pts. These data provide mechanistic insights into the efficacy of FEN in RA patients.

REFERENCE:

[1] Crawford, et al., J Med Chem 2018 61(6) 2227-2245.

Table 1. FEN Treatment Causes Changes in B and Myeloid Cell Biomarkers (median% of baseline at week 12)

	Cohort 1				Cohort 2		
	FEN 50 mg qD (n=37)	FEN 150 mg qD (n=99)	FEN 200 mg BID (n=99)	PBO (n=100)	ADA 40 mg q2w (n=103)	FEN 200 mg BID (n=45)	PBO (n=41)
RF	71	63*	58*	87	66*	56*	120
IgM	88*	86*	84*	100	103	78*	96
IgG	100	96*	91*	100	100	89*	99
CCL4	83*	88*	77*	96	64*	79*	112
IL6	63	63	60	76	43*	60*	83
CRP	66	64	59*	81	37*	42*	98

*significant versus PBO (p-value ≤ 0.05 FDR adjusted); Kruskal-Wallis test

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FRI0130

RELATIONSHIP BETWEEN DEPRESSION AND DISEASE ACTIVITY IN US VETERANS WITH EARLY RHEUMATOID ARTHRITIS RECEIVING METHOTREXATE

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Background: Depression is common in rheumatoid arthritis (RA) patients and exacerbates disease activity and may reduce response to first-line disease-modifying antirheumatic drugs.

Objectives: To determine whether depression affects disease activity in patients with early RA treated with methotrexate (MTX).

Methods: Patients in the Veterans Affairs Rheumatoid Arthritis registry with early RA (onset <2 years) receiving MTX were selected (n=268). Depression was assessed at baseline using International Classification of Diseases codes (296.2-296.39, 300.4, 311). Disease activity was measured using the 28 joint count disease activity score (DAS-28), tender and swollen joint counts (TJC and SJC), patient and provider global assessment (PTGA and PRGA), patient-reported pain, multidimensional health assessment questionnaire (MDHAQ), and erythrocyte sedimentation rate (ESR). Baseline confounders included sociodemographics, anthropometrics, concomitant treatments, and other clinical characteristics. Propensity score weights were used to equate the depressed and non-depressed participants on baseline confounders. Generalized linear survey models were used to compare disease activity trajectories between depressed (n=48) and non-depressed (n=220) patients over two years. Standardized causal mean outcome differences were estimated at 6 months and 1- and 2-years follow-up.

Results: Depression was associated with significantly greater DAS-28 at 6 months ($\beta=0.36$; 95% CI: 0.03, 0.69) but not at 1- or 2-years follow-up (Table 1). Associations for DAS-28 component measures were smaller in magnitude, decreased over time, and not statistically significant. Depression was also associated with significantly greater pain at both 6 months ($\beta=0.47$; 95% CI: 0.11, 0.82) and 1-year ($\beta=0.42$; 95% CI: 0.03, 0.82) follow-up but not the PRGA or MDHAQ at any assessed time interval.

Table 1. Causal mean differences in standardized disease activity at 6 months and 1- and 2-years follow-up comparing those with depression to those without at baseline.

Measure	6 Months(β , 95% CI)	1 Year(β , 95% CI)	2 Years(β , 95% CI)
DAS-28	0.36 (0.03, 0.69)	0.11 (-0.29, 0.51)	-0.20 (-0.75, 0.35)
SJC	0.24 (-0.01, 0.50)	0.03 (-0.28, 0.34)	0.03 (-0.49, 0.54)
TJC	0.29 (-0.02, 0.61)	0.12 (-0.22, 0.47)	-0.16 (-0.75, 0.43)
PTGA	0.30 (-0.06, 0.66)	0.27 (-0.08, 0.61)	0.00 (-0.65, 0.65)
ESR	0.17 (-0.23, 0.57)	-0.07 (-0.47, 0.33)	-0.15 (-0.72, 0.41)
PRGA	0.14 (-0.16, 0.43)	0.15 (-0.20, 0.50)	-0.33 (-1.00, 0.34)
Pain	0.47 (0.11, 0.82)	0.42 (0.03, 0.82)	0.20 (-0.35, 0.75)
MDHAQ	0.18 (-0.15, 0.51)	0.11 (-0.27, 0.48)	0.06 (-0.46, 0.58)

DAS-28: 28 joint count disease activity score; SJC: Swollen joint count; TJC: Tender joint count; PTGA: Patient global assessment; ESR: erythrocyte sedimentation rate; PRGA: Provider global assessment; MDHAQ: Multidimensional health assessment questionnaire.

Conclusion: Findings demonstrate that depression is associated with less robust short-term response to MTX, and despite clinical RA treatment, more persistent and severe pain. Depression in RA patients may be a risk factor for primary non-response to MTX treatment, and interventions targeted at treating depression could result in better initial RA disease control and DMARD persistence.

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FRI0131

ELUCIDATING THE MECHANISM UNDERLYING CREATINE PHOSPHOKINASE UPREGULATION WITH UPADACITINIB

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Background: JAK inhibitors, including Upadacitinib (UPA), have been associated with increased serum levels of creatine phosphokinase (CPK) in patients with inflammatory disorders, but not in patients with myeloproliferative disease or in healthy subjects treated for a limited duration (1). While CPK increases can be indicative of muscle damage, there are no other indicators of muscle pathology observed with JAK inhibitors, suggesting that there may be another mechanism behind the increased CPK levels. Inflammatory diseases including rheumatoid arthritis are often associated with reduced muscle mass (sarcopenia), a process reversed with disease control (2).

Objectives: We hypothesized that one or more cytokines present in the inflammatory milieu may block differentiation of myoblasts into mature myocytes and that JAK inhibition restores differentiation and associated CPK expression. We focused on the gp130-mediated cytokines IL6, Oncostatin M (OSM), CNTF, and LIF as these have been shown to impact myoblast differentiation.

Methods: Human skeletal muscle myoblast (HSMM) cells were cultured in 10% fetal bovine serum, or were serum starved (2% horse serum) to induce differentiation into myocytes, with and without stimulation with OSM (1–100 ng/ml) and/or UPA (0.0007–1 μ M) for up to 5 days. RNA was purified and expression of CPK (M-type) was determined by QPCR using GAPDH as a reference. CPK expression was also measured following stimulation of HSMM cells with other JAK inhibitors (Baricitinib and Tofacitinib).