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The impact of methotrexate and targeted immunosuppression on cellular and humoral immune responses to COVID-19 vaccine BNT162b2: a cohort study

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Atopic-eczema-associated fracture risk and oral corticosteroids: Anti-tumour necrosis factor (TNFi) therapy is widely used to treat immune-mediated inflammatory diseases including psoriasis. However, 2-5% of patients receiving TNFi may suffer from de novo psoriasis-like eruptions (including psoriasiform dermatitis; pDCs). Nevertheless, PXP is still ill-understood and its underlying mechanisms are yet to be fully comprehended. In this study, we investigated molecular and cellular players putatively involved in PXP in the blood of patients with PXP (n=15, of which 5 with resolved PXP) and age, sex and ethnicity-matched controls groups of healthy donors (HD, n=15) and psoriasis patients before (Ps) and after 12 weeks of receiving TNFi without developing PXP (Ps TNFi). IFNα mRNA expression was significantly lower in PXP versus Ps TNFi (p<0.05), with a downward trend in the level of IFNα protein in the serum of PXP patients versus each control group. However, IFN-γ induced expression of IFNγ, IFNα mRNA expression was similar between PXP and Ps TNFi. Next, we used an 11-colour flow cytometry panel inclusive of skin homing, maturation and pDC subtypes markers to deep-phenotype PBMCs of PXP patients. A higher frequency of pDCs expressing tissue-homing markers favouring their migration to the skin, where they may contribute to disease development. Investigation of skin pDC phenotypes and function using image mass cytometry may elucidate mechanisms underpinning PXP and uncover potential prognostic biomarkers to aid patient stratification and treatment.

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First clinical experience with IMU-935, an orally available small molecule inhibitor of IL-17

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The objectives of this clinical trial are to assess safety, tolerability, and pharmacokinetics of IMU-935. This is a first-in-human, double-blind, placebo-controlled clinical trial comprising three parts. In part A, healthy volunteers in cohorts of size 8 subjects each were enrolled and received single ascending doses of IMU-935 (25 to 400 mg) or placebo (ratio 3:1). In part B, healthy volunteers will receive multiple ascending doses of IMU-935 or placebo for 14 days, and in part C, patients with moderate to severe plaque-type psoriasis will take either two different dose levels of IMU-935 or placebo. First clinical experience with IMU-935 comes from part A of this clinical trial which has recently been completed. Pharmacokinetic evaluation showed a half-life of IMU-935 ranging from 6.5 to 11.0 hours, with a marked dose-dependent increase of Cmax and area under the plasma concentration-time curve (AUC). Treatment-emergent adverse events (TEAEs) related to study drug administration were reported in 29 of 71 (41 %) subjects, with a total of 50 drug-related TEAEs. Most related TEAEs were fatigue (6/28, 21%), headache (4/28, 14%), nausea (4/28, 14%), constipation (3/28, 11%), gastroesophageal reflux (3/28, 11%), constipation (3/28, 11%), and nausea (3/28, 11%). Overall, the number or severity of adverse events did not increase with ascending doses. There were no serious adverse events or adverse events that led to study discontinuation. There were no other clinically meaningful findings related to safety and tolerability, as assessed by physical examination, clinical laboratory tests, vital signs, and 12-lead electrocardiograms (ECGs). IMU-935 has linear pharmacokinetics after single oral doses that allow for once daily dosing. IMU-935 is safe and well tolerated with a benign adverse event profile up to 400 mg as single dose. Ongoing recruitment will provide initial data on the anti-psoriasis activity of IMU-935.

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Oxidative stress in atopic dermatitis and cardiovascular disease: urinary bioprints as possible biomarker

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Bioprints are the end products of the oxidation reaction of bilirubin with ROS. An increase in bilirubin consumption, due to oxidative stress, is reflected by increased level of urinary bilirubin. As a result of their hydrophilic properties, bilirubin are immediately excreted in the urine after their production. Therefore, their continuous monitoring can indicate the intensity of oxidation in vivo. To date, the possible role of urinary bilirubin in the pathogenesis of atopic dermatitis (AD) has not been extensively explored. The aim of this study was to investigate the role of bilirubin in the inflammatory-oxidative process of moderate-severe AD. Furthermore, the study proposed to investigate the activity of biotechnological therapy with dupilumab to influence their concentration and action. For this purpose, 10 patients with moderate-severe AD, and 10 healthy control subjects, matched by sex and age, were enrolled. Morning urine samples were collected from all study participants. For AD patients, a collection was planned before to start therapy with dupilumab and after 52 weeks. The analysis of urinary levels of bilirubin was performed by ELISA. Urinary bilirubin concentration was significantly increased in AD patients compared to controls (p<0.05). Furthermore, our results showed reduced levels of urinary bilirubin in AD patients after 52 weeks of dupilumab treatment (p<0.05). The correlation analysis showed a statistically significant positive correlation between the urinary concentration of bilirubin and EASI index (r=0.9), circulating IgG (r=0.7) as well as plasma CRP levels (r=0.9). These data suggest that urinary bilirubin could represent new peripheral markers in AD, with predictive value of disease severity and response to therapy.

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Atopic-eczema-associated fracture risk and oral corticosteroids: a population-based cohort study

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Evidence suggests adults with atopic eczema have increased fracture risk. However, it is unclear whether oral corticosteroids explain the association. The objective of this study was to assess to what extent oral corticosteroids mediate the relationship between eczema and fracture risk. We performed a cohort study using English primary care (Clinical Practice Research Datalink) and hospital admissions (Hospital Episode Statistics) records (1996-2016). Participants were adults with atopic eczema matched on age, sex, and general practice with up to five adults without eczema. We estimated Hazard ratios (HRs) from Cox regression models with eczema and to those with eczema, adjusting for six different definitions of time-updated oral corticosteroid use (ever any prescription; ever high dose; recent, cumulative, current, peak dose). We identified 526,808 individuals with eczema and 2,506,003 controls. We observed an association between eczema and major osteoporotic fractures (e.g., spine HR 1.15 95% CI 1.08-1.21; hip HR 1.11 95% CI 1.08-1.15) that remained after additionally adjusting for oral corticosteroids (e.g., cumulative corticosteroid dose: spine HR 1.09 95% CI 1.03-1.16; hip HR 1.09 95% CI 1.03-1.12). Fracture rates were higher in people with eczema compared to people without eczema and to those with oral corticosteroids (e.g., spine HR 0.99%). confounder adjusted 2.31 [91.2-81.2], additionally adjusted for cumulative dose 1.71 [102.49]. Our findings suggest that little of the association between atopic eczema and major osteoporotic fractures is explained by oral corticosteroid use.

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Clinical and Molecular Characterization of Ichthyosis at King Abdulaziz Medical City, Riyadh KSA

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Ichthyosis is a disorder of abnormal keratinization, characterized by excessive scaling and rough skin that is more than two subtypes varied in severity, mode of inheritance and the genes involved. Our aim is to identify the histopathological features and genetic profile of ichthyosis. It is an observational retrospective case series study conducted in March 2020, unselectively all patients who were diagnosed with ichthyosis and confirmed by histological and the genes involved. We identified a mean age of 13 ±9.2. There is almost equal distribution between female patients (48%) and males (52%). Majority of them were Saudis 94%. More than half of them had scaling (33.5%), followed by bluntness and coarse skin (31.6%) and hyperlinearity (8.33%). Family history and history of consanguinity were seen in 26 (41.3%), 13 (22%), respectively. History of colloidial babies were found in 6 (10%) cases of ichthyosis. The most frequent genes were ALOX12B, ALOXE3, CERS3, CYP4F22, DOLK, MX1 (p<0.05) and STAT1 (p<0.05), with a downward trend in the level of STAT1 protein in the serum of AD patients compared to controls (p<0.05). Furthermore, our results showed reduced levels of urinary bilirubin in AD patients after 52 weeks of dupilumab treatment (p<0.05). The correlation analysis showed a statistically significant positive correlation between the urinary concentration of bilirubin and EASI index (r=0.9), circulating IgG (r=0.7) as well as plasma CRP levels (r=0.9). These data suggest that urinary bilirubin could represent new peripheral markers in AD, with predictive value of disease severity and response to therapy.