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AARS Announcements

Register Now for Our 15th Annual AARS Networking Reception

Please join us for our 15th Annual AARS Member Networking Reception co-hosted with *Practical Dermatology* on Friday, March 20, 2020 from 6:30 PM – 8:30 PM at the Ellie Caulkins Opera House in the Chambers Grant Salon. It's only a one-minute walk from the convention center! Participation is open to all! Come to learn more about the upcoming **AARS Global Research Summit** activities in May 2020! Register now for free as space is limited to see this fabulous venue and spend time with your friends and colleagues!

Click Here to Register!

Save the Date for the inaugural AARS Global Research Summit

The AARS is pleased to launch the largest ***Access*** strategic initiative thus far, the **AARS Global Research Summit 2020.** Please save the date for our upcoming 2-day scientific and networking event will be held in conjunction with the AARS 9th Annual Scientific Symposium during the 78th Annual Meeting of the Society of Investigative Dermatology. This Summit will take place on May 12-13, 2020 at the Westin Kierland in Scottsdale, Arizona. Email info@aarsmember.org for more information!

The three core activities within the inaugural AARS Global Research Summit include:

Tuesday, May 12, 2020 6:00 PM – 8:00 PM Impact of Acne, HS and Rosacea

Join us for a pre-symposium dinner with an audience of scientists, payers and your industry colleagues from managed care, medical affairs, and commercial teams. This evening will feature a unique approach to the discussion of acne and rosacea medication access and the impact felt from these diseases. The payers will hear how important maintaining acne and rosacea therapy is through a moderated panel of patient influencers who will share their own insights into their prescription medication access challenges and success. We will also include thoughts from AARS leadership who fight for this coverage and recent burden of illness data.

Wednesday, May 13, 2020 9:00 AM – 1:00 PM 9th Annual AARS Scientific Symposium

Started by former AARS President, Dr. Diane Thiboutot, this symposium is our largest live scientific symposium during the year. This event will feature presentations and discussion from esteemed researchers co-chaired by AARS President Dr. Mark Jackson and Dr. Diane Thiboutot.

Wednesday, May 13, 2020 1:00 PM – 2:00 PM Research Networking Workshop

During informal sessions we will connect the research communities with industry and patients to learn more from each other and discover potential funding and additional research opportunities. Each presenter from the symposium will have the chance to explain more about their research and introduce their department colleagues.

Industry News

With Foamix merger weeks away, Menlo itching drug fails a phase 2 test. Frank Vinluan, February 26th, 2020. Xconomy. https://xconomy.com/san-francisco/2020/02/26/with-foamix-merger-weeks-away-menlo-itching-drug-fails-a-phase-2-test/

A Menlo Therapeutics drug in testing for various itching conditions has failed a Phase 2 study, but executives say the results won't translate to its lead itching target nor will they affect its pending merger with Foamix Pharmaceuticals. The Menlo (NASDAQ: MNLO) drug, serlopitant, is an experimental treatment for pruritus, itching that's associated with a number of disorders. The Phase 2 failure was in chronic pruritus of unknown origin. The goal for the 10-week, 233-patient study was to show a reduction in itching as assessed by a rating scale. According to results released Wednesday, 37.9 percent of patients treated with serlopitant achieved a 4 point or greater improvement on the rating scale. But that was bested by the placebo group, where 39.3 percent of patients hit that mark. Furthermore, that placebo response was 10 percent higher than in any of the previous studies testing the once-daily pill, CEO Steve Basta said on a conference call to discuss the results. But Basta added that there's no indication that this high placebo response would be duplicated in forthcoming Phase 3 tests of the drug in the Redwood City, CA, company's lead indication, prurigo nodularis. "That would be putting undue weight on the [chronic pruritus of unknown origin] results," he said. "I think what you'll see is this is an outlier." Serlopitant, a small molecule drug, was designed to block neurokinin 1 receptor, a nerve-signaling pathway for itching. In Phase 2 results for prurigo nodularis, a skin disorder that causes hard itchy lumps on the skin, Menlo reported that patients treated with the drug showed statistically significant improvement compared to those given a placebo. Basta said that prurigo nodularis is different in that the nodules and lesions that appear on the skin indicate the underlying cause of a patient's itching. Chronic pruritus of unknown origin, by definition, has no explanation for the itching source. Itching experienced by this diverse group of patients may have different causes, which could explain the high placebo effect, Basta added. The placebo effect has derailed other tests of serlopitant. Before achieving successful Phase 2 results in pruritus nodularis in 2018, the company reported two mid-stage failures, one addressing itching in atopic dermatitis and the other in treating chronic cough. Basta said he does not expect that research will continue in chronic pruritus of unknown origin, but further development of the compound in that indication and others will soon be in the hands of Foamix (NASDAQ: FOMX). Last fall the Israel-based skin drugs developer agreed to an all-stock merger with Menlo. In January, Menlo shareholders approved the transaction, which Basta said is now expected to close on or around March 9. Speaking on the conference call, Foamix CEO David Domzalski said his company was aware that serlopitant was in proof-of-concept testing for chronic pruritus of unknown origin and that the focus of the merger was always around the drug's potential in pruritus nodularis, Menlo's lead indication. "Looking at the results we have today, our focus again is clearly on the [pruritus nodularis] program on a go-forward basis," Domzalski said. Foamix plans to pursue Phase 3 tests of serlopitant in patients with that condition, and if successful, file for FDA review by the end of this year. Assuming the drug is approved, Domzalski projected that Foamix could launch it late next year. Foamix is currently preparing to launch minocycline (Amzeeq), an antibiotic treatment for inflammatory lesions in patients who have moderate-to-severe acne. The FDA approved the topical treatment—a foam formulation of minocycline, an oral medication—in October. The company expects an FDA decision in June for FMX103, a minocycline foam tested as a treatment for rosacea. Menlo isn't the only company with disappointing pruritus news. Late Tuesday, Vanda Pharmaceuticals (NASDAQ: VNDA) reported a Phase 3 failure for its drug, tradipitant, in pruritus in adults with atopic dermatitis. Like Menlo's drug, the experimental Vanda therapy is a small molecule designed to block neurokinin 1. Despite the clinical trial failure, Vanda says the anti-itching effect of its drug was "robust" in patients who have mild atopic dermatitis, which represents 60 percent of the total atopic dermatitis population in the US. Those results will need to be confirmed by additional testing,

and the Washington, DC-based company says it will determine its next steps after assessing results from a second Phase 3 test of the drug in atopic dermatitis. That study is ongoing.

Foamix's rosacea candidate shows promise in phase 3 studies. February 19, 2020. DermWire, Practical Dermatology. https://practicaldermatology.com/news/foamixs-rosacea-candidate-shows-promise-in-phase-3-studies-1?c4src=topic:rosacea:feed

Foamix Pharmaceuticals Ltd.'s FMX103 1.5% Topical Minocycline Foam for rosacea performed well in an integrated efficacy analysis of two pivotal Phase 3 clinical trials presented at the 17th Annual South Beach Symposium in Dermatology in Miami, Florida. The U.S. Food and Drug Administration (FDA) accepted the filing of a New Drug Application for FMX103 for the treatment of moderate to severe papulopustular rosacea in adults with the action date set for June 2nd, 2020 under the Prescription Drug User Fee Act (PDUFA). The integrated efficacy analysis compared FMX103 to vehicle from 2 identical Phase 3 studies (FX2016-11 and FX2016-12) with 1,522 subjects (1,009 subjects received FMX103 and 513 subjects received vehicle) after 12 weeks of once-daily application. In the combined analysis of both pivotal Phase 3 studies, FMX103 demonstrated statistically significant benefit compared to vehicle foam on both co-primary endpoints. There was a significantly greater reduction of inflammatory lesion counts from Baseline to Week 12 for FMX103 compared to vehicle (-18.0 vs. -14.9; $p<0.001$), respectively. Moreover, a significantly greater number of subjects receiving FMX103 achieved Investigator Global Assessment of Rosacea Severity (IGA) success defined as an IGA score of 0 (clear) or 1 (almost clear) and at least a 2-grade improvement at Week 12, (50.6% vs. 41.0%; $p<0.001$), respectively. Statistical superiority of FMX103 when compared to vehicle was observed for both co-primary endpoints for all supporting sensitivity analyses. In a subgroup analysis of disease severity, FMX103 demonstrated statistically significant efficacy over vehicle in both Baseline severity groups: IGA 3 ("moderate") and IGA 4 ("severe"). For subjects assessed as having severe papulopustular rosacea (IGA 4) at baseline in each study: The FMX103 integrated treatment group demonstrated a significantly higher reduction of inflammatory lesions compared to the vehicle integrated treatment group from Baseline to Week 12, (-26.0 vs. -15.1; $p<0.001$), respectively. The FMX103 integrated treatment group demonstrated a significantly higher proportion of subjects achieving IGA treatment success compared to the vehicle integrated treatment group at Week 12, (36.8% vs. 14.9%; $p=0.003$), respectively. The integrated efficacy analysis further demonstrated the effect of FMX103 treatment on disease improvement as early as week 4.

Ortho Dermatologics launches telemedicine on Dermatology.com, US cash-pay prescription program. February 18, 2020. DermWire, Practical Dermatology. https://practicaldermatology.com/news/ortho-dermatologics-launches-telemedicine-on-dermatologycom-us-cash-pay-prescription-program?c4src=news-landing:feed

Bausch Health Companies Inc. and its dermatology business, Ortho Dermatologics, launched a new telemedicine platform on Dermatology.com, the first and only non-reimbursed, cash-pay prescription program in dermatology in the United States. The enhanced website will offer patients the ability to consult with a health care professional, order, and potentially receive a prescription on-demand for many of the branded dermatology products available in the program. Some products, such as Solodyn (minocycline hydrochloride) extended release tablets, Efudex (fluorouracil) topical cream, 5%, and Aldara (imiquimod) cream, 5%, which are for more serious skin conditions, will require an in-office visit instead. "At Ortho Dermatologics, we understand that patients with certain skin conditions, particularly acne and fine lines and wrinkles, can face multiple barriers to getting the skin care treatments they need," says Bill Humphries, president, Ortho Dermatologics. "By providing an on-demand solution where patients can conveniently consult with a medical professional online, order our clinically proven medicines directly, and receive prompt delivery, we believe we can deliver the best possible experience and access for patients." To use the new telemedicine service on

Dermatology.com, patients are required to submit a photo of their skin-related need and other information on their health, medical history, and lifestyle via their mobile device or desktop. Once the submission is placed, which takes approximately three minutes, the patient will receive an email confirmation stating that their submission is being reviewed by a health care provider. Typically within 24 hours, the health care provider will either provide the patient with a prescription for one of the company's branded prescription products available on the site, based on the assessment by the health care provider, or recommend the patient visit a board-certified dermatologist if the skin condition warrants an in-person consultation. To help these patients connect directly to a board-certified dermatologist, the site will feature a direct link to the American Academy of Dermatology Association's Find a Dermatologist locator. Through Dermatology.com, patients have direct access to many of Ortho Dermatologics' proven, high-quality, branded dermatology medicines. The products available on the site include Retin-A (tretinoin) cream as well as newer products such as Altreno (tretinoin) Lotion, 0.05%. The company also recently added four more products to the program, Solodyn (minocycline hydrochloride) extended release tablets, Renova (tretinoin cream 0.02%), Loprox shampoo (ciclopirox 1%), and BenzEFoam (benzoyl peroxide emollient foam 5.3%/9.8%), bringing the total product count to 15. The addition of BenzEFoam 5.3% also marks the site's first over-the-counter option for patients. Since its launch in March 2019, Dermatology.com has helped thousands of patients get access to branded dermatology products at transparent prices through participating pharmacies, including all Walgreens U.S. retail pharmacies.

New Medical Research

Efficacy and safety of plasma gel as a new modality in treatment of atrophic acne scars. Elfar NN, Hasby EA. Int J Dermatol. 2020 Feb 28. doi: 10.1111/ijd.14815. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32108322

Background: Postacne scarring is an unfortunate and frequent complication of acne, with varied morphological forms and associated significant psychological distress to patients. Aim of the work: To evaluate the efficacy and safety of plasma gel injection alone and in combination with microneedling in treatment of atrophic postacne scars. Patients and methods: Sixty patients with atrophic postacne scars were enrolled in this single blinded randomized controlled study. The patients were divided into three groups with 20 patients being treated with intradermal injection of plasma gel, 20 patients treated with dermaroller, and 20 patients subjected to combined plasma gel and dermaroller. Patients received four sessions at monthly intervals and were evaluated by clinical, histopathological, and immunohistochemical analysis. Results: There was statistically significant improvement in postacne scars after treatment in all studied groups with variable degrees; the combined technique showed the best clinical improvement in postacne scars. There was an increase in newly formed collagen and elastic fibers with more organized and condensed bundles after the end of treatment. Conclusion: Plasma gel showed a remarkable improvement for most patients after one session, providing a quick and easy solution for acne scars. The combination of dermaroller and plasma gel potentiated its effect with more improvement in scars.

Can monocyte/HDL show inflammatory activity of isotretinoin treatment in acne patients? Önder S, Ozturk M. Cutan Ocul Toxicol. 2020 Feb 26:1-13. doi: 10.1080/15569527.2020.1734815. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32100587

Aim: There are reports that isotretinoin causes some important diseases such as teratogenicity, inflammatory bowel disease and sacroiliitis by triggering inflammation. (Monocyte/HDL (high density lipoprotein) ratio) MHR is closely related

to inflammation and is thought to be an indicator of atherosclerotic development. We aimed to investigate how isotretinoin (ISO) affects the immunoinflammatory response in acne patients. Materials and Methods: In this study, 116 nodulocystic acne patients who received ISO treatment for at least three months were evaluated retrospectively. ISO treatment was given to patients at a dose of 0.5-1 mg/kg. Pre-treatment and post-treatment white blood cell (WBC), neutrophil, lymphocyte, monocyte, platelet, mean platelet volume (MPV), platelet, plateletcrit, platelet distribution width (PDW), neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), total cholesterol, LDL cholesterol, triglyceride, HDL cholesterol and MHR were evaluated. Results: MPV and MHR values were significantly increased after 3 month treatment ($p < 0.05$). There was no significant change in NLR and PLR values ($p > 0.05$). There was a significant decrease in neutrophil count ($p < 0.05$). There were no significant changes in WBC, lymphocyte, monocyte, platelet, plateletcrit values ($p > 0.05$). Total cholesterol, LDL cholesterol and triglyceride levels were significantly increased after three months of treatment ($p < 0.05$). HDL cholesterol levels decreased significantly after three months of treatment ($p < 0.05$). Conclusion: We concluded that ISO treatment may trigger inflammation due to the increase in MPV and MHR value. MHR can show inflammation after ISO treatment.

Identifying the impacts of acne: A Delphi survey of patients and clinicians. Tan J, Frey MP, Thiboutot D, et al. J Cutan Med Surg. 2020 Feb 25:1203475420907088. doi: 10.1177/1203475420907088. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32096429

Background: Acne can adversely impact those affected in multiple dimensions. The purpose of this study was to determine the most prominent impacts identified by acne patients and by clinicians. Methods: Independent Delphi surveys for acne patients and clinicians were conducted to achieve consensus regarding acne impacts within each group. Acne patients were recruited from outpatient clinics of authors (AL, JT, and DT). The first phase involved qualitative responses, where emergent themes were identified and used to generate items for 2 subsequent phases. Results: The qualitative phase generated 64 items in 3 themes: psychological, sociological, and treatment related. These items were independently ranked in importance by patients and by clinicians. Consensus for importance was achieved for 34 items by patients and 43 by clinicians. Patient-identified highest ranked items were being self-conscious, feeling unattractive, feeling uncomfortable in own skin, unattractive to others, would not want pictures taken, envious of people with clear skin, and time/effort spent concealing scarring; while clinicians identified feeling unattractive. Conclusions: We identify acne impacts within psychological, sociological, and treatment-related domains by acne patients and clinicians. Further, we establish discrepancies between patients and clinicians regarding the impact of acne. This provides evidence for the importance of establishing patient-reported outcomes.

Treatment of hidradenitis suppurativa: Surgery and yeast (Saccharomyces cerevisiae)-exclusion diet. Results after 6 years. Aboud C, Zamaria N, Cannistrà C. Surgery. 2020 Feb 22. pii: S0039-6060(20)30011-8. doi: 10.1016/j.surg.2019.12.015. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32098690

Background: Hidradenitis suppurativa is a complex disorder, the pathogenesis of which is still unsolved. The known association between hidradenitis suppurativa and Crohn's disease, an autoimmune disease diagnosed with the presence of Anti-Saccharomyces cerevisiae antibodies of the IgG family, suggests that a much more complex mechanism than a simple infectious disorder is involved. The goal of this study is to report patients' characteristics and the outcome of 6 years of a yeast (Saccharomyces cerevisiae)-exclusion diet and surgery in the treatment of hidradenitis suppurativa. Method: We analyzed 185 patients with hidradenitis suppurativa with a self-evaluative questionnaire. Thirty-seven patients were treated in our center following our protocol. The other 148 were members of a support group for patients with hidradenitis suppurativa treated by other centers. Results: In 80% of patients who had the onset of hidradenitis

suppurativa before the age of 30, the female to male ratio was 3.34:1, 74% were active smokers, and 5% also had Crohn's disease. In the diet group, 70% had an improvement of hidradenitis suppurativa symptomatology, 81% of whom in less than 6 months. Also, 87% of patients demonstrated an immediate recurrence of skin lesions less than a week after consuming a food containing the yeast. Immunologic testing showed intolerance to yeast, wheat, and cow's milk in 20%, 29%, and 23% of patients, respectively. Conclusion: The analysis confirmed the stabilization and regression of hidradenitis suppurativa with our diet, presumably by decreasing the local and systemic inflammation, leading to a less invasive operative treatment. These new findings seem to link hidradenitis suppurativa to food intolerance and gut dysbiosis.

Alopecia areata and isotretinoin; coincidence or causal relation. Gupta M, Lotti T, Goldust M. Dermatol Ther. 2020 Feb 21:e13280. doi: 10.1111/dth.13280. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32083770

Isotretinoin is a safe and useful medication for acne management. Adverse effects are mostly related to cutaneous and mucous membranes. We present a case of a 24-year-old female patient who was on treatment with isotretinoin for acne vulgaris Grade 4. After 6 months of treatment, the patient presented with localized patch of hair loss. Beginning of alopecia areata in patients with acne vulgaris could be regarded as a side effect of retinoids due to anti-acne therapy. The exact mechanism by which retinoids cause hair loss is not known.

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Baseline characteristics from UNITE: An observational, international, multicentre registry to evaluate hidradenitis suppurativa (acne inversa) in clinical practice. Prens EP, Lugo-Somolinos AM, Paller AS, et al. Am J Clin Dermatol. 2020 Feb 19. doi: 10.1007/s40257-020-00504-4. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32077014

Background: Hidradenitis suppurativa (HS), also known as acne inversa, is a recurring, painful, chronic, and sometimes disfiguring inflammatory skin disease. Objectives: Our objective was to report the baseline clinical characteristics, natural history, and associated outcomes of patients with HS from the ongoing, prospective, non-interventional UNITE registry that is collecting data regarding the natural history and associated outcomes of HS. Methods: Patients with inflammatory HS lesions were enrolled, including adolescents (aged 12 to < 18 years) and adults (aged ≥ 18 years). None had participated in previous or current originator-adalimumab studies/registries. Patients received treatment consistent with site-specific, routine clinical practice. HS disease status was assessed by HS lesions and disease flare; treatment and outcomes data were collected at enrolment and every 6 months for ≤ 4 years. Results: Enrolment (N = 594; 89.1% adults; 10.9% adolescents) occurred from 29 October 2013 to 29 December 2015 at 73 sites in 12 countries. At baseline, the majority were female (69.7%) and White (81.2%), had moderate-to-severe disease (Hurley stage II or III; 93.3%), and had undergone prior procedures/surgery for HS (68.7%). In total, 61.6% of adults and 49.2% of adolescents were obese; 40.2% of patients reported current tobacco use. Scarring due to lesions occurred in 91.2% of patients. The prevalence of comorbidities of interest was as follows: depression (13.3%), other psychiatric disorders (9.6%), inflammatory bowel disease (2.7%), diabetes (9.1%), and polycystic ovary syndrome (5.2%). Conclusions: In this population from the UNITE HS registry, obesity and smoking were common, and disease burden was high, manifesting as multiple lesions, scarring, surgical history, and considerable comorbidities.

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Assessing adherence to evidence-based guidelines of care for acne vulgaris. Dunaway S, Fleischer AB Jr. J Dermatolog Treat. 2020 Feb 19:1-16. doi: 10.1080/09546634.2020.1729950. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32073329

Background: Care guidelines are developed to assist in performing high-quality, cost-effective care. Objective: This study was designed to assess the adherence to evidence-based guidelines of care for acne. Methods: For acne treatment, we analyzed 2008-2015 National Ambulatory Medical Care Survey visits. For each medication mention, a grade was assigned based upon the American Academy of Dermatology 2007 treatment guidelines. Results: Most encounters achieved the grade of A, regardless of specialty or patient population. A proportion of visits involved the use of oral antibiotics monotherapy, which occurred at 11.7% (8.6-14.8) dermatologist and 25.6% (12.4-38.8) of non-dermatologist visits. Although not addressed in the 2007 guidelines, this practice was not recommended in the updated 2016 guidelines. Limitations: Other factors influencing prescribing behaviors cannot be completely assessed using extant data. Conclusions: This study demonstrates that nearly all physicians adhered to the 2007 guidelines. Many prescribed antibiotic monotherapy, a practice not supported by the evidence. Capsule Summary Although acne practice guidelines are published, adherence to these guidelines in unknown. Using a grading system analogous to the United States A to F system, virtually all providers receive a grade of A. We expect that the grade will be lower in the future.

Exploring the anti-acne potential of impepho [helichrysum odoratissimum (l.) sweet] to combat cutibacterium acnes virulence. De Canha MN, Komarnytsky S, Langhansova L, Lall N. Front Pharmacol. 2020 Jan 30;10:1559. doi: 10.3389/fphar.2019.01559. eCollection 2019. https://www.ncbi.nlm.nih.gov/pubmed/32082144

The Gram-positive bacterium Cutibacterium acnes (previously Propionibacterium acnes), plays an important role in the pathogenesis and progression of the dermatological skin disorder acne vulgaris. The methanolic extract of Helichrysum odoratissimum (L.) Sweet (HO-MeOH) was investigated for its ability to target bacterial growth and pathogenic virulence factors associated with acne progression. The gas chromatography-mass spectrometry (GC-MS) analysis of HO-MeOH identified α-humulene (3.94%), α-curcumene (3.74%), and caryophyllene (8.12%) as major constituents, which correlated with previous reports of other Helichrysum species. The HO-MeOH extract exhibited potent antimicrobial activity against C. acnes (ATCC 6919) with a minimum inhibitory concentration (MIC) of 7.81 µg/ml. It enhanced the antimicrobial activity of benzoyl peroxide (BPO). The extract showed high specificity against C. acnes cell aggregation at sub-inhibitory concentrations, preventing biofilm formation. Mature C. acnes biofilms were disrupted at a sub-inhibitory concentration of 3.91 µg/ml. At 100 µg/ml, HO-MeOH reduced interleukin-1α (IL-1α) cytokine levels in C. acnes-induced human keratinocytes (HaCaT) by 11.08%, highlighting its potential as a comedolytic agent for the treatment of comedonal acne. The extract exhibited a 50% inhibitory concentration (IC50) of 157.50 µg/ml against lipase enzyme activity, an enzyme responsible for sebum degradation, ultimately causing inflammation. The extract's anti-inflammatory activity was tested against various targets associated with inflammatory activation by the bacterium. The extract inhibited pro-inflammatory cytokine levels of IL-8 by 48.31% when compared to C. acnes-induced HaCaT cells at 7.81 µg/ml. It exhibited cyclooxygenase-II (COX-II) enzyme inhibition with an IC50 of 22.87 µg/ml. Intracellular nitric oxide (NO) was inhibited by 40.39% at 7.81 µg/ml when compared with NO production in lipopolysaccharide (LPS)-induced RAW264.7 cells. The intracellular NO inhibition was potentially due to the 2.14 fold reduction of inducible nitric oxide synthase (iNOS) gene expression. The HO-MeOH extract exhibited an IC50 of 145.45 µg/ml against virulent hyaluronidase enzyme activity, which is responsible for hyaluronan degradation and scar formation. This study provides scientific validation for the traditional use of H. odoratissimum as an ointment for pimples, not only due to its ability to control C. acnes

proliferation but also due to its inhibitory activity on various targets associated with bacterial virulence leading to acne progression.

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PsAPASH: a rare and recent autoinflammatory syndrome associated with hidradenitis suppurativa. Gadelha RL, Paiva RDSR, Palitot EB, Costa JEFD. An Bras Dermatol. 2020 Jan 21. pii: S0365-0596(20)30023-4. doi: 10.1016/j.abd.2019.02.012. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32063421

Hidradenitis suppurativa is a chronic inflammatory skin disease, which affects 1% of the population, being more common in young, obese and smokers, and mainly affects armpits and groin, with formation of pustules, nodules, abscesses, scars and fistulas. Recently, its association with other autoimmune diseases such as psoriasis, psoriatic arthritis, pyoderma gangrenosum, pyogenic arthritis and ulcerative colitis have been reported. These associated forms are usually resistant to standard treatment, with immunobiologicals as promising therapy. The case of a rare form of association is reported, with only one case previously described in the literature: psoriasis arthritis, pyoderma gangrenosum, acne and hidradenitis suppurativa.

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Clinical Reviews

Long-term safety of adalimumab for patients with moderate-to-severe hidradenitis suppurativa. Tzanetakou V, Stergianou D, Giamarellos-Bourboulis EJ. Expert Opin Drug Saf. 2020 Feb 28:1-13. doi: 10.1080/14740338.2020.1734560. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32098513 Introduction: Hidradenitis suppurativa (HS) is a chronic debilitating inflammatory skin disorder that affects regions rich in apocrine glands. Although the etiology of HS is not clear, inflammatory cytokines, like tumor necrosis factor (TNF)-α, participate in pathogenesis. Adalimumab (ADA), a human IgG1 monoclonal antibody that selectively targets TNFα, is the only EMA/FDA-approved biologic agent available for the therapy of moderate-to-severe HS. Areas covered: A comprehensive literature search was conducted to present existing studies with an emphasis on the safety profile of ADA for the treatment of moderate-to-severe HS. ADA is prescribed for more than 15 years for varied indications and has improved the therapeutic outcomes of many diseases. Clinical trials and real-life safety data from ADA administration in HS were presented, with particular attention to special populations, such as children, elderly, and pregnant women. Expert opinion: Existing data advise for limited safety concerns with long-term ADA treatment provided that patients are thoroughly screened for infections, latent tuberculosis, and history of malignancy before the start of treatment.

Optimizing isotretinoin treatment of acne: Update on current recommendations for monitoring, dosing, safety, adverse effects, compliance, and outcomes. Landis MN. Am J Clin Dermatol. 2020 Feb 27. doi: 10.1007/s40257-020-00508-0. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32107726

Acne vulgaris is the most common skin disease treated by dermatologists. It can be severe and result in permanent scars. Isotretinoin is the most effective treatment for acne and has the potential for long-term clearance. Prescribing and monitoring protocols can vary widely among prescribers. Recent studies, reports, and consensus statements help shed light on optimizing the use of isotretinoin for acne. A recent literature review is summarized in this article to help the

practitioner optimize isotretinoin use for acne. The article outlines the advantages and disadvantages of standard, high-dose, and low-dose isotretinoin regimens; discusses the current status of controversies surrounding isotretinoin (including depression/suicide, pregnancy, and inflammatory bowel disease); reviews monitoring recommendations and treatment for hypertriglyceridemia and elevated transaminase levels; and discusses common adverse effects seen with isotretinoin, along with their treatment and prevention.

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Selective RAR agonists for acne vulgaris: A narrative review. Kassir M, Karagaiah P, Sonthalia S, et al. J Cosmet Dermatol. 2020 Feb 26. doi: 10.1111/jocd.13340. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32100454

Background: Acne vulgaris is a chronic disfiguring inflammatory disease of adolescents and adults affecting up to 90% of the population around the world. The sequence of etiopathogenesis in acne is not completely understood but involves abnormalities in sebum production, follicular plugging, proliferation of propionibacterium acnes, and chronic inflammation. Aims: This review aims to summarize the features of the topical selective RAR agonists in treating acne vulgaris with a special emphasis on the 4th generation topical retinoid trifarotene. Methods: Studies were identified by searching electronic databases (MEDLINE and PubMed) till August 2019 and reference lists of respective articles. Only articles published in English language were included. Results: Topical retinoids have been first line of treatment for more than 30 years now in treating mild to moderate acne vulgaris. Third generation retinoids like adapalene and tazarotene are selective RAR and γ agonists, having an additional anti-inflammatory action along with their comedolytic effects and work well in combinations with topical antibiotics, due to the stability of chemical composition. Conclusion: Trifarotene is a new 4th generation retinoid with selective action on RAR-γ receptor alone, which is specific for skin, and it is safe for long-term maintenance therapy with good efficacy and tolerability.

Surgical and post-surgical wound care in hidradenitis suppurativa. Manfredini M, Garbarino F, Bigi L, et al. Dermatol Ther. 2020 Feb 21. doi: 10.1111/dth.13282. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32083788

Hidradenitis suppurativa (HS) is a chronic inflammatory disorder. Several medical treatments, with varying degree of efficacy, have been developed. However, in most cases of advanced (HS), the definitive treatment option is often represented by surgical excisions. Surgical techniques, reconstructive approach and local wound care should be accurately designed in order to obtain the best result. In this review we analyzed the possible surgical treatments and local wound care. A Medline search was performed on the various surgical treatments, reconstructive techniques and local wound care. Surgical treatment is a common therapeutic modality for HS. Different surgical reconstructive techniques and postsurgical wound care approaches are described for the management of HS patients. There were few high-quality evidence-based studies evaluating the surgical management of HS. Many disparate HS severity scores were used in these studies making comparison between them difficult. Nonetheless research into different surgical approaches and wound care management has increased substantially in the past decade and has given patients more surgical therapeutic strategies. The description of the best combinations and timing of surgery, wound care and medical therapies, will be a matter of future research for the definition of the optimal management of HS patient.

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The top 100 most cited articles in rosacea: A bibliometric analysis. Wang Y, Zhang H, Fang R, et al. J Eur Acad Dermatol Venereol. 2020 Feb 20. doi: 10.1111/jdv.16305. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32078196

Background: Many articles in rosacea have been published. Bibliometric analysis is helpful to determine the most influential studies in a specific field. Objective: To identify the top 100 most cited articles in rosacea using the bibliometric analysis method. Methods: We searched in the Web of Science database on November 20th, 2019. Articles were listed in descending order by their total citations. The top 100 most cited articles in rosacea were identified and analyzed. Results: The top 100 most cited articles were published between 1971 and 2015. The largest number of articles were published in a single interval in 2011-2015. The average annual citations were constantly ascending, and the total citations were positively correlated with annual citations. The 100 articles were classified into different research focuses: treatment (35%), pathogenesis (27%), clinical features and diagnosis (14%), pathophysiology (6%), associated diseases (4%), epidemiology (3%) and others (11%). 19 articles were randomized controlled trials (RCT), 14 focused on the association between rosacea and Demodex, and five focused on the association between rosacea and Helicobacter pylori. 25 publications focused on a specific subtype of rosacea, mainly papulopustular and ocular rosacea. The 100 articles were published in 32 journals. 79 different first corresponding authors were from 20 different countries, mostly in North America and Europe. Steinhoff. M from University of California published the most articles as the corresponding author. Conclusions: This study identified the top 100 most cited articles in rosacea and analyzed their bibliometric characteristics, which may pave the way for further research.

Conventional and novel treatment modalities in rosacea. Engin B, Özkoca D, Kutlubay Z, Serdaroğlu S. Clin Cosmet Investig Dermatol. 2020 Feb 20;13:179-186. doi: 10.2147/CCID.S194074. eCollection 2020. https://www.ncbi.nlm.nih.gov/pubmed/32110082

Rosacea is a common skin disease that is troublesome for both the patients and the dermatologists. Erythema, telengiectasia, papulopustular changes and phymatous changes are the main problems faced by the patients and dermatologists in everyday practice. Due to the chronic and relapsing nature of the disease, patients are usually unsatisfied with conventional treatment methods. This article aims at redefining rosacea according to the 2017 consensus and reviewing the different treatment modalities for different manifestations of the disease in depth.

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Biologic therapies for the treatment of hidradenitis suppurativa. Rosales Santillan M, Morss PC, Porter ML, Kimball AB. Expert Opin Biol Ther. 2020 Feb 20. doi: 10.1080/14712598.2020.1732918. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32077334

Introduction: Hidradenitis suppurativa (HS) is a chronic skin disorder characterized by inflammatory nodules, abscesses, and fistulae. Patients tend to present in young adulthood and are predominantly female. The pathogenesis of HS involves apopilosebaceous gland follicle occlusion and affected areas appear to be located where this type of gland predominates. Treatment selection depends on HS severity, and there are different scoring systems used for severity classification. In recent years, biological therapies have been evaluated and used with increasing frequency for patients with HS, particularly those with moderate-to-severe disease. Areas covered: This review focuses on biological therapies used in patients with hidradenitis suppurativa assessed in case reports, case series, and clinical trials. The efficacy, hidradenitis suppurativa scoring systems, adverse events, and long-term results of these biological therapies are discussed depending on the studies' endpoints. Expert opinion: Adalimumab is currently the only FDA-approved biological therapy

for HS. Some patients do not experience treatment efficacy with adalimumab at 40 mg/week, which may result in increasing the dose of this biologic or seeking other systemic treatment options. Infliximab is the next line of treatment for HS with demonstrated efficacy. However, similar to adalimumab, not all patients respond to treatment. Other biological therapies being studied or reported have demonstrated efficacy in small patient groups, but the results lack study power. Further studies, particularly those using similar regimens to psoriasis, may provide answers to seeking treatment options for patients who fail to improve on current standard HS treatment.

Acne vulgaris and risk of depression and anxiety: A meta-analytic review. Samuels DV, Rosenthal R, Lin R, et al. J Am Acad Dermatol. 2020 Feb 20. pii: S0190-9622(20)30279-6. doi: 10.1016/j.jaad.2020.02.040. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32088269

Background: Several studies have shown an association of acne vulgaris with depression and anxiety but a quantitative review has not yet been conducted. Objective: To conduct a systematic review and meta-analysis that elucidates the association of acne vulgaris with depression and anxiety. Method: A systematic review and meta-analysis of literature published prior to October 1, 2019 from PubMed, PsycINFO, MEDLINE, and Cochrane databases was conducted. We used a meta-analytic approach to perform a random effects analysis comparing individuals with and without acne. Subgroup analyses between studies included age, study setting, and geographic region. Results: In all, 42 studies were included. We found a significant association of acne vulgaris with depression, r = 0.22 (95% CI: 0.17-0.26, p < .00001), and anxiety, r = 0.25 (95% CI: 0.19-0.31, p < .00001). Subgroup analyses and comparisons showed moderating influences based on factors including age, study setting, and geographic region. Limitations: Inconsistency between publications regarding acne and outcome ascertainment, data reporting, and studies with no control group posed considerable barriers to synthesizing all available literature. Conclusion: Because of increased risk for depression and anxiety, clinicians should pursue aggressive treatment of acne and consider psychiatric screening or referrals.

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Treatment of acne with spironolactone: A retrospective review of 395 adult patients at mayo clinic, 2007-2017. Roberts EE, Nowsheen S, Davis MDP, et al. J Eur Acad Dermatol Venereol. 2020 Feb 20. doi: 10.1111/jdv.16302. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32078195

Background: Few large studies have assessed spironolactone treatment of adult female acne. Objectives: To explore the role of spironolactone in the treatment of adult female acne. Methods: We performed a retrospective case series assessing the efficacy of spironolactone treatment of a cohort of women evaluated at Mayo Clinic in Rochester, Minnesota, from 2007 through 2017. Results: In total, 395 patients (median age, 32 years) received a median spironolactone dose of 100 mg daily. Approximately two-thirds of patients (66.1%) had a complete response; 85.1% had a complete response or a partial response greater than 50%. Median times to initial response and maximum response were 3 months and 5 months. Efficacy was observed across all severity subtypes of acne, including those with papulopustular and nodulocystic acne. Patients received long-term treatment with spironolactone (median duration, 13 months) and had few adverse effects. Conclusions: Spironolactone is a safe and effective treatment of acne for women.

Abnormal baseline lab results rarely lead to treatment modification for patients on isotretinoin. Tkachenko E, Sharma P, Mostaghimi A. Dermatology. 2020 Feb 18:1-4. doi: 10.1159/000505451. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32069457

Background: Treatment modification and clinical course for patients initiating isotretinoin with abnormal baseline lab results is currently unknown, and no recommendations exist for monitoring this patient group. Methods: We performed a retrospective review of patients prescribed isotretinoin for acne from 2008 to 2016 at Brigham and Women's and Massachusetts General Hospitals to investigate the characteristics, clinical implications, and management of patients initiating isotretinoin for acne with baseline laboratory abnormalities. Results: We identified a low rate (7.2%) of treatment modification, including interruption (3.6%) and early termination (3.6%), during isotretinoin therapy due to lab abnormalities for patients with baseline lab abnormalities. Abnormal baseline total cholesterol, triglyceride, and liver function tests did not predict management changes, as only 2 of 10 total treatment modifications were due to a lab result that was abnormal at baseline. Treatment modification was driven by ALT elevation not present at baseline that occurred in patients with liver comorbidities. Conclusion: Emphasizing relevant comorbidities, including hepatic disease or alcohol use, to inform our monitoring may be a superior predictor of abnormalities during treatment, as our work demonstrates that the value of baseline lab data prior to isotretinoin is unclear.

Successful use of guselkumab in the treatment of severe hidradenitis suppurativa. Kearney N, Byrne N, Kirby B, Hughes R. Clin Exp Dermatol. 2020 Feb 18. doi: 10.1111/ced.14199. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32068912

Hidradenitis Suppurativa (HS) is a chronic incurable disease of apocrine gland-bearing skin characterized by double comedones, recurrent nodules, draining tracts and scarring predominantly in the axilla, groin and inframammary folds. Adalimumab and Infliximab are recommended for use in HS Hurley stage 2-3 and there are several reported cases and one case series of successful treatment with Ustekinumab which blocks the p40 subunit of IL-12 and IL-231. We report a case of successful treatment of HS with a monoclonal antibody (Guselkumab) to the p19 subunit of IL-23.

Depression in transgender adolescents under treatment with isotretinoin. Campos Muñoz L, López de Lara D, Conde-Taboada A, et al. Clin Exp Dermatol. 2020 Feb 17. doi: 10.1111/ced.14194. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32064651

In adolescents, acne may have severe psychological effects and negatively impact quality of life. Certainly, it is associated with higher rates of social phobia, low self esteem, anxiety, and self-harm. Studies comparing transgender and non-transgender adolescents report clinical depression among the former to be much more common; indeed, some 30% have suicidal thoughts compared to 18% of the general population.

Nanocarriers as versatile delivery systems for effective management of acne. Patel R, Prabhu P. Int J Pharm. 2020 Feb 13;579:119140. doi: 10.1016/j.ijpharm.2020.119140. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32061843

Acne vulgaris is a chronic inflammatory skin disorder affecting mostly females. It has a negative impact on the social life and psychological well-being of the individual. Its pathogenesis involves an exaggerated secretion of sebum, hyperkeratinisation of hair follicles, colonization of anaerobic microbes in the hair follicles, and inflammation. Conventional therapy for acne utilizes antibacterial and anti-inflammatory drugs. Systemic use of these drugs is

associated with undesirable toxicities. Hence, topical delivery of anti-acne drugs is desired. However, topical delivery is hindered by poor aqueous solubility of drug and inadequate penetration across stratum corneum. Nanocarriers are endowed with immense potential to facilitate topical delivery of anti-acne drugs as monotherapy or in combination by a myriad of mechanisms including occlusive nature promoting skin hydration, providing sustained drug release thereby decreasing dosing frequency, follicular targeting, and protecting the labile active from degradation. Further, smart nanocarriers can deliver the anti-acne cargo in response to some stimulus present at the disease site precluding undesirable effects at non target sites. Nanocarriers have also been explored in photothermal and photodynamic therapy of acne for destruction of antibiotic resistant bacteria implicated in acne. This review focuses on the potential of a variety of nanocarriers for treatment of acne.

Minocycline, focused on mechanisms of resistance, antibacterial activity, and clinical effectiveness: Back to future. Asadi A, Abdi M, Kouhsari E, et al. J Glob Antimicrob Resist. 2020 Feb 12. pii: S2213-7165(20)30023-0. doi: 10.1016/j.jgar.2020.01.022. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32061815

The increase of crisis in multidrug-resistant (MDR) or extensively drug-resistant (XDR) microorganisms leads to appealing therapeutic options. During the last 30 years, minocycline has been a wide-spectrum antimicrobial agent, effective against MDR gram-positive and-negative bacterial infections. Alike other tetracyclines, mechanism of action of minocycline is attaching to the bacterial 30S ribosomal subunit and preventing protein synthesis. This antimicrobial agent has been approved for the treatment of acne vulgaris, some sexually transmitted diseases and rheumatoid arthritis. Although many reports have been performed in this field, there remains limited information regarding the prevalence, mechanism of resistance, and clinical effectiveness of minocycline. Thus, we summarize the currently available data concerning pharmacokinetics and pharmacodynamics, mechanism of action and resistance, antibacterial activity, and clinical effectiveness of minocycline.

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Hidradenitis suppurativa, a rare skin disease. Khattak JI, Zahid U. J Pak Med Assoc. 2020 Feb;70(2):348-350. doi: 10.5455/JPMA.5213. https://www.ncbi.nlm.nih.gov/pubmed/32063633

Hidradenitis Suppurativa (HS) is a rare, chronic and recurrent skin disease involving folliculopilosebaceous unit. It is a debilitating disease due to its chronicity, painful relapses and cosmetic outcomes. It affects the patient's personal, family, social and professional life. It is often diagnosed late during its course, due to lack of awareness and knowledge among general practitioners. Management is symptomatic, as ultimate treatment is latest and has limitations due to cost and availability issues. Reported here is a case of HS, being treated at Hearts International Hospital, Rawalpindi, Pakistan.

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Apremilast for the treatment of hidradenitis suppurativa associated with psoriatic arthritis in multimorbid patients: Case report and review of literature. Garcovich S, Giovanardi G, Malvaso D, et al. Medicine (Baltimore). 2020 Jan;99(5):e18991. doi: 10.1097/MD.0000000000018991. https://www.ncbi.nlm.nih.gov/pubmed/32000436

Introduction: Hidradenitis suppurativa is a complex, chronic, difficult to treat condition belonging to the spectrum of cutaneous immune-mediated inflammatory diseases. Systemic treatment options for moderate-severe disease are limited to TNF-alpha antagonists and other biologic agents, with limited clinical evidence. Patient concerns: We report two adult patients with severe hidradenitis suppurativa presenting concomitant psoriatic arthritis and multiple medical

comorbidities. Both were ineligible or resistant to adalimumab, the only biologic drug approved for the treatment of hidradenitis. Diagnosis: Both patients were diagnosed with severe Hurley III-stage disease and psoriatic arthritis, showing resistance to first-line systemic treatments and a complex comorbidity profile. Interventions: Patients underwent treatment with apremilast, an oral phosphodiesterase-4 inhibitor, approved for the treatment of psoriatic arthritis. Outcomes: After 16 weeks of treatment, a clinically relevant improvement of inflammatory lesions, skin- and arthritis-related pain, and patient-reported outcomes was achieved in both patients. Apremilast was well tolerated and continued up to 48 weeks of treatment. Conclusion: We report the "real-life" use of apremilast in the treatment of multimorbid patients with hidradenitis suppurativa and review its potential role in the management of this severe condition.

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