutics; however, these drugs have serious side effects. Fire needle therapy, which is widely used in China, has shown good clinical efficacy for treating moderate-severe acne; moreover, it has fewer side effects, hence, it can be used as a primary treatment (as an alternative to pharmaceutical medications) or in combination with pharmaceutical medications for clinical treatment. However, current clinical evidence regarding its use has not been comprehensively evaluated. Methods: We systematically searched several databases, including PubMed, Embase, Cochrane Central Register of Controlled Trials, China Network Knowledge Infrastructure (CNKI), China Biomedical Literature Service System (SinoMed), China Science and Technology Journal Database (CQVIP), and Wanfang Data Knowledge Service Platform, from their inception time to November 22, 2018. Randomized controlled trials conducted to compare the efficacy, acne recurrence, and adverse events associated with fire needle therapy alone, or in combination with Chinese herbs or conventional pharmaceutical medication, to those of pharmaceutical treatment were selected. RevMan 5.3 software was used to calculate risk ratio (RR) with a 95% confidence interval (CI). Results: Ten trials, with a total of 904 participants, met the inclusion criteria. Meta-analyses showed that fire needle treatment with clindamycin or oral isotretinoin treatment had advantages over pharmaceutical medications alone in the treatment of moderate-severe acne [RR = 2.18, 95% CI (1.19, 3.99), P = 0.03 random model; I2 = 72%]. Moreover, the use of fire needle therapy alone in the treatment of moderate-severe acne had a better effect than pharmaceutical medications, regardless of the type of pharmaceutical medication used [RR = 2.32, 95% CI (1.77, 3.03), P < 0.00001 random model; I2 = 59%]. In terms of recurrence rate, there was no significant difference between fire needle and pharmaceutical medication groups [RR = 0.78, 95% CI (0.54, 1.14), P = 0.20 fixed-effect model; I2 = 0%]. In addition, the use of fire

needles was associated with few adverse reactions, such as burning and tingling; furthermore, the adverse reactions were transient. Conclusion: Fire needle therapy alone or combined with other treatments is effective for moderate-severe acne. However, further large-scale, rigorously designed trials are needed to confirm these findings.

Use of combined fractional carbon dioxide laser and fractional microneedle radiofrequency for the treatment of acne scars: a retrospective analysis of 1-month treatment outcome on scar severity and patient satisfaction. Tatlıparmak A, Aksoy B, Shishehgarkhaneh LR, et al. J Cosmet Dermatol. 2019 May 29. doi: 10.1111/jocd.13004. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31141299

Background: Acne scars lead to social and psychological problems for patients, and they should be treated effectively. Ablative and nonablative lasers have been used for the treatment of acne scars in recent years. Aims: The aim of this study was to evaluate the effectivity of combined FCL and FmRF treatment for acne scars retrospectively. Methods: A total of 72 patients with acne scars who received FCL + FmRF treatment between 2014 and 2016 were included in this study. Photographs of patients before treatment and 1 month following the last treatment session were scored by two blinded researchers, according to the ECCA acne scar scoring method. Patients were contacted via telephone after 1 month following the last treatment and asked to evaluate their satisfaction with the treatment outcome using a 5-point Likert-type scale. Results: A significant decrease was noted in ECCA scores after the treatment along with temporary side effects. Change from pretreatment scores was significantly higher in patients very satisfied vs satisfied with treatment. The number of treatment sessions was positively correlated with treatment-related change in ECCA scores. Conclusions: In conclusion, our findings revealed association of FCL + FmRF treatment with significantly improved ECCA scores, mild pain experience, and low rate of side effects in patients with acne scars, despite usage of high-energy FLC dose and five sessions of treatment on average. More remarkable improvement in ECCA scores during treatment seems to be associated with higher patient satisfaction and to be more likely in patients with darker skin types.

Rosacea associated with dupilumab therapy. Heibel HD, Hendricks AJ, Foshee JP, Shi VY. J Dermatolog Treat. 2019 May 28:1-12. doi: 10.1080/09546634.2019.1624683. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31132923

Background: Dupilumab is used for treatment of atopic dermatitis through blockade of IL-4 and IL-13 signaling of the Th2 pathway. Recent case reports have described alopecia, psoriasis, persistent facial dermatitis, and recall dermatitis at patch test sites after the initiation of dupilumab therapy. Case report: We describe the case of a 67-year-old female with atopic dermatitis who developed recurrent episodic flares of rosacea temporally associated with dupilumab injections that resolved after dupilumab discontinuation. Conclusion: The cause of rosacea-like reaction associated with dupilumab treatment is unknown. Th2 pathway inhibition by dupilumab may promote Demodex proliferation and increased IL-17-mediated inflammation implicated in the pathophysiology of rosacea.

Non-invasive objective skin measurement methods for rosacea assessment: a systematic review. Logger JGM, de Vries FMC, van Erp PEJ, et al. Br J Dermatol. 2019 May 23. doi: 10.1111/bjd.18151. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31120136

Background: Rosacea assessment and therapy monitoring can be challenging to standardize, as most clinical evaluation systems are prone to interobserver variability and not always validated. Objective, reliable and preferably non-invasive measurement tools are therefore needed. Objectives: To give insight into available non-invasive

imaging techniques and biophysical methods in rosacea by performing a systematic review. Methods: PubMed, EMBASE, Cochrane and Web of Science databases were searched until 1 September 2018 in accordance with PRISMA guidelines, identifying studies providing original data about objective non-invasive imaging and/or biophysical skin measurement techniques for diagnosis, assessing severity or therapy monitoring of adult patients with cutaneous facial rosacea. Risk of bias of included articles was assessed with the Cochrane Risk of Bias tool, Newcastle Ottawa Scale and Quality in Prognosis Studies tool. Results: A total of 78 studies was included, describing 14 imaging and biophysical methods. Widespread information about (sub)surface cutaneous morphology and functionality was obtained. Methodological study quality was relatively low and interstudy outcome variability was large. Several tools show promising value in research settings; for treatment follow-up, Demodex mites are countable with reflectance confocal microscopy, spectrometry can quantify erythema, and rosacea severity could be objectified with skin hydration and transepidermal water loss measurements. Conclusions: This systematic review describes the spectrum of non-invasive imaging and biophysical methods in rosacea assessment, giving multifaceted information about structure and properties of rosacea skin, especially useful for research purposes. Larger studies with good methodological quality are needed to create validated protocols for further implementation into research.

Download Reference Document

Staphylococcus epidermidis: a potential new player in the physiopathology of acne? Claudel JP, Auffret N, Leccia MT, et al. Dermatology. 2019 May 21:1-8. doi: 10.1159/000499858. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31112983

Background: Cutibacterium acnes has been identified as one of the main triggers of acne. However, increasing knowledge of the human skin microbiome raises questions about the role of other skin commensals, such as Staphylococcus epidermidis, in the physiopathology of this skin disease. Summary: This review provides an overview of current knowledge of the potential role of S. epidermidis in the physiopathology of acne. Recent research indicates that acne might be the result of an unbalanced equilibrium between C. acnes and S. epidermidis,according to dedicated interactions. Current treatments act on C. acnesonly. Other treatment options may be considered, such as probiotics derived from S. epidermidis to restore the naturally balanced microbiota or through targeting the regulation of the host's AMP mediators. Key Messages: Research seems to confirm the beneficial role of S. epidermidis in acne by limiting C. acnes over-colonisation and inflammation.

Dermatology Reference Document

Non-pharmacologic approaches for hidradenitis suppurativa - a systematic review. Hendricks AJ, Hirt PA, Sekhon S, et al. J Dermatolog Treat. 2019 May 20:1-30. doi: 10.1080/09546634.2019.1621981. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31106609

Importance: Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition presenting with painful nodules and sinus tracts primarily in intertriginous regions. The persistent nature of HS and challenges in symptom management lead many patients to seek non-pharmacologic approaches due to the paucity and limited efficacy of conventional HS therapeutic options. Objective: To evaluate existing evidence for non-pharmacologic modalities in treatment of HS. Findings: Discussed in this review are non-pharmacologic modalities with evidence of efficacy in HS treatment, including weight loss, vitamin B12, vitamin D and zinc supplementation, and dietary avoidance of brewer's yeast. Limitations of the available data on non-pharmacologic therapies in HS include the predominance of pilot and single-armed studies, as well as heterogeneity in study design, subject disease severity, concomitant

treatment and comorbid conditions. Conclusions and relevance: HS patients are becoming increasingly interested in the use of non-pharmacologic approaches to augment conventional treatments. Strength of evidence for non-pharmacologic therapies in HS is limited by small study size and lack of randomized controlled trials. Future large-scale investigations should be pursued to better establish efficacy and dosing regimens for the use of non-pharmacologic treatments in HS.

Combined treatment of recalcitrant papulopustular rosacea involving pulsed dye laser and fractional microneedling radiofrequency with low-dose isotretinoin. Kwon HH, Jung JY, Lee WY, et al. J Cosmet Dermatol. 2019 May 18. doi: 10.1111/jocd.12982. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31102325

Background: While a considerable number of cases with papulopustular rosacea (PPR) are resistant to conventional medications, therapeutic regimens are not currently established. Pulsed dye laser (PDL) and fractional microneedling radiofrequency (FMR) have previously demonstrated satisfactory results for anti-angiogenesis, anti-inflammation, and dermal remodeling. Aims: To evaluate the efficacy and safety of novel combination regimen with low-dose oral isotretinoin, PDL, and FMR in the treatment of recalcitrant PPR. Patients and methods: A retrospective study was undertaken for recalcitrant PPR patients to evaluate the clinical course of novel combination regimen. Twenty-five PPR patients who had failed in previous first-line therapies were enrolled. They were treated with three sessions of PDL and FMR consecutively at 4-week intervals, maintaining daily oral administration of 10 mg isotretinoin for 8 weeks. Objective assessments, erythema index measurement, and patients' subjective satisfaction were evaluated at each visit and 16 weeks after the final treatment. Results: At the final follow-up visit, the number of papules and pustules decreased by 71%, and erythema index by 54% compared with baseline ($P < 0.05$ for both). Physician's global assessment based on rosacea severity score and patients' subjective assessments paralleled with these results. No serious side effect was observed during whole study periods. Conclusion: This novel combination regimen demonstrated satisfactory efficacy with reasonable safety profiles for the treatment of recalcitrant PPR.

Propionibacterium acnes and acne vulgaris: new insights from the integration of population genetic, multi-omic, biochemical and host-microbe studies. McLaughlin J, Watterson S, Layton AM, et al. Microorganisms. 2019 May 13;7(5). pii: E128. doi: 10.3390/microorganisms7050128. https://www.ncbi.nlm.nih.gov/pubmed/31086023

The anaerobic bacterium Propionibacterium acnes is believed to play an important role in the pathophysiology of the common skin disease acne vulgaris. Over the last 10 years our understanding of the taxonomic and intraspecies diversity of this bacterium has increased tremendously, and with it the realization that particular strains are associated with skin health while others appear related to disease. This extensive review will cover our current knowledge regarding the association of P. acnes phylogroups, clonal complexes and sequence types with acne vulgaris based on multilocus sequence typing of isolates, and direct ribotyping of the P. acnes strain population in skin microbiome samples based on 16S rDNA metagenomic data. We will also consider how multi-omic and biochemical studies have facilitated our understanding of P. acnes pathogenicity and interactions with the host, thus providing insights into why certain lineages appear to have a heightened capacity to contribute to acne vulgaris development, while others are positively associated with skin health. We conclude with a discussion of new therapeutic strategies that are currently under investigation for acne vulgaris, including vaccination, and consider the potential of these treatments to also perturb beneficial lineages of P. acnes on the skin.

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An integrated approach to unravel hidradenitis suppurativa etiopathogenesis. Tricarico PM, Boniotto M, Genovese G, et al. Front Immunol. 2019 Apr 25;10:892. doi: 10.3389/fimmu.2019.00892. eCollection 2019. https://www.ncbi.nlm.nih.gov/pubmed/31105704

Hidradenitis suppurativa/acne inversa (HS) is a chronic inflammatory disease involving hair follicles that presents with painful nodules, abscesses, fistulae, and hypertrophic scars, typically occurring in apocrine gland bearing skin. Establishing a diagnosis of HS may take up to 7 years after disease onset. HS severely impairs the quality of life of patients and its high frequency causes significant costs for health care system. HS patients have an increased risk of developing associated diseases, such as inflammatory bowel diseases and spondyloarthropathies, thereby suggesting a common pathophysiological mechanism. Familial cases, which are around 35% of HS patients, have allowed the identification of susceptibility genes. HS is perceived as a complex disease where environmental factors trigger chronic inflammation in the skin of genetically predisposed individuals. Despite the efforts made to understand HS etiopathogenesis, the exact mechanisms at the basis of the disease need to be still unraveled. In this review, we considered all OMICs studies performed on HS and observed that OMICs contribution in the context of HS appeared as not clear enough and/or rich of useful clinical information. Indeed, most studies focused only on one aspect-genome, transcriptome, or proteome-of the disease, enrolling small numbers of patients. This is quite limiting for the genetic studies, from different geographical areas and looking at a few aspects of HS pathogenesis without any integration of the findings obtained or a comparison among different studies. A strong need for an integrated approach using OMICs tools is required to discover novel actors involved in HS etiopathogenesis. Moreover, we suggest the constitution of consortia to enroll a higher number of patients to be analyzed following common and consensus OMICs strategies. Comparison and integration with the findings present in the OMICs repositories are mandatory. In a theoretic pipeline, the Skin-OMICs profile obtained from each HS patient should be compared and integrated with repositories and literature data by using appropriate InterOMICs approach. The final goal is not only to improve the knowledge of HS etiopathogenesis but also to provide novel tools to the clinicians with the eventual aim of offering a tailored treatment for HS patients.

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Development of periungual pyogenic granuloma with associated paronychia following isotretinoin therapy: a case report and a review of the literature. Benedetto C, Crasto D, Ettefagh L, Nami N. J Clin Aesthet Dermatol. 2019 Apr;12(4):32-36. Epub 2019 Apr 1. https://www.ncbi.nlm.nih.gov/pubmed/31119008

The development of periungual pyogenic granulomas while taking the oral acne drug isotretinoin is a known yet uncommon and potentially severe side effect of the oral vitamin A derivative. Previous reports have detailed the development of pyogenic granulomas most commonly arising at sites of previous acne lesions as well as both subungual and periungual locations, with associated paronychia, bleeding, and discomfort. This is thought to arise as a result of the nail bed's fragility and propensity toward spicule formation brought on by the proliferative action of isotretinoin. Here, we report a case of periungual pyogenic granuloma with associated paronychia in a patient taking oral isotretinoin. A review of the pathogenesis and available treatment modalities based on the current literature is provided.

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