BIODERMA
LABORATOIRE DERMATOLOGIQUE

INTERNATIONAL MEDICAL

Bioderma Congress Reports
DUBAI DERMA 2023

Reports written by

Dr. Jelena Mestrovic Stefekov

Dermatologist, Croatia

Acne update in managment

Husain Juma MD, Consultant Dermatologist

1. Acne leaves its marks – physically and emotionally.
Affects: >80% adolescents, > 40% adults over than 25. Associated with: disfigurement, pain, loss of confidence, depression. Effects on quality of life

2. Overview of current acne therapy:
- Topical retinoids (tretinoin (Retin A), adapalene (Differin). Tazarotene (Tazorac)) – effects, advantages and disadvantages, adverse effects
- Topical antibiotics (Erythromycin, Clindamycin) – effects, advantages and disadvantages, adverse effects
- Benzoyl peroxide – effects, advantages and disadvantages, adverse effects
- Azelaic acid – effects, advantages and disadvantages, adverse effects
- Systemic antibiotics (tetracyclin, doxycyclin, minocyclin, erythromycin)
- Hormonal control (OHC, Ortho tri-cyclen (Estrostep), Oral antiandrogens (spirinolactone), corticosteroids - short course in severe inflammatory acne)
- Isotretinoin

3. Whats New:
- Topical oxazolidnone (Radezolid®, antibacterial, phase II)
- Oral sarecycline (Seysara®, antibacterial and anti-inflammatory, phase III)
- CJM112 (anti-inflammatory, phase II)
- Topical suspension of gold microparticles (Sebostatic, phase III)
- Cream contaning chromophores (Klaresca®, killing C.acnes, FDA-approved)
- Transdermal gel containing synthetic cannabidiol (BTX1503, anti-inflammtory and sebostatic, phase Ib)
- Topical minocycline foam 4% (FMX101, antibacterial, anti-inflammatory, antioxidant, blocks inflammasome-pyroptosis ant cleaved IL-1ß, phase III)
- Solubilized topical minocycline gel (BPX-01, antibacterial, anti-inflammatory, antioxidant, inhibits protein synthesis bacteria and inhibits INOS and MMPs in cells, phase III)

- Topical small molecule prodrug (olumacostat glasaretil DRM01, sebostatic, inhibitor of CoA carboxylase involved in FA biosynthesis, phase III)
- Topical botulinum toxin type A (ANT-1207, anti-inflammatory, acetylcholine inhibitors and glutamate-antagonists, phase II)
- Topical tazarotene lotion (DFD-03, anti-inflammatory, retinoid prodrug: suppress keratinocyte hyperproliferation, phase III)
- Oral capsule (acebilustat CT-4430, anti-inflammatory, leucotriene A4 hydrolase inhibitors, phase II)
- Topical spray (B244, anti-inflammatory and microbiome modulation, production of nitrite nd NO to suppress inflammation, phase IIb)
- Topical gel (SB204, antibacterial and anti-inflammatory, release of NO that inhibits IL-1ß, phase III)
- Topical cream (ASC-J9, androgen modulation, synthetic androgen receptor degradation, phase III)
- Topical cream (trifarotene CD-5789, anti-inflammatory, retinoic acid receptor gamma agonists, phase III)
- Topical lupeol cream (Lupeol, suppresed lipogenesis, anti-inflammatory, NF-κB and PI3K/Akt modulator, in clinical trials)
- Topical silver particle suspension (SNA-001, photothermolysis of sebaceous gland, laser-excited particles that convert light energy to heat, phase IIb)

4. Minocyclin 4% foam:
- A unique topical minocycline preparation (Amzeeq®) developed by Foamix
- Case raport – patient picture before and affter 12 weeks, once daily, significantly improved
- Phase III clinical trials
- Inflammatory and noninflammatory lesions, age 9 years and older
- Modrate to severe acne
- Satisfactory or highly satisfactory to use
- Extension trial dana indicated that topical minocycline foam 4% continued to be effective for up to 52 week
- Stein Gold et al. J Am Acad Dermatol 2019

5. Sarecycline (Seysara®, Almirall) – recived FDA approval for acne in 2018
- Tetracyine-derivated, once daily, moderate to severe acne
- Moderate to severe acne, patients age 9 and older
- 1.5mg/kg/day and commercially available at 60mg, 100mg and 150 mg

6. Reinventing Retinoids:
- **Trifarotene (Aklief® cream 0.005%)** – 4th generation retinoid, performs both immunoregulatory and keratoplastic function
- Appears to be effective and safe in the treatment of modetare acne on face and trunk (in 2 independent, randomized, well-controled studies)

7. Suppresing sebum:
- **Clascoterone (Winlevi® cream 1%)** – anti-androgen and copetetive antagonist of DHT for the androgen receptor, moderate-to-severe acne, inhibits production of sebum, pro-inflammatory cytokines and inflammatory folicular activity
- Topically 2x daily, 60g tube, cost 580USA

8. Cannabidiol
Non-psychoactive Cannabis sativa plant, reduce inflammation and expression of inflammatory cytokines

9. Emerging Energy + Laser

- Selective photothermolysis of sebaceous glands with a 1726-nm Raman fiber laser appears to be an efficacious approach toward acne treatment
- Allowing for selective destruction of sebaceous glands for rapid and durable acne control with few treatments and minimal collateral damage

---

A holistic approach with triple peptide combination for facial skin rejuvenation

Emmanouil Dimonitsas MD, Resident in Plastic Surgery Department

1. IMCAS 2023: New beauty trend – minimalisation. Less volume, skin quality is the key of success

2. Aim: deep moisturise, reconstruction of the mid-dermis with collagen stimulation, relaxation of muscle contraction

3. Peptides facelift protocol: 4 session, each session includes:
- 1 ml argireline i.m. (forehead lines, frown lines, crow's feet),
- 2 ml argireline intra-dermally (forehead lines, frown lines, crow's feet),
- 5 ml collagen peptides nd thymopoetin in deep dermis (fine lines all over face)

4. Indications:
- patients age 40+,
- low/medium skin laxity,
- mixed/dry skin with fine lines,
- patient's preferance for non-invasive techniques,
- patients with realistic expectations of a non-invasive facelift

5. Ingredients:
- Argireline (hexapeptide-8): destabilize and interrupts the integral formation of SNARE complex - inhibits ACH release at the synapse – reduces muscle contraction and stimulates collagen production
- Hydrolyzed collagen peptides: boost the collagen self-production – increases firmness and elasticity
- Thymopoetin (Acetyl Tetrapeptyd-2): 4 –aminoacid peptide that reinforces Langerhans cells and triggers cellular reactions against ROS

6. Study: 10 patients were enrolled (Greece and Cyprus)
- Assessment clinicaly and by photographic documentation after each session
- 4 sessions
- Significant hydratation after 1 st session
- Severe improvement of skin quality – tightening and brightness 1 month after the last session

7. 4 best cases:
- women 40s: restoration of volume, skin tightening, hydratation, 4 sessions/15 days,
- women in 60s: 2 session/15 days – improvement from 1 st session of jawline and finelines, improvement in skin quality,
- man in 70s: skin tightening - improvemen of jawline, skin hydratation, smoothing of fine lines, 3 sessions/15 days, 1 session of the protocol combined with PRP

- women in 60s: cutanous lupus and rheumatoid arthritis, 4 sessions/15 days, no adverse effects, improvement from 1st session

8. Complications:
a. Redness
b. Oedema
c. No allergic or other serious adverse effects

9. Satisfaction scale: 90% patients satisfied, 10% patients needed to repeat it in one month for stronger results (deeper wrinkles), 100% all patients repeat protocol, 60% of patients did not continue with other treatment

10. Conclusion:
- Primary goal of aesthetic medicine – deeper lyers – improve skin imperfections from inside to outside.
- Key success is the treatment's combination that responds to different layers.
- A more holistic natural approach is achieved

Novel treatment approaches to scalp psoriasis

Thomas Dirschka MD, Professor of Dermatology

1. Definition and characteristics of psoriasis; immune mediated chronic skin condition of unknown orgin. Can effect the wholw body, but the scalp and limbs are the most frequently affected areas. Genetic factors play a critical rolein the development of the condition, and environental factors can exacerbate it

2. Skalp is often a first manifestation of psoriasis, usually located behind the ears and neck. Lesions varies from fine scaling to thick erythematous crusted plaques throughout the skalp. Common characteristics of scalp psoriasis are intense itching, danduff and scaring alopecia

3. Scalp psoriasis have significant impact on quality of life – several studies validated significant limitations in 30-50% of patients in terms of vacations, sports, work, interpersonal relationships, domestic life and sexual intercourse

4. Therapy:
a. Must be personalized,
b. Should provide long-lasting response,
c. There is no treatment for an absolute remission,
d. Therapeutic measures focus on partial and temporary control of the lesions. Therapy: phototherapy/oral/injectible/topical. Phototherapy (sunlight, UVB long band, UVB narow band, psoralen plus UV light A (PUVA), excimer laser). Oral/injectable (steroids, retinoids, MTX, cyclosporine, biological drugs, other)

5. Topical therapy is the therapeutic basis for scalp psoriasis and it is considered the firs line treatment in guides, but also have disadvantages:
- Corticosteroids (long-term – thinning of the skin),
- Vitamin D analogs (expencive, facial irritation),

- Retinoids (frequently causes skin irritation and increased sensitivity to light. Not recomended in pregnancy or lactation),
- Calcineurin inhibitors (not recomended in pregnancy or lactation, long-term use increase risk of skin cancer and lymphoma).
- Salicylic acid (not recomended in combination with vitamin D analogues)
- Coal tar (it may irritate skin. It is uncomfortable, stain clothes, strong odor)
- Anthralin (can irritate the skin, stain)

6. Despite the wide range of therapeutic options and a large number of studies, scalp psoriasis remains difficult to treat. A topical treatment is required secure, great penetration, fast acting, convenient application, simple regimen.

7. Corticosteroids are so far the most effective topical therapy, and first line treatment according to guides

8. Clobetasol propionate 500ug/g shampoo. Clobetasol propionate: fifth generation of corticosteroids, stable, penetration peak is more then double that the solution, greater efficiency, better safety profile, good short-term safety profile, better adhesion. Application – 15min/day 4 weeks, than maintenance 1-2x per week.

9. After 6 months, 40.3% patients did not experience a relapse. Reference supported.

10. Also, clinical evidence present that short contact application of clobetasol proprionate may be affective and safe alternative to ketoconazole in the treatment of scalp seborrhoic dermatitis. Reference supported

---

Radiofrequency micro needling in long-term acne remission and reduction of acne scar load

Fadi Hamadani MD: Professor of Plastic Surgery, Division Chief, Plastic & Reconstructive Surgery

1. Acne – causes, pathophysiology

2. Acne - isotretinoin versus Morpheus (synergy with low dose isotretinoin)
- Isotretinoin: 1/3 no responce, 55% relapse in 5 years, 30/100 scar improvement
- Morpheus (synergy with low dose isotretinoin): 0.1/3 no responce, 10% relapse in 5 years, 60-90/100 scar improvement

3. Technique:
- blast the acne with the right settings (Table: depth, energy, mode)
- Prednisone cream % 2x day for 3 days for inflammation
- Anti-histamine for 1 month
- Tretinoin or adapalene between sessions or (even better) low dose isotretinoin

4. Case (picture) before-after of female patient with acne and acne scars – notice the improvement in facial structure
- Low dose isotretinoin 20mg p.o. 2x/week for 8 months
- 2 Morpheus sessions
- Spaced 2 months apart

5. Another case (picture) before-after of female patient with acne and acne scars – (obvious improvement)
- Low dose isotretinoin 20mg p.o. 2x/week for 1 year
- 5 Morpheus sessions
- Spaced 2 months apart

6. My modality: internal subcision of acne scars using bipolar RF:
- RF energy travels from +ve internal probe to ve external pobe
- Unprecedented thermal control (int. And ext. Temp. Cut-off)
- Delivers mechanical subcision as well as coagulative remodelingof the skin from within
- Safety features including temp. surge protection, safe for all skin types

7. Video – method technique

8. The rationale:
- Subcision is a key procedure for acne scar revision
- Especially in scars that are deep and tethered (boxscars, rolling) – non monomorphic
- RF induces a coagulative necrosis with the release of many cytokines, fibroblast proliferation and induction of collagen/elastin/angiogenesis
- This is achieved both internally and externally, inducing dermal remodeling as well
- In my hands, less sessions and faster results than subcision with other modalities

9. Picture of female patient before-after - (obvious improvement)

10. Summary
- Isotretinoin fails 1/3 of patients, even adolescents, with high recurrence
- Not ideal for scar remodeling
- Fractional RF works through several mechanisms to reduce acne load (sebaceous gland ablation, anti-inflammatory cytokine release, dermal remodeling)
- Excellent adjunctfor scar revision
- Safe in all skin types with low pain and downtime

Exosomes: The new frontier of regenerative medicine - Fact or fiction?

Naina Sachdev MD, Medical Director

Goals of the presentation:
1. Real definition of exosomes,
2. Hallmarks of exosomes,
3. Regenerative potential of exosomes in aesthetic,
4. What is fact ant what is fiction for exosomes.

1. Real exosomes definition/clarification: Exosomes are biological vesicles 30-100 (150 nm) in diameter that originate as intraluminal vesicles (ILVs) in multivesicular body (MVB's) and become relesed as extracellular vesicles (EVs) upon MVB fusion with plasma membrane. EV's are all-encompassing term for cell-derivated small vesicles; include exosomes, microvesicles, and apoptotic bodies (AB,s) (Riazifar M, 2017)

2. Exosomes skin/hair benfits:
a. Aging and skin rejuvenation and regeneration
b. Scar revision
c. Atopic dermatitis
d. Wound healing
e. Ingrediants in skin-products

3. Exosomes can contain growth factors: TGFB3 – very important, HGF, ICAM-1, DAN, PF4, IGFBP2-3, IL-1B, PDGF-AA, BFGF, OPN

4. Exosome biomarkers: CD63, CD81, CD9, HSP 60, HSP 70, HSP 90, ALIX, TSG

5. Extracellular vesicles (EV's)/Exosomes: previously considered as cellular debris or excreting toxic products from cells. Essential in physiology of cell-cell communication, found in all bodily fluids. Some cell types release EV's under homeostasis, other, particularly immune stem cells, can be induced by various stimuli, including metabolic stress to release EV's. Emerging functions of EV's may be in the maintanance of tissue homeostasis, as EV's released from injured tissue have been found to influence stem cells, and conversely, stem cell-derivated EV's have been found to support injured tissue

6. Human Adipose-Derived Stem Cell (HADSC) EV'S/Exosomes: select diverse biomolecules (human adipose mesenchymal stem cell derivated exosomes). miRNA and mRNA (miRNA non-coding rnas that play important roles in regulating gene expresion), tRNA, protein, lipids, nucleic acid, GFs

7. HADSC,s Exosomes/Hair: dermal papilla cells-derivated exosomes promoted the development of hair follicles

8. Exosomes: multiple therapeutic skin efficacy: increase angiogenetic ability, increase collagen and elastin synthesis, decrease skin inflmmation (Yang et al. Biomaterials Research 2021, Ahmed MI et al, J Cell Biol 2014, Wang M et al J Dermatol Treat 2020)

9. Exosomes: tissue injury and regeneration: accelerated wound closure, enhanced collagen deposition and collagen remodeling, enhanced revascularisation, faster growth of granulation tissue , angiogenesis“.

10. Exosome concerns:
a. Mass production of high-quality exosomes should be possible,
b. Challenge with the current culture and isolation methods,
c. A multi-functional system should be developed with highly efficient isolation technique and real-timequantification and analysis technology,
d. Cell debris is removed during purification process. Label-free technology uses a 0.2um filter system in final processand test to make sure no cell culture contaminants including fragmented cell debris exsist in the final product

11. Safety testing exosomes: testing should be above the strictest guidelines for human cell and tissue culture

12. Exosome therapeutic application:
a. High extraction efficiency and mass productionof high-quality exosomes are crucial
b. Cell culture is crucial

c. Isolation manufacturing process is crucial
d. 2D skin cell culture multilayer flask processes
e. 3D skin cell culture increased particle number and quantity: scaffolds, bioreactors and spheroids

13. Goal: Highly concentrated bioavailable exosomes delivering proprietary GF for skin/hair repair and enhanced cell cohesion, stem cell regulators for skin/hair rgneration, targeted peptides, to optimize collagen and elastin production, cytokines to decrease skin/hair inflammation, hyaluronic acid for maximum hydratation and skin/hair vitamines clinically shown to decrease oxidative stress for ultimate total skin rejuvenation and repair

---

Post-inflammatory hyperpigmentation (PIH): the other side of inflammation

Giovanni Pellacani MD, Chairman of Dermatology Department

1. Definition: prmarily affects darker skin types, prevalence (0.42%-9.99%)

2. Triggers for PIH: acne, atopic dermatitis, impetigo, iatrogenic (chemical peels, laser procedures). As such, individuals with darker skin tones cannot recive certain treatments safely (Taylor 2009, Lawrence 2021)

3. Histopatology: increases in the number (hyperplasia), size (hypertrophy), and activity of melanocytes. Epidermal type (increase in epidermal melanin and minimal dermal changes), dermal type (melanine granules and melanophages in the dermis), other findings (epidermal hyperplasia/lymphocites infiltration)

4. PIH pathogenesis:
a. UV/injury/trauma
b. Hormons
c. Inflamation

5. Differential dg: melasma, solar lentigines, ephelides, drug-induced pigmentations, actinic lichen planus, facial acanthosis nigricans, frictional melanosis, Hori's nevus, Ota nevus – sometimes can indistinguishable or coexist in patients- important when devising treatment plans or enrolling patients for clinical trials

6. PIH clinical examination:
a. Distribution of pigment: uniform/patchy, symmetry, sites,
b. Wood lamp (enhancement of contrast in epidermal type, no enhancement of contrast in dermal type)
c. Dermoscopy
d. In vivo confocal microscopy

7. Dermoscopy: light to dark brown = epidermis, bluish to grey = dermis

8. Confocal microscopy: Vivascope – in vivo imaging of the skin at cellular level resolution, horizontal sections of the skin. High refractility structures: melanin contaning cells: melanocytes, pigmented keratinocytes, reactive Langerhans cell cytoplasm

9. Confocal microscopy and PIH: epidermis: polycyclic papilary conturs, dermo-epidermal junction: melanophages in the dermis

10. Confocal microscopy and PIH: MELANIN: epidermis (motted pigmentation), DEJ level (increased brightness of rings), dermis (melanophages/bright particles)

11. Mild PIH: few light brown spots: epidermis regular, DEJ small bright particles

12. Moderate PIH: few light brown spots: DEJ increased brightness of rings

13. Confocal microscopy provides:
a. A fast evoluton of PIH
b. Differentiation between epidermal or dermal involvement
c. Posibility to better classiy PIH
d. Possibility to precisely choose and monitor the best treatment

14. PIH treatment: due to different beckgrounds treatment should be better targeted on pathogenic mechanisms, atomic alterations and causes. Laser treatment, medical treatment (superficial to deep peeling, topical products)
- **Part II of the lecture:** Conflicts of intrest Beiersdorf supported with samples a case series and sponsored: "Eucerin" anti pigment: Thiamidol (thyrosinase inhibitor), Licochalcone (anti-oxidative and anti-inflammatory). Study.
- **Part III of the lecture:** Before and after laster treatment: PIH and hand freckles

15. Conclusion: PIH is a complex phenomenon, with different causes, signaling and effectors, resulting in different clinical and pathological expressions. Confocal microscopy helps to understand causes and type, to choose and monitor treatment efficacy

---

The role of antihistamine in the treatment of acne vulgaris (Effect of adding desloratadine to isotretinoin in the treatment of moderate and severe acne)

Shakir Al Saedy MD, Consultant Dermatologist and Venereologist

1. In a few words, simplified definition, epidemiology, etiology and pathogenesis, trigger factors and therapy of acne vulgaris, side effects of oral isotretinoin
2. Role of histamine in acne: the histamine have inflammatory effects in the pathogenesis of acne vulgaris. Mast cell mediators cause keratinocytes proliferation which is one of the pathogenic mechanism of acne formation, mast cell histamine stimulates fibroblast release of fibroblast GF-2 which leads of keratinocytes proliferation“
3. Presentation of the study: "Effect of adding desloratadine to isotretinoin in the treatment of moderate and severe acne" - without explanation for the idea of that particular combination (isotretinoin-desloratadine).
4. Aims of the study:
a. To assess the effect of using long acting anti histamine (desloratadine) with isotretinoin in daily protocol for treatment of moderate to severe acne.
b. To compare the efficacy, safety, adverse effects with both treatment regimes
5. Groups: Cases group (30 patients) recived 5 mg of oral desloratadine (Aerius) daily and 20 mg of isotretinoin (Dermatane) after meal at morning for 12 weeks. Control group (30 patients) recived oral

isotretinoin 20 mg after meal for a total period of 12 weeks
6. Results: the results revaled that in both groups, there was significant reduction of the inflammatory lesions at the end of trial compared to baseline ($p<0.05$).
7. Conclusion: safety of desloratadine and its low cost made it highly recommended as adjuvant therapy for standardized acne treatment.

Tomorrow's treatment for alopecia areata

Annunziata Dattola MD, Researcher at The Department of Dermatology University of Rome Tor Vergata, Italy

1. Introduction: hair cycle, classifications: scarring and non-scarring alopecia, non-scaring 6 major categories (alopecia reata, androgenetic alopecia, telogen effluvium, traumatic alopecia/trichotillomania, tinea capitis, anagen effluvium)
2. Alopecia areata: autoimmune disorder, 2% population worldwide, autoantibodies attack follicular hair cells of the bulb disturbing the anagen phase. AA - patchy, totalis and universalis. Can be associated with atopic diseases and other autoimmune diseases
3. Damage to the hair follicle occurs when there is disruption of the protective shield of growing hair, resulting in formation of autoreactive CD8+ T-cells directed against the follicular cells
4. Prevalence of alopecia areata is 0.2%, no racial or sexual predilection, it may affect any age group
5. In patients with alopecia areata there is a peribulbar lymphocytic infiltrate with a decrease in the ratio of anagen to telogen hair
6. JAK inhibitors for alopecia areata: Tofacitinib (JAK1 and JAK 3), Baricitinib (JAK 1 and JAK 2), Upadacitinib (JAK 1)
7. JAK inhibitors are small molecules which bind to Janus kinases and disrupt the signalling cascade. In contract to biologic therapy which uses large molecules-antibodies administratedusually subcutaneously, JAK inhibitors are orally administrated, rapidly absorbed and have short half-lives mostly between 4-8 hours
8. In alopecia areata autoreactive CD8+ effector T-cells produce IFNγ receptors on follicular epithelial cells and via JAK1/2-STAT pathway induces the production of IL-15. IL-15 binds to receptors on CD8+ T-cells and via JAK1/3 STAT pathways signals the production of more IFNγ. The positive feedback loop potentiates the inflammatory response and leads to disruption of anagen phase with consequent hair loss
9. Baricitinib is JAK1/2 inhibitor but can also block JAK3 (Triyangkulsri 2018). In EU is licensed for the treatment of severe resistant rheumatoid arthritis and atopic dermatitis (EMA 2017). As of 13th June 2022 it is also the first drug which is licensed for the treatment of alopecia areata in the USA and has pending approval in the EU (FDA 2022)
10. The decision was based on the results of two clinical trials (BRAVE-AA1 and BRAVE-AA2). Around 40% of the patients who received baricitinib 4mg tablets ad at least 80% scalp covered by hair in contrast to 6% of the placebo group after 36 weeks. Side effects include upper respiratory and urinary tract infections, acne, increased LDL and CK levels, and HSV infections
11. Clinical Case: 32-year-old woman affected by rheumatoid arthritis with low activity presented 2018 alopecia areata patches. Initially treated with cyclosporine 250mg/day and complete hair regrowth, maintained up to 2 years even after tapering the cyclosporine dosage down to 200mg/daily. After 2 years severe episode of acne fulminans occurred (o history of acne), requiring therapy with isotretinoin 60mg/day for 24 weeks. Alopecia areata showing new patches on the scalp, she lost eyebrows and lashes (at), and then alopecia universalis. Topical therapy with squaric acid dibutyl ester (SADBE) started for 24 weeks – with no improvement

12. In addition, due to the rheumatological disease the decision of staring baricitinib 4 mg per day orally was made.
13. After 8 weeks regrowing hair was observed. After 3-month complete regrowth. No adverse event. Published in Ital J Dermatol Venerol 2022.

Update in treatment of rosacea

Husain Juma MD, Consultant Dermatologist

Complete overview of rosacea (definition, pathogenesis, quality of life, connection with other diseases, subtypes and variants of rosacea, stages, characteristics, triggers, contributing factors). Overview of the entire therapy with news: topical: brimonidine, azelaic acid, ivermectin, metronidazole, minocycline (foam), and systemiv (doxycicline 40mg, isotretinoin, minocycline, ß-blockers), laser, botox and IL-17 inhibitors injections, and agents under development.

Conclusions:
1. Topical ivermectin (high-certainty evidence) was demonstrated to be the most effective topical treatment for papulopustular rosacea and provide the greatest psychological benefit to these patients. Also, can be applied not onlyto skin almost clear of papulopustular rosacea, bit also to skin with moderate to severe rosacea.
2. Topical minocycline (moderate-certainty evidance) foam and gel (in studies) show efficacy and safety for the treatment of moderate to severe papulopustular rosacea (Amzeeq®)
3. Tranexamic acid (topical or systemic) is a conventional treatment for melasma. It may improve the symptoms of patients with rosacea by regulating the immune response and angiogenesis. There a re notable decreases in the visual scale scores for itching, flushing and burning, and no significantadverse events observed (Kim e al 2013)
4 ß-blockers might be useful to treat persistant erythema – carvedilol, propranolol)
5. PDL and IPL therapy (low-to-moderate evidence) recommended for the treatment of erthema and mainly teleangiectasia)
6. Injections (?) – botulinum toxin, IL-17 inhibitors.
- Botox has beed demonstrated to be useful in rosacea treatment (two studies) - some of the possibilities - requires experience, considerations of cost and need for repeated injections.
- IL 17-inhibitors (Cosentyx® 150mg (sucukinumab) – IL-17 links Demodex folliculorum to angiogenesis, teleangiectasias, inflammation, and pustules. It is costly, might be used to treat severe and treatment-resistant papulopustular rosacea (refers to the study 20 patients receiving secukinumab). Need larger studies to evaluate the efficacy and safety of IL-17 inhibitors)

Agents under development:
1. Encapsulated benzoyl peroxide cream 5% (Epsolay ®). Nearly 70% reduction of inflammatory lesions of rosacea by the end of 12 week. (PRICE +500 USD)
2. B244 spray
3. DMT210 5% gel
4. Hydroxychloroquine 200mg twice daily
5. Minocycline: extended relase capsules (DFD-29 20mg and 40mg), minocycline (1.5% and 3% foam, minocyclin 1% and 3% gel, omiganan gel
6. Rifaximin (Xifaxan®)
7. Secukinumab 300mg weekly for 5 weeks then monthly (Cosentyx®)

Lip fillers different techniques for best results

Dina Ahmed Dorgham MD, Associate Professor of Dermatology

1. 4 point injection technique (Sahan A et al. Acta Dermatovenerol Alp Panonica Adriat 2018)
2. Phi technique (Karamidas E et al. Plast Reconst Surg Glob Open 2021)
3. Inverted Mercedes Benz sign technique (Adel N. Plast Reconst Surg Glob Open 2021)
4. Bi-Bi technique: uses 2 different fillers – one for conturing and the second for volumizing (Smarrito S et al. JCD)
5. French Kiss technique (Trevidic P et al. Dermatologic Sugury 2020)
6. Minimalistic approach (Goel A et al. J Cosmet Dermatol 2022)
7. Take home message:

- Filling the lips has mainly 2 axes:

a. Vermilion border (including the philtrl columns and cupid bow).
b. Body of lips (tubercles)

- When you use cannulas instead of needles: it could be less likely to cannulate a vessel but it is not impossible
- Knowing the anatomy is of ulmost importance
- Picking the proper depth as well as direction of injection might help you to relatively safer injections

---

Current and Future Uses of Phosphodiesterase -4 Inhibitors in Dermatology

Isam Oumeish MD, Consultant Dermatology and Venereology and Laser

1. Phosphodiesterase inhibitors (PDE) – a group of drugs inhibiting specific phospohodiesterase enzymes in various cells. FDA approved for: COPD, erectile dysfunction, psoriasis, psoriatic dermatitis, atopic dermatitis

2. PDE inhibitors: exert their effects, depending on the specific enzyme they target:

- PDE3: inhibitors for heart diseases
- PDE4: inhibitors for psoriasis, PA, AD, IBD, COPD
- PDE5: inhibitors for erectile dysfunction

3. Mechanism of action: block one or more of the five subtypes of the enyme (PDE) thereby block the degradative action on: cAMP, cGMP

4. PDE4 inhibitors effects:
a suppress generation of inflammatory cytokine,
b. Reduce superoxide generation and chemotaxis,
c. Upregulate anti-inflammatory cytokines such as IL-10

5. FDA Approval:

- Crisaborole: Dec. 2016 for mild and moderate AD in patients older than 2 years. In 2020 for children at least 3 months of age
- Apremilast: Mar. 2014 for psoriatic arthritis. Sept. 2014 for plaque psoriasis

6. Apremilast: until now, only aprroved oral PDE-4 inhibitor for the treatment of psoriasis

7. Apremilast dosing: available in 10mg, 20mg and 30mg tablets (start with 10mg morning dose with daily increment of 10mg until day 6 when the recommended dose (30mg bid) for adults is reached

8. Apremilast side effects: GIT symptoms: nausea, vomiting, diarrhea (most common side effect), headaches, worsening depression, suicidal thoughts, weight loss, upper respiratory infections

9. Apremilast induced diarrhea – most cases are reported within the first 2 weeks of Tx and are self-resolving within 1 month even with ongoing treatment. Intractable diarrhea may necessitate dose reduction or even Tx dicontinuation

10. Apremilast drug-drug interaction: apremilast level is reduced decreasing its efficacy when given with CYP450 inducers such as:
a. Rifampin,
b. Phenobarbital,
c. Carbamezapine,
d. Phenytoin

11. Topical Apremilast: Nanocrystal and micronized-based formulations (gel and cream) to improve topical delivery are under invastigation. Recently, a nail lacquer formulation for nail psoriasis is under trial

12. Trials on off-label indications od Apremilast: Review of Literature (perforating dermatosis, granuloma annulare, genital erosive lichen planus in women, disseminated granuloma annulare, Behcets disease, Bechcets syndrome (3 trials)).

13. Crisaborole:
- topical PDE4 as 2% ointment
- a nonsteroidal alternative for treating AD
- modifies inflammation by inhibitinh degradation od cAMP by PDE4 thus increasing cAMP level which result in downregulation of Th2 pathway

14. Crisaborole side effects:
- burning and/or stinging at site of application
- hypersensitivity: prutitus, swelling, erythema, contact urticarial (in this case should be discontinued)

15. Pefcalcitol: an analog of topical vitamin D3 with PDE4 inhibitory activity. Preclinical studies suggested its efficacy in plaque psoriasis with fewer side effects than topical vitamin D3

16. Roflumilast: in 2022 the FDA approved roflumilast 0.3% cream once daily as the firs topical PDE inhibitor for Tx of plaque psoriasis, including psoriasis in intertriginous areas, in patients 12 years of age and older

17. Roflumilast: a presentiation at EADV Congress Sep. 2021 showed: topical Roflumilast has caused significant itch reduction in many conditions including body and skalp psoriasis as well as in seborrhoic dermatitis. Published Am J Clin Dermatol 2022

18. Conclusion:
- PHD inhibitors are relatively new development in treatment of psoriasis and atopic dermatitis
- Examples of already approved PDE inhibitors are: oral apremilast, topical crisaborole and topical roflumilast

- More PDE inhibitors are currently in the pipeline
- Wide range of off-labelindications are under clinical trial awaiting licensing

Don't miss any congress reports