EA DV CONGRESS
BERLIN 11-14 OCTOBER 2023
EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY

Abstract N°: 19

A convergent synthetic platform of hydrogels enclosing prednisolone-loaded nanoparticles for the treatment of chronic actinic dermatitis.

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[1]Guangzhou Institute of Dermatology

Introduction & Objectives:

Recurrent eczematous lesions and acute itching occurring on the sun-exposed area was the main feature of chronic actinic dermatitis (CAD). Topical corticosteroid is the first-line treatment of CAD, however, continuous use of corticosteroids might result in a dermal adverse effect. Effective and precise treatment options are made possible by modern drug delivery technologies.

Materials & Methods:

Chitosan (CS)-coated PLGA nanoparticles encapsulated prednisolone (PDS) and co-encapsulated to poloxamer hydrogel to enhance anti-inflammatory action and reduce side effects. The PDS@NPs were synthesized using the solvent-emulsification evaporation method, and their physical and chemical properties were analyzed. The hydrogels' rheological characteristics, such as viscosity and the temperature at which the sol-gel transition occurs, with and without nanoparticles, were investigated. Ex vivo drug absorption experiment was conducted utilizing the Franz diffusion cells in vitro.

Results:

Toxic effects on human fibroblasts and keratinocytes were not observed in the nanoparticle formulations; however, they all stimulated the production of reactive oxygen species. Nanoparticles and hydrogels altered PDS's release kinetics, but not by the non-encapsulated molecule. Nanoparticles could not penetrate the stratum corneum of removed the skin, which shows the nano encapsulation of PDS improved skin absorptions. Pseudoplastic and non-Newtonian behavior was seen in all hydrogels, whether they contained nanomaterial.

Conclusion:

The nanoformulations appear to be a promising option for glucocorticoid delivery to individuals with chronic actinic dermatitis (CAD).

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Abstract N°: 148

A Case of Eosinophilic Annular Erythema Treated Successfully with Colchicine

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Introduction & Objectives:

Eosinophilic annular erythema (EAE) is a rare eosinophilic dermatosis presented with recurrent urticarial and annular or polycyclic erythematous plaques with central healing. The disease usually appears on the trunk and proximal extremities, and is chronic and relapsing. Histologically, EAE is characterized by a superficial perivascular and interstitial mixed infiltrate with prominent eosinophils. To date, only a few cases of EAE have been reported in the literature. Herein, we report a case of EAE successfully treated with colchicine therapy.

Materials & Methods:

A 75-year-old woman presented to our clinic with itchy and painful erythematous plaques with a central clearing of 6 months duration on her extremities and torso. Dermatological examination revealed annular erythematous plaques with elevated borders, and central healing on her abdomen, back, upper, and lower extremities. She had no response to antihistamines, montelukast, topical corticosteroids, or emollients. She had a personal history of chronic lymphocytic leukemia (CLL) and hypertension.

Results:

Laboratory studies, including renal and liver function tests, total immunoglobulin E, anti-nuclear antibody, and complement levels, were normal. She had lymphocytosis and leukocytosis due to CLL. Malignancy screening showed no pathological results.

Histopathological examination revealed mild acanthosis, mild spongiosis, edema in the papillary dermis, and mixed perivascular interstitial inflammatory cell infiltration rich in eosinophil leukocytes. There were no signs of vasculitis, granuloma formation, flame figures, dermal mucin, or vacuolar changes (Figure 1).

Based on clinicopathological findings, the diagnosis of EAE was made. The patient was administered 1 milligram of colchicine, and the lesions completely cleared after one month, with no recurrence in two years of follow-up.

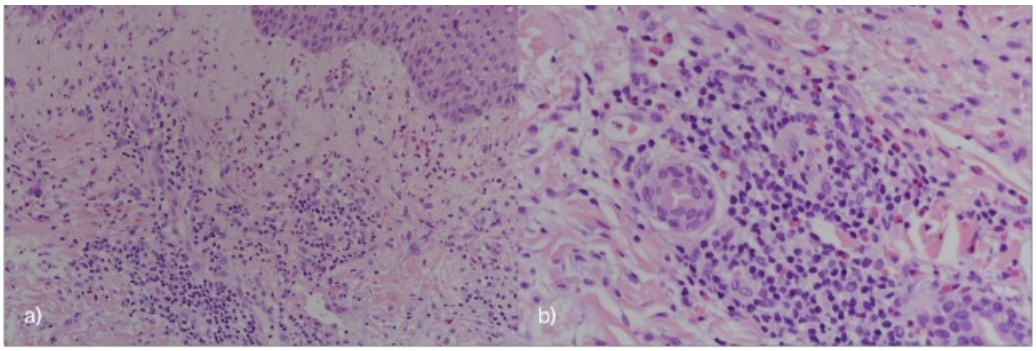

Figure 1. (a,b) Histopathology showed mild acanthosis, mild spongiosis, papillary dermal edema, and mixed perivascular interstitial inflammatory cell infiltration rich in eosinophil leukocytes in the epidermis. (H&E; 40X &

100X respectively)

Conclusion:

EAE is a rare eosinophilic dermatosis with a differential diagnosis of Wells Syndrome, figurate erythemas, granuloma annulare, erythema multiforme, and urticarial phase of bullous pemphigoid. The pathogenesis of EAE remains unclear. Associated disorders consist of malignancies, chronic infections, and autoimmune diseases. Due to its potential association with malignancies, EAE patients can be candidates for cancer screening.

Effective and safe therapeutic options for EAE management are needed. Therapeutic options reported in the literature include topical corticosteroids, antimalarials, dapsone, thalidomide, and various biologic agents.

Colchicine is an alkaloid that inhibits tubulin polymerization, leading to subsequent downregulation of multiple inflammatory pathways and modulation of innate immunity. Because of its anti-inflammatory effect, colchicine's inhibition of microtubule polymerization and altered expression of adhesion molecules and chemotactic factors could explain the adequate clinical response in our case.

In conclusion, we report a case of EAE successfully treated with colchicine without any relapse. The efficacy and safety of colchicine make this drug a new therapeutic option for this rare and difficult-to-treat disease. Further studies are necessary to confirm our findings.

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Abstract N°: 334

A novel formulation of Sildenafil-loaded lipid-based nanocarrier for treatment of alopecia areata: A randomized clinical study

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Introduction & Objectives: Alopecia areata (AA) is a nonscarring patchy hair loss. Numerous treatment options are available with variable outcome. Sildenafil, a phosphodiesterase 5 inhibitor, might promote hair growth. This study evaluated the safety and efficacy of topical sildenafil vs minoxidil in the treatment of AA.

Materials & Methods: Twenty-eight patients, with patchy AA of the scalp, were treated by either topical 5% minoxidil gel or topical 1% sildenafil-loaded liposomes twice daily for 8 weeks. Results were assessed by the percentage of clinical improvement, severity of alopecia tool (SALT), and by dermoscopic evaluation at baseline, 4, and 8 weeks.

Results: Both groups demonstrated hair regrowth after treatment with reduction in SALT scores. Significant improvement was detected at 4 weeks in sildenafil treated patients ($p=0.007$), but only at 8 weeks in minoxidil treated patients ($p=0.011$). There was significant decrease in dystrophic hairs by dermoscopic evaluation in both groups ($p<0.05$). The differences between both groups were insignificant. All patients in sildenafil group had regrowth of new vellus hair and 13 (81.3%) patients had pigmented hair regrowth compared to 7 (58.3%) and 10 (83.3%) patients in minoxidil group.

Conclusion: Sildenafil-loaded liposomes is a safe and promising therapeutic option in AA. Dermoscopy is very useful to identify signs of early clinical response.

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Abstract N°: 458

Maffucci's angiochondromatosis: an unusual form, Rapamycin trial

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Introduction & Objectives:

Angiochondromatosis or Maffucci syndrome is a very rare, constitutional, non-hereditary condition of unknown etiology. Classically defined by the association of multiple enchondromatoses of the metaphyses and diaphyses of the bones and a hemangiomatosis of the soft tissues.

The evolution is characterized by the high risk of emergence of neoplastic processes which considerably affect the prognosis. The transformation of chondromas into chondrosarcomas is the most frequent.

We return to a case of Maffucci syndrome described 24 years ago by O.Boudghen Stambouli et all, to highlight on the one hand the evolutionary aspect of the disease and on the other hand the satisfactory response to Rapamycin.

Materials & Methods:

Patient aged 52 years, from a non-consanguineous marriage, single and without any particular family history. Known for a Maffucci syndrome evolving since early childhood, the diagnosis was established 20 years ago thanks to clinical examination, imaging and histology data

Results:

The evolution was marked by multiple ray amputations .

Indeed, an amputation of the first and second radius of the left hand and the left big toe was performed because of their massive involvement in the tumor process, with an exeresis of multiple enchondromatosis and hemangiomatosis lesions of the proximal phalanx of the left ring finger, the wrist and the left foot. Other radii were also involved but to a lesser extent.

The histological study of these surgical specimens did not reveal any evidence of mitotic activity or tumor necrosis related to sarcomatous degeneration.

A significant shortening of the left upper and lower limbs occurred progressively, leading after many years to a flagrant inequality of the limbs, causing a significant scoliotic attitude and a genu valgum, further altering the quality of life of our patient.

The use of Rapamycin in this indication is all the more interesting as it would reduce the risk of emergence of neoplasia as reported by Alberu et al in renal transplant patients receiving Rapamycin.

The use of Rapamycin at 2.5 mg/m2 of body surface area, allowed to obtain in our patient a clinical benefit, with almost complete disappearance of pain and decrease in the size of the vascular lesions, as well as a beginning of the improvement of the function of the left hand, after 20 days of treatment. And without signs of intolerance. It will be continued for a few more months

Conclusion:

Follow-up of patients with Maffucci syndrome is crucial and should aim at early detection of associated neoplasia as well as sarcomatous degeneration of vascular and cartilaginous lesions.

The case reported above shows a satisfactory response to the use of Rapamycin from the first days of treatment, but the lack of hindsight does not allow us to conclude the definitive effectiveness of the molecule in our patient.

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Abstract N°: 522

use of alpha, beta and poly hydroxyacids (aha, bha, pha) in cosmeceuticals

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[1]Mohammed VI University of Health Sciences

Introduction & Objectives:

Formulations containing hydroxy acids have been used in clinical practice for decades to treat various skin conditions. The aim of our study is to constitute a repository of good practices for the use of cosmeceuticals containing hydroxy acids.

Materials & Methods:

In this study, we conducted an exhaustive literature search according to the PRISMA guidelines. A total of 42 publications were retained in the final qualitative analysis. The information extracted was the mechanisms of action, classification, indications and the side effects of hydroxyacids (HA). The use of HA for medical peeling purpose at high concentrations (> 20%) was excluded from our study.

Results:

AHAs are organic acids (glycolic acid, lactic acid, malic acid, tartaric acid…), widely used in cosmetic formulations. Their main properties are: exfoliation, hydration, improvement of the skin texture and anti-inflammatory action. However, caution is required given their side effects (photosensitivity, irritation, edema, pruritus…). BHA (lipohydroxyacid, salicylic acid) are fat-soluble acids that penetrate deep into the pilosebaceous follicle, used at maximum concentrations of 4% in retentional and inflammatory acne. Bionic acids are a recent non-irritating class, widely used in patients with rosacea, acne and reactive skin.

Conclusion:

Our study is the first literature review covering original articles from 1980 to 2022. The conception of new topical, less irritating, fat-soluble formulas that act against clinical and biological impact of the exposome on the skin represents one of the promising advances in cosmetology.

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Abstract N°: 543

Evaluation of clinical and perceived efficacy of an anti-aging filler stick

Renato Pinto[1], Jayme Filho*[2], Neise Orru Cerqueira[1], Beatriz Mendonça[1]

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Evaluation of clinical and perceived efficacy of an anti-aging filler stick

Introduction & Objectives:

Facial skin aging is a progressive degenerative process, resulting from a physiological decline in skin tissue functions due to a combination of intrinsic and extrinsic factors. The extrinsic factors that expose the skin to various aggressions, such as ultraviolet radiation and atmospheric pollution, induce alterations in morphological and biophysical properties of the skin, clinically manifested as wrinkles and change in skin texture, for instance. Considering this context, extrinsic aging acts as an intensifier of chronological aging.

Several cosmetic ingredients can play an important role to prevent extrinsic aging and improve the quality of the skin. Vitamin A is known to promote beneficial effects in the treatment of photoaging, significantly reducing from superficial to deeper lines. Retinol palmitate, an ester of retinol, is the main form of vitamin A found in the epidermis and is the most stable ester of vitamin A, also presenting less irritability to the skin compared to other forms.

Hyaluronic acid is a glycosaminoglycan, fundamental substance of the dermis recognized by its anti-aging actions due to its ability to hydrate, lubricate and elasticize the skin, maintaining the shape of the tissues. Furthermore, the application of topical hyaluronic acid helps to support the synthesis of collagen.

This study aims to evaluate clinical and perceived efficacy of an anti-aging filler stick formulated with retinol palmitate and two types of hyaluronic acid, under facial anti-aging criteria. The product should help reducing lines and wrinkles, while promoting firmness and preventing signs of aging.

Materials & Methods:

The evaluation of clinical and perceived efficacy of an anti-aging filler was conducted following an unicentric, blinded, non-comparative clinical study that included 30 female participants aged 30 to 60 years with signs of mild facial aging (wrinkles and expression lines).

The product was applied on clean and dry skin with circular movements on the affected areas by signs of aging and/or regions that need texture improvement. The perceived evaluation was made under the application of a subjective questionnaire and concluded after 30 days.

Results:

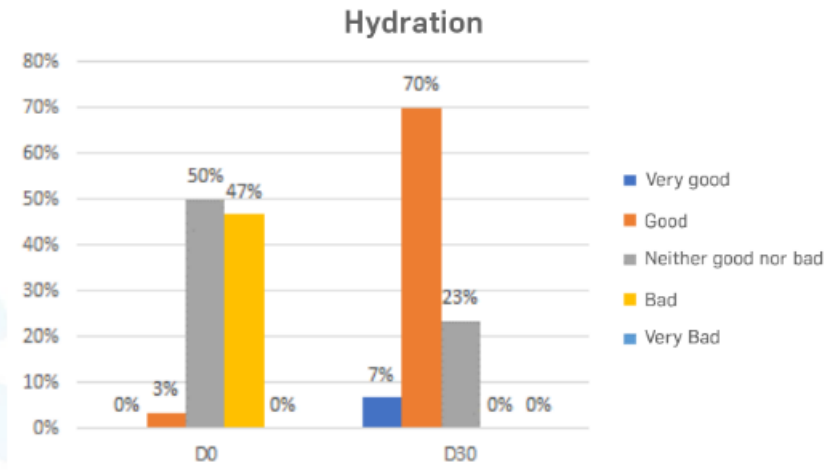

Figure 1. Evaluation of clinical efficacy - D0 and D30 - N=30

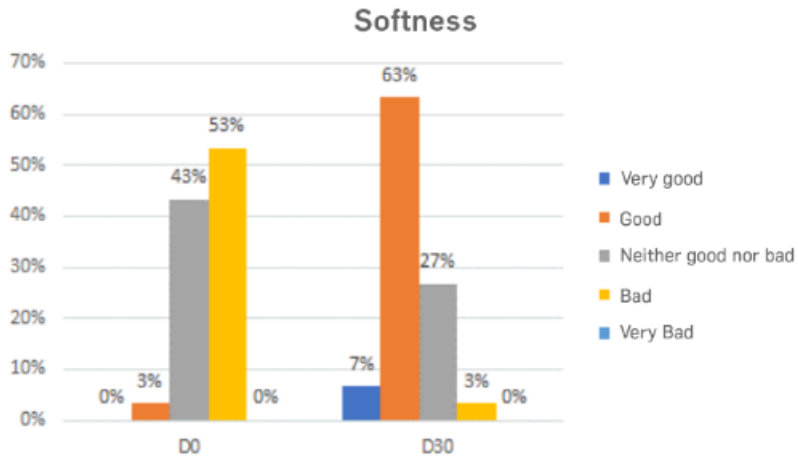

Figure 2. Evaluation of clinical efficacy - D0 and D30 - N=30

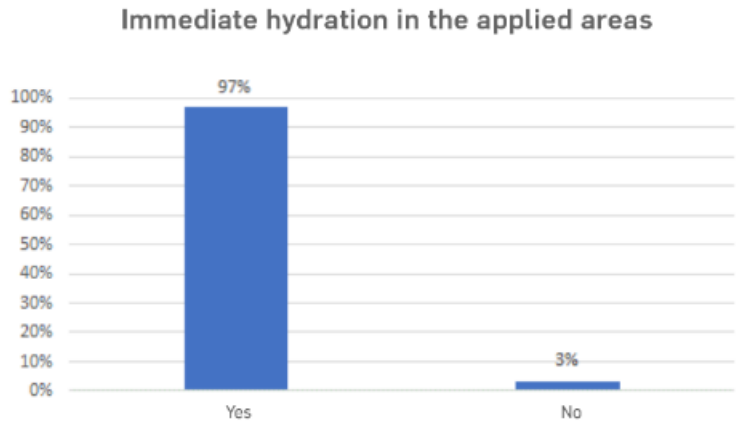

Figure 3. Evaluation of perceived efficacy at D30

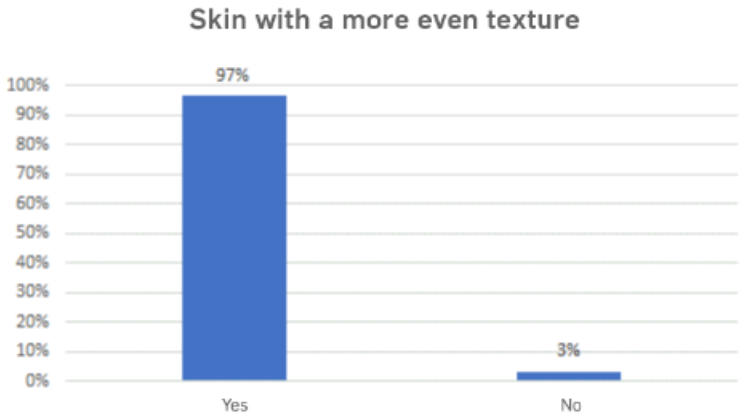

Figure 4. Evaluation of perceived efficacy at D30

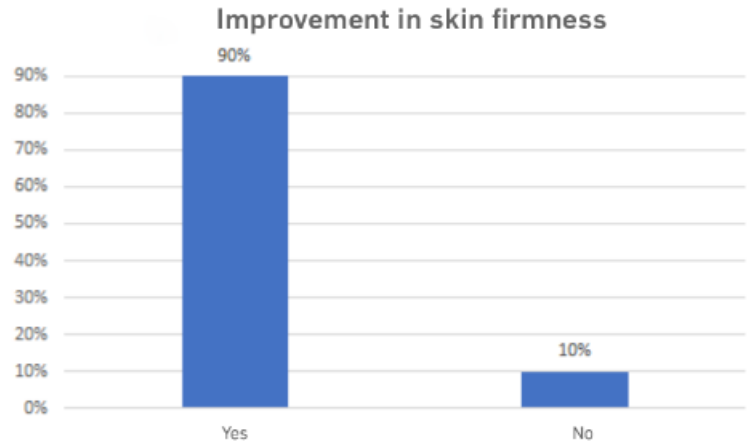

Figure 5. Evaluation of perceived efficacy at D30

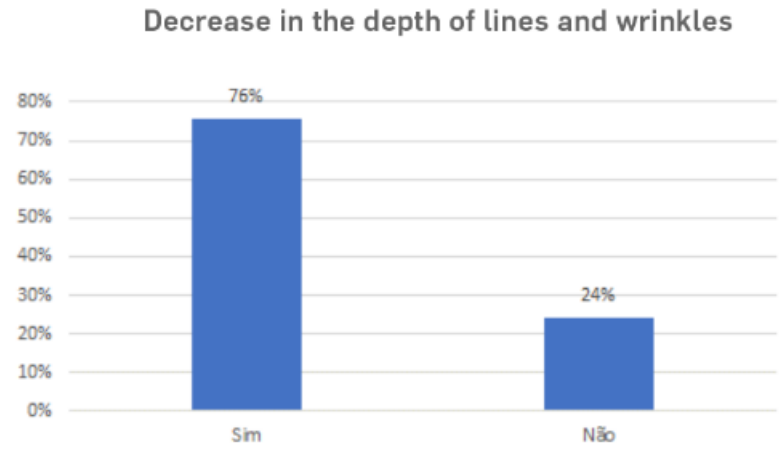

Figure 6. Evaluation of perceived efficacy at D30

Conclusion:

The anti-aging filler stick showed proven effectiveness in the evaluated parameters. The clinical efficacy of the product showed an improvement of 67% in skin hydration and an improvement of 60% in skin softness. According to the perceived efficacy, 97% of the participants perceived immediate hydration; 90% perceived a more even skin texture; 90% perceived an improvement in skin firmness and 76% perceived a decrease in the

depth of wrinkles and lines.

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Abstract N°: 647

Evaluation of antioxidant potential of topically nanoencapsulated Vitamin C

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Evaluation of antioxidant potential of topically nanoencapsulated Vitamin C

Introduction & Objectives:

As a potent antioxidant, Vitamin C is able to donate electrons and neutralize the free radicals present in the intra and extracellular matrix, avoiding lipid membrane, DNA and proteins damage that would be caused by oxidative stress and eventually lead to a photoaging proccess.

Paradoxically, once solubilized, vitamin C degrades rapidly into less active species by atmospheric oxygen, catalyzed by light, heat, and metal ions. In order to avoid this oxidation, many derivatives of Vitamin C have been introduced, including ascorbylpalmitate (AP), that has improved stability and better skin penetration. The deceleration in the AP degradation has been obtained by nanoencapsulation, a delivery system that offers several advantages such as increased surface area, higher solubility and stability, improved permeation through epithelia barriers and reduced skin irritancy.

This study aims to evaluate and compare the antioxidant potential -represented by free radicals production- of nanoencapsulated Vitamin C (as ascorbylpalmitate), in different concentrations.

Materials & Methods:

To compare the antioxidant potential of a Vitamin C nanoencapsulated system, it was conduced an in vitro study using cultured human dermal fibroblast cells and evaluated the production of reactive oxygen species, also known as free radicals.

The identification of free radicals is performed with a fluorescent probe in 3 samples: (1) 10% Nanoencapsulated Vitamin C; (2) 20% Nanoencapsulated Vitamin C and (3) 30% Nanoencapsulated Vitamin C. The solutions containing the control and sample groups were applied to the cell culture, in quintuplicate for each group, followed by incubation for 24 hours. The values obtained after the application of the samples are compared with the values of the control group (basal state of the cells producing free radicals).

Results:

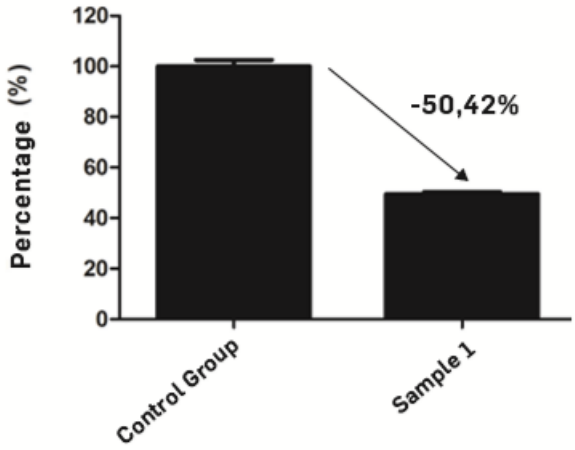

Figure 1. Percentage of free radical production after 24 hours compared to the control group referring to sample 1.

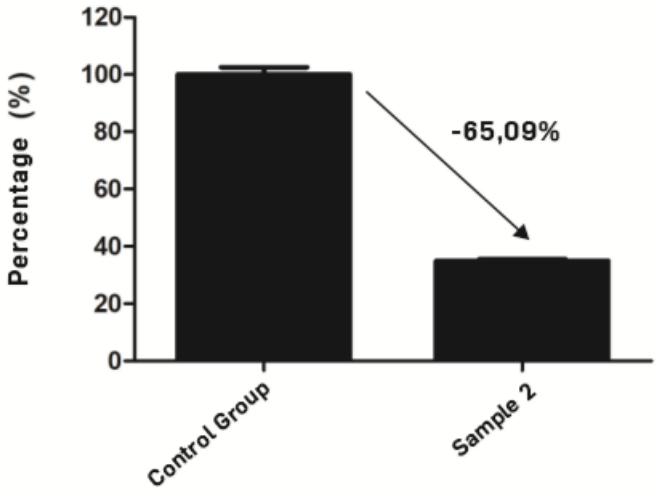

Figure 2. Percentage of free radical production after 24 hours compared to the control group referring to sample 2.

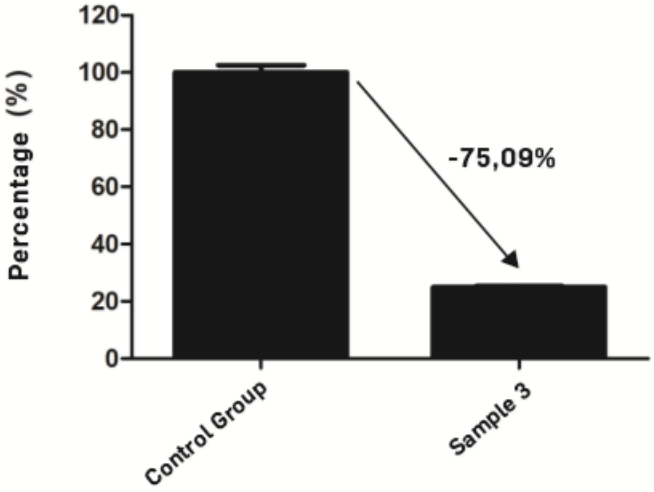

Figure 3. Percentage of free radical production after 24 hours compared to the control group referring to sample 3.

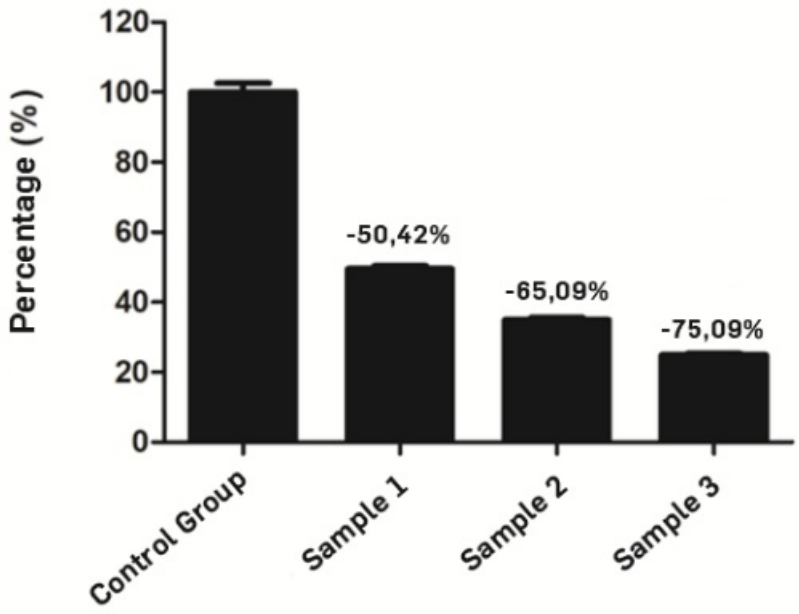

Figure 4. Percentage of free radical production with comparison between control group and evaluated samples.

According to the obtained results, all evaluated samples showed significant reduction in the production of free radicals in relation to the control group. It was observed that sample 3 showed the highest percentage of free radical reduction (reduced 75,09% of free radical production compared to the control group after 24h of exposure).

Conclusion:

These finding suggests that a Vitamin C nanoencapsulated system (with its derivate ascorbylpalmitate) presents higher antioxidant action as the concentration increases, once the free radical production decreases. This could motivate even more its use as topical antioxidant in cosmetic preparations, in order to strengthen antioxidant capacity and thus reduce reactive oxygen species-induced skin damage.

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EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY

Abstract N°: 750

Safety, Tolerability and Pharmacokinetics of GT20029 Gel and GT20029 Solution in Healthy Subjects

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[1]National Clinical Research Center for Geriatric Diseases (Huashan Hospital), Shanghai, China; 200040,[2]Phase I Clinical Research Center, Huashan Hospital, Fudan University, Shanghai, China, [3]Kintor Pharmaceuticals, Suzhou , China

GT20029-CN-1001 Abstract for EADV Congress in Berlin 2023

Introduction & Objectives:

The interaction of dihydrotestosterone (DHT) and the androgen receptors (AR) is one of the pathophysiologies of Androgenetic Alopecia (AGA) and Acne. GT20029 is a topical AR-Proteolysis Targeting Chimera (PROTAC), which recruits AR in proximity to an E3 ubiquitin ligases to initiate AR ubiquitination and subsequent degradation. In preclinical studies, GT20029 can promote hair growth significantly in dihydrotestosterone (DHT)-induced AGA mouse model and inhibit testosterone propionate (TP)-induced flank organ enlargement with statistically significance in hamster flank organ acne model. Therefore, it showed potential treatment efficacy in promoting hair growth and inhibiting sebaceous gland development. GT20029 also exhibited low systemic exposure and a good safety profile. In light of the above, this phase I clinical trial to evaluate GT20029 gel and solution safety, tolerability and pharmacokinetics (PK) in healthy volunteers (HV) was initiated at China.

Materials & Methods:

This was a single-center, randomized, double-blinded, placebo-controlled, parallel group, dose escalation study with two stages. Stage 1: HVs were treated with GT20029 gel or placebo. 28 HVs were planned to enter single ascending dose (SAD) group with 4 different doses, and 40 HVs to multiple ascending dose (MAD) group, of whom can be recruited from SAD cohorts (after 14 days wash out period) or from other sources. Stage 2: HVs were treated with GT20029 solution or placebo. 24 HVs were planned to enter MAD group with 3 different doses. All drugs/placebo were topically administrated to the subjects on a fixed 8cmX 8cm area of the back. The study design and dose assignement table are in Figure 1. PK blood samples were collected regularly. Safety assessment included monitoring of adverse events (AEs), vital signs, laboratory findings, electrocardiogram, physical exams and assessment of the application site skin. Study endpoints included evaluation of safety and recommended phase II dose (primary) , PK characters and systemic exposure (secondary) of GT20029.

Results:

From July2021 to Aug2022, 95 subjects were randomly enrolled, including 69 in stage 1 and 26 in Stage 2 (Figure 2). HVs' baseline demographics is listed in Table 1.

Total 92 HVs were included in the safey analysis set, treatment emergent AEs (TEAEs) were reported in 68 subjects (73.9%), of whom 64 and 4 subject's TEAEs were grade 1 and grade 2, respectively. 64 subjects' AEs were deemed as drug-related AEs (DRAEs). The most reported DRAEs (≥10%) were rash, skin exfoliation, and pruritus. Less DRAEs incidences were observed in Stage 2 compared to that treated with gel (Table 2). No DRAEs were ≥ grade 3 nor led to cessation of treatment or death.

There was no systemic exposure after single dose of gel application. Since blood concentrations were Below

Limit of Quantification (1pg/ml) at the most points, PK showed linear characteristics after multi-dose application of gel/solution in the range of 2-10 mg and 5-20 mg, respectively.

Conclusion:

Overall, HVs who received a single application of GT20029 gel (1, 2, 5 and 10 mg) or 14-days topical GT20029 gel (2 mg QD, 2mg BID, 5mg QD, 5mg BID, 10 mg QD) or solution (5mg QD, 10mg QD and 20 mg QD) showed low system exposure and good safety. Combined with the obtained PK characteristics and overall safety data, it is recommended to explore the safety and efficacy of multi-dose application of GT20029 solution (5 mg 0.5% QD, 10 mg 1.0% QD) in follow-up studies.

EA CONGRESS DV
BERLIN 11-14 OCTOBER 2023
EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY

Abstract N°: 989

Real-world evidence of tirbanibulin for actinic keratosis in Germany - First insights into patient-reported outcomes

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Introduction & Objectives: Tirbanibulin is a synthetic tubulin polymerization inhibitor developed as a 1% ointment for the topical treatment of actinic keratoses (AK). The efficacy and safety of tirbanibulin has been demonstrated in two pivotal phase 3 clinical trials [1]. Tirbanibulin was approved by the EMA in July 2021 and launched in Germany in September 2021 [2]. A non-interventional study has been conducted in Germany aiming to evaluate patient-reported outcomes (PROs), effectiveness and safety of tirbanibulin in AK in dermatology outpatient clinics and practices.

Materials & Methods: The following visits have been conducted in this multicentre, prospective trial: V1 (day 0), V2 (optional, day 8-29), V3 (day 57), and V4 (optional follow-up, day 240). Evaluated endpoints were clearance of the AK lesions, safety and tolerability of tirbanibulin ointment (including local skin reactions [LSRs]), PROs, adherence and treatment satisfaction from the physicians' and patients' perspectives.

Results: In the interim analysis, data from 320 patients (67% male) at V3 from 40 dermatological clinics and practices were available. The mean age was 72.8 years (range 42-91). The average number of AK lesions in the treatment area of 25 cm2 at baseline was 6.4 per patient. Treatment locations were face (55%), scalp (24%), and face and scalp simultaneously (20%). 89.3% of patients adhered to a once daily 5-day application regimen. 57% of patients had received prior treatments, mainly with topical therapies. During the observation period until V3, the average number of lesions decreased from 6.4 to 1.9, corresponding to a 70.3% lesion count reduction. LSRs were documented in 98.4% of patients. The LSRs (total values over all visits) were predominantly erythema (97.8%) and scaling (87%). Crusting (59.4%), swelling (19.4%), erosions/ulcerations (16.2%) and blistering (7.6%) were also reported. LSRs were mostly mild to moderate. A total of 83.4% of patients rated the treatment results as completely healed, clearly improved and moderately improved (Patient Global Improvement Index, PGII). 88% of patients assessed the cosmetic outcome as much improved (61%) or somewhat improved (27%). Most patients (97%) would consider tirbanibulin again for treatment of their AK lesions (45% definitely, 26% certainly, 15% probably and 11% maybe). The mean total AK quality of life sum score was 6.64 at baseline and improved to 4.76 at V3.

Conclusion: In the interim analysis of these first German real-world data on tirbanibulin in the treatment of AK, the results regarding tolerability and effectiveness of the pivotal trials were supported [1]. No new adverse reactions have been observed. The 5-day short-term application regimen of tirbanibulin 1% showed a high level of acceptance. Most patients reported a convincing treatment result demonstrated by PGII assessment and improvement of cosmetic appearance in the treated areas. More than 90 % of patients would consider tirbanibulin again for the treatment of their AK lesions. These PRO data highlight the benefits associated with this therapeutic option from a patient perspective.

[1] Blauvelt A, et al. N Engl J Med. 2021;384(6):512-520.

[2] SmPC Klisyri, July 2021

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BERLIN 11-14 OCTOBER 2023
EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY

Abstract N°: 1118

A systematic review of clinical trials using single or combination therapy of oral or topical finasteride for women in reproductive age and postmenopausal women with hormonal and nonhormonal androgenetic alopecia

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Introduction & Objectives: Female pattern hair loss (FPHL) is a hereditary form of hair loss in women and the most common patterned progressive hair loss in female patients with androgenetic alopecia (AGA). One of the best methods for treating hair loss in women is the finasteride treatment.

Materials & Methods:

This systematic review includes a summary of the pharmacology of finasteride and the effect of the drug on women, especially those in the menopausal age group, and is aimed at elucidating methods of preventing systematic side effects. A search of all published literature from 1999 to 2020 has been conducted with the use of PubMed/MEDLINE, Embase, PsycINFO, TRIP Cochrane, as well as Cochrane Skin databases. A total of 380 articles were found, of which 260 articles were removed and 87 review studies were excluded. Lastly, full texts of 33 original articles were reviewed and 14 articles that met the inclusion criteria were selected.

Results:

Ten out of the 14 articles reported a high rate of alopecia recovery in women taking finasteride.

Conclusion:

Based on the results, it can be stated that 5 mg of oral finasteride per day could be an effective and safe treatment in normoandrogenic women with FPHL, especially when used in combination with other drugs, such as topical estradiol and minoxidil. We also found that topical finasteride is more effective than other topical formulas for treating hair loss.

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Abstract N°: 1188

Fibrosis-4 index as a non-invasive screening tool for detecting liver fibrosis in adult patients aged 18-35 years old taking methotrexate

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Introduction & Objectives:

Methotrexate (MTX) is widely used as a first line systemic treatment option for patients with moderate to severe inflammatory skin disease. Whilst it is accepted that MTX can cause a transient transaminitis, its role in the pathogenesis of liver fibrosis is debate and other co-morbidities such as metabolic syndrome may contribute to a greater extent.

UK and European guidelines recommend screening for MTX-induced liver fibrosis in adult patients with psoriasis by testing Procollagen III N-terminal peptide (P3NP) three monthly. If abnormal then a dose reduction or indeed cessation may be considered. In recent years, more sensitive and cost-effective non-invasive markers of liver fibrosis have been validated in other patient cohorts. In the UK the Fibrosis 4 (FIB-4) index is widely recommended by hepatologists to screen for liver fibrosis in patients with non-alcoholic fatty liver disease. In dermatology, FIB-4 is increasingly being used as a replacement for P3NP. However this test is not validated in those aged <35 years as liver fibrosis is a rarity in this population and therefore data is lacking. We sought to evaluate the use of the FIB-4 index in screening for liver fibrosis in adult patients taking MTX aged 18-35 years.

Materials & Methods:

Electronic medical records were searched to identify patients aged 18-35 years who had an AST requested and had been prescribed MTX in a single UK dermatology department. A FIB-4 score was retrospectively calculated, and all were offered a Fibroscan, a more direct measure of liver fibrosis which is validated in adults ≥18 years and is often used as a second line test when FIB -4 is raised. Data from a second cohort in the region is currently being collected.

Results:

Forty-one patients were identified in the primary cohort. Thirty-one patients underwent a Fibroscan, whilst ten did not attend. Of those who had a Fibroscan, FIB-4 could not be calculated in one patient due to sample haemolysis and they were excluded. The average age of the cohort was 28.12 years (range 18-35 years). The mean FIB-4 score was 0.52 (range 0.2 – 1.0, normal reference range <1.3 in 23–64-year-olds). The median liver stiffness score was 4.8 kPa (<7kPa indicates normal liver stiffness). Three patients aged 23, 24 and 35 years had a raised median liver stiffness (8.6 kPa, 9.5 kPa and 12.2kPa respectively) with normal FIB-4 scores (0.3, 0.34 and 0.36 respectively). Hepatology reviews are pending to ascertain the significance of these results.

Conclusion:

The negative predictive value of FIB-4 in > 35 year olds is 90%, which is similar to our findings when the reference range for an older age group is applied. As a younger age will reduce the FIB-4 score, a lower normal reference range may be required to accurately detect fibrosis in this group. A minority of patients in our cohort had an abnormal Fibroscan with a normal FIB-4 result. Based on this preliminary data, we suggest a combined

assessment of BMI, alcohol intake, lipid profile and diabetic status alongside FIB-4 and referral for Fibroscan if these risk factors are present.

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Abstract N°: 1437

Additional external methods of treatment of patients with seborrheic dermatitis

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Introduction & Objectives: Today, the use of platelet-rich plasma is increasing in clinical practice in various fields of medicine. The plasma therapy is used by dermatologists, dentists, gynecologists, traumatologists and many other specialists in daily practice.

Currently, there is a large number of patients seeking medical help with seborrheic dermatitis. However, the complexity of the pathogenesis of seborrheic dermatitis and its sensitivity to medications require from the dermatologist a differential approach in choosing the local therapy.

Objective. Evaluation of the effectiveness of plasma therapy in the treatment of patients with seborrheic dermatitis

Materials & Methods: To evaluate the effectiveness of the injection of platelet-rich plasma in patients with seborrheic dermatitis, 21 patients with this pathology were examined and treated (15 patients - main group, 7 - control group). The control group included patients treated using conventional methods. All examined patients had at least two episodes of exacerbation of the disease during a year. The severity of clinical manifestations in patients of both groups did not differ significantly before the start of therapy. The patients of the main group had their plasma injected intradermal around the lesions. The plasma injections were made up of several cycles up to four times with an interval of 7 days.

Results: During the therapy, clinical improvement was observed in all patients of the main group after the second course of treatment, in contrast to the control group where the treatment lasted much longer, we observed a complete absence of clinical manifestations of the disease after the fourth course. The remission of patients of the main group (15 patients) lasted a year, while in the control group (11 patients), we observed an exacerbation of the disease after three months.

Conclusion: The use of platelet-rich plasma in the treatment of seborrheic dermatitis gives a pronounced therapeutic effect, increases clinical remission and reduces the frequency of relapses. Therefore, this method of treatment can be considered as an effective adjuvant therapy, which further helps to reduce the intensity of exacerbations of seborrheic dermatitis.

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Abstract N°: 1529

Efficacy, safety, tolerability, and satisfaction of N-acetylcysteine and pentoxifylline in lichen planopilaris patients under treatment with topical clobetasol: A triple arm blinded randomized controlled trial

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Introduction & Objectives:

Lichen planoplaris (LPP) is one of the most common causes of inflammatory cicatricial alopecias. There is no definitive cure for the disease and most of the available therapeutic options can potentially lead to serious complications following their use for extended durations. In this study, we aimed to evaluate the efficacy, safety and tolerability of N-acetylcysteine (NAC) and pentoxyfillin (PTX), as adjunctive therapies, in the management of LPP.

Materials & Methods:

In a randomized, assessor- and analyst-blinded controlled trial, patients with proven LPP were randomly assigned to three groups of 10. Group I (the control group) received clobetasol 0.05%lotion; Group II, a combination of clobetasol 0.05% lotion and oral PTX; Group III, a combination of clobetasol lotion 0.05% and oral NAC. Lichen planopilaris activity index (LPPAI), the possible side effects, tolerability and patients satisfaction were assessed before and two and four months after the initiation of the treatments.

Results:

Thirty patients, 96.7% women, with a mean age of 46.8 ± 13.3 years old, were included in the study. Four months into the treatments, the overall LPPAI and the severity and/or frequency of most of its determinants significantly decreased in all groups. In a comparison among the groups, patients who received either of the combination therapies showed more decline in their LPPAI than those receiving only clobetasol. The decline was more noticeable and statistically significant only in the NAC group. Three patients in the PTX group developed complications that were not statistically significant when compared with the other groups. There were no substantial differences in the tolerability of the treatments among the study arms.

Conclusion:

The use of oral NAC and PTX added to the therapeutic efficacy of topical clobetasol in the treatment of LPP, suggesting that they might be beneficial and safe adjuvant therapies and add to the efficacy of topical treatment without any noticeable impact on the adverse effects experienced by patients.

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Abstract N°: 1585

Topical metformin as a potential treatment for alopecia areata

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Introduction & Objectives:

Alopecia areata (AA) is an autoimmune and inflammatory disease of the hair follicles. Both genetic and environmental factors may contribute to the development of this condition. Environmental factors may include microtrauma, bacterial superantigens, viral infections, stress, diet, vaccines, and hormones.

Materials & Methods:

These factors can cause an inflammatory process that destroys the immune privilege of hair follicles, causing the attraction of immune cells, including T lymphocytes, and the production of inflammatory cytokines. The autoimmune reaction then destroys the hair follicles in a cytotoxic manner.By inhibiting the mitochondrial respiratory chain, metformin increases cellular AMPK, which inhibits the mTOR pathway and reduces the generation of cytotoxic lymphocytes and inflammatory cytokines, which are important in developing alopecia areata.

Results:

Metformin also blocks the transmission of cytokines to the cell nucleus by blocking the JAK-STAT pathway. This medicine can also suppress NF-B, an inflammatory mediator, and inhibit CD4 + T cells from differentiating into Th1, Th2, and Th17. Another anti-inflammatory effect of metformin is promoting the proliferation of regulatory T cells, which are crucial for maintaining immune tolerance and preventing autoimmune reactions. Other autoimmune and inflammatory disorders like Sjogren's syndrome, SLE, rheumatoid arthritis, and vitiligo have responded favorably to metformin therapy. By promoting stem cell proliferation and autophagy in hair follicle cells, metformin can also contribute to hair regrowth. These characteristics of metformin make it appropriate for evaluation as a topical immunomodulator for the treatment of alopecia areata.

Conclusion:

We hypothesized that topical metformin as an anti-inflammatory and immunomodulatory medication can be effective in the treatment of alopecia areata.

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Abstract N°: 1606

Achieving the desired results in acne therapy: difficulties and their solutions

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Introduction & Objectives: Nowadays dermatologist's arsenal contains numerous pharmacological agents with high efficiency, but achieving the desired results in acne therapy is still not the easiest problem.

The aim - to study the modern possibilities of medical and cosmetological correction of acne manifestations based on the analysis of foreign and domestic sources.

Materials & Methods: We conducted a review with further analysis of foreign and domestic sources, domestic, European and American recommendations for the treatment of acne. Publications were searched through the National Center of Biotechnology Information, PubMed, StudMed and GoogleBooks resources.

Results: The undisputed leader in the treatment of acne, taking into account the frequency of prescriptions, effectiveness, active substances as mono- and combined forms, lack of systemic influence, are topical medicines.

Among them, benzoyl peroxide, antibiotics and retinoids are prescribed more often than others. Studies have shown higher effectiveness of combined fixed forms in comparison to the use of their components separately. Thus, the use of a combination of clindamycin phosphate 1% with BPO 5% in the form of a gel showed higher efficiency and a lower frequency of antibiotic resistance development compared to 1% clindamycin as monotherapy. In turn, the combination of adapalen 0.1% and BPO 2.5% showed better tolerability and less pronounced local side effects of retinoid, as well as an effective reduction of inflammatory and non-inflammatory elements of the rash compared to the use of these components separately.

The combination of stabilized and solubilized 0.025% trethionine and 1.2% clindamycin phosphate in the form of a gel showed a statistically significant advantage over the use of these components separately. A reduction in the total number of rash elements was recorded in 55% of patients who used this combination, while when using clindamycin - in 49%, trethionine - in 50%. A more pronounced reduction in the number of non-inflammatory elements is noted (when using the combined drug by 51%, clindamycin - by 42.9%).

An important step in the optimization of acne therapy was also the appearance of new agents, among which sarecycline, which was created specifically for dermatological needs and is an antibiotic of the tetracycline group, studies on its use in the treatment of acne have shown high efficiency, good tolerance, it is used once a day for treatment of acne in adults and children aged 9 years and older. Worthy of attention is triparoten, the first new retinoid molecule approved by the FDA in the last 20 years. The uniqueness of the molecule lies in its exclusive effect on RAR-γ, widely distributed in the skin, the expression of which has not been detected in other organs (lungs, spleen, prostate, heart, kidneys, etc.), which allows safe use of this retinoid on large areas of the skin (back , chest).

Conclusion: As a result, groups of the most effective medical agents for acne therapy, features of their use in different forms and degrees of severity, possible side effects and factors that can provoke them, ways to minimize their occurrence without reducing effectiveness were identified.

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Abstract N°: 1904

Non-Invasive Physical Plasma for Preventing Radiation Dermatitis in Breast Cancer

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Introduction & Objectives:

Radiation dermatitis (RD) is the most common acute side effect of breast irradiation. It occurs in up to 85% of patients and can be moderate to severe in up to 30%. Clinically characterised by erythema, itching, oedema, dry and moist desquamation, RD not only affects quality of life, but may also require treatment interruptions in severe cases, compromising tumour control. Despite ongoing research efforts, effective preventive and therapeutic options are still not available.

Non-invasive physical plasma (NIPP) has already proven to be a viable and promising new therapeutic approach for a number of skin diseases. Dielectric barrier discharges (DBE) are a form of NIPP that can be generated using ambient air alone (without a carrier gas). The reactive mixture of electrons, ions, excited atoms, reactive oxygen and nitrogen species (RONS), UV radiation and heat has a beneficial and dose-dependent effect on tissue healing.

We have previously established the feasibility and safety of NIPP in combination with simultaneously applied radiotherapy in humans. Here, we report the preliminary results of a prospective clinical trial with DBE-generated NIPP for the prevention of RD in whole-breast irradiation (DRKS00026225).

Materials & Methods:

Patients who received adjuvant hypofractionated whole-breast irradiation after breast-conserving surgery were included. The breast received daily NIPP treatment (120 seconds) parallel to radiotherapy. As standard skin care, all patients used a urea-based lotion which was applied twice daily on the irradiated breast. At the end of treatment, an experienced breast radiation oncologist assessed the radiation-induced skin reaction (RD, dry and moist desquamation) using CTCAE v5.0. Patient-reported outcomes (pain, itching, burning, impairment in everyday activities) and experiences were recorded using a modified RISRAS scale. For patients with grade ≥ 2 RD, moist desquamation and/or acute pain, topical corticosteroids were prescribed until symptoms resolved.

Results:

Since March 2022, 38 patients have been included. Complete follow-up data are available for 25 patients, with a median age (range) of 58 (30–82) years. The results are presented in *Table 1* and compared with a comparable high-quality study cohort with equal standard skin care and acute toxicity assessment. None of the patients found the treatment uncomfortable and 96% would recommend NIPP for prevention of RD. No adverse device events, side effects or interactions associated with NIPP were documented.

Conclusion:

While the data collected to date are currently insufficient for a powered analysis, the prophylactic use of a topical NIPP generator appears effective in preventing RD in the context of modern, adjuvant hypofractionated whole-

breast irradiation. The observed prevalence and severity of RD are less frequent and milder compared to recent literature, as are the symptoms experienced by patients.

Table 1. Radiation toxicity assessment at the end of treatment.

trial	**year**	***n***	**boost (%)**	**RD (CTCAE v5.0) (%)**	**desquamation (%)**	**subjective symptoms (mean ± SD)**	**corticosteroid use (%)**
				0	**1**	**2**	**3**
Current	2023	25	56	28	68	4	0
Control	2020	70	44	21	51	27	0

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Abstract N°: 2068

Upadacitinib for an adolescent with alopecia areata and concomitant atopic dermatitis - case report and a review

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Introduction & Objectives:

Upadacitinib is a selective Janus Kinase 1 (JAK1) inhibitor that was recently approved by the FDA for moderate to severe atopic dermatitis (AD) above 12 years of age. JAK inhibitors (tofacitinib, ruxolitinib and baricitinib) are also proven to be effective in the treatment of alopecia areata (AA). However, data regarding upadacitinib as a treatment option for AA is lacking. We present a case of an adolescent with AA and AD that was treated successfully with upadacitinib. In addition, we review the five previously published reports and recommend a treatment protocol for adolescent and adult patients with concomitant AA and AD.

Materials & Methods:

Case report: 14-year-old boy presented with severe AD and widespread multifocal AA. He was diagnosed with AD in infancy and with AA when he was 11-year-old. Topical therapy did not improve both conditions. Systemic therapy for AD included cyclosporine for several exacerbations which caused headaches. Methotrexate was attempted and stopped due to significant increase in liver enzymes. Later on dupilumab was introduced but had only a mild effect and resulted in severe conjunctivitis. Baricitinib treatment was subseqeunly given, unfortunately without substantial improvement. Due to the recalcitrant nature of the disease and the significant deterioration in the AA, upadacitinib was tried with remarkable improvement both in the AD and AA. Complete hair regrowth was noticed 8 weeks after commencing upadacitinib. No side effects were observed.

Results:

Upadacitinib has emerged in recent years as a promising therapy for AD. It was shown that upadacitinib has a favorable benefit-risk profile, with sustained efficacy responses in adolescents and adults with moderate to severe AD. In the past two years few cases demonstrated the efficacy of upadacitinib in patients with concomitant AA and AD. All patients reported to date (Table 1) as well as our patient had a complete or near complete regrowth of hair and a significant improvement in the AD condition.

Conclusion:

We believe the newly introduced upadacitinib may hold the potential to treat both AA and AD and may be especially beneficial for adolescent and adult patients with concomitant diseases.

Table 1

Article	Sex	Age	Severity and duration of AD	Severity and duration of AA	Previous therapies	Treatment protocol	Result	Side effects
Gambardella A. et al	M	30	Severe N/A	AA universalis 5 years	Corticosteroids, cyclosporine and dupilumab	Upadacitinib 30 mg/day	Complete regrowth of all hair after 4 months of therapy,	None
Gambardella A. et al (SECOND CASE)	W	42	Severe N/A	Resistant patch of AA of the vertex N/A	Cyclosporin, azathioprine and dupilumab	Upadacitinib 30 mg/day	Dramatic patchy hair regrowth of the vertex after 4 months of treatment.	None
Asfour L et al	W	59	Moderate to severe AD N/A	Relapsing–remitting multifocal AA 35 years	Baricitinib	N/A	Regrowth of chronic preauricular AA patches within 4 weeks of therapy. Partial regrowth in eyebrows area	None
Cantelli M et al	M	24	Severe AD From infancy	AA totalis 10 years	Corticosteroids, cyclosporine and dupilumab	Upadacitinib 30 mg/day	Complete regrowth of hair in the scalp after 3 months of therapy	None
Bourkas AN et al	M	14	moderate to severe AD N/A	AA Near totalis 13 years	Topical and intralesional corticosteroid injections, 0.1% protopic cream spironolactone, cyclosporine and low-dose systemic minoxidil (1.25 mg daily)	N/A	Complete regrowth of hair in the scalp after 6 weeks of therapy	None

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Abstract N°: 2078

Efficacy of Jessener solution versus intralesional steroid in treatment of alopecia areata

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Introduction & Objectives:

Alopecia areata is an autoimmune condition that causes non-scarring hair loss. To date, there is no single cure and treatment remains challenging.

The recent use of janus kinase inhibitors (JAK) was reported to be effective in severe AA as well as

alopecia universalis.

Aims:

To evaluate the efficacy of Jessener solution versus intralesional steroid

in treatment of Alopecia Areata.

Materials & Methods:

This study included 40 patients who presented with multifocal patchy alopecia areata (AA).For each patient, three patches were randomly selected to be treated one with intralesional steroid, another with topical Jessner solution and the third with normal saline. Three sessions were done 3 weeks apart and were followed up for 3 months.Response was assessed clinically and by trichoscope.

Results:

Fifteen percent of patches coated with Jessner or injected with steroids

showed an excellent response while 20% of patches coated with Jessner and 32.5%

patches injected with steroids showed a good response. A significant difference was

observed between the three modalities of treatment regarding the prognostic score

for response ($p < 0.001$) as patches coated with Jessner and those steroid injected

showed a significant higher response rate than patches injected with saline ($p < 0.001$)

while no significant difference was reported between patches either treated with

Jessner or steroids ($p > 0.05$)

Jessners solution can be a novel and feasible and well tolerated modality

of treatment for patients suffering from alopecia areata.

Conclusion:

Jessners solution can be a novel and feasible and well tolerated modality

of treatment for patients suffering from alopecia areata.

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Abstract N°: 2081

Azelaic acid in dermatology

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Introduction & Objectives:

=Azelaic acid is a dicarboxylic acid molecule with anti-inflammatory and antioxidant properties, effective in the treatment of acne vulgaris and papulopustular rosacea, among other cutaneous conditions.

=Azelaic acid is available at many forms and concentrations.

=It has antibacterial,keratolytic,comedolytic and anti-inflammatory properties.

=It is used as topical treatment for mild to moderate acne alone or in combination with oral antibiotics or hormonal therapy.

=AS a tyrosine inhibitor,reduce pigmentation,it is particularly useful for darker skinned patients with postinflammatory pigmentation melasma.

=Azelaic acid inhibit the activation of PI3K/AKT signaling pathway and angiogenesis, thereby improving the symptoms of psoriasis.

=Azelaic acid 15% gel is FDA approved for treating mild-to-moderate rosacea with very mild adverse effecta which do not warrant discontinuation of therapy.

Materials & Methods:

This study included 80 patients who presented with different diseases who were treated using azelaic acid.

Our patients were:

- Mild-to-moderate rosacea

-Psoriasis

-Cases of for mild-to-moderate papulopustular acne

- Cases of melasma and Hyperpigmentation

- cases of alopecia…

-Hidradenitis suppurativa (HS)

-Male pattern baldness

-Keratosis pilaris

-Periorificial dermatitis

Results:

=We reached an excellent results with more than 70% of cases..

results for more than 80% of cases

=We used azelaic acid as topical treatment for mild to moderate acne alone or in combination with oral antibiotics or hormonal therapy.

= AS a tyrosine inhibitor,reduce pigmentation,it was particularly useful for darker skinned patients with postinflammatory pigmentation melasma.

=We used Azelaic acid for improving the symptoms of psoriasis.

= Azelaic acid 15% gel treating mild-to-moderate rosacea with very mild adverse effecta which do not warrant discontinuation of therapy.

= Azelaic acid can be used for mild-to-moderate papulopustular acne as monotherapy or in combination with other treatments and that is suitable as maintenance therapy.

=AS a broadspectrum antibacterial agent, azelaic acid can act as a pillar in acne therapy minimizing the potential risk of emergence of resistance

Conclusion:

=Azelaic acid is a promissing dermatological drug with excellent results in improving many diseases…

=AS a broadspectrum antibacterial agent, azelaic acid can act as a pillar in acne therapy minimizing the potential risk of emergence of resistance…

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Abstract N°: 2285

Treatment of Prurigo Nodularis: A Canadian Retrospective Study

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Introduction & Objectives:

Prurigo Nodularis (PN) is a chronic skin disorder characterized by severe pruritic nodules. PN poses significant physical and psychological harm, and is commonly associated with other chronic comorbidities. Several treatment options, such as methotrexate, cyclosporine, and narrow band UV therapy (UVB), are used to treat PN, but their efficacy has not yet been evaluated in a Canadian population. This study aims to describe the demographic, clinical characteristics, and comorbidities associated with PN. Also, we aim to describe the effectiveness of systemic therapies, including methotrexate, cyclosporine, and UVB, and the predicting factors associated with improvement.

Materials & Methods:

This is a retrospective chart review of adult patients diagnosed with PN at Hamilton Health Science Center and McMaster Dermatology Clinics in Hamilton, Ontario, between 2015 and 2023.

Results:

The study included 81 patients, 60% of which were female. The mean age of the study population was 52.8 years (range: 30-77 years). The average age of diagnosis with PN was 50 years. All patients experienced itching and 17% of patients experienced pain. Mental health comorbidities included anxiety (52%), depression (58%), personality trait disorder (7%), bipolar disorder (5%), and post-traumatic stress disorder (5%). Atopic dermatitis was the most common skin comorbidity noted in this population (22%). Other skin comorbidities included psoriasis (5%), lichen planus (3%), pityriasis lichenoides chronica (1%), and vitiligo (1%). Additional associated conditions were diabetes mellitus (12%), thyroid disease (9%), chronic kidney disease (11%), and chronic liver disease (4%). Treatments used included methotrexate, cyclosporine, and narrow band UVB, which elicited symptom improvement rates of 31%, 38%, and 35%, respectively, at week 16 of therapy.

Conclusion:

PN is associated with increased risk of mental health disorders. Methotrexate, cyclosporine, and UVB therapy may be effective treatments at improving symptoms in PN patients, but clinicians must consider the side effects and the unknown long-term effects of these treatments before providing them to PN patients.

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EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY

Abstract N°: 2336

Baricitinib for treatment of nail dystrophy

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Introduction & Objectives:

Nail dystrophy is very common in children, which may be associated with various inflammatory skin diseases. The more serious cases of nail dystrophy were treated with acitretin, cyclosporine previously. However, the treatment of nail lesions is challenging.

To evaluate the efficacy and safety of baricitinib in the treatment of nail dystrophy.

Materials & Methods:

We report 11 pediatric patients with nail dystrophy with a mean age of 7.73 ± 2.15 years (range 3–11 years) treated with baricitinib. After fully informed the patients and their parents, baricitinib was used for treatment. The baseline demographic, clinic data of patients were collected

Results:

Clinical responses to treatment were evaluated at baseline and on weeks 12 and 24. In view of the similar changes with nail psoriasis, the severity of nail lesions was evaluated based on the Nail Psoriasis Severity Index (NAPSI). At week 12, seven patients (63.6%) had achieved NAPSI25 (25% decrease in NAPSI score), one patient (9%) had achieved NAPSI50. At week 24, one patient showed no obvious change, one patient (9%) had achieved NAPSI25, three patients (27.3%) had achieved NAPSI50, two patients (18.2%) had achieved NAPSI75, and four patients (36.4%) had achieved NAPSI90. The physician global assessment showed 36.4% (4/11) patients with almost complete resolution, 45.5% (5/11) patients with significant improvement (>50% improvement), 1 patient with slight improvement (<50% improvement) and 1 patient with no change

Conclusion:

This study showed that baricitinib administration yielded significant remission of nail dystrophy in pediatric patients and was well tolerated.

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Abstract N°: 2540

Diffuse dermal angiomatosis of the breasts successfully treated with topical propranolol: A case report

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Introduction & Objectives:

Diffuse dermal angiomatosis of the breast (DDAB) is a rare cutaneous reactive angiomatosis that typically presents as ulcerated erythematous-violaceous plaques, commonly observed in women with macromastia. In this case report, we aim to describe the successful use of topical propranolol 1% in cold cream for the treatment of DDAB in a frail patient with multiple comorbidities, including diabetes mellitus type 2, Alzheimer's disease, and recent COVID-19 infection.

Materials & Methods:

We present a case report of a 92-year-old woman who presented to the emergency department with asymptomatic lesions in both breasts, 10 days after a COVID-19 infection. The physical examination revealed erythematous-violaceous symmetric plaques over pendulous and macromastic breasts. The dermatoscopic features are also described. Laboratory tests, including hematology, biochemistry, coagulation, and autoimmune screening, were negative or normal. A skin biopsy demonstrated a diffuse proliferation of endothelial cells without atypia, forming small elongated vessels among collagen fibers. Immunohistochemistry was positive for CD31 and CD34. Due to fragility and pharmacodynamic concerns, topical propranolol 1% in cold cream was preferred and started early, and the treatment was discontinued after one month when antiproliferative and antiangiogenic effects were observed. A reepithelializing cream was used until the superficial ulcers healed.

Results:

The use of topical propranolol 1% in cold cream was effective in treating DDAB in this patient. No recurrence was observed during the follow-up period.

Conclusion:

DDAB is a rare cutaneous reactive angiomatosis with limited treatment options. Our case report suggests that topical propranolol 1% in cold cream could be a safe and effective treatment option for DDAB, especially in elderly patients with multiple comorbidities. Further studies are needed to better understand the pathogenesis of DDAB and improve the available treatments.

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Abstract N°: 3760

Use of lyophilized purified adipocyte-derived stem cell exosomes in various medical dermatology cases in Filipino skin

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Introduction & Objectives:

The use of lyophilized, purified, human adipocyte-derived stem cell exosomes, which are nano vesicles delivering functional proteins, lipids, miRNA, mRNA, tRNA and siRNA to recipient cells, has a great potential in the dermatology practice. Its current uses include wound management, burn treatments, scar therapy, acne scars, and anti-aging. The primary mechanism of exosomes in focus is the protein-rich cargo it carries which are highly immunomodulatory and attenuates inflammation by enhancing secretion of anti-inflammatory cytokines. The transferable and functional RNA content also has the ability to modulate the expression of mammalian protein encoding genes. Literature reports that for scarring mechanisms, exosomes have been shown to induce the synthesis of type I collagen and elastin in human dermal fibroblasts. For pigmentation, exosomes have shown to reduce intracellular melanin levels. Our objective is to start seeking to expand the therapeutic application of adipocyte-derived stem cell exosomes beyond the current uses to cutaneous inflammatory cases. This is a collection of isolated medical dermatology cases.

Results:

The outcomes of use of adipocyte-derived stem cell exosomes in this series are variable. The most significant improvement was noted in a case of exfoliative dermatitis in an elderly where the redness, scaling and pruritus improved in minutes after topical application. Granuloma annulare on the dorsal hands improved with visible flattening and fading of erythema the next day after lesional injection of exosomes as monotherapy. Rosacea symptoms of stinging sensation, sensitivity and erythema improved after one topical application of exosomes after a few days. Brightening of the general skin area of the face including the dark patches were noted after weekly application on exosomes monotherapy in a melasma case. Other cases with variable results include localized psoriasis vulgaris, hidradenitis suppurativa, seborrheic dermatitis, hypertrophic scar and keloid, atopic dermatitis, trauma wounds, and milia rubra. With our limited collection of cases, a constant pattern noted is that a few repeat exosome therapies are needed for a more substantial improvement but signs and symptoms do not revert back to the baseline condition. The patients have given their consents to undergo exosomes therapy. No adverse effect is seen in any of the cases.

Conclusion:

Lyophilized, purified, human adipocyte-derived stem cell exosomes in medical dermatology progress to become a safe alternative or adjunctive therapy to many cutaneous conditions because of its benefit to repair rather than control like what current drugs do. As patient safety prevails, more studies are needed to solidify the position of exosomes in day-to-day clinical cases and therapies but great strides have been made in a matter of a few years. A more extensive safe use of exosomes in medical dermatology will eventually define the protocols of therapy.

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Abstract N°: 3798

Safety, Tolerability and Pharmacokinetics (PK) of GT20029 Following Topical Single Ascending Dose (SAD) Administration in Healthy Volunteers and Multiple Ascending Dose (MAD) Administration in Subjects with Androgenetic Alopecia (AGA) or Acne

Ting Huang[1], Min Dong[1], Janet Dubois[2], Seth Forman[3], Huiliu Wang[1], Zhihua Ren[1], Meiyu Wang[1], Jie Chen[1], Joel Neutel[4], Todd Bertoch[5], J. Scott Overcash[6], Xiang Ni[1]

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GT20029-US-1001 Abstract for EADV Congress in Berlin 2023

Introduction & Objectives:

The interaction of dihydrotestosterone (DHT) and the androgen receptors (AR) is one of the pathophysiologies of Androgenetic Alopecia (AGA) and Acne. GT20029 is a topical AR-Proteolysis Targeting Chimera (PROTAC), which recruits AR in proximity to an E3 ubiquitin ligase to initiate AR ubiquitination and subsequent degradation. In preclinical studies, GT20029 can promote hair growth significantly in dihydrotestosterone (DHT)-induced AGA mouse model and inhibit testosterone propionate (TP)-induced flank organ enlargement with statistically significance in hamster flank organ acne model. Therefore, it showed potential treatment efficacy in promoting hair growth and inhibiting sebaceous gland development. GT20029 also exhibited low systemic exposure and achieved a good safety profile. In light of the above, the phase I clinical trial to evaluate its safety, tolerability and Pharmacokinetics (PK) in healthy volunteers (HV) and subjects with AGA or Acne was initiated in United Status (USA) only.

Materials & Methods:

This was a randomized, double-blinded, placebo-controlled, parallel group, dose escalation study with two stages. Stage 1: topical single ascending dose (SAD), planned to enroll 40 HV with 5 different dosage groups, with drug applied on the back on Day 1 and serial blood samples collected for PK analysis.

Stage 2 with two multiple ascending dose (MAD) cohorts:40 male subjects with AGA and another 40 male and female subjects with acne to recieve different doses. Randomized in the same way as SAD (**Table 1**). PK blood samples were collected regularly and safety was monitored. Dose escalation for SAD and MAD did not occur until safety review was completed.

Safety assessments included monitoring of adverse events (AEs), vital signs, laboratory findings, electrocardiograms (ECG), physical exams, subject skin self-assessments and investigator evaluated skin irritation assessment.

The study endpoints included evaluation of safety and tolerability (primary) and PK characteristics (secondary) of GT20029.

Results:

From December, 2021 throught December, 2022, 8 sites contributed 123 subjects: (Table 2 A-C Subjects Disposition by Dose Cohort). Subjects' demographic information listed in Table 3.

For safety analysis, almost all treatment emergent (TE) AEs were assessed as mild and no TEAEs were serious, severe or resulted in early withdrawal or death occurred. The most common TEAE across all study cohorts was headache (not related to study treatment). The most common TEAEs among both MAD Cohorts were application site dryness, application site pain, and application site pruritis (all mild in severity and all related to study treatment). All TEAEs summarized in Table 4A-4C. Laboratory results, post-baseline mean values of the vital signs, and ECG parameters were similar across all cohorts in the study. Subject skin self-assessments and investigator-evaluated skin irritation assessments also showed minimal cutaneous reaction to treatment.

For PK analysis, overall quantifiable GT20029 concentration was low. GT20029 concentrations were higher in subjects with acne as compared to those with AGA, yet remained close to the LLOQ for all cohorts.

Conclusion:

Overall GT20029 was safe and well tolerated. No significant safety concerns were identified in the study.

PK parameters such as AUC, Cmax, Tmax, t1/2 were assessed, however, following topical administration, systemic exposure of GT20029 was low. Page 2** of 2**

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Abstract N°: 3843

Invasive SCC and tirbanibulin: experience in patient with epidermodysplasia verruciformis

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Introduction & Objectives: Epidermodysplasia verruciformis (EV) is an autosomal recessive skin disease with an increased susceptibility to humanpapilloma virus (HPV) cutaneous infection. Patients present multiple lesions in sun-exposed sites, including papules resembling flat warts and erythematous or hypopigmented scaling macules. In early adult life, an increased risk of developing actinic keratoses (AKs), Bowen disease and invasive squamocellular carcinoma (iSCC) has been demonstrated. There are no curative therapies for EV. Several treatments have been used with transient benefit and recurrence when treatment is discontinued.

Results: We report a 37-year-old patient with EV who had performed multiple therapies (topical imiquimod, ingenol mebutate, 5-fluorouracil, PDT) for flat wart-like lesions and AKs of the frontal region, with low benefit. Following the clinical and histological finding of SCC (HPV-related) on forehead, an excisional biopsy was performed with histological diagnosis of iSCC keratinizing and ulcerated, G2, pT3 according to VIII edition UICC, 2017, with depth of invasion of 8 mm and incompletely removed with focally infiltrated lateral excision margin.

SCC is quickly clinically relapsed, however wide local excision was complicated due to aesthetic area, the field of cancerization and the presence of concomitant classic EV warty lesions. For these reasons, we used tirbanibulin ointment on the area of previous surgery and on the peripheral area, applying it once a day for 2 cycles of 5 days with 14 days of break between the 2 cycles. We observed no recurrence of SCC, confirmed histologically 6 months after the excisional biopsy, clinically maintained after a further follow-up period of 6 months and a concomitant reduction of keratotic lesions in the area. This result was associated with well tolerated, moderate, local inflammation.

Conclusion: Tirbanibulin is a novel anti-proliferative and pro-apoptotic agent, recently approved to treat mild AKs on the face and scalp, with a selective action against cells that most express microtubules and its action is more effective the greater the number of mitoses. It inhibits cell growth and induces cell death and its efficacy on SCC, melanoma and other cancer lines are being studied as well. Moore et al. successfully used tirbanibulin to eradicate a periungueal HPV-positive in situ SCC. Braasch et al. also described the use of tirbanibulin for HPV-related anogenital warts with clinical and histologic benefit and resolution of superficial lesions. Based on this reasoning, we used tirbanibulin in the treatment of iSCC as an adjuvant approach in a selected patient to reduce the risk of progression, waiting for a possible surgical excision which always remains the first-line of therapy. Finally, we believe that due to its mechanism of action and tolerability, cycles of tirbanibulin application may be a viable option for the treatment of actinic keratoses and typical lesions in EV-patients.

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Abstract N°: 4024

Therapeutics in immune-mediated diseases and fertility: what is the evidence of safety?

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Introduction & Objectives

Changes in society, with an increasing participation of women in the labor market, have been promoting a postponement of the dream of motherhood. Additionally, there has been an increase in homoaffective and transgender couples who wish to have children. Consequently, there is a growing demand for treatments for ovule and sperm cryopreservation and even assisted reproduction techniques. Faced with this scenario, many patients have asked us: given my immune-mediated disease, what is the evidence of safety in the therapies so that I can undergo these fertility treatments?

Materials & Methods

A literature review was carried out on the evidence published in articles indexed in Pubmed until May 2023.

Results

Articles are more frequent on the subjects of pregnancy and spermogenesis.

Case reports and case series were found on treatments with methotrexate, acitretin, cyclosporine, fumaric acid esters, infliximab, etanercept, adalimumab, certolizumab pegal, ixekizumab, risankizumab, guselkumab, brodalumab, tildrakizumab, secukinumab, ustekinumab, omalizumab, anakinra, rituximab, apremilast, prednisone , PUVA, anthralin, calcipotriol, coaltar, corticosteroids, salicylic acid, tacrolimus and tazarotene.

Conclusion:

The evidence are mostly dependent on low level evidence and will be demonstrated but it is certain that more studies and even case series need to be conducted in this area.

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Abstract N°: 4202

Microdosing retinol strategy : improves skin ageing clinical parameters and its associated molecular mechanism leading to keratinocytes proliferation

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Introduction & Objectives:

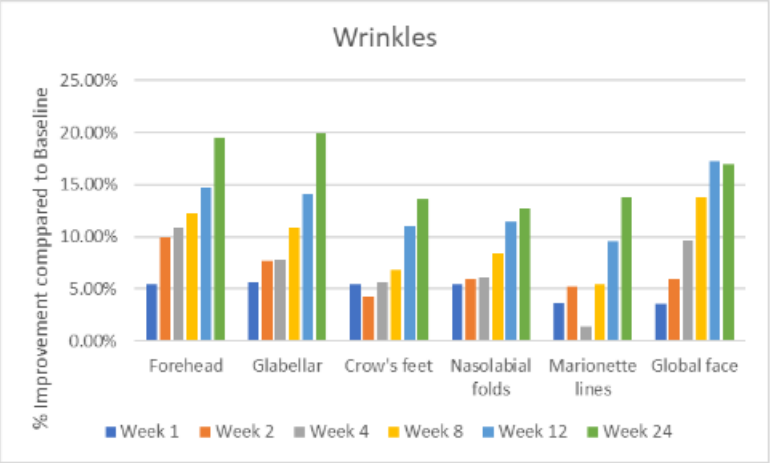
Topical retinoids and their derivatives have gained recognition for their extensive research and proven clinical benefits in skin age management. However, the associated side effects, including redness, peeling, and irritation, pose significant challenges. Microdosing, a strategy aimed at achieving the desired physiological effects of an active ingredient while minimizing adverse reactions, offers a promising solution. This study aimed to evaluate the effectiveness of a low-dose, 0.1% retinol skin cream formulated with skin-soothing and barrier-strengthening ingredients, complemented by a transient receptor potential vanilloid 1 (TRPV-1) inhibitor to manage potential retinoid-induced discomfort.

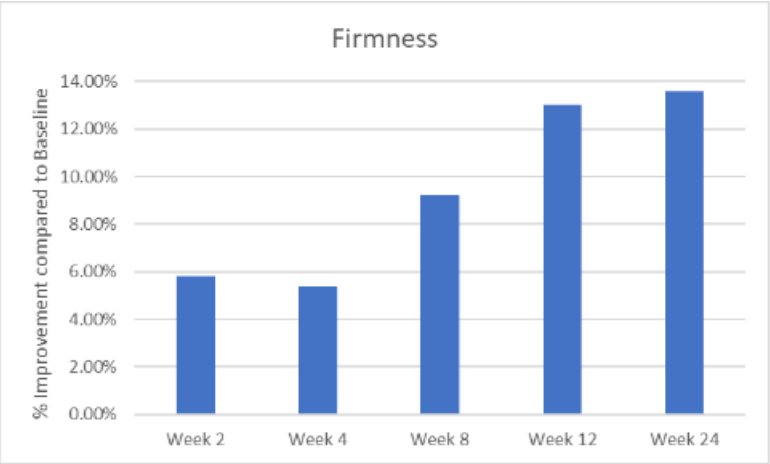
Materials & Methods:

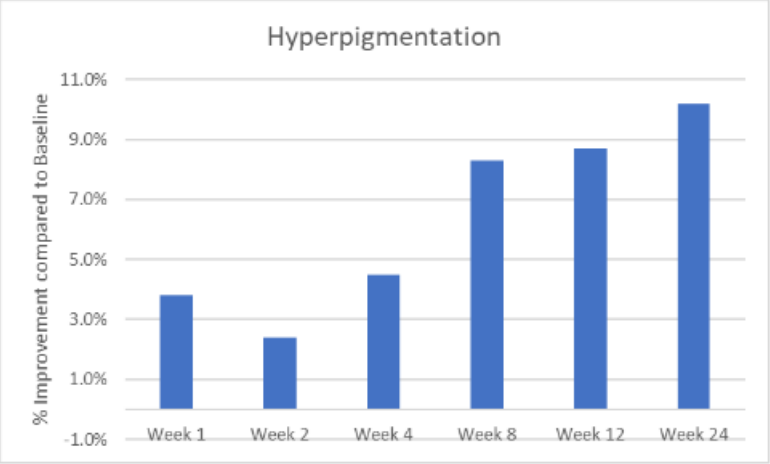
A 6-month, multi-center clinical study enrolled 132 women with mild to moderate photodamaged facial and neck skin, encompassing diverse Fitzpatrick skin types. Efficacy assessments, employing blinded expert grading on attributes such as wrinkles, texture, firmness, and pigmentation using a 10-point scale, were conducted at baseline and intermittently throughout the once-nightly 6-month application period. Instrumentation evaluation encompassed Corneometer measurements of cutaneous hydration, transepidermal water loss (TEWL) measurements, and optical coherence tomography (OCT) to assess epidermal thickness. Furthermore, a non-invasive untargeted label free proteomic analysis from tape strips was performed to elucidate the retinol protein signature. Self-assessment surveys, tolerance evaluations, and cell renewal evaluation via dansyl chloride labeling were also implemented.

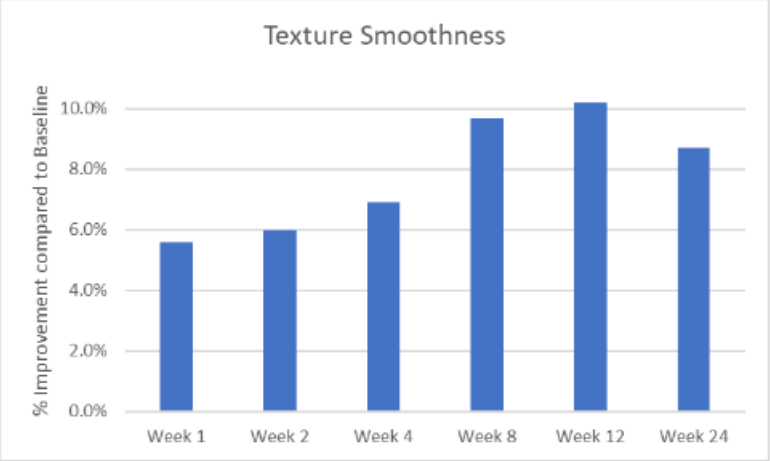
Results:

Statistically significant ($p<0.05$) clinical parameters as assessed by blinded expert grader were observed as early as 1 week into the study, with continued enhancements throughout the 6-month test period:









Cutaneous hydration levels showed a progressive increase overtime (+19.6%, $p<0.001$), with no observed disruption to the skin barrier at month 6 as indicated by TEWL (-10.6%, $P=0.004$). OCT analysis revealed a

statistically significant increase (+12.3%, $p<0.001$) in epidermal thickness at month 6 relative to baseline. Proteomic analysis showed an upregulation of fatty acid-binding protein 5 (FABP5) expression at month 6, indicative of the activation of peroxisome proliferator-activated receptor delta/beta (PPARδ/β) target genes in keratinocytes which can lead to a decrease in cell cycle arrest, apoptosis, and senescence. Furthermore, upregulation of key aerobic glycolytic enzymes, including α-enolase and fructose bisphosphate aldolase A, implied increased cellular energy demands. These findings collectively suggest increased keratinocyte proliferation, a characteristic mechanism of action for retinol. Cell renewal evaluation showed accelerated cell proliferation compared to untreated control ($p<0.001$). Tolerance evaluations, self-assessment surveys, and instrumental measurements confirmed the formula's well-tolerated nature without compromising the integrity of the skin barrier, even among individuals new to retinol usage.

Conclusion:

These studies provided convincing evidence supporting the efficacy of microdose retinol formula, complemented by skin-soothing and barrier-strengthening ingredients, in delivering biologically effects to the skin with minimal discomfort. C1 - Internal use

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Abstract N°: 4465

Chemical matricectomy with phenol 50% in the treatment of the ingrown toenail : about 145 cases

Asmaa Elkissouni[1], Fatima-Zahra Elfatoiki[1], Hayat Skalli[1], Hali Fouzia[1], Soumia Chiheb[1]

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Introduction & Objectives:

Ingrown toenail is a common pathology of the big toe, which results from a painful conflict between the nail bed and the adjacent tissues. Recourse to surgery is necessary when medical care fails, nevertheless recurrences are not rare, the aim of this study is to evaluate the efficacy of chemical matricectomy of the ingrown toenail with phenol 50%.

Materials and methods

This study was conducted between 2018 and 2022.

All patients underwent avulsion of the lateral part of the nail followed by an application of phenol 50% on the matrix for 2 minutes

Clinical evaluation was performed at day 1, day 7, day 30 and after 6 months

Results

145 patients were included in this study, the average age was 30 years (4- 68 years), the average course was 13 months, 50 patients (34) had already benefited from an avulsion without phenolisation with recurrence, on clinical examination 93 patients (64%) had a unilateral nail ingrowth, 52 (36%) patients had a bilateral ingrowth, and a lateral bud was noted in 31 patients (21%) .after avulsion of the lateral part of the nail followed by an application of phenol 50% on the matrix for 2 minutes . treatment with analgesics and daily dressing changes were indicated after the intervention

The evolution was favourable in 142 (98%) of the patients, only 3 patients (2%) had recurrence, no case of infection was observed.

Conclusion

The chemical destruction technique using phenol has shown superiority over conventional surgical methods. This is due to the properties of phenol: analgesic effect by demyelination of the terminal nerve fibres, cauterisation by protein coagulation and antiseptic properties. Several studies have examined the efficacy of phenol 88% in the treatment of ingrown toenails, however, to our knowledge, this study is the first to test phenol 50%, which has similar efficacy and safety to phenol 88%, as well as a low recurrence rate.Nevertheless, randomised double-blind studies are desirable to confirm these results

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Abstract N°: 4485

Treatment of Lichen Planus with Roflumilast

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Introduction & Objectives:

In the recent years, together with an improved understanding of the complex pathogenesis of some dermatoses, we are witnessing a major revolution in dermatological treatments. Lichen Planus (LP) is a chronic inflammatory disease that, in symptomatic cases, can heavily affect the quality of life of our patients. Its treatment is nothing short of challenging, especially in the case of patients with contraindications to classic immunosuppressors or that do not tolerate those treatments. Therefore, we are sometimes forced to look for off-label alternatives.

Materials & Methods:

Through a comprehensive review of the literature we managed to identify potential treatments useful for those patients with moderate-to-severe LP refractory to conventional topical and systemic therapies. Based on its pathogenesis and recent reports we considered phosphodiesterase-4 inhibitors as potential therapeutical alternatives for LP. Apremilast was the first medication from this group that has been used in Dermatology. Thanks to its mechanism of action, it reduces the production of TNF-alpha, IFN-gamma, IL-2, IL-4, IL-8 and IL-12. Cases of oral LP treated with apremilast have been reported. In the last year, roflumilast has also been of increased interest in many inflammatory dermatoses. It has achieved satisfactory results in mucocutaneous diseases such as nummular eczema, hidradenitis suppurativa, psoriasis, aphthosis, periodontitis, and more recently in another case of oral erosive lichen planus. Hereby, we present the results of patients with contraindications or intolerance to other alternatives that have been successfully treated at our Departement with roflumilast.

Results:

A woman in her 70s, without any relevant medical history, presented with LP lesions on her tongue and leg for almost a year. Diagnosis was confirmed on both locations with compatible dermoscopy and histopathological findings, and patch testing was negative. After the beginning of treatment with roflumilast, the patient progressively experienced major improvements of her lesions and was capable of returning to her previous dietetic habits.

A man in his 60s, with hypertension and diabetes, consulted in our Department for flat-topped, violaceous, pruritic papules on his chest and lumbar region. Mucous membranes were sparred. Histopathology corroborated the clinical suspicion of LP. Roflumilast was prescribed after failure of other alternatives achieving full control of his pruritus.

Conclusion:

Roflumilast could become considered as a cost-efficient alternative to other new biologic therapies and novel molecules, for the treatment of refractory LP opening a new window of opportunity for patients in which immunosuppressive therapy is contraindicated or has failed.

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Abstract N°: 4492

the efficacy of photobalneotherapy in the treatment of children's palmoplantar keratosis

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Introduction & Objectives:

The management of palmoplantar keratosis (PPK) in children represents a therapeutic challenge given the modest efficacy of local treatments and the innumerable side effects of systemic treatments. The aim of our study is to evaluate the efficacy of photobalneotherapy in the treatment of children's PPK.

Material and methods:

This is a prospective study, carried out over a period of 5 years, were included children with PPK initially treated by dermocorticoids without clear improvement, regardless of the etiology of the PPK.

The sessions took place twice a week as follows: after immersion of the hands and or feet in 2 mL of Methoxsalene diluted in 5 L of water for 15 minutes, then drying for 15 minutes, the patients received local phototherapy (UVA) at a dose of 0.3 J with a gradual increase in the dose of 0.1 J at each session

An evaluation was made after 24 sessions and the effectiveness of the treatment was classified as "clear improvement", "partial improvement" and "no improvement".

Results:

Twenty-seven patients were enrolled, with a predominance of females and a sex ratio of 0.41: M/F. The average age was 13 years with extremes of 4 to 16 years, the average duration of evolution of the PPK was 6 months, the acquired PPK came at the head of the list with psoriasis 40% (n=11), eczema 29% (n=8), mycosis fungoides 7% (n=2), hereditary PPK represented 22% of cases (n=6), palmo-plantar involvement was present in 66% of patients (n=18), isolated palmar involvement occupied 22% (n=6), while isolated plantar involvement was present in 11% of patients (n=3)

The average duration of the treatments was 16 weeks, with an average total number of sessions of 32. The result after 24 sessions showed a "clear improvement" in 66% of patients (n=18), a "partial improvement" in 25.9%, while 7.4% of patients (n=2) had no improvement.

Conclusion :

Balneophototherapy consists of the administration of psoralens topically in baths then irradiation with UVA. This technique has several advantages over conventional PUVA, including the use of a reduced dose of UVA, which causes less irritation, as well as the complete elimination of the product by the skin within three hours of treatment. On the other hand, contrary to systemic treatments, balneopuvatherapy does not pose a problem of drug interactions or systemic effects.

The PUVA bath has shown its effectiveness in the treatment of many chronic inflammatory dermatoses, several studies have reported its effectiveness in the treatment of PPK in adults, the originality of our study is that it has been tested in children with a good totality and good improvement in 66% of cases. Balneopuvatherapy can be an interesting therapeutic approach easy, effective and inexpensive.

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Abstract N°: 4960

"Intelligent" combination of skin identical moisturizers and lipids in emollients boosts moisturization and barrier repair in patients with Xerosis cutis

Barbara Schuster[1], Dylan Griffiths[1], Schölermann Andrea[1]

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Introduction & Objectives:

Xerosis cutis is characterized by decreased stratum corneum (SC) hydration and impaired skin barrier function. According to modern corneotherapy, preparations with skin identical moisturizers and lipids can restore the impaired intracellular lipid bilayer and substitute the lack of natural moisturizing factors (NMFs) observed in Xerosis. Urea, a potent natural NMF, is considered gold standard in the treatment of Xerosis cutis. In the following we summarize findings of three studies (in vivo and ex vivo) to explore if the application of an "intelligently" formulated, biomimetic emollient has advantages compared to standard moisturizers in terms of moisturization, depth of moisturization and skin's own repair processes.

Materials & Methods:

An "intelligently" formulated, biomimetic emollient containing 10% urea + 17 further skin identical NMFs as well as ceramides and gluco glycerol was tested in three studies:

1. Double-blind, vehicle-controlled clinical study (N=44, very dry skin). Application of biomimetic emollient and two vehicles (vehicle and vehicle "plus" with added urea and lactate) twice daily to inner forearms for 2 weeks. Skin hydration levels were measured using Corneometer CM 825, transepidermal water loss (TEWL) was measured using Tewameter 300.
2. Randomized, controlled study (N=26, normal skin). Application of the biomimetic emollient and two vehicles (vehicle and vehicle "plus" with 10% urea added) twice daily to inner forearms for 2 weeks. Deep SC hydration was measured using KOSIM IR, which enables the depth-resolved determination of water content in vivo.
3. Double-blind, vehicle-controlled clinical study (N=22, very dry skin). Application of the biomimetic emollient and vehicle twice daily to inner forearms for 2 weeks. Suction blister samples were obtained for gene expression analysis using RT-PCR.

Results:

1. Corneometry showed a significant improvement in skin hydration in all groups after 2 weeks compared to baseline, with the biomimetic emollient showing superior efficacy compared to vehicle and vehicle plus ($p<.05$). Furthermore, TEWL was significantly reduced after 2 weeks of treatment with biomimetic emollient and vehicle plus ($p<.05$), but not with vehicle alone.
2. KOSIM IR showed a significantly higher water content in the SC up to a depth of 10 µm in treated compared to untreated skin ($p<.05$). Water content was significantly higher in areas treated with the biomimetic emollient and vehicle plus compared to vehicle ($p<.05$), with the highest water content observed for areas treated with the biomimetic emollient.
3. Relative gene expression data of suction blister roofs showed a significant upregulation of markers of barrier function (FLG, FLG2, IVL, TGM1, Krt10, KLK7, CASP14, CDSN, OCLN, CLDN1, KLK5, LOR), skin hydration (AQP3, AQP9, ELOVL4) and skin lipid metabolism (SMPD1, FADS1, HMGCR) compared to vehicle (all $p < .05$).

Conclusion:

The results show that the efficacy of moisturizers containing Urea can be further enhanced when combined with further skin identical NMFs, gluco glycerol and lipids. More precisely, this combination showed superior moisturization of the skin in vivo, also in deeper layers of the SC. Furthermore, the analysis of gene expression data suggests that treating the skin with intelligently formulated emollients could support skin's own barrier repair processes, going beyond passive skin hydration and barrier stabilization.

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Abstract N°: 4988

Topical Application of Microencapsulated Epidermal Growth Factor Device Dose Not Promote the Progression of B16-F10 Melanoma in vitro and in vivo

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Introduction & Objectives:

Microencapsulated recombinant human epidermal growth factor (Me-rEGF) has been topically applied to promote wound healing. This study aims to evaluate the probable risk of topical Me-rEGF in stimulating skin cancer *in vitro* and *in vivo*.

Materials & Methods:

Mouse B16-F10 melanoma models were employed to investigate the oncogenic potential of Me-rEGF and its ingredients to induce skin cancer. We studied melanoma cell growth form mouse B16-F10 melanoma cells by cell proliferation and colony formation assays and primary melanoma mice model. Western blot assay was performed to assess the expression of epidermal growth factor receptor (EGFR) and HER2. Immunohistochemistry was used to assess the marker of proliferative index in melanoma tissues.

Results:

The cell proliferation assay indicated that Me-EGF did not stimulate the viability nor the anchorage-dependent growth of B16-F10 melanoma cells *in vitro*. Western blot analysis showed that Me-EGF treatment increased the total and phosphorylated EGFR expression without affecting the HER2 expression in B16-F10 melanoma cells. Further assessment of melanoma tumor growth using B16-F10 cells induced primary melanoma mice model also showed that Me-EGF did not promote the growth of B16-F10 melanoma. Immunohistochemistry staining revealed that there was no difference on the expression of proliferative index marker Ki-67 among Me-EGF, other adjuvant and control groups.

Conclusion:

Administration of Me-EGF does not promote melanoma tumor growth *in vitro* and *in vivo*.

Key words: Melanoma; Tumor; EGF; Microencapsulation; Me-EGF

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Abstract N°: 4993

Impact of tirbanibulin 1% treatment on symptoms, emotions, and functioning in different subgroups of patients with Actinic Keratosis in routine clinical practices across the U.S. (PROAK Study)

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Introduction & Objectives: Actinic Keratosis (AK) has been shown to negatively affect emotional and social functioning and skin-related quality of life (QoL). The objective of this analysis was to evaluate changes in patient-reported AK symptoms, emotions, and functioning, among different subgroups of patients with AK treated with tirbanibulin 1% in routine clinical practice across the U.S.

Materials & Methods: This single-arm, prospective cohort study (PROAK: NCT05260073) was conducted in adults with AKs on the face or scalp who were newly initiated with once-daily tirbanibulin 1% ointment treatment (5-day course) as part of usual care. Patients and clinicians completed surveys and clinical assessments at baseline, Week-8, and Week-24. Skindex-16 (completed at baseline and Week-8) is a 16-item survey with 3 domains: symptoms (4 items), emotions (7 items) and functioning (5 items); each item potential score of 0 (never bothered) to 6 (always bothered); each domain score range: 0-100 (higher score indicates severe impairment). The change from baseline to Week-8 in Skindex-16 domains in subgroups of patients according to gender, age, baseline Fitzpatrick skin type, baseline skin photodamage, baseline history of skin cancer, and prior treatment experience (cryosurgery, other topical treatments, and treatment naïve at baseline) was assessed.

Results: A total of 290 AK patients completed the study assessments at Week-8 (mean age: 66.3 years; female: 31.4%; history of skin cancer: 61.7%; Fitzpatrick skin type: I: 7.6%, II: 71.4%, III: 18.6%, IV: 1.4%, V: 1.0%). At Week-8, a statistically significant ($p<0.0001$) decrease in scores from baseline was observed for all Skindex-16 domains (symptoms: 22.3 at baseline vs 8.2 at Week-8; emotions: 38.2 vs 13.5; functioning: 14.4 vs 4.6). After dividing the sample by subgroups, a statistically significant difference ($p<0.03$) was observed for all Skindex-16 domains in all subgroups of patients except for the subgroup ≤49 years in the functioning domain (16.38 at baseline vs 6.41 at Week-8, $p=0.0886$). The table shows the mean value for each domain at baseline and Week-8 by subgroups.

Conclusion: QoL is impaired in patients with AK. In our study, baseline values were quite high compared to the maximum in each of the Skindex-16 domains. Patients with AKs who used once-daily tirbanibulin 1% treatment for 5-days reported a significant reduction in AK burden, as indicated by the improvement in AK symptoms, emotional, and functional impact from baseline to as early as Week-8, independently to gender, age, baseline Fitzpatrick skin type, baseline skin photodamage, baseline history of skin cancer, and prior treatment experience. Younger (≤49 years) patients had a not statistically significant improvement in functioning domain.

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Abstract N°: 5105

Do topical steroids influence the cutaneous microbiome composition in lichen sclerosus patients?

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Introduction & Objectives:

Microbiome research is booming. Dermatological clinical trials routinely analyse the microbiome composition as clinical endpoint or as exploratory biomarker. A plethora of new compounds are being developed targeting microbiome perturbations for a range of dermatological and gynaecological indications. Examples include endolysin treatment targeting *Staphylococcus aureus* for atopic dermatitis and acne, and *Lactobacillus*-based compounds for bacterial vaginosis. However, have microbiome-modulating effects of topical corticosteroids, dermatology's golden standard, ever been described? The aim of this study was to understand the influence of topical corticosteroids on the microbiome composition in lichen sclerosus patients.

Materials & Methods:

The effect of clobetasol on the microbiome composition was analysed in patients with lichen sclerosus in a prospective, open-label clinical trial. Women with vulvar lichen sclerosus (n=10) were enrolled and vaginal, vulvar and anal swabs were collected. The microbiome composition was characterized with metagenomic shotgun sequencing. Clobetasol was applied on the affected vulvar area for a duration of 4 weeks, compliance was measured with an e-diary application. Pre- and post-dose samples were analysed.

Results:

All patients completed the treatment period with 99% compliance. The vulvar microbiome composition did not significantly alter after clobetasol treatment. Literature review revealed few descriptions of microbiome analyses during corticosteroid treatment. The findings were extrapolated for other dermatological diseases with pharmacological considerations considering the working mechanism of corticosteroids.

Conclusion:

No alterations to the vulvar microbiome composition were observed after 4-week clobetasol treatment of lichen sclerosus. We conclude that corticosteroids do not directly affect the microbiome composition of the skin. However, indirect, immunomodulatory effects from corticosteroids cannot be ruled out at this stage. These findings raise questions for the applicability for other new compounds that target dysbiosis.

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Abstract N°: 5143

An Evaluation of Conjunctivitis Among Individuals with Moderate-to-Severe Atopic Dermatitis Treated with Dupilumab in the United States

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Introduction & Objectives:

Conjunctivitis has been reported in patients with moderate-to-severe atopic dermatitis (MTS-AD). In clinical trials, ophthalmic adverse events occurred at higher rates among individuals with AD treated with dupilumab than with placebo . The objective of this study was to investigate the incidence of conjunctivitis among individuals with MTS-AD and treated with dupilumab in comparison to non-dupilumab therapies in a real-world setting using algorithms validated for this purpose.

Materials & Methods:

An observational cohort study was conducted using medical and pharmacy claims data from the Optum Research Database. Using a validated algorithm, an MTS-AD study population was identified among patients at least 12 years of age from 28 March 2017 through 30 November 2019.

Within this study population, initiators of dupilumab and dupilumab-naïve patients treated for MTS-AD were identified and propensity score (PS)-matched in a 1:1 ratio. Patients were required to have continuous enrollment in the health plan with complete medical and pharmacy benefits during baseline (12 months prior to cohort entry, defined as initiation of dupilumab or dispensing/administration of other AD therapy). Following exclusion of patients with conjunctivitis or keratitis in the 30 days before cohort entry, covariate balance between the PS-matched treatment cohorts (PS included 81 variables) was evaluated to confirm that both groups were similar with respect to AD severity and baseline comorbidities before analyzing study outcomes. Conjunctivitis was identified using a validated algorithm beginning on the day after cohort entry. Incidence rates and incidence rate ratios (IRRs) for conjunctivitis with 95% confidence intervals (CIs) were estimated for the PS-matched cohorts via Poisson regression models that adjusted for number of AD diagnosis codes on unique days, number of dermatologist visits, and number of unique AD therapies; variables that were not fully balanced in the PS matching.

Results:

In the moderate-to-severe AD study population, 2,446 dupilumab initiators and 12,117 other AD therapy users meeting cohort inclusion criteria were identified. After PS matching and removing patients with recent conjunctivitis or keratitis codes, 2,175 dupilumab initiators and 2,189 other AD therapy users remained. Nearly all measured baseline characteristics were well-balanced between the dupilumab and comparator cohorts (Table 1).

The adjusted IRR for conjunctivitis comparing the dupilumab and other AD therapy cohorts was 1.86 (95% CI 1.51, 2.30), indicating an increased incidence of the outcome among dupilumab initiators (Table 2). The incidence of conjunctivitis was similar between cohorts during the first 8 weeks of follow-up and differentiated after 8 weeks. In a complementary analysis of patients who experienced conjunctivitis while on dupilumab, only 8.6% discontinued treatment.

Conclusion:

Results from this study indicated an increased risk of conjunctivitis in patients initiating dupilumab versus other AD therapy users. In general, the results are in line with existing literature and clinical trials and do not alter the known benefit-risk profile for dupilumab. Strengths of the study include the use of validated algorithms to identify both the study population and the outcome events, the large list of baseline covariates intended to balance AD severity and risk of ocular events between treatment cohorts, and the large sample size.

Table 1. Baseline Covariate Distributions After Propensity Score Matching among moderate-to-severe AD patients in the Dupilumab Initiator Cohort and Other AD Therapy Cohort, Identified 28 March 2017 through 30 November 2019

Baseline Covariates[a]	Dupilumab (N = 2,175)[b]	Other AD Therapy (N = 2,189)[b]	Std. Diff.
	N (%)	N (%)	
Demographics			
Age (years), median (IQR)	40 (24 - 54)	41 (25 - 54)	-0.03
Sex			
Female	1,166 (53.6%)	1,151 (52.6%)	0.02
Male	1,009 (46.4%)	1,038 (47.4%)	-0.02
Health Plan Enrollment and Health Care Utilization			
Length of health plan enrollment (years), median (IQR)	3 (2 - 4)	3 (2 - 4)	0.02
No. AD diagnosis codes on unique days, median (IQR)	3 (2 - 4)	2 (2 - 3)	0.21
No. allergist visits, median (IQR)	0 (0 - 1)	0 (0 - 1)	0.03
No. dermatologist visits, median (IQR)	2 (1 - 4)	2 (1 - 4)	0.12
No. emergency department visits, median (IQR)	0 (0 - 1)	0 (0 - 1)	0.00
No. hospitalizations, median (IQR)	0 (0 - 0)	0 (0 - 0)	0.00
No. ophthalmologist visits, median (IQR)	0 (0 - 0)	0 (0 - 0)	-0.01
No. physician visits, median (IQR)	9 (5 - 13)	9 (5 - 14)	-0.04
No. unique AD therapies, median (IQR)	4 (3 - 6)	3 (3 - 4)	0.44
Total hospital length of stay (days), median (IQR)	0 (0 - 0)	0 (0 - 0)	0.00
Prior AD Therapy			
Crisaborole	346 (15.9%)	317 (14.5%)	0.04
Oral corticosteroids	1,218 (56.0%)	1,288 (58.8%)	-0.06
Parenteral corticosteroids	784 (36.0%)	859 (39.2%)	-0.07
Phototherapy	150 (6.9%)	152 (6.9%)	0.00
Systemic immunosuppressants			
Azathioprine	33 (1.5%)	26 (1.2%)	0.03
Belimumab	2 (0.1%)	0 (0.0%)	0.04
Cyclosporine	4 (0.2%)	7 (0.3%)	-0.03
Interferon gamma	0 (0.0%)	0 (0.0%)	0.00
Leflunomide	3 (0.1%)	3 (0.1%)	0.00
Methotrexate	161 (7.4%)	155 (7.1%)	0.01
Mycophenolate	74 (3.4%)	58 (2.6%)	0.04
Rituximab	0 (0.0%)	0 (0.0%)	0.00
Topical corticosteroids	1,806 (83.0%)	1,844 (84.2%)	-0.03
High potency	1,186 (54.5%)	1,260 (57.6%)	-0.06
Medium potency	1,165 (53.6%)	1,218 (55.6%)	-0.04
Low potency	483 (22.2%)	527 (24.1%)	-0.04
Topical tacrolimus, pimecrolimus	649 (29.8%)	659 (30.1%)	-0.01
Ocular Conditions and Prescription Medications			
Artificial tears	0 (0.0%)	0 (0.0%)	0.00
Blepharitis	0 (0.0%)	0 (0.0%)	0.00
Conjunctivitis	212 (9.7%)	216 (9.9%)	0.00
Contact lens wear	3 (0.1%)	7 (0.3%)	-0.04
Dry eye syndrome	71 (3.3%)	77 (3.5%)	-0.01
Ectropion	4 (0.2%)	6 (0.3%)	-0.02
Keratitis/Keratoconjunctivitis	23 (1.1%)	31 (1.4%)	-0.03
Ocular herpes	7 (0.3%)	9 (0.4%)	-0.01
Ocular mucous membrane pemphigoid	0 (0.0%)	0 (0.0%)	0.00
Ocular rosacea	54 (2.5%)	50 (2.3%)	0.01
Ocular surface squamous neoplasia	0 (0.0%)	0 (0.0%)	0.00

Baseline Covariates[a]	Dupilumab (N = 2,175)[b]	Other AD Therapy (N = 2,189)[b]	Std. Diff.
	N (%)	N (%)	
Ophthalmic antibiotics (including antibiotic-steroid combinations)	146 (6.7%)	144 (6.6%)	0.01
Ophthalmic antifungals	1 (0.0%)	1 (0.0%)	0.00
Ophthalmic antihistamines	71 (3.3%)	70 (3.2%)	0.00
Ophthalmic antivirals	191 (8.8%)	206 (9.4%)	-0.02
Ophthalmic cholinergic agonists	1 (0.0%)	3 (0.1%)	-0.03
Ophthalmic corticosteroids	74 (3.4%)	63 (2.9%)	0.03
Ophthalmic mast-cell stabilizers	4 (0.2%)	4 (0.2%)	0.00
Topical immunomodulators	431 (19.8%)	442 (20.2%)	-0.01
Topical nonsteroidal anti-inflammatory drugs (NSAIDs)	16 (0.7%)	18 (0.8%)	-0.01
Comorbidities Relevant to Inflammatory Diseases			
Allergic contact dermatitis	362 (16.6%)	373 (17.0%)	-0.01
Allergic rhinitis	751 (34.5%)	767 (35.0%)	-0.01
Asthma	587 (27.0%)	577 (26.4%)	0.01
Cardiovascular disease	172 (7.9%)	170 (7.8%)	0.01
Cerebrovascular disease	25 (1.1%)	26 (1.2%)	0.00
Chlamydia	1 (0.0%)	1 (0.0%)	0.00
Crohn's disease/ulcerative colitis	17 (0.8%)	15 (0.7%)	0.01
Erythema multiforme major	1 (0.0%)	3 (0.1%)	-0.03
Food allergies	72 (3.3%)	70 (3.2%)	0.01
Gonorrhea	0 (0.0%)	2 (0.1%)	-0.04
Herpes simplex virus	81 (3.7%)	84 (3.8%)	-0.01
Hypertension	506 (23.3%)	530 (24.2%)	-0.02
Hyperthyroidism	13 (0.6%)	17 (0.8%)	-0.02
Hypothyroidism	170 (7.8%)	181 (8.3%)	-0.02
Pruritus	578 (26.6%)	601 (27.5%)	-0.02
Psoriasis	213 (9.8%)	196 (9.0%)	0.03
Rheumatoid arthritis	22 (1.0%)	17 (0.8%)	0.02
Sinusitis	322 (14.8%)	330 (15.1%)	-0.01
Sjogren's syndrome	11 (0.5%)	12 (0.5%)	-0.01
Stevens-Johnson syndrome	1 (0.0%)	3 (0.1%)	-0.03
Systemic lupus erythematous	15 (0.7%)	19 (0.9%)	-0.02
Systemic sclerosis	0 (0.0%)	0 (0.0%)	0.00
Toxic epidermal necrolysis	1 (0.0%)	2 (0.1%)	-0.02
Type 1 Diabetes	17 (0.8%)	12 (0.5%)	0.03
Type 2 Diabetes	137 (6.3%)	142 (6.5%)	-0.01
Urticaria	235 (10.8%)	248 (11.3%)	-0.02
Vasculitis	2 (0.1%)	5 (0.2%)	-0.03
Empirically-Identified Variables			
Hydroxyzine Hcl (Rx Dispensing)	615 (28.3%)	624 (28.5%)	-0.01
Other And Unspecified Dermatitis	1,226 (56.4%)	1,257 (57.4%)	-0.02
Rash And Other Nonspecific Skin Eruption	504 (23.2%)	538 (24.6%)	-0.03
Unspecified Contact Dermatitis	227 (10.4%)	255 (11.6%)	-0.04

Abbreviations: AD, atopic dermatitis; IQR, interquartile range; NSAID, nonsteroidal anti-inflammatory drugs; PS, propensity score; SD, standard deviation; Std. Diff., standardized difference

[a] Some baseline covariates have been excluded from the table due to space considerations.

[b] Number remaining after excluding patients with conjunctivitis or keratitis codes in the 30 days prior to cohort entry.

Table 2. Incidence Rates and Incidence Rate Ratios (IRRs) of Conjunctivitis, Overall and Separately by Follow-up Time, among Propensity Score-Matched Dupilumab Initiators versus Other Moderate-to-severe AD Therapy Users, Identified 28 March 2017 through 30 November 2019

Outcome	Dupilumab			Other AD Therapy			Adjusted[a] IRR (95% CI)
	N	PY	IR	N	PY	IR	
Overall	260	1,612.7	161.2	148	1,789.7	82.7	1.86 (1.51, 2.30)
Up to 8 Weeks Follow-up	63	323.7	194.7	45	312.8	143.9	1.23 (0.82, 1.84)
After 8 Weeks Follow-Up	197	1,289.0	152.8	103	1,476.9	69.7	2.14 (1.67, 2.75)

Abbreviations: AD, atopic dermatitis; CI, confidence interval; IR, incidence rate per 1,000 person-years; IRR, incidence rate ratio; PY, person-years

[a] In addition to PS matching, outcome model was adjusted for number of AD diagnosis codes on unique days, number of dermatologist visits, and number of unique AD therapies.

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Abstract N°: 5187

Safety and Tolerability of Tirbanibulin Ointment 1% Treatment on 100 cm2 of the Face and Scalp in Patients with Actinic Keratosis: A Phase 3 Study

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Introduction & Objectives: Actinic keratosis (AK) is a pre-cancerous skin disease resulting from the atypical proliferation of keratinocytes that may progress to squamous cell carcinoma [1]. Tirbanibulin ointment 1% has demonstrated efficacy, tolerability, and safety for AK and is approved in the US and Europe for treating AK on the face or scalp over an area up to 25 cm2 [2,3]. The objective of this study was to evaluate the safety, tolerability, and efficacy of tirbanibulin ointment 1% applied to a larger area, a field of 100 cm2, on the face or balding scalp in adult patients with AK.

Materials & Methods: A phase 3, multicenter, open-label, single-arm study (NCT05279131) was conducted among adult patients having a treatment field on the face (excluding lips, eyelids, inside nostrils, and ears) or balding scalp that measured 100 cm2 and contained 4 to 12 clinically typical, visible, and discrete, non-hypertrophic, non-hyperkeratotic AKs. Enrolled patients received 350 mg of tirbanibulin once daily to the treatment area for 5 consecutive days and a follow-up period up to Day 57. All patients were evaluated for safety, tolerability, and the presence of AKs until Day 57. Safety was assessed by evaluating treatment emergent adverse events (TEAEs). Tolerability endpoints included scores of 6 local signs (erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, erosion/ulceration) scored at each timepoint from 0 (absent) to 3 (severe).

Results: A total of 105 patients (20 sites in US) were included in the safety analysis set (males: 69%; ≥65 years: 65%; Fitzpatrick skin type II: 63%; AK on the face: 68%; mean number of AKs: 7.7). The most common local tolerability signs after 100 cm2 tirbanibulin administration were erythema (96% of patients) and flaking/scaling (85% of patients), which were mild-to-moderate in severity, peaked at Day 5 to 8, and resolved or returned to baseline by Day 29 (Figure 1). Severe erythema was only reported in 6% of patients and severe flaking/scaling in 9% of patients. Overall, the tolerability profile of treating a 100 cm2 area was consistent with that seen when treating an area of 25 cm2. The most frequent TEAEs were application site pruritus (11% of patients) and application site pain (9%), consistent with previous Phase 3 study results (25 cm2 treatment area) [2]. No serious TEAEs related to the drug were reported. The maximum local tolerability composite score was 4 out of 18, consistent with prior pivotal trials. Patients initiated the study with a mean of 7.7 AKs and completed the study with a mean of 1.8 AKs, indicating outstanding efficacy.

Conclusion: Safety, local tolerability, and efficacy in patients with AK treated with tirbanibulin over a 100 cm2 area were consistent with those previously reported in patients with AK treated in pivotal trials with tirbanibulin over a smaller area.

[1] Siegel JA et al. Br J Dermatol. 2017;177(2):350-358.

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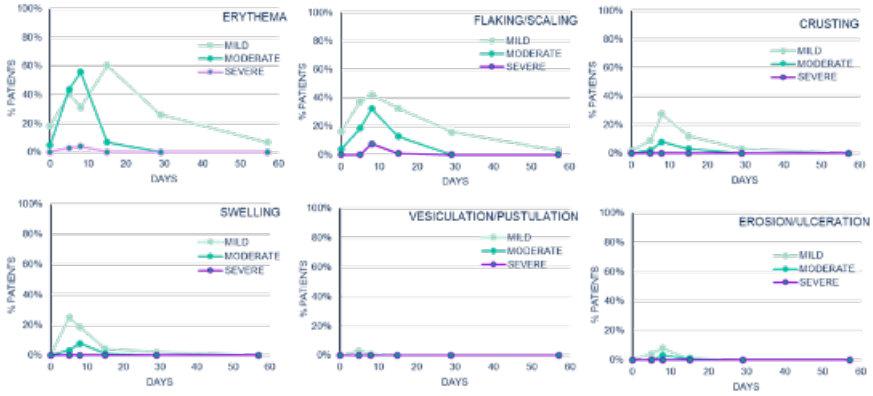
Figure 1. Local tolerability signs after tirbanibulin administration (local tolerability severity scale: 0=absent, 1=Mild, 2=Moderate, 3=Severe)



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Abstract N°: 5707

Chronic actinic dermatitis: treated with topical Tacrolimus

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Introduction & Objectives: Chronic actinic dermatitis (CAD) is a rare photodermatosis of the elderly, characterized by a chronic disabling photosensitivity. Apart from external photoprotection and sometimes darkrooming, the treatment aims at obtaining sufficient sun tolerance. Our observation illustrates a case of stable remission with the application of tacrolimus ointment at 0.1%.

Observation : A 60-year-old woman consulted for a chronic photodistributed erythematous rash predominantly on the face. The patient had no previous history of the disease. Routine biological parameters were normal as well as total serum IgE. Histological examination showed chronic actinic dermatitis.

Photoprotection and dermocorticoids resulted in a slight improvement. Topical treatment with tacrolimus 0.1% ointment, initially at a rate of two applications per day, was then instituted. It allowed the reduction, then the cessation of dermocorticoids, at the cost of a moderate skin irritation during the applications. After two months of treatment, the patient's skin and psychiatric status were satisfactory.

After 6 months of treatment, the patient was in complete remission and the application became daily.

Discussion : This observation shows a stable remission of a case of CAD under topical tacrolimus 0.1%. The treatment of CAD involves first-line photoprotection, dermocorticoids and UVA phototherapy. The combination of systemic corticosteroids and PUVA therapy is often relatively effective.In the literature, as in our patient, the efficacy of tacrolimus on CAD is obtained on average in two weeks (four to 20 days), and complete remission after two months of treatment. The maximum follow-up in the literature is 32 months. Tacrolimus is used alone, in combination with emollients or phototherapy. All observers Chronic actinic dermatitis is one of the most frequently encountered photodermatoses in patients over the age of 50. It is characterized by a persistent redness of the face and other exposed areas, it presents a rare entity, and a diagnostic and therapeutic challenge.report a transient irritation at the beginning of treatment, already known with other indications of tacrolimus ,This undesirable effect has never led to discontinuation of treatment; as with atopic dermatitis, the irritation does not persist in the long term, but fades with time.

Conclusion : Chronic actinic dermatitis is one of the most frequently encountered photodermatoses in patients over the age of 50. It is characterized by a persistent redness of the face and other exposed areas, it presents a rare entity, and a diagnostic and therapeutic challenge.

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Abstract N°: 5710

Safety, Tolerability and Pharmacokinetics (PK) of GT20029 Following Topical Single Ascending Dose (SAD) Administration in Healthy Volunteers and Multiple Ascending Dose (MAD) Administration in Subjects with Androgenetic Alopecia (AGA) or Acne

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GT20029-US-1001 Abstract for EADV Congress in Berlin 2023

Introduction & Objectives:

The interaction of dihydrotestosterone (DHT) and the androgen receptors (AR) is one of the pathophysiologies of Androgenetic Alopecia (AGA) and Acne. GT20029 is a topical AR-Proteolysis Targeting Chimera (PROTAC), which recruits AR in proximity to an E3 ubiquitin ligase to initiate AR ubiquitination and subsequent degradation. In preclinical studies, GT20029 can promote hair growth significantly in dihydrotestosterone (DHT)-induced AGA mouse model and inhibit testosterone propionate (TP)-induced flank organ enlargement with statistically significance in hamster flank organ acne model. Therefore, it showed potential treatment efficacy in promoting hair growth and inhibiting sebaceous gland development. GT20029 also exhibited low systemic exposure and achieved a good safety profile. In light of the above, the phase I clinical trial to evaluate its safety, tolerability and Pharmacokinetics (PK) in healthy volunteers (HV) and subjects with AGA or Acne was initiated in United Status (USA) only.

Materials & Methods:

This was a randomized, double-blinded, placebo-controlled, parallel group, dose escalation study with two stages. Stage 1: topical single ascending dose (SAD), planned to enroll 40 HV with 5 different dosage groups, with drug applied on the back on Day 1 and serial blood samples collected for PK analysis.

Stage 2 with two multiple ascending dose (MAD) cohorts:40 male subjects with AGA and another 40 male and female subjects with acne to recieve different doses. Randomized in the same way as SAD (**Table 1**). PK blood samples were collected regularly and safety was monitored. Dose escalation for SAD and MAD did not occur until safety review was completed.

Safety assessments included monitoring of adverse events (AEs), vital signs, laboratory findings, electrocardiograms (ECG), physical exams, subject skin self-assessments and investigator evaluated skin irritation assessment.

The study endpoints included evaluation of safety and tolerability (primary) and PK characteristics (secondary) of GT20029.

Results:

From December, 2021 throught December, 2022, 8 sites contributed 123 subjects: (Table 2 A-C Subjects Disposition by Dose Cohort). Subjects' demographic information listed in Table 3.

For safety analysis, almost all treatment emergent (TE) AEs were assessed as mild and no TEAEs were serious, severe or resulted in early withdrawal or death occurred. The most common TEAE across all study cohorts was headache (not related to study treatment). The most common TEAEs among both MAD Cohorts were application site dryness, application site pain, and application site pruritis (all mild in severity and all related to study treatment). All TEAEs summarized in Table 4A-4C. Laboratory results, post-baseline mean values of the vital signs, and ECG parameters were similar across all cohorts in the study. Subject skin self-assessments and investigator-evaluated skin irritation assessments also showed minimal cutaneous reaction to treatment.

For PK analysis, overall quantifiable GT20029 concentration was low. GT20029 concentrations were higher in subjects with acne as compared to those with AGA, yet remained close to the LLOQ for all cohorts.

Conclusion:

Overall GT20029 was safe and well tolerated. No significant safety concerns were identified in the study.

PK parameters such as AUC, Cmax, Tmax, t1/2 were assessed, however, following topical administration, systemic exposure of GT20029 was low.

Table 1, Planned Treatment Alignment of Stage 1 (Cohort 1) and Stage 2 (Cohort 2A and 2B)

Cohort 1 Treatment Assignment with Healthy Volunteers		
Group	**Dose of GT20029**	**Subjects**
1	1 mg [0.5% (20g: 0.1g)]	8 (6 active + 2 placebo)
2	2 mg [0.5% (20g: 0.1g)]	8 (6 active + 2 placebo)
3	5 mg [0.5% (20g: 0.1g)]	8 (6 active + 2 placebo)
4	10 mg [1% (20g: 0.2g)]	8 (6 active + 2 placebo)
5	20 mg [2% (20g: 0.4g)]	8 (6 active + 2 placebo)
Cohort 2 Treatment Assignment in Subjects with AGA (A) or Acne (B)		
Group	**Dose of GT20029**	**Subjects**
6 (A/B)	2 mg [0.5% (20g: 0.1g)] QD, Days 1-14	8 (6 active + 2 placebo)
7 (A/B)	2 mg [0.5% (20g: 0.1g)] BID, Days 1-14	8 (6 active + 2 placebo)
8 (A/B)	5 mg [0.5% (20g: 0.1g)] QD, Days 1-14	8 (6 active + 2 placebo)
9 (A/B)	10 mg [1% (20g: 0.2g)] QD, Days 1- 14	8 (6 active + 2 placebo)
10 (A/B)	20 mg [2% (20g: 0.4g)] QD, Days 1-14	8 (6 active + 2 placebo)

BID=twice daily; QD=once daily.

Table 2A Subject Disposition by Dose Cohort (Stage 1 SAD) – All Screened Subjects

		GT20029 Doses					
	Placebo	**1 mg (0.5%)**	**2 mg (0.5%)**	**5 mg (0.5%)**	**10 mg (1.0%)**	**20 mg (2.0%)**	**Total**
Screened Subjects							102
Treated Subjects (Safety Population)	11	6	6	6	6	5	40
Subjects Completed the Study	11 (100%)	6 (100%)	6 (100%)	6 (100%)	6 (100%)	5 (100%)	40 (100%)
Subjects Terminated Early from the Study	0	0	0	0	0	0	0

Table 2B Subject Disposition by Dose Cohort (Stage 2 MAD 2A, Androgenetic Alopecia) – All Screened Subjects

		GT20029 Doses					
	Placebo	**2 mg (QD)**	**2 mg (BID)**	**5 mg (QD)**	**10 mg (QD)**	**20 mg (QD)**	**Overall**
Screened Subjects							65
Treated Subjects (Safety Population)	10	8	6	6	6	6	42
Subjects Completed the Study	10 (100%)	6 (75.0%)	6 (100%)	6 (100%)	6 (100%)	6 (100%)	40 (95.2%)
Subjects Terminated Early from the Study	0	2 (25.0%)	0	0	0	0	2 (4.8%)

Table 2C Subject Disposition by Dose Cohort (Stage 2 MAD 2B, Acne) Randomized Subjects

		GT20029 Doses					
	Placebo	**2 mg (QD)**	**2 mg (BID)**	**5 mg (QD)**	**10 mg (QD)**	**20 mg (QD)**	**Overall**
Screened Subjects							60
Treated Subjects (Safety Population)	10	7	6	6	6	6	41
Subjects Completed the Study	10 (100%)	6 (85.7%)	6 (100%)	6 (100%)	6 (100%)	6 (100%)	40 (97.6%)
Subjects Terminated Early from the Study	0	1 (14.3%)	0	0	0	0	1 (2.4%)

BID=twice daily; QD=once daily.

SAD=single ascending dose. MAD=multiple ascending dose;

Percentage is based on the number of Safety Population.

Table 3 A Summary of Demographic Characteristics of All Cohorts – Safety Population

			Cohort 1-Healthy Volunteers						Cohort 2A- Subjects with AGA						Cohort 2B-Subjects with Acne					
				GT20029 Doses						GT20029 Doses						GT20029 Doses				
Variables	Category	Statistic	Placebo	1 mg	2 mg	5 mg	10 mg	20 mg	Placebo	2 mg	2 mg	5 mg	10 mg	20 mg	Placebo	2 mg	2 mg	5 mg	10 mg	20 mg
				-0.50%	-0.50%	-0.50%	-1.00%	-2.00%	QD or BID	(QD)	(BID)	(QD)	(QD)	(QD)	QD or BID	(QD)	(BID)	(QD)	(QD)	(QD)
			(N=11)	(N=6)	(N=6)	(N=6)	(N=6)	(N=5)	(N=10)	(N=8)	(N=6)	(N=6)	(N=6)	(N=6)	(N=10)	(N=7)	(N=6)	(N=6)	(N=6)	(N=6)
Age (years)		Mean (SD)	28.7 (8.24)	39.0 (10.94)	42.8 (15.09)	30.3 (4.72)	37.0 (9.84)	46.8 (11.65)	40.4 (8.44)	49.8 (6.11)	45.8 (9.15)	47.5 (11.17)	49.5 (8.41)	50.8 (5.56)	37.1 (12.84)	25.4 (6.63)	27.8 (6.82)	26.3 (8.26)	35.3 (9.11)	36.0 (8.99)
		Min - Max	19.0 - 45.0	27.0 - 57.0	19.0 - 56.0	25.0 - 37.0	22.0 - 50.0	28.0 - 56.0	27.0 - 53.0	41.0 - 58.0	31.0 - 58.0	28.0 - 58.0	34.0 - 58.0	45.0 - 58.0	20.0 - 58.0	18.0 - 38.0	19.0 - 35.0	20.0 - 41.0	23.0 - 46.0	25.0 - 48.0
Sex at Birth	Male	N (%)	3 (27.3%)	4 (66.7%)	4 (66.7%)	4 (66.7%)	4 (66.7%)	1 (20.0%)	10 (100%)	8 (100%)	6 (100%)	6 (100%)	6 (100%)	6 (100%)	4 (40.0%)	4 (57.1%)	3 (50.0%)	3 (50.0%)	5 (83.3%)	5 (83.3%)
	Female	N (%)	8 (72.7%)	2 (33.3%)	2 (33.3%)	2 (33.3%)	2 (33.3%)	4 (80.0%)	0	0	0	0	0	0	6 (60.0%)	3 (42.9%)	3 (50.0%)	3 (50.0%)	1 (16.7%)	1 (16.7%)
Race	American Indian / Alaska Native	N (%)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Asian	N (%)	2 (18.2%)	1 (16.7%)	0	0	0	0	0	0	0	0	0	1 (16.7%)	0	1 (14.3%)	0	0	0	0
	Black or African American	N (%)	3 (27.3%)	0	0	2 (33.3%)	0	0	4 (40.0%)	3 (37.5%)	1 (16.7%)	2 (33.3%)	2 (33.3%)	2 (33.3%)	2 (20.0%)	1 (14.3%)	0	0	0	2 (33.3%)
	Native Hawaiian / Pacific Islander	N (%)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	White	N (%)	6 (54.5%)	5 (83.3%)	6 (100%)	3 (50.0%)	6 (100%)	5 (100%)	5 (50.0%)	5 (62.5%)	5 (83.3%)	4 (66.7%)	4 (66.7%)	3 (50.0%)	7 (70.0%)	5 (71.4%)	6 (100%)	6 (100%)	6 (100%)	4 (66.7%)
	Other	N (%)	0	0	0	1 (16.7%)	0	0	0	0	0	0	0	0	1 (10.0%)	0	0	0	0	0
Weight (kg)		Mean (SD)	70.45 (16.247)	74.72 (13.215)	72.21 (10.447)	80.35 (15.901)	78.22 (12.324)	80.06 (11.781)	87.42 (9.884)	91.64 (11.109)	84.80 (9.327)	80.20 (11.647)	82.57 (11.713)	77.82 (9.668)	72.17 (10.599)	72.10 (9.722)	62.32 (9.284)	67.28 (13.636)	77.60 (10.446)	79.40 (13.943)
		Min - Max	51.70 - 102.80	58.30 - 91.70	56.90 - 82.64	53.00 - 95.90	58.40 - 90.40	68.20 - 94.00	69.20 - 100.00	80.90 - 107.00	77.80 - 102.00	68.70 - 95.80	69.50 - 102.00	65.70 - 87.50	59.90 - 90.20	60.40 - 86.40	46.80 - 72.11	53.90 - 88.80	60.00 - 89.80	63.60 - 104.50
BMI (kg/m2)		Mean (SD)	24.535 (3.6986)	25.637 (2.9127)	24.542 (3.2958)	25.048 (3.2124)	25.267 (3.1531)	27.408 (2.1420)	27.132 (1.4124)	27.641 (1.8818)	27.257 (1.8790)	25.423 (3.5360)	27.067 (2.4662)	25.855 (3.4635)	26.395 (2.8947)	23.697 (2.1562)	22.608 (2.9858)	24.228 (4.5648)	26.652 (2.4718)	25.417 (3.0352)
		Min - Max	20.120 - 29.910	20.560 - 29.030	20.220 - 28.530	21.580 - 29.270	19.070 - 28.090	25.420 - 29.740	24.260 - 28.910	24.830 - 29.620	24.690 - 29.800	20.630 - 29.730	22.640 - 29.670	19.640 - 29.760	20.440 - 29.880	20.550 - 26.270	18.280 - 25.720	19.190 - 29.600	22.040 - 29.530	20.370 - 29.600

Percentage is based on the number of Safety Population.

Table 4A Summary of TEAE (Stage 1 SAD, healthy volunteers) – Safety Population

		GT20029 Doses					
MedDRA SOC/Preferred Term	**Placebo (N=11) n (%)**	**1 mg (0.5%) (N=6) n (%)**	**2 mg (0.5%) (N=6) n (%)**	**5 mg (0.5%) (N=6) n (%)**	**10 mg (1.0%) (N=6) n (%)**	**20 mg (2.0%) (N=5) n (%)**	**Combined (N=29) n (%)**
Subjects with at least One TEAE	0	1 (16.7%)	1 (16.7%)	0	0	0	2 (6.9%)
Gastrointestinal Disorders	0	1 (16.7%)	0	0	0	0	1 (3.4%)
Diarrhea	0	1 (16.7%)	0	0	0	0	1 (3.4%)
Nervous System Disorders	0	0	1 (16.7%)	0	0	0	1 (3.4%)
Headache	0	0	1 (16.7%)	0	0	0	1 (3.4%)

Table 4B Summary of TEAE (Stage 2 MAD Cohort 2A, Subjects with AGA) – Safety Population

		GT20029 Doses					
MedDRA SOC/Preferred Term	**Placebo (N=10)**	**2 mg (QD) (N=8) n (%)**	**2 mg (BID) (N=6) n (%)**	**5 mg (QD) (N=6) n (%)**	**10 mg (QD) (N=6) n (%)**	**20 mg (QD) (N=6) n (%)**	**Combined (N=32) n (%)**
Subjects with at least One TEAE	2 (20.0%)	1 (12.5%)	1 (16.7%)	3 (50.0%)	1 (16.7%)	0	6 (18.8%)
General Disorders and Administration Site Conditions	1 (10.0%)	1 (12.5%)	1 (16.7%)	2 (33.3%)	1 (16.7%)	0	5 (15.6%)
Application Site Dryness	0	1 (12.5%)	1 (16.7%)	0	0	0	2 (6.3%)
Application Site Erythema	0	0	0	1 (16.7%)	0	0	1 (3.1%)
Application Site Pain	1 (10.0%)	0	0	1 (16.7%)	0	0	1 (3.1%)
Application Site Pruritus	1 (10.0%)	0	1 (16.7%)	1 (16.7%)	1 (16.7%)	0	3 (9.4%)
Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)	0	0	0	1 (16.7%)	0	0	1 (3.1%)
Melanocytic Naevus	0	0	0	1 (16.7%)	0	0	1 (3.1%)
Nervous System Disorders	1 (10.0%)	0	0	1 (16.7%)	0	0	1 (3.1%)
Headache	1 (10.0%)	0	0	0	0	0	0
Migraine	0	0	0	1 (16.7%)	0	0	1 (3.1%)

Table 4C Summary of TEAE (Stage 2 MAD Cohort 2B, Subjects with Acne) – Safety Population

MedDRA SOC/Preferred Term	Placebo (N=10)	GT20029 Doses					
		2 mg (QD) (N=7) n (%)	2 mg (BID) (N=6) n (%)	5 mg (QD) (N=6) n (%)	10 mg (QD) (N=6) n (%)	20 mg (QD) (N=6) n (%)	Combined (N=31) n (%)
Subjects with at least One TEAE	3 (30.0%)	3 (42.9%)	3 (50.0%)	6 (100.0%)	1 (16.7%)	2 (33.3%)	15 (48.4%)
General Disorders and Administration Site Conditions	2 (20.0%)	3 (42.9%)	2 (33.3%)	6 (100.0%)	1 (16.7%)	2 (33.3%)	14 (45.2%)
Application Site Dryness	1 (10.0%)	3 (42.9%)	2 (33.3%)	4 (66.7%)	1 (16.7%)	1 (16.7%)	11 (35.5%)
Application Site Pain	1 (10.0%)	3 (42.9%)	0	3 (50.0%)	1 (16.7%)	0	7 (22.6%)
Application Site Pruritus	2 (20.0%)	2 (28.6%)	1 (16.7%)	2 (33.3%)	1 (16.7%)	1 (16.7%)	7 (22.6%)
Infusion Site Discomfort	1 (10.0%)	0	0	0	0	0	0
Infusion Site Irritation	1 (10.0%)	0	0	0	0	0	0
Infections and Infestations	0	1 (14.3%)	0	1 (16.7%)	0	0	2 (6.5%)
Urinary Tract Infection	0	1 (14.3%)	0	1 (16.7%)	0	0	2 (6.5%)
Musculoskeletal and Connective Tissue Disorders	1 (10.0%)	0	0	0	0	0	0
Myalgia	1 (10.0%)	0	0	0	0	0	0
Nervous System Disorders	0	0	1 (16.7%)	0	0	0	1 (3.2%)
Headache	0	0	1 (16.7%)	0	0	0	1 (3.2%)
Skin and Subcutaneous Tissue Disorders	0	0	0	1 (16.7%)	0	0	1 (3.2%)
Pruritus	0	0	0	1 (16.7%)	0	0	1 (3.2%)

MedDRA=Medical Dictionary for Regulatory Activities; SOC=system organ class; TEAE=treatment-emergent adverse events.
A subject with more than one finding within a SOC/Preferred Term was counted once for that SOC/Preferred Term.
BID=twice daily; QD=once daily; SAD=single ascending dose; MAD=multiple ascending dose.
Percentage is based on the number of subjects in the safety population.
Adverse Events coded using MedDRA version 25.0

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Abstract N°: 5711

Safety, Tolerability and Pharmacokinetics of GT20029 Gel and GT20029 Solution in Healthy Subjects

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GT20029-CN-1001 Abstract for EADV Congress in Berlin 2023

Introduction & Objectives:

The interaction of dihydrotestosterone (DHT) and the androgen receptors (AR) is one of the pathophysiologies of Androgenetic Alopecia (AGA) and Acne. GT20029 is a topical AR-Proteolysis Targeting Chimera (PROTAC), which recruits AR in proximity to an E3 ubiquitin ligases to initiate AR ubiquitination and subsequent degradation. In preclinical studies, GT20029 can promote hair growth significantly in dihydrotestosterone (DHT)-induced AGA mouse model and inhibit testosterone propionate (TP)-induced flank organ enlargement with statistically significance in hamster flank organ acne model. Therefore, it showed potential treatment efficacy in promoting hair growth and inhibiting sebaceous gland development. GT20029 also exhibited low systemic exposure and a good safety profile. In light of the above, this phase I clinical trial to evaluate GT20029 gel and solution safety, tolerability and pharmacokinetics (PK) in healthy volunteers (HV) was initiated at China.

Materials & Methods:

This was a single-center, randomized, double-blinded, placebo-controlled, parallel group, dose escalation study with two stages. Stage 1: HVs were treated with GT20029 gel or placebo. 28 HVs were planned to enter single ascending dose (SAD) group with 4 different doses, and 40 HVs to multiple ascending dose (MAD) group, of whom can be recruited from SAD cohorts (after 14 days wash out period) or from other sources. Stage 2: HVs were treated with GT20029 solution or placebo. 24 HVs were planned to enter MAD group with 3 different doses. All drugs/placebo were topically administrated to the subjects on a fixed 8cmX 8cm area of the back. The study design and dose assignement table are in Figure 1. PK blood samples were collected regularly. Safety assessment included monitoring of adverse events (AEs), vital signs, laboratory findings, electrocardiogram, physical exams and assessment of the application site skin. Study endpoints included evaluation of safety and recommended phase II dose (primary) , PK characters and systemic exposure (secondary) of GT20029.

Results:

From July2021 to Aug2022, 95 subjects were randomly enrolled, including 69 in stage 1 and 26 in Stage 2 (Figure 2). HVs' baseline demographics is listed in Table 1.

Total 92 HVs were included in the safey analysis set, treatment emergent AEs (TEAEs) were reported in 68 subjects (73.9%), of whom 64 and 4 subject's TEAEs were grade 1 and grade 2, respectively. 64 subjects' AEs were deemed as drug-related AEs (DRAEs). The most reported DRAEs (≥10%) were rash, skin exfoliation, and pruritus. Less DRAEs incidences were observed in Stage 2 compared to that treated with gel (Table 2). No DRAEs were ≥ grade 3 nor led to cessation of treatment or death.

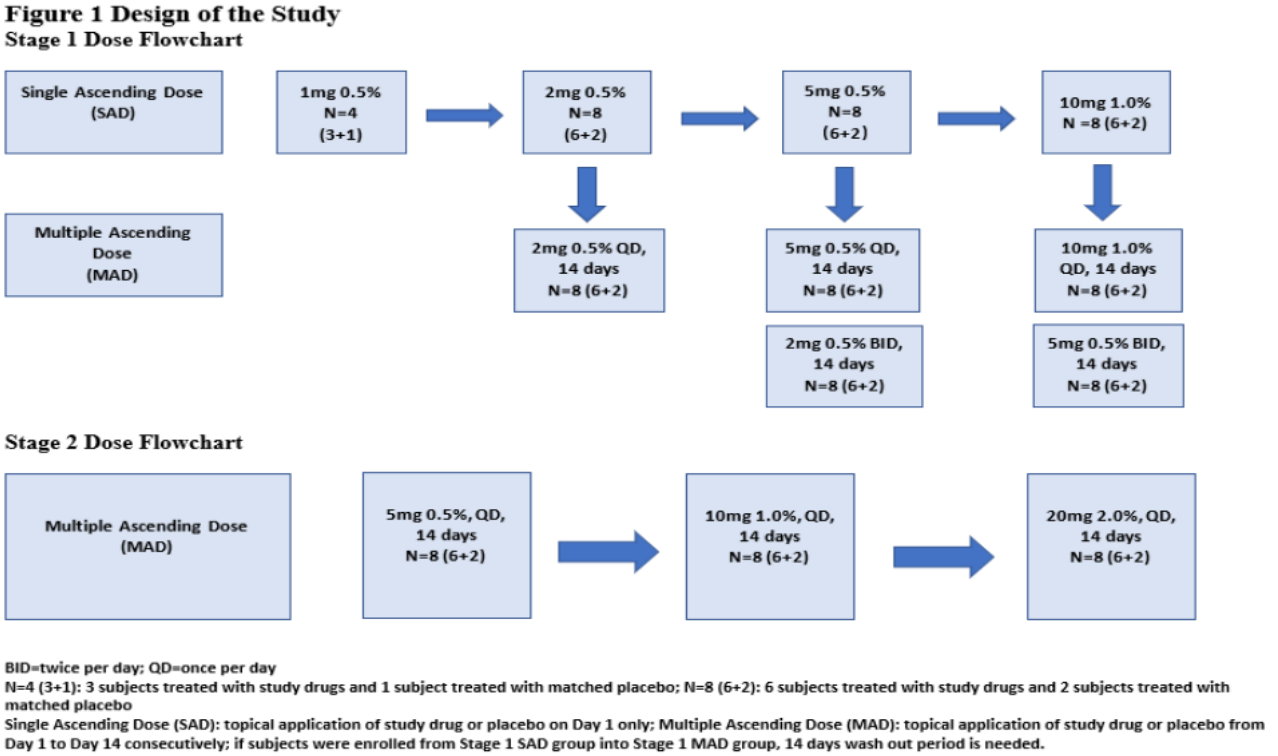
There was no systemic exposure after single dose of gel application. Since blood concentrations were Below Limit of Quantification (1pg/ml) at the most points, PK showed linear characteristics after multi-dose application

of gel/solution in the range of 2-10 mg and 5-20 mg, respectively.

Conclusion:

Overall, HVs who received a single application of GT20029 gel (1, 2, 5 and 10 mg) or 14-days topical GT20029 gel (2 mg once per day [QD], 2mg twice per day [BID], 5mg QD, 5mg BID, 10 mg QD) or solution (5mg QD, 10mg QD and 20 mg QD) showed low system exposure and good safety. Combined with the obtained PK characteristics and overall safety data, it is recommended to explore the safety and efficacy of multi-dose application of GT20029 solution (5 mg 0.5% QD, 10 mg 1.0% QD) in follow-up studies.

Figure 1 Design of the Study



BID=twice per day; QD=once per day
N=4 (3+1): 3 subjects treated with study drugs and 1 subject treated with matched placebo; N=8 (6+2): 6 subjects treated with study drugs and 2 subjects treated with matched placebo
Single Ascending Dose (SAD): topical application of study drug or placebo on Day 1 only; Multiple Ascending Dose (MAD): topical application of study drug or placebo from Day 1 to Day 14 consecutively; if subjects were enrolled from Stage 1 SAD group into Stage 1 MAD group, 14 days wash out period is needed.

Figure 2 CONSORT Flow Diagram of Subjects

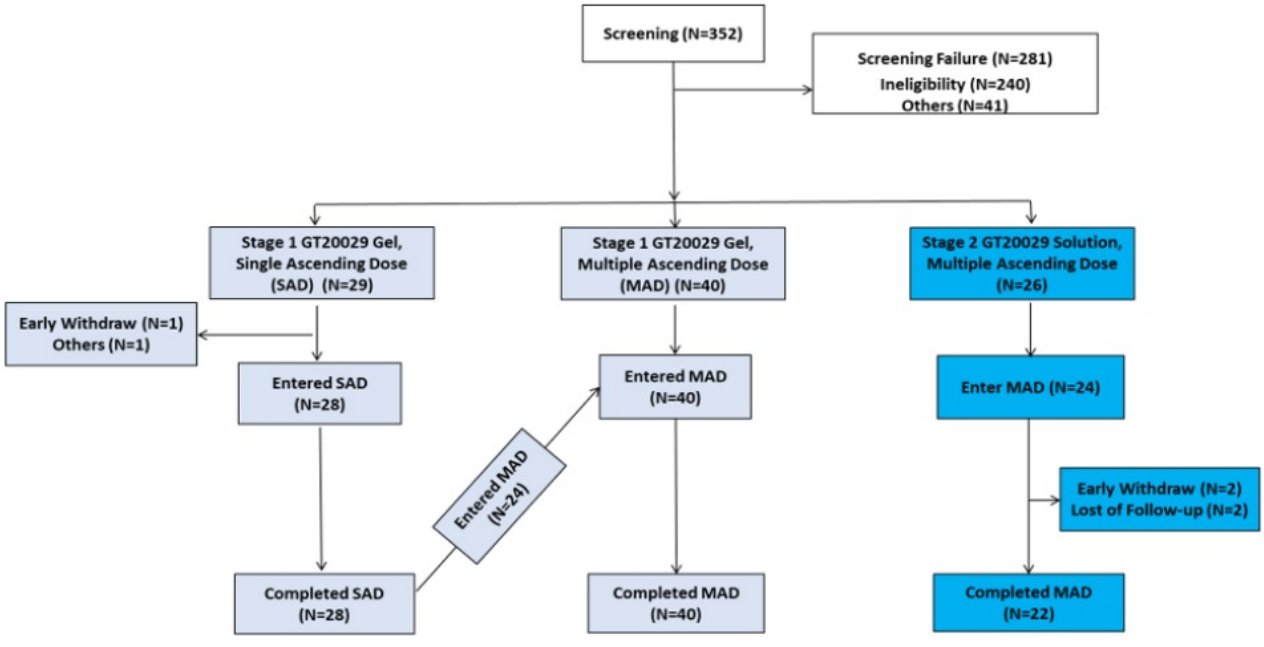


Table 1 Demographic Characteristics of All Cohorts

Characteristics		Stage 1 GT20029 Gel	Stage 2 GT20029 Solution	All
		(N=68)	(N=24)	(N=92)
		n (%)	n (%)	n (%)
Age (Years)	Mean (SD)	31.0 (5.64)	30.8 (6.86)	31.0 (5.94)
Genders	Male	43 (63.2)	16 (66.7)	59 (64.1)
	Female	25 (36.8)	8 (33.3)	33 (35.9)
Races	Han	68 (100.0)	23 (95.8)	91 (98.9)
	Others	0	1 (4.2)	1 (1.1)
Height (cm)	Mean (SD)	165.03 (7.991)	163.84 (8.144)	164.72 (8.003)
Weight (kg)	Mean (SD)	62.48 (7.454)	60.90 (8.934)	62.07 (7.847)
BMI (kg/m²)	Mean (SD)	22.90 (1.653)	22.62 (2.172)	22.83 (1.794)

N (%): Percentages are calculated using the number of non-missing subjects in each group as the denominator.
Percentage is based on the number of Safety Population.
SD=Standard Deviation
Body mass index (BMI): =Weight(kg) /Height (m^2)

Table 2 Summary of Drug Related TEAE

Drug Related TEAE																			
	Stage 1 GT20029 Gel													Stage 2 GT20029 Solution				
	SAD						MAD							MAD				
System Organ Class	1mg 0.5%	2mg 0.5%	5mg 0.5%	10mg 1.0%	Placebo	All	2mg 0.5% QD	2mg 0.5% BID	5mg 0.5% QD	5mg 0.5% BID	10mg 1.0% QD	Placebo	All	5mg 0.5% QD	10mg 1.0% QD	20mg 2.0% QD	Placebo	All
	(N=3)	(N=6)	(N=6)	(N=6)	(N=7)	(N=28)	(N=6)	(N=6)	(N=6)	(N=6)	(N=6)	(N=10)	(N=40)	(N=6)	(N=6)	(N=6)	(N=6)	(N=24)
Preferred Term	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)	HV (%)
All	0	0	5 (83.3)	1 (16.7)	0	6 (21.4)	3 (50.0)	6 (100.0)	5 (83.3)	6 (100.0)	6 (100.0)	8 (80.0)	34 (85.0)	6 (100.0)	6 (100.0)	6 (100.0)	6 (100.0)	24 (100.0)
Diseases of Skin and Subcutaneous Tissue	0	0	4 (66.7)	1 (16.7)	0	5 (17.9)	3 (50.0)	5 (83.3)	5 (83.3)	6 (100.0)	5 (83.3)	8 (80.0)	32 (80.0)	6 (100.0)	6 (100.0)	6 (100.0)	6 (100.0)	24 (100.0)
Laboratory Test	0	0	1 (16.7)	0	0	1 (3.6)	0	2 (33.3)	2 (33.3)	0	1 (16.7)	0	5 (12.5)					
Systemic Diseases and Reactions Drug Application Site							0	0	0	1 (16.7)	1 (16.7)	1 (10.0)	3 (7.5)					

TEAE=treatment-emergent adverse events.
BID=twice per day; QD=once per day.
SAD=Single Ascending Dose; MAD=multiple ascending dose.
HV: healthy Volunteer.
Percentage is based on the number of subjects in the safety population.
Adverse Events coded using MedDRA version 25.0

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Abstract N°: 5720

Clinical and dermoscopic improvement of angiokeratomas in a child: Topical Rapamycin as a promising agent

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Introduction & Objectives:

There is no standard treatment guideline e or stepwise approach for the treatment of angiokeratomas. Treatment is usually difficult, especially in children.

Clinical improvement of vascular lesions with topical application of rapamycin has been reported in several cases, suggesting that administration of the topical form of this drug may be a potentially promising option for the treatment of angiokeratomas

Materials & Methods:

We report a 5-year-old boy with clinical and dermoscopic features of a plaque of angiokeratomas from infancy. There is no standard treatment guideline for angiokeratoma treatment. After three months of topical administration of rapamycin 0.4 %, the vascular component of the lesions disappeared.

Results: ____

Conclusion:

Our case provides new clinical evidence for topical rapamycin's efficacy in treating vascular components without change in the hyperplastic component angiokeratoma in children.

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Abstract N°: 5798

Efficacy and tolerability of subcutaneous v/s oral methotrexate in the management of moderate to severe psoriasis and palmoplantar psoriasis.

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Introduction:

Psoriasis is a chronic proliferative and inflammatory condition of the skin.

Methotrexate is an antiproliferative, immunomodulating FDA approved agent for psoriasis. There is paucity in literature on comparison of efficacy and tolerability of various routes of administration of MTX in dermatology.

Objective:

Compare efficacy and tolerability of oral versus subcutaneous MTX in chronic plaque psoriasis(CPP) and palmoplantar psoriasis(PPP) and enhance the available evidence in methotrexate utilization.

Methods:

It was a prospective, single blind randomized comparative study. Sample size was calculated using Pocock's sample size formula. 75 patients with moderate to severe psoriasis (PASI 10 and above) were enrolled. 55 patients (CPP-Arm1) and 20(PPP-Arm2) were randomly assigned into two groups. Group A received SC MTX and Group B received oral MTX in a dose of (0.3-0.5mg/kg bodyweight) (approx. 15mg) MTX/week for 12 weeks. Patient's clinical responses were evaluated according to PASI score, PGA, VAS and DLQI. Complete blood picture, liver function test, renal function test were assessed before treatment and every 2 weeks in first month and then every 4 weeks in the next 2 months. Follow-up was done every month for 3 months to detect any recurrence.

Results:

Group A patients in Arm1 showed reduction in mean PASI score from 29.49 pre- treatment to 0.67 post-treatment while patients in Group B(Arm1) showed reduction from 26.94 pre-treatment to 1.73 post-treatment with statistically significant difference between both groups.

Similar findings were noticed in m-PASI reduction of patients of Arm2. Clinical improvement was complete in 72% of Group A versus 68% of Group B. PASI 50 was achieved faster with subcutaneous MTX in the first month. There was no significant difference in the side-effects between the groups over the visits. Gastrointestinal side effects were seen equally in both the groups. Relapse rate was more in SC group.

Conclusion:

SC MTX had faster onset of action in both chronic plaque psoriasis and palmoplantar psoriasis initially. However, at the end of 3 months, both SC and oral MTX were equally effective in achieving PASI 90. Gastro intestinal side effects were seen in both the routes given at the same dose.

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Abstract N°: 5837

Generalized lichen sclerosus interest of the combination of general corticosteroid therapy and acitretin

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Generalized lichen sclerosus interest of the combination of general corticosteroid therapy and acitretin

Introduction & Objectives:

Lichen sclerosus (LS) is an inflammatory and fibrotic dermatosis first described in 1887 by Hallopeau. It mainly affects the genital area. We report a case of generalized LS in a prepubertal girl, highlighting the value of combining general corticosteroid therapy and acitretin in this clinical form.

Results:

A 10-year-old girl with no previous pathological history consulted for diffuse pruritic whitish lesions with vulvar pruritus. Examination showed multiple shiny achromic sclerotic papules, confluent in places in patches located on the upper and lower limbs, back, abdomen and trunk. There was vulvitis with erythema and white patches on both labia majora. A skin biopsy was performed confirming the diagnosis of cutaneous LS. The patient was initially put on a general corticosteroid (prednisone (1 mg/kg/d) with significant improvement. Acitretin at a dose of 10 mg per day was added three weeks later when the general corticosteroid therapy began to wear off and was maintained for one year. The evolution at 6 months was marked by a clear improvement with regression of skin lesions and improvement of vulvar signs. No recurrence was noted at 1 year follow-up.

Conclusion:

In contrast to genital LS, extra-genital involvement is relatively rare in only 2.5% of cases. Generalized involvement affecting more than 2 anatomical regions, as in our case, is very rare. It is essentially an aesthetic and functional problem due to its chronic and atrophic evolution. The treatment of this form remains poorly established. Acitretin has been shown in a randomised controlled trial to reduce both the signs and symptoms of moderate to severe vulvar lichen sclerosus. Given the extent of the lesions, we opted in our patient to initiate treatment with a general corticosteroid therapy which proved to be effective, acitretin allowed this improvement to be maintained without recurrence when corticosteroids were stopped.

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Abstract N°: 5872

Diffuse hypertrophic lichen interest of Acitretin, about two cases

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Diffuse hypertrophic lichen interest of Acitretin, about two cases

Introduction & Objectives:

Hypertrophic lichen planus (HLP) is a little known subtype of lichen planus, characterised by verrucous and highly pruritic lesions, often resistant to topical treatments. We report two observations of a rare form of HLP that is unusual in its extent and response to Acitretin.

Results:

Two patients (A) and (B), aged 57 and 53 years respectively, consulted us for diffuse and pruritic verrucous papulo-nodules. On skin examination, multiple whitish verrucous plaques of varying sizes were found on the hands and fingers, legs, thighs and feet. There were pigmented macules on the sub-mammary and axillae (patient B). Mucosal examination showed an endooral lichen network (patient A) and keratotic patches on both labia majora (patient B). Dermoscopy showed follicular plugs filled with yellowish keratin, surrounded by clear halo, blue-grey globules. Histological examination of a skin lesion was consistent with hypertrophic lichen planus. The work-up confirmed Gougerot-Sjögren's syndrome in patient B. Treatment with Acitretin 20mg/day was recommended for both cases. The evolution was marked by a beginning of improvement (patient A) and very satisfactory results (patient B).

Conclusion:

HLP, a form of lichen planus which is characterised by verrucous patches, extremely pruritic and localised to the lower legs. It may result in sequelae of dyschromia and may progress to squamous cell carcinoma. It is frequently associated with venous insufficiency. We present two cases of HLP that are unique in their extensive spread, genital involvement and association with Gougerot-Sjögren's syndrome. We thus underline the interest of dermoscopy as an aid to eliminate differential diagnoses, mainly nodular prurigo. Acitretin remains an effective therapeutic option, allowing a favourable response in our cases.

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Abstract N°: 5910

Successful management of idiopathic knuckle pads with salicylic acid and urea topical keratolytics

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[1]Chu Mohamed Vi Marrakesh

Introduction & Objectives:

Knuckle pads or Garrods nodules are benign subcutaneous fibrotic nodules developed in the dorsal surface of feet and/or more frequently in finger joints. Usually, they are painless, asymptomatic and characterized by a progressive growth. Primarily (idiopathic) KPs are the most common in children and young adults, and they are poorly tolerated for aesthetic and social reasons.

Here we report a case of a children successfully treated with a combination of high-dose salicylic acid and urea topical keratolytic.

Materials & Methods:

A 12-year-old girl presented with a 4 years history of idiopathic knuckle pads on the proximal interphalangeal joint of the thumb and the index finger. Multiple previous treatment have been used without success.

Physical examination revealed firm, well-demarcated, mobile nodules and the dermoscopy revealed

skin-colored lesions without thrombosed capillaries, and a clinical diagnosis of knuckle pads was made.

The patient was prescribed a topical preparation with 40% urea-based emollient-keratolytic cream and 30% salicylic acid ointment, we recommend one overnight application per day under occlusion with a careful removal of dead skin. The two KPs disappeared totally after 6 months with great cosmetic and psychological benefit. No recurrences observed after 2 years of the treatment.

Results:

Knuckle pads (KP) or “Garrod’s nodes” are benign fibromas located over the small joints of the hands and feet.

Clinically, they present as painless, well-circumscribed, mobile subcutaneous nodules that typically involve the dorsum of the proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints.

The differential diagnosis includes warts, rheumatoid nodules, gouty tophi, Bouchard’s and Heberden’s nodes, synovial cysts, tumors (giant cell tumor of the tendon sheaths, neurofibromas), and retained foreign bodies. In cases of diagnostic doubt, ultrasound and plain radiographs may be helpful. Magnetic resonance imaging has only been rarely described.

No effective treatment for KP has been reported in the literature, Spontaneous resolution of primarily KPs has never been described, although in rare cases they can become smaller without disappearing. Surgery has also been used, usually without leading to an aesthetic improvement with recurrences, post-operational loss of joint flexibility, scars, and keloids as possible side effects. Recently, few treatments are turning out to be effective, but they are mostly based on case reports and are often moderately to highly invasive.

In the case of acquired KPs, they may disappear after elimination of the source of friction/trauma like those typical of some professional and athletic activities

Conclusion:

idiopathic KPs are the most common in children and young adults, and they are poorly tolerated for cosmetic reasons. topical salicylic acid and urea keratolytic could be one of the good therapeutic options in the treatment of KPs.

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Abstract N°: 6170

Pseudopitheliomatous keratotic and micaceous balanitis of Lortat-Jacob and Civatte. Presentation of a case.

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Introduction & Objectives: Pseudoepitheliomatous keratotic and micaceous balanitis of Lortat-Jacob and Civatte (PKMB) is a rare entity that presents keratotic plaques on the glans. Its etiopathogenesis is unknown. Four clinical-pathological stages are distinguished: initial or plaque, late or tumor, verrucous carcinoma and transformation to squamous cell carcinoma.

Histopathology reveals hyperkeratosis, parakeratosis, acanthosis, elongated papillary ridges, and mild dysplasia in the basal layers. In the superficial dermis there is an inflammatory infiltrate with lymphocytes and eosinophils.

The malignant potential of this rare form of balanitis is debatable, but there has been an increase in the number of reported cases of verrucous carcinoma or squamous cell carcinoma originating from PKMB lesions. Therefore, close follow-up of these patients is important.

Materials & Methods: We analysed the clinical history of a patient with diagnosis of Pseudoepitheliomatous keratotic and micaceous balanitis of Lortat-Jacob and Civatte (PKMB) in our institution and we made a literature review in order to have a correct diagnosis and a suitable treatment for our patient.

Results: We present the case of a 58-year-old male patient, with a history of meatotomy in 2021 due to meatal stenosis, under follow-up for penile lesions of four years of evolution.

In the first visit on the physical examination, he presented an erythematous scaly plaque with defined limits located on the glans. With suspicion of psoriasis vs. lichen sclerosus vs. porokeratosis vs. PKMB, a skin biopsy was performed, the pathology revealed extensive parakeratosis, mild acanthosis of the epithelium, and moderate focal perivascular lymphocytic and neutrophil infiltrates in the chorion.

With the diagnosis of pseudoepitheliomatous, keratotic and micaceous balanitis of Lortat-Jacob and Civatte, treatment was started with clobetasol propionate 0.05% and topical keratolytics.

After two months of treatment there was no improvement, so treatment was changed to 20% salicylic acid associated with 5% 5-Fluorouracil cream. Two years later, the lesions persisted, so methylprednisolone cream associated with 0.1% tacrolimus ointment was indicated; however, there was no improvement, so treatment with acitretin 10 mg/day and 10% topical salicylic acid was started. He is under strict monitoring.

Conclusion: We present the case because it is a rare entity, which seriously affects the life quality, is refractory to multiple therapeutic lines and requires strict clinical monitoring due to its malignant potential.

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Abstract N°: 6220

Efficacy and safety of topical timolol for the treatment of facial angiofibroma in children with tuberous sclerosis complex

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Introduction & Objectives:

The objective of this study was to assess the efficacy and safety of topical timolol in the treatment of facial angiofibromas (FAs) in pediatric patients with tuberous sclerosis complex (TSC).

Materials & Methods:

A prospective clinical trial was conducted involving fifteen children diagnosed with TSC and presenting with FAs. The participants were administered topical timolol gel 0.5% twice daily. Prior to the intervention, the severity of FAs in each patient was evaluated using the Facial Angiofibroma Severity Index (FASI), which assessed erythema, size, and extent of lesions. Clinical response was assessed at weeks 2 and 4 during the intervention period, as well as one month after discontinuation of treatment.

Results:

Four weeks after discontinuing topical timolol 0.5%, statistically significant reductions were observed in the mean FASI score, erythema, size, and extent of lesions ($P < 0.0001$, $P < 0.0001$, $P = 0.012$, $P = 0.008$, respectively). FASI scores at four and twelve weeks post-intervention, as well as four weeks after treatment cessation, demonstrated a significant decrease compared to baseline ($P < 0.001$). Erythema and extension scores also exhibited a significant decrease one month after treatment cessation compared to baseline ($P < 0.05$), while the mean size of lesions before and after the intervention did not show a statistically significant difference ($p = 0.004$).

Conclusion:

Topical timolol 0.5% represents a cost-effective and readily available treatment option for pediatric patients with facial angiofibromas associated with tuberous sclerosis.

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Abstract N°: 6228

Bevacizumab as adjuvant therapy in the treatment of keloid: A randomized clinical trial

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Introduction & Objectives:

Despite the availability of numerous therapies, keloid treatment remains a challenging clinical issue. Intralesional triamcinolone has been established as an effective corticosteroid treatment for keloids, while sporadic reports suggest the efficacy of intralesional verapamil. This study aimed to evaluate the safety and efficacy of bevacizumab as an adjuvant therapy for keloid treatment.

Materials & Methods:

This randomized controlled trial involved 38 patients diagnosed with keloid according to clinical criteria. The study compared the effects of intralesional triamcinolone combined with bevacizumab injections with intralesional triamcinolone alone. Patients were randomly assigned to either the combination treatment group, which received Intralesional triam HEXAL® (20 mg/ml, monthly for 3 months) plus Avastin® (2.5 mg/ml monthly for 2 months), or the single treatment group, which received intralesional triamHEXAL® alone. The Vancouver scar scale (VSS) was used for serial photographic records of scar evaluation, with differences in VSS scores considered the primary outcome, and changes in height and patient satisfaction visual analog score (VAS) as secondary outcomes.

Results:

A total of 38 patients participated, with a mean age (SD) of 35.32 (14.02) years and 50% being male. No significant differences in age, BMI, duration of disease, gender, causing, family history, or site were observed between the two groups. The single treatment group exhibited a mean reduction of 0.60 (95% CI: (-1.18, -0.01); P= 0.045) in pigmentation score and a mean reduction of 1.37 (95% CI: (-2.68, -0.07); P=0.039) in total score compared to the combination treatment group after three months of treatment. There was a significant reduction in keloid height in the combination group after the end of the treatment (P=0.024). No significant differences in side effects were observed between the two groups.

Conclusion:

Our study demonstrates that bevacizumab can be considered an effective and safe adjuvant therapy option for keloid treatment, suggesting its potential as a promising treatment for the management of keloids.