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VIRTUAL MEETING  
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2020



# RESIDENTS & FELLOWS FINALISTS

## Exosomal lncRNA XIST regulates CD4+ T cell autophagy by acting as a ceRNA of miR-98 in human SLE through mTOR pathway

Background: Abnormal T cell activation and autophagy play important parts in systemic lupus erythematosus (SLE). Long non-coding RNAs (lncRNAs) and exosomes have recently been found to play vital regulatory or communication roles in SLE. However, the roles and mechanisms of exosomal lncRNAs in SLE remain unknown.

Methods: The expression and cellular function of lncRNA XIST was determined. lncRNA XIST and miR-98 expression was determined by RT-qPCR. Potential target genes were verified using bioinformatic analysis and luciferase reporter assays. Effects of lncRNA XIST and miR-98 on CD4+ T cell activation and autophagy were analyzed.

Results: lncRNA XIST was significantly upregulated in CD4+ T cells from SLE patients compared with those in healthy donors, whereas miR-98 expression was downregulated. Luciferase reporter assays demonstrated that miR-98 directly targeted Rictor (a core component of mTORC2) mRNA and miR-98 is a gene target of lncRNA XIST. Moreover, in healthy donor CD4+ T cells, overexpression of lncRNA XIST promoted cell activation and inhibited cell autophagy as a ceRNA of miR-98 by regulating mTOR pathway. However, inhibition of lncRNA XIST induced completely opposite effect in SLE CD4+ T cells. Furthermore, lncRNA XIST was also upregulated in plasma exosomes of SLE patients and could transfer lncRNA XIST to CD4+ T cells to increase their ability of cell activation and autophagy inhibition.

Conclusion: The study revealed that the exosomal lncRNA XIST promotes T cell autoreactivity and inhibits autophagy by acting as a ceRNA of miR-98 in human SLE, providing potential novel strategies for therapeutic intervention in SLE.

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## An Expert Panel Consensus on Opioid-Prescribing Guidelines for Dermatologic Procedures

**Background:** Opioid overprescribing is a major contributor to the opioid crisis, and the lack of procedure-specific guidelines contributes to the vast differences in prescribing practices. Opioid-prescribing consensus guidelines for common dermatologic procedures are needed to help curb unnecessary prescription of opioids in dermatology.

**Methods:** We utilized a four-step modified Delphi method to conduct a systematic discussion amongst a panel of providers in the fields of general dermatology, dermatologic surgery, and cosmetics/phlebology to develop opioid-prescribing guidelines for some of the most common dermatologic procedural scenarios. Guidelines were developed for opioid-naïve patients undergoing routine procedures. Opioid tablets were defined as an oxycodone 5-mg oral equivalent.

**Results:** Postoperative pain after most uncomplicated procedures (76%) can be adequately managed with acetaminophen and/or ibuprofen. Group consensus identified no specific dermatological scenario that routinely requires more than 15 oxycodone 5-mg oral equivalents to manage postoperative pain. Group consensus found that 23 percent of the procedural scenarios routinely require 1-10 opioid tablets, while only one procedural scenario routinely requires 1-15 opioid tablets.

**Conclusions:** Procedure-specific opioid-prescribing guidelines may serve as a foundation to produce effective and responsible postoperative pain management strategies after dermatologic interventions. These recommendations are based on expert consensus in lieu of quality evidence-based outcomes research. These recommendations must be individualized to accommodate patients' comorbidities.

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## The randomized trials of 10% Urea cream and 0.025% tretinoin cream in the treatment of acanthosis nigricans

**Background:** There have been no published randomized trials in the topical management of acanthosis nigricans. This study aimed to assess the efficacy of topical 10% urea cream compared to 0.025% tretinoin cream in the treatment of acanthosis nigricans.

**Methods:** This was an 8-week trial, double-blind, randomized, comparative study of 10% urea and 0.025% tretinoin for the treatment of the neck hyperpigmentation. The Mexameter MX18 was used for assessing treatment efficacy which

expressed as Melanin indices (M). The investigator's global evaluation (IGE) and parent's global evaluation (PGE) were also used to evaluate the overall success rate at week 2, week 4 and week 8 of the study.

**Results:** A total of 40 participants with acanthosis nigricans completed the study. There was statistically significant difference between 10% urea and 0.025% tretinoin in treatment acanthosis nigricans ( $p < 0.01$ ). Mean different of M indices between week 0 and week 8 of 10% urea treatment was 36.7 (95% CI, 18.8-54.5), with  $6.3 \pm 9.5\%$  improvement. Mean different of M indices between week 0 and week 8 of 0.025% tretinoin treatment was 111.5 (95% CI, 87.6-135.4), with  $16.6 \pm 10.2\%$  improvement. The treatment efficacy using the IGE found that 36.8% and 52.6% of participants had skin improvement more than 75% in 10% urea and 0.025% tretinoin treatment, respectively and the PGE found that 21.0% and 47.3% of participants had skin improvement more than 75% in 10% urea and 0.025% tretinoin treatment, respectively.

**Conclusion:** We found significant difference between topical 10% urea and 0.025% tretinoin in treatment acanthosis nigricans.

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## State-level variation in Medicare spending and provider availability for the treatment of actinic keratosis and skin cancer

**Introduction:** Actinic keratosis (AK) treatment cost varies significantly among different parts of the US with less variability in non-metropolitan areas.<sup>1,2</sup> The purpose of our study is to analyze the inter-state variability in Medicare spending and provider availability for different treatment procedures for AK and skin cancer.

**Methods:** The state spending on different treatment procedures for AK and skin cancer, and number of providers who billed Medicare for the treatments of interest were extracted from the 2013-2014 Medicare database files<sup>3,4</sup> and analyzed using descriptive statistics.

**Results:** Payments for topical AK treatment accounted for 18.47% of spending in Georgia but up to 56.67% in New York, for cryotherapy from 40.76% in New York to 77.93% in District of Columbia, and for photodynamic therapy from 2.44% in Minnesota to 9.28% in Georgia. Payments for excision of skin cancer accounted for 3.11% of spending in Minnesota compared to 13.71% in Georgia, 73.46% for Mohs Micrographic Surgery in Florida to 92.85% in Minnesota, and 3.91% for destruction in District of Columbia to 14.82% in Florida.

The average number of providers that billed Medicare for cryotherapy exceeded that for PDT by 9.53-fold. Dermatologists comprised a low of 60.9% in Oregon for providers who billed Medicare for excisions to a high of 90% in District of Columbia.

**Conclusion:** In this study, we demonstrated significant inter-state variation in Medicare spending and provider availability for the treatment of AK and skin cancer. These data may reflect differences in patient population, environmental exposures, and treatment preference of patients and providers.

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## Machine learning for prediction of cutaneous adverse events in patients receiving anti-PD-1 immunotherapy

Background: PD-1 inhibition with cancer immunotherapy is associated with development of cutaneous immune-related adverse events [1,2]. Artificial intelligence may offer a possible approach for identifying patient factors that predict development of these events.

Methods: Patients with metastatic melanoma and non-small cell lung cancer who received either Nivolumab or Pembrolizumab therapy were followed. Predictive parameters of interest were baseline age, cancer type, drug received, autoimmune history, derived neutrophil-to-lymphocyte ratio, lactate dehydrogenase, albumin, body mass index, ECOG performance status, and tumor M-stage [3,4]. Of 410 patients with completed data, we identified 54 patients who developed a cutaneous immune-related adverse event (AE+) and random oversampling resulted in 71 AE+ cases used in our models. After randomly selecting 71 patients who did not develop a cutaneous immune-related adverse event (AE-) from remaining data, a feedforward deep neural network was trained. Hyperparameters were tuned to optimize predictive accuracy on the remaining data, and performance characteristics were calculated. This was repeated using the same neural network architecture 5 times.

Results: Neural networks were trained to have a mean ( $\pm$ SD) positive predictive value of 76.5% ( $\pm$ 10.5%), negative predictive value of 79.4% ( $\pm$ 11.9%), sensitivity of 85.3 ( $\pm$ 8.8%), specificity of 67.6% ( $\pm$ 15.8%), area-under-the-ROC-curve of 76.5 ( $\pm$ 4.5) and accuracy of 78.1% ( $\pm$ 4.3%) in predicting development of cutaneous immune-related adverse events.

Conclusion: Artificial intelligence methods may aid in identifying patients at risk of cutaneous immune-related adverse events from PD-1 inhibitor therapy using only baseline metrics, potentially allowing for early dermatologic intervention. Further model development and exploration of clinical utility is warranted.

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## Predictors for Requirement of Systemic Therapies in Children with Moderate-Severe Eczema

Background: Many atopic dermatitis (AD) patients have moderate-severe disease that cannot be controlled with first-line therapies.[1] Systemic therapies may be considered for these patients, but they often carry significant burden in term of cost and side effects.[2] Although many potential risk factors [3] and outcome prognosticators [4,5] have been identified for AD, it is not clear which of them can help predict if a patient will eventually require systemic therapy.

Methods: This is a retrospective case-controlled study between 6/1/2012-5/20/2019. 111 pediatric patients with the qualifying diagnoses and the pertinent laboratory data were included in the study. With the start of any systemic therapy as the end point, odds ratios of potential covariates (including age of onset, age of presentation, race, socioeconomic status,

other atopic comorbidities, serum IgE, peripheral eosinophils, pneumococcal titers, vitamin D level, and history of HSV infections) were analyzed both independently and in combination with a multivariate logistic regression model.

Results: Elevated serum IgE level (OR 9.6, 95%CI 2.6-36,  $p = 0.001$ ), comorbid allergic rhinitis (OR 12.5, 95%CI 2.1-76,  $p = 0.006$ ), delayed age of presentation (OR 1.21, 95%CI 1.08-1.37,  $p = 0.002$ ), and Caucasian race (OR 3.1, 95%CI 1.1-8.3,  $p = 0.03$ ) were associated with increased likelihood of the patient eventually requiring a systemic therapy.

Conclusion: Assessment of serum IgE level and comorbid allergic rhinitis may help predict the need of systemic treatment in pediatric patients with moderate-severe AD. The increase risk of delayed presentation supports early and aggressive treatment of AD.

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## Microwave Thermoablation for the Treatment of Residual Limb Hyperhidrosis

Background: Up to 66% of lower limb amputees report residual limb hyperhidrosis with a significant association between sweating and decreased prosthetic function.<sup>1</sup> Current strategies for treatment such as botulinum toxin are focused on temporary relief of this problem. Microwave thermoablation is an effective permanent solution for axillary hyperhidrosis.<sup>2</sup> The purpose of this study was to evaluate the use of microwave thermoablation for the treatment of residual limb hyperhidrosis.

Methods: This study was a prospective non-randomized feasibility trial. Tricare-eligible lower limb amputees with residual limb hyperhidrosis were eligible for this study. Dermatology Life Quality Index (DLQI) scores, Severity of Prosthesis Problem Scale (SPPS) scores, and gravimetric measurements of sweat after 10 minutes of exercise were taken at baseline and 3 months after treatment. Study participants underwent treatment of half of their limbs followed by treatment of the other half 2 weeks later to avoid risk of compartment syndrome. Pre and post treatment measurements were compared using the Wilcoxon signed-rank test using SPSS (IBM, Armonk, NY).

Results: A total of 9 limbs in 8 patients (one double amputee) underwent treatment. There was a statistically significant decrease in DLQI ( $Z=-2.136$ ,  $p=0.033$ ) and SPPS ( $Z=-2.521$ ,  $p=0.012$ ) scores indicating improvement in quality of life and increased ease of prosthetic use, respectively. There was a statistically significant decrease gravimetric amount of sweat produced ( $Z=-2.032$ ,  $p=0.042$ ).

Conclusion: Microwave thermoablation significantly improves quality of life, increases ease of prosthetic use, and decreases amount of sweat produced in lower limb amputees. These effects are expected to be permanent.



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## Particle Content of The Plume Generated by Laser Tattoo Removal

**Background:** Aerosolized laser-generated plume can represent a safety hazard for patients, and laser-operators.<sup>1</sup> Ultrafine particulate matter (<2.5 $\mu$ g) and particulate matter (<10 $\mu$ g) are well-established occupational hazards that have been reported at high levels during laser hair removal procedure. <sup>2</sup> High velocity plume particles were found during laser tattoo removal; <sup>3</sup> however, particle content of this plume is unknown. The aim of this study was to identify particle content in the laser tattoo removal induced plume.

**Methods:** Patients presenting for laser tattoo removal were recruited from a university-based practice. Laser settings were chosen based on the physician's discretion using a picosecond multi-wavelength system. Tattoos of all colors were included in the study and treated to the endpoint of whitening. Gas chromatography-mass spectrometry analysis was used to identify the chemical compounds. Ultrafine particle counters were used to measure levels of particulate matter.

**Results:** Twenty-one patients completed this study. Preliminary identification of compounds showed benzene, butane, cycloalkenes, phenol, silane, styrene, and trimethyl sulfate. Levels of particulate matter next to the tattoo rose up to 43 $\mu$ g/m<sup>3</sup> after 5 minutes of treatment. Levels of ultrafine particulate matter next to the tattoo were significantly higher than those in the waiting room (P<0.01).

**Conclusion:** This is the first report of identification and quantification of particle content in plume generated by tattoo removal. Levels of particulate matter during tattoo removal procedure were above the level recommended by The Environmental Protection Agency's Clean Air Act (15 $\mu$ g/m<sup>3</sup>). Chronic exposure to the levels of tattoo removal induced plume may represent an occupational health hazard.

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## Factors associated with appointment non-attendance in outpatient dermatology

**Background:** Appointment non-attendance in outpatient dermatology clinics wastes resources and limits access to care. The purpose of this study was to assess baseline “no-show” rates and understand factors associated with “no-shows” at Beth Israel Deaconess Medical Center (BIDMC) dermatology clinics.

**Methods:** A retrospective cross-sectional study was performed across one academic site and four community-based faculty practices at BIDMC. Patient demographics, appointment characteristics, and appointment attendance were collected for all dermatology appointments between 6/1/17 - 9/30/18. Differences between appointment attendance groups (“no show,” same-day cancellation, and kept appointments) were analyzed via Chi-Square test.

**Results:** 68,442 appointments and 34,005 patients were included. Overall, 79.9% of scheduled appointments were kept, 9.2% were same-day cancellations, 10.5% were “no shows,” and 0.4% had unrecorded attendance. Self-pay (36.1%) and Medicaid (20.6%) had highest “no-show” rates, while Medicare (6.7%) had the lowest ( $p < 0.0001$ ). “No-show” rates varied by appointment type, with lowest rates for pigmented lesion clinic (4.1%) and excisions (2.1%) ( $p < 0.0001$ ). There were several other statistically significant differences in likelihood to “no-show” based on age, race, primary language, distance lived from clinic, attending tenure, and lead time (number of days between appointment booking and the appointment).

**Conclusion:** Understanding how these factors are associated with non-attendance allows future development of interventions to reduce non-attendance, such as altering appointment scheduling strategies, targeting outreach to patients with high likelihood to “no-show”, and double booking patients with high likelihood to “no-show.”

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## Increased Expression of IL-17 in Scalp Psoriasis; an Implication of a New Targeted Therapy

Scalp psoriasis can be a psychologically and socially distressing presentation of psoriasis and can present in up to 79% of patients with chronic plaque psoriasis. The current treatment of this condition is difficult due to the limited drug delivery to the scalp and also time-consuming and cosmetically undesirable treatments. Several studies have been shown that the Interleukin-17 (IL-17) level is increased in lesional skin and blood of patients with psoriasis, and the level is correlated with disease severity. Neutralization of IL-17 in psoriasis patients has been led to histological improvement in skin biopsy specimens of these individuals. The objective of our study was to find out if the IL-17 has increased expression in the psoriatic scalp compared to normal scalp as a possible treatment target. For this purpose, ten specimens of biopsy-proven

plaque psoriasis of the scalp and ten specimens of telogen effluvium of the scalp with no evidence of psoriasis were pulled from our database to serve as the scalp cases and clinically normal scalp controls, respectively. Standard immunohistochemistry staining was performed on formalin-fixed paraffin-embedded tissue sections with polyclonal IL-17 antibodies. Results indicated strongly positive IL-17 antibody staining in the psoriatic scalp specimens and negative IL-17 antibody staining in the telogen effluvium specimens. The results of this study demonstrate a potential role of IL-17 in psoriatic scalp lesions and suggest a possible first-line application of IL-17 inhibitors in the treatment of scalp psoriasis.

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## The standardized extract of *Centella asiatica*, ECa 233 enhances post-laser resurfacing wound healing on the face; A split face, double-blind, randomized, placebo-controlled trial

**Background:** *Centella asiatica*, a medicinal plant, has been used traditionally to promote wound healing. Its efficacy on promoting post-laser resurfacing wound healing is lacking.

**Methods:** Thirty individuals with facial acne scars, underwent a treatment with 2,940 nm Er:YAG laser. Half side of the face was randomized to receive 0.05% ECa 233 gel, a standardized extract of *Centella asiatica*, and the other half with placebo gel. The gels were applied four times daily for 7 days then twice daily for 3 months. Erythema (E) and texture index (TI) from Antera3D® and skin biophysics were obtained at baseline, days 2, 4 and 7, then every two weeks for the first month and every month for three months. Three blinded dermatologists assessed the photographs and provided a grading scale of wound appearances.

**Results:** ECa 233 treated side exhibited significantly less EI at the overall follow-up period by 0.03 units (coefficient = -0.03 (95%CI-0.06 to -0.0006); p = 0.046). In keeping with the physicians' assessment that showed significantly higher improvements in skin erythema at days 2, 4 and 7 (p = 0.009, 0.0061, 0.012), crusting at days 2 (p = 0.02) and general wound appearance at day 2, 4 and 7 (p = 0.008, 0.001, 0.044). TI showed a trend toward better outcome in the ECa 233 group. However, skin biophysics did not differ between the two.

**Conclusion:** ECa 233 might be an option for post-laser treatment to enhance wound healing process.

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## Dupilumab Drug Survival, Treatment Failures, and Insurance Approval at a Tertiary Care Center

**Background:** Dupilumab, an IgG4 monoclonal antibody that targets the IL-4 receptor alpha chain, is FDA approved for the treatment of moderate-severe atopic dermatitis (AD) in adults.

**Objective:** To better characterize dupilumab drug survival, treatment failures, insurance approval rate, and reasons for insurance denial.

**Methods:** Electronic medical review (EMR) of patients greater than 18 years-old who were prescribed dupilumab at UPMC between January 2017-March 2019.

**Results:** 179 patients were prescribed dupilumab, and 67 patients did not initiate mainly due to insurance denial (34/67) and high co-payments (20/67); a higher percentage of Medicare patients (40.7% versus 17.7%,  $p=0.007$ ) is noted among these patients. Reasons for insurance denial included lack of moderate-severe AD documentation and/or lack of treatment with topical or oral immunomodulating therapy. Of 112 treated patients, 9 discontinued dupilumab due to lack of AD improvement (5/9), conjunctivitis (3/9), and patient preference (1/9). 11 patients with dyshidrotic eczema showed improvement; a history of positive patch testing is noted both among dupilumab survivors (18/29, 62.1%) and dupilumab failures (4/6, 66.7%).

**Limitations:** This was a retrospective single institution study with data limited to EMR.

**Conclusion:** Our study demonstrates dupilumab efficacy among patients with AD, dyshidrotic eczema, or history of positive patch testing while also revealing the difficulty of insurance approval.

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## Pulsed Dye Laser (PDL) is More Cost-Effective than Topical Brimonidine and Topical Oxymetazoline for the Treatment of Erythematotelangiectatic Rosacea: A Systematic Review of the Literature and Meta-analysis

We performed a cost-analysis comparing pulsed dye laser (PDL), topical brimonidine, and topical oxymetazoline for treatment of erythematotelangiectatic rosacea (ETR). For the topicals, we calculated the number needed to treat to achieve a two-grade Clinician Erythema Assessment (CEA) improvement. For PDL, physician-reported 50% erythema improvement was used as CEA was not frequently assessed in PDL studies. For the topicals, data was obtained from their phase III trials. For PDL, we performed a meta-analysis of prospective studies evaluating PDL for ETR identified through systematic literature review. Six studies containing 93 patients were analyzed as they reported the outcome of interest.<sup>1-6</sup>

To assess cost, we used the lowest price for the topicals listed on goodrx.com and our institutional PDL cost. In the topical brimonidine and oxymetazoline trials, 55% and 40.1% achieved a two-grade improvement in CEA respectively.<sup>7,8</sup> In our PDL meta-analysis, 60.2% (56/93) achieved a 50% reduction in physician-reported erythema. PDL patients required an average of 2.96 treatments. Based on the average length of PDL follow-up (14.3 weeks), cost to achieve our outcome of interest was \$2,159.47 for PDL, \$2,923.77 for topical brimonidine, and \$4,567.72 for topical oxymetazoline. This suggests PDL is the most cost-effective modality for treating ETR. Our study likely overestimated PDL cost as PDL likely creates durable improvement beyond the 14.3-week cost-analysis period; whereas, topicals require continued daily application to maintain benefit. Limitations of our study include use of a surrogate outcome to compare efficacy and heterogeneity and poor quality of the PDL studies (e.g. no control groups).

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## **Atopic dermatitis: psychological distress, sleep disturbance and alcohol use disorder**

The burden of illness associated with atopic dermatitis (AD) is significant and multidimensional, especially in relation to patients with moderate-severe disease activity.

**Objectives:** To evaluate the disease burden of patients with AD in relation to psychological distress, sleep disturbance and alcohol misuse.

**Methods:** Patients with AD, attending the outpatient Dermatology department of two University Teaching Hospitals in Dublin, Ireland were recruited. A series of validated questionnaires were used: Patient Orientated Eczema Measure (POEM), Dermatology Life Quality Index (DLQI), The Center for Epidemiologic Studies – Depression (CES-D), Quality of Life in Atopic Dermatitis Questionnaire (QoLIAD), Alcohol Use Disorders Identification Test (AUDIT), Pittsburgh Sleep Quality Index (PSQI) and Eczema Area and Severity Index (EASI).

**Results:** One hundred patients completed the questionnaire; the majority were female (52%). Despite current treatment, 67% of patients had ongoing moderate to (very) severe AD according to EASI. Half of the patients (50%) reported taking sick leave due to their AD in the previous 12 months. According to DLQI, 63% were suffering from a moderate to extremely large impact on their quality of life. Risk of clinical depression was identified in 30% of patients. Higher CES-D scores correlated with decreasing age. Patients with moderate to severe AD were more likely to score higher on AUDIT; 25% met criteria for alcohol use disorder. In relation to sleep, 73% of patients scored over 5 on the PSQI, signifying poor sleep quality.

**Conclusion:** Patients with AD endure a significant burden on health in relation to mental wellbeing, alcohol use and sleep quality.

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## **Allergenic Ingredients in Tattoo Aftercare Products**

**Background:** Aftercare of a new tattoo is essential to ensure proper healing and to achieve maximal cosmesis. Common recommendations for tattoo aftercare include careful washing and application of topical products. Little is known about tattoo aftercare products.

**Methods:** Tattoo aftercare products were identified from a previous study of 700 tattoo aftercare instructions and a search on Amazon using the phrase "tattoo aftercare." Duplicates and products without complete ingredient lists were excluded.

All ingredients were entered in Excel and grouped according to CAMP (Contact Allergen Management Plan) categories. Comparison of ingredients to NACDG (North American Contact Dermatitis Group) screening and ACDS (American Contact Dermatitis Society) core allergens were conducted. Marketing claims were also tabulated.

Results: A total of 84 tattoo aftercare products from 52 distinct brands were found. Forty-eight distinctive market claims were identified, the use of "natural ingredient(s) (n=36)" was most common. There were 4 to 28 ingredients per product (average 11.8, SD 5.5) with a total of 369 distinct ingredients used. Products contained 0 to 18 ACDS core allergens with average of 7.9 (SD 3.9) allergens per product and 0 to 17 NACDG allergens with average of 7.0 (SD 3.7) allergens per product; Most common are fragrance/botanicals (n=529), Tocopherol/Vitamin E derivatives (n=43), and Panthenol/Vitamin B5 derivatives (n=11).

Conclusions: Tattoo aftercare products are recommended after tattoo placement. This review of 84 products found that tattoo aftercare products contain an average of 8 ACDS core and 7 NACDG allergens. Clinicians should be aware of potential allergens in commonly recommended tattoo aftercare products.

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## Pemphigus Oral Lesions Intensity Score (POLIS)-Responsiveness to change

Background: Pemphigus Oral Lesions Intensity Score (POLIS) is a yet unpublished validated scale encompassing both quality of life and clinical disease severity parameters. It was developed to fill the void in validated scales that can exclusively and accurately capture the clinical variability of oral lesions in patients with pemphigus vulgaris (PV).

Objective: To assess the responsiveness to change of the POLIS scale and to assess its correlation with mucosal Pemphigus Disease Area Index (mPDAI), oral Autoimmune Bullous Skin disorder Intensity Score (oABSIS) and Physician Global Assessment (PGA) scores.

Methods: Oral lesions of patients with pemphigus vulgaris were graded with POLIS, oABSIS, mPDAI and PGA scales at baseline and at monthly intervals for 6 months or till complete lesion resolution, whichever is earlier. Correlations between POLIS, mPDAI, oABSIS and PGA at each visit were assessed. R programme was used to perform linear mixed effects analysis of the relationship between the new score and time.

Results: Significant correlations were observed between POLIS and oABSIS, mPDAI and PGA scores at successive visits ( $p < 0.001$ ) except during the last visit, owing to decreasing sample size in each successive visit. Minimum value information criteria like Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), log likelihood ratio test, chi square and deviance was adopted to select the final model. POLIS score decreased significantly with time (likelihood ratio test =  $< 0.001$ ).

Conclusion: Being a valid and reliable scale with adequate responsiveness to change, POLIS can be used to assess oral lesions of PV patients in clinical practice or research.



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## Factors Influencing Patient Satisfaction in Dermatology

**Background:** Patient satisfaction is a proxy for healthcare quality, with physicians evaluated and reimbursed based on patient satisfaction scores.(1) Despite the growing influence of patient satisfaction, factors that impact patient satisfaction in dermatology remain unclear.

**Methods:** We analyzed 225 responses to a 50-question survey evaluating patient expectations, willingness, and satisfaction regarding dermatology appointments. Patient willingness and satisfaction were measured on a 1-5 Likert scale.

**Results:** Respondents were most willing to discuss their condition and to be examined with a dermatoscope. Respondents were least willing to wear a patient gown without underwear and to be photographed. Highly satisfying factors included a written treatment plan, provider medication recommendations, and use of gloves during physical exams. Highly dissatisfying factors included waiting 60 minutes, taking off underwear with a patient gown, and being photographed with a cellphone.

Patient willingness and satisfaction differed significantly by gender and age. Male respondents reported less satisfaction than female respondents if a nurse explained the treatment plan. Older respondents were significantly more willing to change into a patient gown, to be photographed, to be examined with a dermatoscope, and to undergo a biopsy than younger respondents. Older and female respondents preferred written plans, while younger and male respondents preferred verbal plans. Younger respondents reported higher satisfaction with an email follow-up compared to older respondents, who preferred a phone call.

**Conclusion:** These findings may represent relatively easy ways to improve patient satisfaction scores. Further insight into factors affecting patient satisfaction may enhance patient experience and engagement, thereby improving clinical outcomes.(2)

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## Occupational and Non-occupational Allergic Contact Dermatitis from Colophonium: A Retrospective, Cross Sectional Study from Turkey between 1996 and 2018

Introduction: Colophonium is a well-known occupational and non-occupational contact allergen.

Materials and Methods:

A retrospective, cross-sectional study on 2451 patients patch tested in our clinic between 1996-2018.

Results: 60 of 2451 (2.45%) patients had a positive patch test reaction to colophonium. Male: female ratio was 1:1.6. The age range was 3-79 (median: 40.0). Five patients had atopic skin/dermatitis. Current/past clinical relevance was established in 46 patients (76.7%). Hands were most frequently affected, followed by airborne, and generalized eczema. Non-occupational allergic contact dermatitis (ACD) (n=45, 75.0%) was most frequently induced by wound plaster/adhesive glues, followed by epilating wax, mascara, neoprene shorts, elastic bandage, wig adhesive, rosin soap, vinyl chair upholstery, and topical preparation including rosin gum. Occupational ACD was diagnosed in 25.0% (n=15) comprising construction workers handling cement, printer worker and illumination artist handling paper and ink, textile workers using glues, jeweler using modeling wax, nurse handling adhesive medical tapes, carpenter exposed to wood dust, basketball player using elastic bandage, and billboard worker handling adhesives. Late positive patch test reactions were observed in 12 patients (20.0%). Nine patients co-reacted with abitol and/or abietic acid. Seventeen patients co-reacted with fragrances. In five of them, colophonium was solely a marker for fragrance allergy.

Conclusions: Colophonium sensitization seems to be an important problem in Turkey. Clinicians and patients should be aware of its ubiquity both in occupational and non-occupational settings in order to determine its relevance properly, and to avoid the eliciting causes accordingly.

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## John Cunningham Virus seroconversion in a psoriasis cohort

John Cunningham virus (JCV) is a human polyomavirus infecting between 30-70% of the population .1 In the immunosuppressed it may cause a rare complication- Progressive multifocal leukoencephalopathy (PML).2 Concerns regarding PML have resulted in stringent recommendations for psoriasis patients on dimethylfumarate (DMF).3

**Methods:** We examined the prevalence of JCV infection and seroconversion rates in psoriasis over 5 years. We analysed antibodies to JCV in serum of 248 psoriasis patients using a polyomavirus enzyme immunoassay©. 95 were receiving Systemic/Biologic therapy, 84 on DMF and 69 were not on systemics therapies. We re-tested serum from 54 patients of the original study using the same assay 5 years later.

**Results:** In our earlier work, JCV seroprevalence was 52%, 50% and 48% in the Systemic/Biologic group, DMF and non-systemic group. This year we reassessed 54 patients from the original cohort; 50% were seropositive. 7 patients had seroconverted bringing up a total of 63%.

**Discussion:** PML is a rare condition which has occurred in JCV seropositive psoriasis patients following immunosuppression. PML occurred in patients treated with efalizumab in 2009, resulting in its withdrawal from the market.4 Recent concern has been raised regarding DMF and PML. Without JCV infection, there is no risk of PML. Therefore 50% of our cohort are not at risk. To date, this is the first study to assess JCV seroprevalence in psoriasis patients in a longitudinal cohort study. After 5 years, 63% of patients were seropositive. JCV antibody status may be of importance in some patients on DMF.

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## Single ablative fractional resurfacing laser treatment (FLR) for forearm treatment of actinic keratoses and prevention of non-melanoma skin cancer

**Introduction:** Fractional laser resurfacing (FLR) has demonstrated to effectively treat facial actinic keratoses (AK), but has not been studied in detail on other sites commonly afflicted with AK. Previously, our group has reported that treatment of aged skin with ablative FLR results in removal of senescent fibroblasts and normalizes the pro-carcinogenic acute ultraviolet B radiation responses associated with aged skin. This study was designed to test the effectiveness of FLR on forearm skin of subjects age 60 and older to remove AKs.

**Methods:** Between February 2018 and March 2019, 30 subjects were enrolled in the study in which they underwent a single FLR treatment using the Er:YSSG 2,790-nm laser of one extremity (15 subjects randomized to each arm) including dorsal forearm, wrist, and dorsal hand. Numbers of AKs were recorded on both extremities at baseline, then at three and six months post treatment. Side effects of the FLR were documented.

Results: We noted a 62% decrease in the numbers of AKs on the treated area vs a 167% increase in AKs on the untreated area ( $P < .00001$ ). With at least 10 subjects followed for 12 months, we have noted 9 non-melanoma skin cancers (NMSC) on the untreated area, and 1 on the treated area ( $P < .00001$ ). The laser treatment was well-tolerated without complications.

Conclusions: This study demonstrates that FLR of the upper extremity is an effective and safe field treatment for treatment of upper extremity AK and helps to prevent NMSC.

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## **Clinical outcomes in patients on dupilumab in a specialist adult atopic dermatitis service: A single centre, prospective, observational cohort study of the first 100 patients treated**

Dupilumab is a monoclonal antibody targeting (IL)-4 receptor alpha. In trials, 44-52% of patients with atopic dermatitis (AD) achieved  $\Delta$ EASI75. This single-centre, investigator-led prospective observational study aimed to assess real-world effectiveness and tolerability of dupilumab in a tertiary service.

The first 100 patients initiated on dupilumab to treat AD were prospectively recruited (May 2017-November 2018). Data was collected at pre-determined time points using a structured data collection tool. Primary outcome was proportion of patients achieving  $\Delta$ EASI75 from baseline at 24 weeks.

63% were male, mean age 41.0 years, high incidence of atopy (74% asthma, 59% allergic rhinitis, 42% allergic conjunctivitis); 97% had received systemic therapy (mean 2.6 agents). At baseline, mean EASI was 19.9 (SD10.4), POEM 19.5 (SD7.2) and DLQI 15.0 (SD7.7) and 85.1% had PGA of moderate/severe.

At 24 weeks, 54.8% achieved  $\Delta$ EASI75 (n=46/84; 13/100=missing data (7 clinic schedule; 3 treatment discontinued (AE); 3 lost-to-follow-up); 3=incomplete data) with a mean reduction in POEM of 11.9 (SD7.8; n=81, 6=incomplete data) and DLQI 9.4 (SD7.5; n=85, 2=incomplete data). 29.0% achieved PGA of clear/almost clear (n=25/86, 1=incomplete data).

90% had an AE in the first 24 weeks; 62% reported any eye symptom; 16% cutaneous HSV; 8% joint/muscle pains; 5% flare of head/neck dermatitis. 4% had a SAE, one of which was possibly dupilumab-related (community acquired pneumonia). 4% had an AE causing treatment discontinuation (allergic conjunctivitis (n=2), systemic symptoms (n=1), enthesitis (n=1)).

In summary, these data demonstrate effectiveness of dupilumab in a real world cohort of patients with difficult-to-control AD, with ophthalmological side-effects.

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## A Topical Product Against Visible Light-Induced Effects on the Skin

Studies have demonstrated that visible light (VL) produces sustained pigmentation and combination with ultraviolet (UV) (VL+UVA1) is synergistic.<sup>1,2</sup> Ex vivo studies using topical antioxidant complex demonstrated efficacy in preventing formation of free radicals in skin<sup>3</sup>. This study evaluated in vivo effects in 20 subjects. Three concentrations (0.2%, 0.5%, 1.0%) of the antioxidant complex and placebo were applied to the backs of subjects followed by irradiation with VL+UVA1. Colorimetric assessments were performed at each visit, and 2 punch biopsies were obtained at the placebo and 1.0% product sites after 24 hours.

For lighter skin subjects, there was no statistically significant difference in erythema between the product sites compared to placebo immediately after irradiation, but the 0.5% site had statistically significantly ( $p=0.013$ ) less pigmentation compared to placebo after 7 days. There were no statistically significant differences in histopathologic staining between the product and placebo for lighter skin subjects. For darker skin subjects, there were no statistically significant differences in pigment formation between any of the product treated sites when compared to placebo immediately after irradiation or after 7 days. However, there was a statistically significant ( $p=0.02$ ) decrease in cell proliferation as measured by cyclin D1 staining between the 1.0% product compared to placebo.

The reduced intensity of the VL+UVA1-induced effects in some of the treatment sites with this product supports the hypothesis that the effects of VL+UVA1 can be mitigated by antioxidants. This clinical effects and biomarker protection cannot be generalized to all concentrations. The mechanism of action and variability in response between skin-types warrants further studies.

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## A multicentric, spectrophotometric analysis to determine the role of the follicular SULT1A1 sulfotransferase gene in minoxidil conjugation, its prevalence and regulation – Deciphering the mystery behind the variable therapeutic efficacy of minoxidil.

Introduction: Topical minoxidil, the licensed topical formulation for androgenetic alopecia, has a clinical response rate between 30% and 40%, allegedly due to incongruous sulfation of minoxidil. We attempted to discern the same, through the follicular sulfotransferase enzyme system, predominantly SULT1A1, and did accessory studies to understand its regulation.

Methodology: This transverse, multicentric cross-sectional study was done over three years, involving 164 patients. 10 anagen bulbs, with intact outer root sheaths were plucked from a standardized 1x1 cm<sup>2</sup> area from alopecic scalps, and bio-assayed in a patented solution. Spectrophotometric analysis was done at 405 nm, and a lower optical density (OD) limit of <0.4 arbitrary units (AUs) was pre-allocated, for SULT1A1, the lower limit for Minoxidil 'non-responders'. We have,

in prior studies, demonstrated that these levels predict minoxidil response. Two accessory cohorts were studied, for therapeutic effects with oral acetylsalicylic acid (SA) and topical retinoic acid (RA).

Results: Of clinical significance, 40.83% subjects (n=49/120) showed a low prevalence point for SULT1A1 level, which was matched demographically. Sulfotransferase activity predicted treatment response with 93% sensitivity and 83% specificity. Of the upregulatory cohort with RA, 60% of subjects (n=12) initially predicted to be non-responders to topical minoxidil were converted to responders following 5 days of RA application. The downregulatory cohort had subjects on OTC acetylsalicylic acid (75-81mg). In this accessory cohort, 54.16% (n=13/24) were initially predicted to be responders to minoxidil. Following 14 days of SA, only 29.16% (n=7/24) of the subjects were predicted to respond to topical minoxidil, rendering 25% (n=6/24) subjects non-responsive to minoxidil.

Conclusion: This is the first study to elucidate the interaction between topical minoxidil, retinoids and oral acetylsalicylic acid, and is a pioneer prevalence study for the follicular sulfotransferase enzyme, an efficacy predictor and biomarker, and thus provides a pathway for development of future alopecia treatments.

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**Topical osteopontin inhibition targets molecular anti-fibrotic mechanism for hypertrophic scar prevention**

Hypertrophic and keloid scarring represent excessive fibrosis and extracellular matrix (ECM) deposition, which can be functionally and cosmetically problematic. Our recent findings show that osteopontin (SPP1), a secreted chemokine-like protein involved in intracellular signaling, modulates ECM remodeling in fibroblasts by focal adhesion kinase (FAK) activation; MYO1E/FAK-induced SPP1 plays a role in scar formation as SPP1 is known to drive tissue fibrosis. Previous studies have shown that SPP1 local knockdown leads to accelerated repair and decreased granulation tissue and scar formation. Using a dual-Glo-tagged SPP1 promoter drug screening, we evaluated pharmaceutically active library that inhibit SPP1 promoter and identified an FDA-approved drug, pentamidine isethionate, which inhibits SPP1 activity by  $\geq 80\%$  with minimal in vitro cell toxicity. Topical pentamidine gel was tested using serial dilutions in a novel hypertrophic scar formation rabbit ear model. Following partial ischemic ligation of leporine auricular vessels and linear full-thickness wounding, relative ischemia was assessed with a fluorescent light assisted angiography (Spy Elite, LifeCell) and resulted in hypertrophic scar formation. Rabbits were then assigned to treatment groups: (1) control group with synthetic bandage (no treatment), (2) PCCA base only, or (3) pentamidine (anti-fibrotic SPP1 inhibitor) in PCCA base. Treatment with 2% topical pentamidine in PCCA base demonstrated scar reduction following 4 weeks as observed in gross and histological studies in addition to 3D ultrasonography (n=18). These results provided proof-of-concept data for this new topical therapeutic agent for patient care, currently under clinical trial investigation (ClinicalTrials.gov Identifier: NCT03403621), to enhance clinical practice in wound healing.

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# RESIDENTS & FELLOWS DISCLOSURES

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**Abdullah Aleisa, MD;** No financial relationships exist with commercial interests.

**Abigail Cline, MD, PhD;** No financial relationships exist with commercial interests.

**Aleksi Suo, MD;** No financial relationships exist with commercial interests.

**Alexander Meves, M.D.;** SkylineDx B.V. - Investigator (Grants/Research Funding);

**Alexis Lyons;** Bayer - Investigator (Grants/Research Funding); Biofrontera - Investigator (Grants/Research Funding); General Electric - Investigator (Equipment); Incyte - Investigator (Grants/Research Funding); Lenicura - Investigator (Equipment); Loreal - Investigator (Grants/Research Funding); Miragen - Investigator (Grants/Research Funding); Pfizer - Investigator (Grants/Research Funding); Unigen Inc - Investigator (Grants/Research Funding);

**Alison Sears\*, MBChB;** Medimmune - Investigator (Grants/Research Funding);

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**Amanda Nahhas;** No financial relationships exist with commercial interests.

**Andrew Pink;** Abbvie - Advisory Board (Honoraria), Speaker (Honoraria); Almirall - Advisory Board (Honoraria), Speaker (Honoraria); Janssen - Advisory Board (Honoraria), Speaker (Honoraria); La Roche Posay - Advisory Board (Honoraria); La Roche Posay - Speaker (Honoraria); Leo - Advisory Board (Honoraria), Speaker (Honoraria); Lilly - Advisory Board (Honoraria), Speaker (Honoraria); Novartis - Advisory Board (Honoraria), Speaker (Honoraria); Pfizer - Advisory Board (Honoraria), Speaker (Honoraria); Sanofi - Speaker (Honoraria); Sanofi - Advisory Board (Honoraria); UCB - Advisory Board (Honoraria), Speaker (Honoraria);

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**Anna Malara;** No financial relationships exist with commercial interests.

**Annemarie Tobin;** No financial relationships exist with commercial interests.

**Arucha Treesirichod;** No financial relationships exist with commercial interests.

**Aseem Sharma;** Janssen Pharmaceuticals, Inc - Speaker (Honoraria); Menarini Group - Speaker (Honoraria);

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## B

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**Brian Kirby;** No financial relationships exist with commercial interests.

## C

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**Carla Thomas;** No financial relationships exist with commercial interests.

**Catherine Smith;** Regeneron - Investigator (Grants/Research Funding); Sanofi - Investigator (Grants/Research Funding);

**Chanat Kumtornrut;** No financial relationships exist with commercial interests.

**Chang Ye Wang, MD, MSc;** No financial relationships exist with commercial interests.

**Ciara O'Grady;** No financial relationships exist with commercial interests.

**Cillian F De Gascun;** No financial relationships exist with commercial interests.

## D

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**Darren Roche;** No financial relationships exist with commercial interests.

**Dipankar De;** No financial relationships exist with commercial interests.

**Don G. Morris, MD, PhD;** No financial relationships exist with commercial interests.

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**Elaine C. Siegfried**; No financial relationships exist with commercial interests.

**Elissa Norton, M.D.**; No financial relationships exist with commercial interests.

**Erin M. Warshaw**; Wen - Consultant (Honoraria).

**Esen Özkaya**; No financial relationships exist with commercial interests.

**Esen Özkaya, MD.**; No financial relationships exist with commercial interests.

## G

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## H

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**Henry Lim**; Eli Lilly and Company - Speaker/Faculty Education (Honoraria); Ferndale Laboratories, Inc. - Advisory Board (Honoraria); Galderma Laboratories, LP - Advisory Board (Honoraria); Incyte Corporation - Investigator (Grants/Research Funding); ISDIN - Consultant (Fees); Johnson and Johnson - Speaker/Faculty Education (Fees); L'Oreal USA Inc. - Investigator (Grants/Research Funding); Pfizer Inc. - Investigator (Grants/Research Funding); Pierre Fabre Dermatologie - Consultant (Fees), Speaker/Faculty Education (Honoraria); RaMedical - Speaker/Faculty Education (Fees).

## I

**Iltefat Hamzavi**; AbbVie - Advisory Board (No Compensation Received); Allergan - Investigator (Grants/Research Funding); Beiersdorf - Investigator (Grants/Research Funding); Clinuvel - Investigator (Grants/Research Funding); Estee Lauder - Investigator (Grants/Research Funding); Ferndale - Investigator (Grants/Research Funding); Galderma - Investigator (Grants/Research Funding); General Electric - Investigator (Equipment), Investigator (Grants/Research Funding); Global Vitiligo Foundation - Other (No Compensation Received); HS Foundation - Other (No Compensation Received); Incyte - Consultant (Fees), Investigator (Grants/Research Funding); Janssen Biotech - Investigator (Grants/Research Funding); Johnson & Johnson - Investigator (Grants/Research Funding); Lencicula - Investigator (Equipment); L'Oreal - Investigator (Grants/Research Funding); PCORI - Investigator (Grants/Research Funding); Pfizer - Investigator (Grants/Research Funding); Unigen Inc. - Investigator (Grants/Research Funding).

**Indermeet Kohli**; Allergan, Inc - Investigator (Grants/Research Funding); Bayer - Consultant (Fees), Investigator (Grants/Research Funding); Estee Lauder -

Investigator (Grants/Research Funding); Ferndale Laboratories, Inc. - Investigator (Grants/Research Funding); Johnson & Johnson Pharmaceutical Research & Development - Consultant (Fees); Johnson and Johnson - Investigator (Equipment); L'Oréal Research and Innovation - Investigator (Grants/Research Funding); Pfizer Inc. - Consultant (Fees); Unigen - Investigator (Grants/Research Funding).

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**Julianne Clowry**; No financial relationships exist with commercial interests.

**Julie Mac Mahon**; No financial relationships exist with commercial interests.

**Justin M. McLawhorn, MD**; No financial relationships exist with commercial interests.

## K

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**Kamal kishore**; No financial relationships exist with commercial interests.

**Kimberly Shao, MD**; No financial relationships exist with commercial interests.

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## L

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**Liz Lin**; No financial relationships exist with commercial interests.

**Louise Griffiths**; No financial relationships exist with commercial interests.

**Lucien Rizzo, MD, MS**; No financial relationships exist with commercial interests.

## M

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**Maritza Perez**; No financial relationships exist with commercial interests.

**Martina Porter, MD**; AbbVie - Consultant (Fees), Investigator (Grants/Research Funding); AnaptysBio - Investigator (Grants/Research Funding); Janssen Pharmaceuticals, Inc - Investigator (Grants/Research Funding); National Psoriasis Foundation - Speaker (Honoraria); Novartis - Consultant (Fees), Investigator (Grants/Research Funding); Pfizer Inc. - Investigator (Grants/Research Funding); UCB - Investigator (Grants/Research Funding).

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**Mohsen Mokhtari**; No financial relationships exist with commercial interests.

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## O

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## P

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**Raheel Zubair**; No financial relationships exist with commercial interests.

**Rahul Mahajan**; No financial relationships exist with commercial interests.

**Ratchathorn Panchaprateep**; No financial relationships exist with commercial interests.

**Reid Waldman**; No financial relationships exist with commercial interests.

**Richard Woolf\* (\*contributed equally)**; Abbvie - Advisory Board (Honoraria), Other (Honoraria); Biogen - Speaker (Honoraria); Eli Lilly - Speaker (Honoraria); Leo - Other (Honoraria), Speaker (Honoraria); Sanofi - Speaker (Honoraria).

**Roy Chen**; No financial relationships exist with commercial interests.

**Ryan T. Lewinson, MD, PhD**; Alberta Innovates - Investigator (Grants/Research Funding); Glacier Rx - Founder (No Compensation Received).

## S

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**Shane Grace**; No financial relationships exist with commercial interests.

**Sharon Blackford**; No financial relationships exist with commercial interests.

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**Sonal Choudhary**; No financial relationships exist with commercial interests.

**Sonu Goel**; No financial relationships exist with commercial interests.

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**Soulmaz Boroumand, Ph.D.**; No financial relationships exist with commercial interests.

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**Steven Moran, M.D.**; No financial relationships exist with commercial interests.

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**Wilawan Damkerungsuntorn, MD**; No financial relationships exist with commercial interests.

**Williams Howard**; No financial relationships exist with commercial interests.