AARS HOT TOPICS MEMBER NEWSLETTER

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Industry News

Almirall, LLC is the new name of Aqua. DermWire, Practical Dermatology. Tuesday, October 23, 2018. http://practicaldermatology.com/dermwire/2018/10/23/aqua-is-now-almirall

Almirall, LLC is the new name of Aqua Pharmaceuticals. Almirall, LLC is part of the larger Almirall, S.A. family, an internationally-recognized global dermatology pharmaceutical company, with a strong focus on skin health. The name change, was announced jointly by Almirall LLC President and General Manager, Ron Menezes and Almirall, S.A. CEO, Peter Guenter. "Almirall acquired Aqua at the end of 2013 and both companies have long shared the vision of improving skin health conditions through scientific advances. It was a natural progression for Aqua to assume the Almirall name in the U.S.," explains Menezes. "We want to continue to explore new therapies in dermatology in order to grow and provide new solutions to healthcare professionals and patients." Guenter adds, "Without question, Aqua established a strong presence in dermatology in the U.S. through delivering quality products and offering effective solutions to dermatologists and their patients. Similarly, Almirall has created a global reputation as a provider of significant medical advances to patients and a commitment to medical dermatology that was shown in the recent acquisition of key brands from the Allergan portfolio. By bringing Aqua under the Almirall name, we are offering healthcare providers and their patients greater and more cohesive support, aligned with our shared resources and innovation in the U.S., as well as globally." Almirall LLC is launching the campaign "We're all in, we're Almirall," which the company says speaks to its deep commitment to dermatology. With nearly 14% of sales revenue being invested into research and development by Almirall S.A. in 2017 the company trusts that they are in a strong position to achieve their goal of being a leader of innovation in medical dermatology.

Aclaris acquires Rhofade from Allergan. DermWire, Practical Dermatology. Wednesday, October 17, 2018. http://practicaldermatology.com/dermwire/2018/10/17/aclaris-acquires-rhofade-from-allergan

Aclaris Therapeutics, Inc. has entered into a definitive asset purchase agreement with Allergan Sales, LLC to acquire worldwide rights to Rhofade® (oxymetazoline hydrochloride) cream, 1% and additional intellectual property. The acquisition includes an exclusive license to certain intellectual property for Rhofade, which is approved for the topical treatment of persistent facial erythema associated with rosacea in adults. This transaction, which is subject to customary closing conditions, including certain governmental regulatory clearances, is expected to close in the fourth quarter of 2018. Allergan has agreed to provide support to Aclaris to allow for a smooth transition of Rhofade. Under the terms of the agreement, the purchase price includes an upfront cash payment of $65 million due at closing, a development milestone payment related to the potential development of an additional dermatology product, and tiered royalties on net sales. Allergan developed and brought Rhofade to market in 2017 after acquiring the drug as part of its 2011 acquisition of Vicept Therapeutics, Inc., a company established by certain members of the current senior management team of Aclaris. “We are excited to acquire Rhofade. Our team is very familiar with the asset and the market opportunity,” says Neal Walker, DO, President and Chief Executive Officer of Aclaris. “It is a rare opportunity to acquire an asset which was on a good trajectory with this level of initial launch activities completed.”

Study: Positive safety and tolerability results for Ortho Dermatologics' Altreno for acne. DermWire, Practical Dermatology. Thursday, October 11, 2018. http://practicaldermatology.com/dermwire/2018/10/11/study-positive-results-for-ortho-dermatologics-altrenos-safety-and-tolerability-for-acne

Ortho Dermatologics shared results of two identical Phase 3, multicenter, randomized, double-blind, vehicle-controlled, parallel group studies examining the efficacy and safety of Altreno (tretinoin) Lotion, 0.05%, the first formulation of tretinoin, a retinoid, in a lotion indicated for the topical treatment of acne vulgaris in patients 9 years of age and older. The FDA approved the New Drug Application for Altreno Lotion on Aug. 24, 2018. In the studies, Altreno Lotion was shown to have significantly greater efficacy compared to vehicle in achieving treatment success, which was defined as at least a two-grade improvement from baseline in a global severity by Evaluator Global Severity Score (EGSS) and 'clear' or 'almost clear' skin. By week 12, 17.7 percent of Altreno Lotion patients had achieved treatment success, compared to 9.3 percent of patients receiving vehicle. Altreno Lotion also demonstrated statistically significant reductions in both inflammatory and noninflammatory lesion counts (both P<.001) at week 12 compared to vehicle (52.1 percent versus 41.0 percent for inflammatory lesion counts and 46.1 percent versus 29.9 percent in noninflammatory lesion counts). The most common adverse reactions were application site pain (3.1 percent), dryness (3.7 percent) and erythema (1.4 percent). Altreno Lotion was found to be generally well-tolerated among treatment groups. "Extensive clinical data have shown that topical retinoids are highly effective in acne and are recommended as the cornerstone of topical therapy; however, retinoids are perceived to have limited efficacy in inflammatory acne and that tolerability issues are barriers to their use. The results from the two Phase 3 clinical trials demonstrated that Altreno can provide physicians and their patients a new treatment option that significantly reduces inflammatory and noninflammatory acne lesions along with a favorable tolerability profile," says Sabrina Fabi, MD, a dermatologist and dermatologic cosmetic surgeon from Cosmetic Laser Dermatology, San Diego, and assistant clinical professor, University of California, San Diego. Patient satisfaction was also shown to be significantly greater with Altreno Lotion compared to vehicle, increasing from baseline to week 12 by 53 percent compared to 43 percent with vehicle (P<.001), and with nine out of 10 patients reporting satisfaction with their treatment. Patient satisfaction was measured using the acne-specific quality of life (Acne-QoL) questionnaire. The 19-item Acne-QoL is a validated psychometric instrument designed for use in clinical trials. "Helping to make a difference in the lives of people living with skin conditions, such as acne, is the driving force behind our work at Ortho Dermatologics," says Bill Humphries, president, Ortho Dermatologics. "We believe these new data further demonstrate the value that Altreno Lotion provides patients with acne vulgaris, and we look forward to bringing the product to market by the end of the month."

New Medical News

Effectiveness and safety of acne scar treatment with nonanimal stabilized hyaluronic acid gel. Dierickx C, Larsson MK, Blomster S. Dermatol Surg. 2018 Nov;44 Suppl 1:S10-S18. doi: 10.1097/DSS.0000000000001689. https://www.ncbi.nlm.nih.gov/pubmed/30358630

Background: Acne scarring affects most patients with acne and have a negative impact on quality of life. New effective treatment options offering minimal downtime are therefore needed. Objective: To evaluate improvement in overall facial appearance after hyaluronic acid (HA) treatment of atrophic acne scars. Methods: Twelve subjects with moderate-to-severe acne scars were treated at 3 sessions 4 weeks apart. At each session, up to 2-mL HA gel was injected into each side of the face. Acne scar severity, global facial aesthetic improvement, and subject satisfaction were assessed up to 36 weeks after treatment. Safety assessments included subject diaries and adverse events.

Results: The overall facial appearance and the appearance of atrophic acne scars improved after treatment. Scar severity and subject satisfaction with the overall facial appearance and with the sensation and perception of the skin improved in most subjects. Subjects' self-esteem and self-confidence also improved. Adverse events were typically mild to moderate, expected, and procedure-related. Conclusion: Hyaluronic acid gel injections were effective and safe for treatment of moderate-to-severe atrophic acne scars. The treatment effect developed gradually over time with the highest improvement observed at the end of the study.

Comparison of efficacy and safety of topical 1% nadifloxacin and tretinoin 0.025% combination therapy with 1% clindamycin and tretinoin 0.025% combination therapy in patients of mild-to-moderate acne. Deshmukh SN, Badar VA, Mahajan MM, et al. Perspect Clin Res. 2018 Oct-Dec;9(4):161-164. doi: 10.4103/picr.PICR_109_17. https://www.ncbi.nlm.nih.gov/pubmed/30319945

Background: Topical retinoids in combination with antimicrobials have been proven to reduce acne lesions faster and to a greater degree than antimicrobial therapy alone. Aims and objectives: To compare the efficacy and safety of topical combination of 1% Nadifloxacin [NAD] and 0.025% Tretinoin [Tr] with 1% Clindamycin [CLN] and 0.025% Tr in patients of mild to moderate acne vulgaris of the face. Material and methods: There were two groups (40 patients in each group): Group A received (NAD+Tr) combination therapy and group B received (CLN+Tr) combination therapy. Efficacy was assessed by any reduction in the mean number of inflammatory lesions(IL), non-inflammatory lesions(NIL) and/or total lesions(TL) as well as by using Evaluator's Global Severity Scale (EGSS) of acne and safety was assessed by adverse effects of study medications at 0, 6 and at 12 weeks follow-up. Results: Both the study groups showed statistically significant intragroup reduction in NIL, IL and TL after 12 weeks of therapy. There was no statistically significant reduction at the end of 6 weeks of therapy in both the groups. At the end of 12 weeks of therapy there was a statistically significant reduction in IL, NIL and TL in group A. There was no statistically significant difference in the occurrence of adverse effects in both the groups. Conclusion: Overall the study proved better efficacy of NAD+Tr compared to CLN+Tr. Medications of both the groups were safe and well tolerated.

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Adolescent-onset hidradenitis suppurativa: Prevalence, risk factors and disease features. Molina-Leyva A, Cuenca-Barrales C. Dermatology. 2018 Oct 26:1-6. doi: 10.1159/000493465. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30368494

Background/aims: Hidradenitis suppurativa (HS) is a chronic inflammatory and destructive skin disorder. Early diagnosis and treatment are critical to stop its progression. Data concerning adolescent-onset HS are scarce. The aims of this study are to describe the prevalence of adolescent-onset HS and to explore potential risk factors and the disease features of these patients. Patients and methods: A cross-sectional study including 134 patients was performed. Results: Adolescent-onset HS occurred in 51.5% (69/134) of patients. Adolescent-onset HS was associated with female sex, positive family history, presence of pilonidal sinus, acne conglobata, longer disease duration and a worse perception of disease severity. Conclusion: Adolescent-onset HS might be more frequent than previously reported. Female sex, positive family history and the presence of elements of the follicular occlusion tetrad identify individuals with a higher risk of early onset. These patients experience a longer disease duration and perceive their disease as severer.

Evaluation of the safety and efficacy of the dual wavelength picosecond laser for the treatment of benign pigmented lesions in Asians. Kung KY, Shek SY, Yeung CK, Chan HH. Lasers Surg Med. 2018 Oct 25. doi: 10.1002/lsm.23028. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30357871

Background and objectives: Cutaneous pigmentary disorders are both more common and more difficult to treat in patients with skin color given the higher melanin content in the epidermis. Although Q-switched lasers are widely considered to be the standard treatment for both epidermal and dermal pigmentary conditions, a very high risk of post-inflammatory hyperpigmentation (PIH) of up to 25% is seen in patients with skin of color. Recently, the novel picosecond laser with pulse durations operating at sub-nanosecond domains has been shown to be effective in tattoo removal and in the treatment of acne scars. The objective of this study is to examine the safety and efficacy of the dual wavelength picosecond laser for the treatment of benign pigmented skin lesions in Asian patients. Methods: Twelve subjects with benign pigmentary disorders and Fitzpatrick skin types III to IV were recruited in a prospective clinical study to examine the safety and efficacy of the dual wavelength picosecond laser. Patients were treated at approximately 2-6 week intervals depending of the type of lesion. The primary efficacy endpoint is the global percent of clearance which was evaluated by blinded observers using post treatment photographs compared to baseline photographs. Safety was evaluated before and after each laser treatment and patients were asked to rate the level of pain according to the Visual Analog Scale after each treatment session. Patient satisfaction was assessed at the completion of treatment with questionnaires. All patients were followed up at 4, 8, and 12 weeks after the last treatment session. Results: The pigmentary conditions treated included melasma, freckles, lentiginies, café au lait macules, and Hori's macules. Three months after treatment, 53.8% of all pigments achieved excellent response (75-94% lightening,) 30.8% of pigments achieved good response (50-74% lightening,) and 7.7% of pigments achieved both fair (25-49% lightening) and poor responses (0-24% lightening), respectively. The average number of treatment sessions required to reach at least 50% clearance was 4.5 for melasma, 1 for freckles, 1.5 for lentigines and 1 for café au lait. The patient with Hori's macules did not reach 50% clearance after a total of six treatments. Sixty three percent of patients reported satisfaction in the subjective assessment, while 27.3% were neutral and 9.1% were very dissatisfied. The post inflammatory hyperpigmentation rate was 4.8% and 6.5% of subjects developed blistering as a side effect of treatment. Conclusion: The dual wavelength picosecond laser is a safe and effective treatment of benign pigmentary conditions in patients with skin of color. In particular, superior clinical efficacy is demonstrated for treatment of freckles and lentigines with a low risk of PIH.

Effects of isotretinoin on the hair cycle. İslamoğlu ZGK, Altınyazar HC. J Cosmet Dermatol. 2018 Oct 23. doi: 10.1111/jocd.12800. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30350907

Background/ objectives: Isotretinoin is a synthetic vitamin A agent that affects all of the pathogenic factors that suppress sebum production and play a role in the formation of acne. It is frequently used in the treatment of moderate-severe acne vulgaris. However, there are some mucocutaneous and systemic side effects that limit the use of isotretinoin. In this study, we aimed to determine the effect of isotretinoin on hair growth parameters. Material and methods: Isotretinoin treatment at 0.5 mg/kg per day dose was started to patients with moderate-severe acne vulgaris, and hair growth parameters were evaluated before treatment and after 3 months of treatment. Parameters were measured by Fotofinder dermatoscopy device using the TrichoScan Professional program. Results: In the TrichoScan analysis, the total hair count, hair density, percentage of anagen and telogen hair, density, count, and ratio of vellus and terminal hairs in the 0.73 area were calculated. As a result, there were differences in some values between the first analysis and the second analysis. However, these differences were not statistically significant. Conclusion: Our study was based on the mucocutaneous side effects of isotretinoin which are telogen effluvium and

thinning hair. Our results support that the drug does not alter hair growth parameters in the short term and when very high doses are not used.

Highly efficient and biocompatible nanoparticle-based photosensitizer for treatment of acne vulgaris. Wang P, Tang H, Zhang P. Nanomedicine (Lond). 2018 Oct 19. doi: 10.2217/nnm-2018-0125. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/30338704

Aim: Nanoparticle-based photosensitizers containing silver core and mesoporous silica shell with hematoporphyrin IX embedded were developed to treat vulgaris photodynamically. Materials & methods: The hybrid photosensitizers were dispersed in 30% polyethylene glycol (PEG-200) solution and used for the photodynamic treatment of Staph epidermidis and Propionibacterium acnes under the illumination of a portable LED (~410 nm). Results: After a 5 min illumination by the LED, the hybrid photosensitizers of 50 µg/ml displayed killing efficacy of approximately 5-log for S. epidermidis and approximately 4-log for P. acnes. Results indicated that hybrid photosensitizers in PEG-200 matrix perform better than in deionized (DI) water (~1-log increase in killing efficacy). Conclusion: Under short illumination of a portable LED, hybrid photosensitizers demonstrated immense potential for treatment of acne vulgaris without involving antibiotics.

Outcome of pedicled thoracodorsal artery perforator flap in the surgical treatment of stage II and III hidradenitis suppurativa of axilla. Elgohary H, Nawar AM, Zidan A, et al. Ann Plast Surg. 2018 Oct 15. doi: 10.1097/SAP.0000000000001658. [Epub ahead of print]. https://www.ncbi.nlm.nih.gov/pubmed/30325840

Background: Hidradenitis suppurativa (HS) is a chronic, inflammatory disease affecting the apocrine glands of the axillary, groin, and mammary regions with significant physical and psychosocial sequelae. Surgical excision of the affected tissue is the criterion standard treatment. Advanced cases of axillary HS are associated with high rates of recurrence and require extensive surgical resection with challenging reconstruction associated with risk of postoperative complications. The most effective method for reconstruction of the axilla after excision of HS is yet to be identified. Objectives: The aim of the study was to evaluate the results of the use of pedicled thoracodorsal artery perforator (TDAP) flap as a method of reconstruction for axillary effect result from wide surgical excision as a line of treatment for stage II and III HS of the axilla. Patient and methods: The study included 20 patients with stage II and III (Hurley staging system) HS of the axilla, 18 male and 2 women treated by wide local excision and reconstruction by rotational TDAP flap. At the end of follow-up, outcome is judged by complete remission of disease, comparing preoperative shoulder function (using Constant-Murley shoulder outcome score), and quality of life (using dermatology life quality index) with postoperative results after 1 year, plus durability of reconstruction, donor site morbidity, overall aesthetic outcome, and patient's satisfaction. Results: The mean ± SD follow-up period was 30 ± 5.2 months (range = 12-60 months). Four patients (20%) were treated for their right side, 8 patients (40%) for their left side, and 8 patients (40%) were treated bilaterally, so we perform 28 operations for 20 patients. The treated patients with stage II disease were 16 (57.14%) and with stage III disease were 12 (42.85%). The size of the defects was usually approximately 10 × 15 cm. By the end of follow-up period, all patient showed complete remission of the disease with improvement in both shoulder function and quality of life, whereas 1 flap (3.57%) was complicated by bleeding treated by reoperation, 2 flaps (7.14%) complicated by wound infection that was treated conservatively, 3 other flaps (10.71%) showed wide scare at insight of the flaps, and 1 flap (3.57%) developed hypertrophic scare at donor site of the flap. Conclusions: Surgical treatment of stage II and III HS of axilla and reconstruction by rotational TDAP flap provides good aesthetic and functional results with 100% success rate in eradicating and complete remission of the disease during follow-up period and accepted complication rate.

Effects of combined oral doxycycline and topical cyclosporine treatment on ocular signs, symptoms, and tear film parameters in rosacea patients. Bilgin B, Karadag AS. Arq Bras Oftalmol. 2018 Oct 8. pii: S0004-27492018005002101. doi: 10.5935/0004-2749.20180093. [Epub ahead of print]. https://www.ncbi.nlm.nih.gov/pubmed/30304088

Purpose: This study reports the effects of combined use of oral doxycycline and topical cyclosporine on ocular signs, symptoms, and tear film parameters in rosacea patients. Methods: Fifty-four right eyes of 54 patients were included in this study. All patients underwent full ophthalmologic examination-including best corrected visual acuity measurement, slit-lamp anterior segment and fundus examination, tear film break-up time, and Schirmer test-before treatment and six months post-treatment. Patients were divided into two treatment groups. The first group was treated with oral doxycycline 100 mg twice daily for the first month and once daily for the following two months. The second group received topical 0.05% cyclosporine emulsion drops twice daily for six months in addition to the oral doxycycline treatment regimen. All patients received preservative -free artificial tear drops, warm compress, eyelash cleaning, and topical corticosteroid drops three times daily for one month. Results: A significant improvement in ocular signs and symptoms was recorded for all patients in groups 1 and 2 after treatment. There was not a significant difference in terms of itching, burning, meibomian gland inspissation, corneal neovascularization, and conjunctival hyperemia score changes between groups 1 and 2. The increases in Schirmer test and break-up time scores were significantly higher in group 2 than in group 1. Conclusions: Our results support the finding that topical cyclosporine in addition to the standard regimen improves tear function, as shown by Schirmer test and break-up time scores, in ocular rosacea patients.

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Treatment of moderate acne vulgaris in Fitzpatrick Skin Type V or VI: Efficacy and tolerability of fixed combination clindamycin phosphate 1.2%/benzoyl peroxide 3.75% gel. Amar L, Kircik LH. J Drugs Dermatol. 2018 Oct 1;17(10):1107-1112. https://www.ncbi.nlm.nih.gov/pubmed/30365592

Background: Acne vulgaris (acne) is the most common skin disease in patients who have darker skin with most frequent sequelae of post inflammatory hyperpigmentation (PIH). Methods: Open label study in 20 patients (mean age 32 years) with Fitzpatrick Skin Type V or VI and with moderate facial acne treated with clindamycin phosphate 1.2%/benzoyl peroxide 3.75% gel (CL-BP 3.75%) once-daily for 16 weeks. Assessments included improvement in Investigator Global Assessment (IGA) of acne severity, PIH severity and distribution, and lesion count reduction. Adverse events (AEs) were assessed throughout. Results: Significant reductions in inflammatory, noninflammatory and total lesions occurred within the first 4 weeks compared to baseline. At week 16, percent changes from baseline were 76%, 62%, and 71%, respectively (all P less than equal to .0002). There was also a significant reduction in IGA to week 16 (P equals.0001); 70% (N=14) of patients were 'clear' or 'almost clear' and all patients experienced at least a 1-grade improvement in IGA. Additionally, PIH severity and distribution were also significantly reduced by week 16. In 40% of patients PIH severity was rated as 'none' or 'slight'; 19 (95%) and 15 (75%) of patients experienced at least a 1-grade improvement in PIH severity or distribution. Ten patients experienced a total of 21 AEs. There were no serious AEs. Only one AE was possibly related to study drug (facial tattoo tightening) and resolved with no residual effects at the end of the study. Conclusions: Patients with Fitzpatrick Skin Type V and VI treated with clindamycin phosphate 1.2%/ benzoyl peroxide 3.75% gel experienced significant reductions in facial acne severity, lesion counts and PIH severity/distribution. Tolerability was excellent.

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Novel tretinoin 0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris: Assessment of efficacy and safety in patients aged 9 years and older. Tyring SK, Kircik LH, Pariser DM, et al. J Drugs Dermatol. 2018 Oct 1;17(10):1084-1091. https://www.ncbi.nlm.nih.gov/pubmed/30365589

Background: Topical tretinoin has been extensively studied in clinical trials, and its essential role in the treatment of acne vulgaris (acne) established through evidence-based guidelines. Objective: To evaluate efficacy, safety, and tolerability of a novel tretinoin 0.05% lotion in moderate-to-severe acne in patients aged 9 years and older. Methods: A total of 1640 patients, 9-58 years of age were randomized to receive tretinoin 0.05% lotion or vehicle in two double-blind, placebo-controlled 12-week, 2-arm, parallel group studies evaluating safety and efficacy (inflammatory and noninflammatory lesion counts and acne severity using Evaluator Global Severity Scores [EGSS]). In addition, patients completed a patient satisfaction survey (PSS), Acne-specific quality of life (QoL) questionnaire and assessed their facial skin for shininess/oiliness improvement. The data from these two independent studies were pooled and analyzed. Results: Tretinoin 0.05% lotion demonstrated statistically significant superiority to vehicle in reducing inflammatory and noninflammatory lesion counts (both P less than .001) at week 12 and improving acne severity (P less than .001). At week 12, mean percent change in inflammatory and noninflammatory lesions were 52% and 46%, respectively. Treatment success (a 2-grade improvement in EGSS and 'clear' or 'almost clear' was reported in 18% of patients. Tretinoin 0.05% lotion also showed significantly greater benefits relative to vehicle control in terms of patient satisfaction (P less than .001) and acne-specific QoL domains. Tretinoin 0.05% lotion was very well tolerated with no substantive differences in cutaneous tolerability among treatment groups. No patients discontinued treatment because of adverse events. Limitations: Data from controlled studies may differ from clinical practice. Conclusions: Tretinoin 0.05% lotion provides statistically significant greater efficacy than vehicle with a highly favorable safety and tolerability profile in moderate-to-severe acne patients.

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Clinical and laboratory characteristics of patients with adolescence acne and acne tarda. Azanbayeva D, Batpenova G, Tarkina T, et al. Georgian Med News. 2018 Sep;(282):103-106. https://www.ncbi.nlm.nih.gov/pubmed/30358551

Acne is a chronic recurrent androgen-mediated disease of the pilosebaceous complex with a multifactorial genetically determined development mechanism. Currently, there is a tendency to persistent course of the disease, resistance to therapy forms of acne, late debut and change the clinical picture of acne. This could be due to various factors, such as polycystic ovary syndrome, microadenoma and pituitary adenoma, congenital adrenal hyperplasia, SAHA syndrome, etc. Objective - to study the degree of incidence of hyperprolactinemia in patients with acne and features of the clinical course of juvenile and late acne with a background of hyperprolactinemia. We conducted a case-control study, which included 267 patients with varying disease severity. All patients underwent clinical and dermatological examination and determination of prolactin level. The study found that hyperprolactinemia, associated and nonassociated with adenoma, or pituitary microadenoma, can act as a primary factor in the development of acne, promote the persistence of the disease, as well as change skin manifestations in the form of an increase in the area of skin lesions with a smaller accumulation of sebaceous follicles and low androgen-sensitivity, such as the lower third of the back. Thus, in the diagnosis of acne vulgaris, it is necessary to evaluate the hormonal profile of patients, in particular prolactin, especially in the presence of a persistent course, a late start, resistant to therapy forms.

TNIP1 regulates cutibacterium acnes-induced innate immune functions in epidermal keratinocytes. Erdei L, Bolla BS, Bozó R, et al. Front Immunol. 2018 Sep 24;9:2155. doi: 10.3389/fimmu.2018.02155. eCollection 2018. https://www.ncbi.nlm.nih.gov/pubmed/30319618

Human skin cells recognize the presence of the skin microbiome through pathogen recognition receptors. Epidermal keratinocytes are known to activate toll-like receptors (TLRs) 2 and 4 in response to the commensal Cutibacterium acnes (C. acnes, formerly known as Propionibacterium acnes) bacterium and subsequently to induce innate immune and inflammatory events. These events may lead to the appearance of macroscopic inflammatory acne lesions in puberty: comedos, papules and, pustules. Healthy skin does not exhibit inflammation or skin lesions, even in the continuous presence of the same microbes. As the molecular mechanism for this duality is still unclear, we aimed to identify factors and mechanisms that control the innate immune response to C. acnes in keratinocytes using a human immortalized keratinocyte cell line, HPV-KER, normal human keratinocytes (NHEK) and an organotypic skin model (OSM). TNIP1, a negative regulator of the NF-κB signaling pathway, was found to be expressed in HPV-KER cells, and its expression was rapidly induced in response to C. acnes treatment, which was confirmed in NHEK cells and OSMs. Expression changes were not dependent on the C. acnes strain. However, we found that the extent of expression was dependent on C. acnes dose. Bacterial-induced changes in TNIP1 expression were regulated by signaling pathways involving NF-κB, p38, MAPKK and JNK. Experimental modification of TNIP1 levels affected constitutive and C. acnes-induced NF-κB promoter activities and subsequent inflammatory cytokine and chemokine mRNA and protein levels. These results suggest an important role for this negative regulator in the control of bacterially induced TLR signaling pathways in keratinocytes. We showed that all-trans retinoic acid (ATRA) induced elevated TNIP1 expression in HPV-KER cells and also in OSMs, where TNIP1 levels increased throughout the epidermis. ATRA also reduced constitutive and bacterium-induced levels of TNFα, CCL5 and TLR2, while simultaneously increasing CXCL8 and TLR4 expression. Based on these findings, we propose that ATRA may exhibit dual effects in acne therapy by both affecting the expression of the negative regulator TNIP1 and attenuating TLR2-induced inflammation. Overall, TNIP1, as a possible regulator of C. acnes-induced innate immune and inflammatory events in keratinocytes, may play important roles in the maintenance of epidermal homeostasis.

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Clinical Reviews

The toxic edge-A novel treatment for refractory erythema and flushing of rosacea. Friedman O, Koren A, Niv R, et al. Lasers Surg Med. 2018 Oct 12. doi: 10.1002/lsm.23023. [Epub ahead of print]. https://www.ncbi.nlm.nih.gov/pubmed/30311683

Purpose: Rosacea is a common, chronic facial skin disease that affects the quality of life. Treatment of facial erythema with intradermal botulinum toxin injection has previously been reported. The primary objective of the study was the safety and efficacy of thermal decomposition of the stratum corneum using a novel non-laser thermomechanical system (Tixel, Novoxel, Israel) to increase skin permeability for Botulinum toxin in the treatment of facial flushing of rosacea. Methods: A retrospective review of16 patients aged 23-45 years with Fitzpatrick Skin Types II to IV and facial erythematotelangiectatic rosacea treated by Tixel followed by topical application of 100 U of abobotulinumtoxin. A standardized high-definition digital camera photographed the patients at baseline and 1, 3, and 6 months after the last treatment. Objective and subjective assessments of the patients were done via Mexameter, the Clinicians Erythema Assessment (CEA), and Patients self-assessment (PSA) scores and the dermatology life quality index (DLQI) validated instrument. Results: The average Maxameter, CEA, and PSA scores at 1, 3, and 6 months were

significantly improved compared with baseline (all had a P-value <0.001). DLQI scores significantly improved with an average score of 18.6 at baseline at 6 months after treatment (P < 0.001). Self-rated patient satisfaction was high. There were no motor function side-effects or drooping. Conclusion: Thermal breakage of the stratum corneum using the device to increase skin permeability for botulinum toxin type A in the treatment of facial flushing of rosacea seems both effective and safe.

Androgens in women: Hormone modulating therapies for skin disease (Part II). Azarchi S, Bienenfeld A, Lo Sicco K, et al. J Am Acad Dermatol. 2018 Oct 9. pii: S0190-9622(18)32673-2. doi: 10.1016/j.jaad.2018.08.061. [Epub ahead of print]. https://www.ncbi.nlm.nih.gov/pubmed/30312645

Androgen-mediated cutaneous disorders (AMCDs) in women including acne, hirsutism, and female pattern hair loss (FPHL) can be treated with hormone-modulating therapies. In the second part of this Continuing Medical Education series, we discuss the hormone-modulating therapies available to dermatologists for the treatment of AMCDs including combined oral contraceptives, spironolactone, finasteride, dutasteride, and flutamide. Available hormone-modulating treatments utilized for each AMCDs are reviewed, along with mechanisms of androgen modulation, safety profile, contraindications, monitoring parameters, and evidence of efficacy. Medications discussed include ones that are FDA-approved for certain AMCDs as well as some that are used off-label. Despite the ubiquity of hormone-modulating therapies used for AMCDs, this review highlights the need for more rigorous studies to evaluate these therapies for acne, hirsutism, and FPHL.

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Predictive role of skin rash in advanced pancreatic cancer patients treated with gemcitabine plus erlotinib: a systematic review and meta-analysis. Zeng M, Feng Q, Lu M, et al. Onco Targets Ther. 2018 Oct 8;11:6633-6646. doi: 10.2147/OTT.S168418. eCollection 2018. https://www.ncbi.nlm.nih.gov/pubmed/30349297

Purpose: The survival benefit from gemcitabine plus erlotinib was on average marginal for advanced pancreatic cancer (APC) patients. Skin rash developed shortly after starting treatment seemed to be associated with better efficacy and might be used to assist clinical decision-making, but the results across studies were inconsistent. Thus, we conducted a systematic review and meta-analysis. Methods: PubMed, Embase, Cochrane Central Register of Controlled Trials, three Chinese databases, and the abstracts of important conferences were searched for eligible studies. The primary outcome was overall survival (OS), and the secondary outcomes were progression-free survival (PFS) and objective response. The random-effects model was used to pool results across studies if heterogeneity was substantial. Otherwise, the fixed-effect model was used. Results: A total of 16 studies with 1,776 patients were included. Patients who developed skin rash during treatment had longer OS (8.9 vs 4.9 months, HR=0.57, 95% CI 0.50-0.64) and longer PFS (4.5 vs 2.4 months, HR=0.53, 95% CI 0.40-0.68) than those who did not. A dose- response relationship was also observed for both OS (HR=0.64 for grade-1 rash vs no rash and HR=0.46 for ≥grade-2 rash vs no rash) and PFS (HR=0.72 for grade-1 rash vs no rash and HR=0.43 for ≥grade-2 rash vs no rash). Conclusion: Skin rash was associated with better OS and PFS in APC patients treated with gemcitabine plus erlotinib. It might be used as a marker for efficacy to guide clinical decision-making toward a more precise and personalized treatment.

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Long-term adalimumab treatment of hidradenitis suppurativa: Results and practical insights from a real-life experience. Bettoli V, Manfredini M, Calamo G, et al. Dermatol Ther. 2018 Oct 8:e12737. doi: 10.1111/dth.12737. [Epub ahead of print]. https://www.ncbi.nlm.nih.gov/pubmed/30295378

Data on the long-term management of patient receiving adalimumab for hidradenitis suppurativa (HS) are scarce and mainly derived from the period 2 of the PIONEER studies (Alexa B Kimball et al. 2016; Theut Riis, Thorlacius, and Jemec 2018; Alexa B Kimball et al. 2012). The aim of our retrospective study was to review epidemiological data and analyze the therapeutic response, adverse effects, duration, and reasons of short suspension periods (SSP) during long-term anti-TNFα therapy, in a real-life setting. The medical records of HS patients receiving adalimumab therapy at the O.U. of Dermatology of the University of Ferrara were reviewed from January 2015 to February 2018. Modified Sartorius score (mSS), International HS Severity-Score System (IHS4) and HiSCR50 were considered (A B Kimball et al. 2014; Giamarellos-Bourboulis et al. 2017; Zouboulis et al. 2017; Sartorius et al. 2009). Every suspension ≤6 weeks from the standard adalimumab administration schedule was considered SSP. Student t-test, Pearson's r and linear regression of mSS and IHS4 numerical scores were calculated (Prism 6.0, Graph- Pad Software, Inc., CA). Pearson's r was considered sufficient (≥0.4, <0.6), good (≥0.6, <0.8) or excellent (≥0.8).

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The utility of understanding atrophic acne scar formation for prevention and treatment. Wang JV, Saedi N. Br J Dermatol. 2018 Oct;179(4):819. doi: 10.1111/bjd.17020. https://www.ncbi.nlm.nih.gov/pubmed/30318805

This issue of the BJD contains a thorough examination of the immunological processes behind atrophic scar formation in patients with acne. Acne is a very common skin condition that affects a large population of patients. In those who ultimately develop scars, the psychological and social impact can be immense, especially for patients in their formative teenage years. The treatment of acne and scars can sometimes be quite difficult. Even with the most innovative scar treatment techniques, outcomes may be less than ideal and the cost can be a barrier for many. Although a previous study in the literature had examined the inflammatory response of patients with scar-prone acne, Carlavan et al. have compared these lesions over a 3-week period in order to offer more comprehensive evidence. This study shows that the inflammatory response of acneiform lesions in those prone to scars differs significantly from that of patients not prone to scars. In general, the inflammation is stronger, more robust and more durable in patients with scar-prone acne. Perhaps this can be directly attributable to differences in innate immune responses or a combination of genetic and environmental factors. In recent years, research has revealed a large amount of clinically relevant information pertaining to inflammatory skin conditions such as acne conglobata and hidradenitis suppurativa. Both conditions are characterized by significant inflammation and have also been shown to demonstrate improvement with either steroids or tumor necrosis factor antagonists. Perhaps patients with acne that is prone to atrophic scars may have somewhat of a distinct, yet milder, form of inflammation. Possibly in the future, we can learn to select for this by the discovery or innovation of targeted therapies. The study by Carlavan et al. begins to fill an important gap in the literature for this skin condition, but additional experimental and translational studies are still needed. For patients with scar-prone acne, their data suggests an alteration of sebaceous gland structures, presumably as a result of inflammatory remodeling with increased matrix metalloproteinases. This is largely consistent with what is known about atrophic scars, which are characterized by disorganized tissue structure with decreased and thinned collagen bundles. Current cosmetic treatment strategies have revolved around increasing the amount of dermal collagen. This can be accomplished either through inducing the skin's own synthesis and regeneration of collagen, termed neocollagenesis, or through the injection of external collagen from soft tissue fillers. Chemical peels, dermabrasion and laser treatments have been shown to be variably effective in increasing levels of collagen and improving the clinical appearance of

scars. In clinical practice, the effectiveness of these techniques generally depends on the severity of lesions in terms of depth, surface area and chronicity. In our current climate, further research should focus on identifying and improving more cost-effective techniques.

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Diagnostic value of ultrasonography in synovitis-acne-pustulosis-hyperostosis-osteitis (SAPHO) syndrome: A case report. Asano T, Furuya MY, Fujita Y, et al. Medicine (Baltimore). 2018 Oct;97(41):e12725. doi: 10.1097/MD.0000000000012725. https://www.ncbi.nlm.nih.gov/pubmed/30313072

Rationale: Synovitis-acne-pustulosis-hyperostosis-osteitis (SAPHO) syndrome is a rare condition that affects the skin, bones, and joints. Diagnosis of SAPHO syndrome is established based on clinical manifestations and imaging features on radiography or magnetic resonance imaging. Patient concerns: We report a 44-year-old male with a 20-year history of pustulosis who presented with pain in the lower extremities. Plain radiography demonstrated hyperostosis with subperiosteal erosions in the right tibia. Magnetic resonance imaging and computed tomography showed inflammatory accumulation, whereas musculoskeletal ultrasonography clearly depicted a periosteal reaction, osteitis, and enthesitis with abnormal blood flow in the surface of the right tibia. Diagnoses: A diagnosis of SAPHO syndrome was made. Interventions: The patient was treated with combination therapy comprising prednisolone, methotrexate, and infliximab, which resulted in clinical improvement. Outcomes: The elevated levels of C-reactive protein and matrix metalloproteinase-3 normalized, and the abnormal ultrasonographic findings disappeared. Lessons: The present case report demonstrates that multiple imaging modalities are important for the definitive diagnosis of SAPHO syndrome. Ultrasonography might be a useful tool for evaluating local musculoskeletal inflammation in patients with SAPHO syndrome.

Occurrence of an invasive cervical epidermoid carcinoma in a patient receiving TNF-α blocking therapy for hidradenitis suppurativa. Ram A, Noël JC, Marmol VD, Benhadou F. JAAD Case Rep. 2018 Oct 3;4(9):857-859. doi: 10.1016/j.jdcr.2018.06.014. eCollection 2018 Oct. https://www.ncbi.nlm.nih.gov/pubmed/30306109

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease affecting apocrine gland areas leading to recurrent abscesses and nodules, forming scars and sinus tracts. Adalimumab, a tumor necrosis factor (TNF)-α monoclonal antibody is the first treatment approved by the US Food and Drug Administration for HS. TNF-α plays a primary and critical role in the mechanism of autoimmune disease by binding to TNF-α receptors, and initiating the immune response. Biological therapies have dramatically changed the management of chronic inflammatory skin disorders. The association between cervical dysplasia and TNF-α blocking therapy is well documented. TNF-α plays a critical role in the control of viral infection, including human papilloma virus (HPV). Therefore, the therapeutic TNF-α inhibition may increase the risk of HPV reactivation and lead to cervical dysplasia and carcinoma. We report, for the first time to our knowledge, the impressive case of an HS patient who went on to have a cervical epidermoid carcinoma 6 months after starting adalimumab therapy.

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