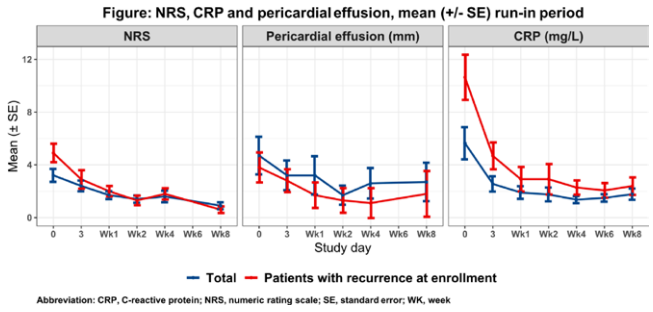



**Conclusion:** The first data show ability to achieve and maintain IRP remission on goflikicept monotherapy with favorable risk-benefit ratio. Final data will be provided.

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## OP0046 EVALUATION OF THE EFFICACY OF TOPICALLY APPLIED TACROLIMUS IN THE TREATMENT OF ORAL ULCERS IN BEHCET'S DISEASE: A DOUBLE BLIND PLACEBO CONTROLLED STUDY

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**Background:** Treatment of Behcet disease (BD) associating oral ulcers is still challenging despite the advances in the systemic treatment modalities.
**Objectives:** We aimed to evaluate the clinical efficacy of topical Tacrolimus for treatment of BD.
**Methods:** In this double blind placebo controlled trial, forty BD patients with persistent active oral ulceration were equally randomized into group I (20 patients received oral colchicine plus topically applied tacrolimus) and group II (20 patients received oral colchicine plus placebo oral gel). All participants were evaluated based on Behcet's Disease Current Activity Form (BDCAF), Ulcer Severity Score (USS) and visual analog scale (VAS) before treatment, and at four-time points post-treatment (15 days, 1st, 2nd, and 3rd months).
**Results:** VAS was significantly lower in group I after 2 weeks (p= 0.037) and 3 months (0.025) than in group II. USS was significantly lower in group I after 3 months of follow up regarding the number of ulcers (p=0.014), ulcer size (p=0.022), and duration (p=0.009). BDCAF showed significant improvement in 3 months follow up within each group (p<0.001 for both groups), while there was insignificant difference between both groups(p=0.347).
**Conclusion:** Topical Tacrolimus has been proven to be a safe and effective adjunctive therapy in the management of oral ulcerations in BD.

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## OP0047 IMPAIRED JAK-STAT PATHWAY IN PATIENTS WITH PYODERMA GANGRENOSUM

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**Background:** Pyoderma gangrenosum (PG) is an inflammatory disease with an unknown etiology. Currently there is an unmet need in the of PG. In recent years, JAK/STAT pathway have been shown to have an important role in the etiology of inflammatory conditions particularly in the field of dermato-rheumatology. However, current data on JAK/STAT pathway in PG is significantly limited.
**Objectives:** Herein we aimed to investigate the JAK/STAT signaling pathway in the skin biopsies of PG patients and compared with psoriasis (PSO) and healthy subjects (HS).

**Table 1. Summary of the findings**

| | | | Healthy Subjects (n=26) | Pyoderma Gangrenosum (n=31) | Psoriasis (n=35) |
|---|---|---|---|---|---|
| | **Age, mean ± SD** | | **60,3 ± 18,3** | **58,1 ± 16,1** | **46,5 ± 18,4** |
| | **Women/men (%)** | | **14/12** | **18/13** | **15/20** |
| Dermal staining | **JAK1** | Positive, n (%) | 0 | 7 (22.6)* | 3 (8.5) |
| | **JAK3** | Positive, n (%) | 0 | 27 (87)* | 31 (88.5)** |
| | **TYK2** | Positive, n (%) | 0 | 31 (100)* | 34 (97.2)** |
| | **STAT1** | Positive, n (%) | 0 | 20 (64.5)* | 27 (77.1)** |
| | **STAT3** | Positive, n (%) | 0 | 29 (93.6)* | 1 (2.8) |
| | **STAT4** | Positive, n (%) | 0 | 7 (22.6)* | 11 (31.4)** |
| | **STAT5** | Positive, n (%) | 0 | 9 (29.3) | 27 (77.1)** |
| | **STAT6** | Positive, n (%) | 0 | 3 (9.7) | 33 (94.3)** |
| cytoplasmic parts of epidermis | **JAK1** | Negative, n (%) | 0 | 1 | 0 |
| | | Mildly positive, n (%) | 0 | 0 | 0 |
| | | Moderately positive, n (%) | 23 (88.4) | 6 (19.4) | 24 (68.5) |
| | | Strongly positive, n (%) | 3 (11.5) | 24 (77.4)* | 11 (31.5)** |
| | **TYK2** | Negative, n (%) | 0 (0) | 1 (3.2) | 2 (5.7) |
| | | Mildly positive, n (%) | 0 (0) | 4 (12.9) | 1 (2.8) |
| | | Moderately positive, n (%) | 18 (69.2) | 18 (58.1) | 11 (31.4) |
| | | Strongly positive, n (%) | 8 (30.8) | 8 (25.8) | 21 (60)** |
| | **STAT3** | Negative, n (%) | 0 | 1 (3.2) | 0 |
| | | Mildly positive, n (%) | 0 | 1 (3.2) | 0 |
| | | Moderately positive, n (%) | 12 (46.1) | 1 (3.2) | 1 (2.8) |
| | | Strongly positive, n (%) | 14 (53.9) | 28 (90.4)* | 34 (97.2)** |
| | **STAT4** | Negative, n (%) | 0 | 1 (3.2) | 0 |
| | | Mildly positive, n (%) | 0 | 1 (3.2) | 0 |
| | | Moderately positive, n (%) | 12 (46.1) | 3 (9.7) | 6 (17.1) |
| | | Strongly positive, n (%) | 14 (53.9) | 26 (83.9) * | 29 (82.9) ** |
| | **STAT6** | Negative, n (%) | 18 (69,2%) | 15 (48,4%) | 1 (2,8%) |
| | | Mildly positive, n (%) | 8 (30,8%) | 16 (51,6%) | 0 |
| | | Moderately positive, n (%) | 0 | 0 | 20 (57,2%) |
| | | Strongly positive, n (%) | 0 | 0 | 14 (40%)** |
| nuclear part of epidermis | **TYK2** | Negative, n (%) | 22 (84,6%) | 1 (3,2%) | 2 (5,7%) |
| | | Mildly positive, n (%) | 4 (15,4%) | 10 (32.2%) | 6 (17,1%) |
| | | Strongly positive, n (%) | 0 | 20 (64,6%)* | 27 (77,2%)** |
| | **STAT3** | Negative, n (%) | 0 | 1 (3,2%) | 0 |
| | | Mildly positive, n (%) | 16 (61,5%) | 2 (6,5%) | 5 (14,3%) |
| | | Strongly positive, n (%) | 10 (38,5%) | 28 (90,4%)* | 30 (85,7%)** |

Data were shown mean±SD and n (%), *= significant expression HS vs PG, **= significant expression HS vs PSO.

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**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 the dermis the staining intensity was recorded as 'positive' or 'negative. The epidermal part is divided into cytoplasmatic and nuclear parts and staining intensity recorded by semi-quantitively 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, there were 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 ($p<0.001$). TYK2 and STAT6 were highly expressed in the PSO versus PG in cytoplasmic parts of the epidermis ($p = 0.024$, $p<0.001$). In the investigation of nuclear parts of epidermis STAT1, 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 up 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.
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OP0048

### FIRST INTERIM ANALYSIS OF THE INTERNATIONAL X-LINKED HYPOPHOSPHATAEMIA (XLH) REGISTRY: ADULT POPULATION BASELINE CHARACTERISTICS

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**Background:** X-Linked Hypophosphataemia (XLH) is a rare, progressive, lifelong, hereditary phosphate wasting disorder characterised by a pathological increase in fibroblast growth factor 23 concentration/activity.[1] Despite XLH being increasingly recognised as a chronic progressive disease, there are few data documenting its natural history or the impact of treatment and other medical interventions on patient outcomes.[2] The multicentre, international, XLH patient registry was established to address this lack of information in XLH to help inform future clinical practice.
**Objectives:** To report data from the first interim analysis of the International XLH Registry (NCT03193476), focusing on baseline characteristics of adults (aged ≥18 years [y]).
**Methods:** The International XLH Registry was initiated August 2017 to collect information on the natural history of XLH and will run for 10 years, aiming to recruit 1,200 people with XLH. Subjects diagnosed with XLH were enrolled from 81 sites in 16 countries (Last Patient In: 30/11/2020; Database Lock: 29/03/2021). Parameters collected at baseline included demographics, medical/treatment history, and clinical presentation.
**Results:** In total, 217 adults were eligible for inclusion in this analysis (18–<30y, n=56; 30–<50y, n=96; ≥50y, n=65); and 150 (69.1%) were female. Mean (SD) age was 41.9y (15.5y); median 41.1y. Mean height was 155.8 cm (n=79); mean weight, 70.0 kg (n=96); mean BMI 26.5 kg/m$^2$ (n=48). Most subjects resided in the UK (50.7%, n=110) and in France (18.9%, n=41). Treatment data were available for 118 subjects: conventional therapy (phosphate salts and active vitamin D), 83.9% (99/118); burosumab, 11.0% (13/118); no treatment recorded 5.1% (6/118). Of 163 subjects with available data, a genetic test result was recorded for 68 (41.7%), of whom 62 (91.2%) had a confirmed *PHEX* mutation. Data on XLH family history were available for 187 subjects; 56/140 (40.0%) reported their biological mother was affected; and 22/141 (15.6%) reported their biological father was affected. The mean time to diagnosis from first symptoms was longer in older vs younger adults: 18–<30y, 25 months (mo) (n=21); 30–<50y, 21mo (n=21); ≥50y, 112mo (n=13).
Retrospective XLH clinical data were available at study entry for 110 adult subjects. Among these subjects, joint conditions were reported by 36.4% (40/110), with osteoarthritis of the knees (60%), hips (42.5%), and shoulders (22.5%) the most frequently affected. Skeletal abnormalities were noted for 71.8% (79/110) of subjects; most common conditions were *genu varum* 53.2% (42/79), *genu valgum* 26.6% (21/79), and enthesopathy 21.5% (17/79). Historical fracture data ("yes/no") were available for 111 subjects; 41 were reported to have had a fracture. Femur fracture was reported for 22 subjects, and hip fractures for 5 subjects. Details of historical orthopaedic surgery were reported for 99 adults; osteotomy was reported for 89 subjects, and hip replacements reported in 14 subjects.
**Conclusion:** The demographics and baseline characteristics of subjects in the International XLH Registry are as expected for adults with XLH. The shorter time to diagnosis in younger vs older adults may indicate improved recognition and diagnosis of XLH in recent years. The analysis of this young population treated with conventional therapy highlights the frequency of musculoskeletal involvement (osteoarthritis, enthesopathies, etc). The information collected within this rare-disease registry during these 10 years provides an exciting opportunity to integrate large-scale real-world evidence into clinical practice, with the aim of improving the care and quality of life of people living with this debilitating disease.
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OP0049

### 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 monoclonal 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 (15.5%), 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 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.
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## Managing chronic pain in RMDs

OP0050

### INTRAARTICULAR MORPHINE IN CHRONIC KNEE-ARTHRITIS – RESULTS OF A RANDOMIZED PLACEBO-CONTROLLED TRIAL

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**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

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