Methods: 31 patients with PG, 35 patients with PSO and 26 HS were included. Immunohistochemical methods were used to evaluate the expression of JAK1, JAK2, JAK3, Tyrosine Kinase 2 (TYK2), STAT1, STAT3, STAT4, STAT5, and STAT6 in cytoplasmic parts of the epidermis. The epidermal part is divided into cytoplasmatic and nuclear parts and staining intensity recorded by semi-quantitatively as follows: negative, mildly positive, moderately positive and strongly positive.

Results: In total, there were 92 biopsies. Dermal staining was significant for all the JAK/STAT proteins for patients with PG and PSO when compared to HS. On the other hand, no differences in the staining patterns of PG and PSO. For the investigation of cytoplasmic parts of epidermis JAK1, STAT3, and STAT4 were highly expressed in the PG and PSO, STAT6, and TYK2 were only significantly overexpressed in psoriasis. JAK3 was overexpressed in healthy skin, PG, and psoriasis. The assessment of the nuclear part of epidermis TYK2 and STAT3 were highly expressed in the PG and PSO. JAK1 was overexpressed in PG versus PSO in cytoplasmic parts of the epidermis (p<0.001). STAT2 and STAT6 were highly expressed in the PSO versus PG. The summary of the findings is given in Table 1.

Conclusion: In this study, the JAK/STAT inflammatory pathway is significantly activated in PG patients which is adding new information to the current literature. Considering the unmet need in PG targeting of this pathway could be beneficial for the treatment of refractory PG.

Disclosure of Interests: None declared.


Further characterization of clinical and laboratory features occurring in VEXAS syndrome in a large-scale analysis of multicenter case-series of 116 French patients

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Background: A new autoinflammatory syndrome related to somatic mutations of UBA1 was recently described and called VEXAS syndrome.

Objectives: To describe clinical characteristics, laboratory findings and outcomes of VEXAS syndrome.

Methods: Case-series. Patients referred to a French multicenter registry between November 2020 and May 2021. 116 patients with VEXAS syndrome. Frequency and median of parameters and vital status, from diagnosis to the end of the follow-up.

Results: Main clinical features were skin lesions (83.5%), non-infectious fever (63.6%), weight loss (62%), lung involvement (49.6%), ocular symptoms (38.8%), relapsing chondritis (36.4%), venous thrombosis (34.7%), lymph nodes (33.9%), and arthralgia (27.3%). Hematological disease was present in 58 cases (50%), considered as myelodysplastic syndrome (MDS, n=58) and monogonic gammapathy of unknown significance (n=12). UBA1 mutations included p.M41T (44.8%), p.M41V (30.2%), p.M41L (18.1%), and splice mutations (6.9%). After a median follow-up of 3.0 years, 18 patients died (15.3%), from infectious origin (n=9) and MDS progression (n=3). Unsupervised analysis identified 3 clusters: cluster 1 (47%) with mild-to-moderate disease; cluster 2 (16%) with underlying MDS and higher mortality rates; cluster 3 (37%) with constitutional manifestations, higher C-reactive protein levels and less frequent chondritis. Five-year survival probability of survival was 84.2% in cluster 1, 50.5 % in cluster 2, and 89.6% in cluster 3. UBA1 p.Met41Leu mutation was associated with a better prognosis.

Conclusion: VEXAS syndrome displays a large spectrum of organ manifestations and shows different clinical and prognostic profiles. It also raises a potential impact of the identified UBA1 mutation.

Disclosure of Interests: None declared.


Managing chronic pain in RMDs


Background: Patients with chronic inflammatory arthritis (e.g. rheumatoid arthritis; RA) or inflammatory exacerbations of chronic degenerative joint diseases (e.g. osteoarthritis; OA) suffer from recurrent pain, restricted function...
and reduction of daily activities. The current standard of intraarticular (i.a.) therapy is the injection of steroids, which can increase risk of infection, cartilage degenerations, and other well-known systemic side effects. A novel approach without such complications could be the activation of peripheral opioid receptors, e.g. by i.a. application of small, systemically inactive doses of morphine.

Objectives: The aim of this randomized placebo-and active drug controlled double blind trial was to investigate reduction of pain in chronic knee arthritis patients following i.a. injections of morphine, a standard steroid (triamcinolone), or placebo. The primary hypothesis was that i.a. morphine results in significantly lower pain scores than placebo. The primary outcome parameter was reduction of the Visual Analogue Scale (VAS) pain at day 7.

Methods: Adult patients with chronic knee arthritis because of osteoarthritis (OA) or inflammatory arthritis (IA, rheumatoid arthritis, psoriatic arthritis, spondyloarthritis, oligoarthritis or monarthritism) and a high level of pain (VAS pain ≥ 4 out of 10) at baseline received a single dose of either morphine 3 mg i.a., or triamcinolone 40 mg i.a., or placebo (NaCl 0.9%) i.a.. Patients were monitored closely throughout the entire study period with a total of 4 visits over weeks and documented pain in the morning and evening in a patient’s diary. Safety data was collected during the entire study period. P-values were calculated using two-sided T-Tests.

Results: 114 patients were screened, 93 were treated and 89 (96%) completed day 7 of these n= 61 (66%) were diagnosed with OA and n= 32 (34%) with IA 48 (52%) patients were female, mean age was 58.5 (SD 14 years) and mean disease duration 6.7 years (median 2 years, range <1 year – 42 years, IQR <1 – 10 years). The mean VAS pain improvement at day 7 for morphine, triamcinolone and placebo was -22.8, -37.7, and -19.8 respectively. The differences were not significant (p=0.069) for placebo vs. morphine, but significant for placebo vs. triamcinolone and for triamcinolone vs. morphine (p=0.013 and p=0.006). Mean improvements of the everyday pain documentation are shown in Figure 1. During the study period, there were no serious adverse events and 45 adverse events, most of them were mild.

Conclusion: In this randomized, placebo and active controlled double blind trial a single dose of 3mg i.a. administered morphine did not lead to significant improvements in comparison to placebo and was inferior to triamcinolone at day 7. The same was true during the first 7 days as shown in the pain documentation in patient diaries. These data does not support the use of i.a. morphine for pain reduction in patients with chronic arthritis.

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Figure 1. Mean VAS pain over one week in patients with chronic knee arthritis treated with morphine, triamcinolone or placebo as a single intraarticular injection.

TRENDS FOR OPIOID PRESCRIPTIONS AMONG PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES BETWEEN 2006-2020

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Background: Opioid prescribing has contributed to a North American epidemic with increasing trends in several European countries1. Rheumatic and musculoskeletal diseases (RMDs) are one of the most common indications for prescribed opioids despite there being little evidence on opioid prescribing and the benefit of long-term use in RMDs.

Objectives: To investigate national UK opioid prescribing trends by studying the patterns of opioid prescribing in new users with the following six RMDs: rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthritis (AxSpA), systemic lupus erythematosus (SLE), osteoarthritis (OA) and fibromyalgia.

Methods: Patients aged 18 years and older with a diagnosis of RA, PsA, AxSpA, SLE and OA with a new episode of opioid use without cancer in the Clinical Practice Research Datalink (CPRD) were included between 01/01/2006 and 31/12/2020. CPRD is a database of anonymised UK primary care electronic health records representative of the national population. New opioid users were defined as individuals with RMDs who had a new episode of opioid use in a 2-year time window up to 6 months before or after an RMD diagnosis. Rates of new opioid users were calculated by dividing the number of new opioid users with an RMD per year by the number of eligible patients registered in CPRD per year. Age- and gender-standardised rates for new opioid users were obtained using direct standardisation for each RMD. Rates of opioid prescriptions among new users for each RMD were calculated by dividing the number of opioid prescriptions among new users with an RMD in the year they had new opioid episodes by patient-years of the new users with an RMD. Trends for the rates in the study period were tested using negative binomial regression. Significant change points were identified by looking at the points where the derivative (i.e. rate of change) of the trends for the rates crossed zero. Recurrent opioid users were defined as patients who had at least 3 opioid prescriptions issued within 3 months after a new opioid episode. Results: This study included 21,505 RA patients, 8,392 PsA patients, 4,491 AxSpA patients, 4,508 SLE patients, 944,078 OA patients, and 33,829 fibromyalgia patients, who had new opioid episodes between 2006-2020. Whilst the overall trend for RA (2.7 vs 3.9), PsA (1.0 vs 1.8) and fibromyalgia (3.7 vs 8.3) has significantly increased over 15 years, from 2018 onwards, trends of new opioid users appeared to stabilise/decrease (Figure 1). The year 2018 was found to be a significant decreasing change point in the trends of new opioid users for RA, AxSpA, and SLE, whilst this was 2013 in OA and 2019 for fibromyalgia. Opioid prescription rates among new opioid users increased in SLE (4.6# vs 4.9#) and fibromyalgia (5.6# vs 6.5#) but decreased in RA (5.7 # vs 5.3#) from 2006 to 2020, despite fluctuations in the rates observed in this period. The highest proportions of recurrent opioid users among the 6 RMDs were patients with RA (32.6%) and fibromyalgia (31.9%).

The number of new opioid users per 10000 persons

* The number of opioid prescriptions in new users per patient years

Figure 1. Trends of new opioid users by RMD, 2006-2020.