adverse effects (1 deranged LFTs, 3 infection, 1 rash, 1 headache, 2 flares of IBD, 1 dizziness, 1 malignancy). Despite the refractory nature of their RA, 14 patients responded sufficiently to remain on Tofacitinib for an average of 24.5 months to date. 1 Patient who failed 3 bDMARDs achieved remission (DAS28 1.82) with 4 confirmed as having moderate disease activity (Mean DAS 3.58, SD 0.42). Of the 39 patients to receive Baricitinib, three had primary non-response, whilst the others remain on therapy. Response is to be determined in 16, 4 have achieved remission (Mean DAS 2.2, SD 0.32) and 14 MDA (Mean DAS 4.04, SD 0.44). 5 patients received both JAKis sequentially, switching from Tofacitinib to Baricitinib, 2 due to adverse events (both flares of IBD) and 3 due to non-response. Of these 5, 1 patient to date has shown a good response at 3 months, 2 have shown no response, with results pending for others. **Conclusion:** Our experience of patients treated with JAKi for RA indicates improvement in disease activity. Benefit was observed in a severely refractory subgroup that had previously failed multiple biologic therapies.

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THU0170

A MULTICENTER STUDY ASSESSING THE EFFICACY AND SAFETY OF REPOSITORY CORTICOTROPIN INJECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS: INTERIM DATA FROM THE OPEN-LABEL TREATMENT PERIOD

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Background: Rheumatoid arthritis (RA) is an autoimmune disorder associated with chronic inflammation and is treated with disease-modifying anti-rheumatic drugs (DMARDs) for active disease. Both American College of Rheumatology (ACR) and EULAR recommend that short-term administration of corticosteroids (CSs) may be beneficial for its anti-inflammatory effects. Repository corticotropin injection (RCI) is a complex mixture containing purified porcine pituitary adrenocorticotropic hormone (ACTH)-analogue and an agonist for all 5 melanocortin receptors (MCRs). Activation of MCRs by ACTH has been shown to have direct and indirect anti-inflammatory and immunomodulatory effects. RCI is approved in the United States as adjunctive therapy for short-term administration in RA.

Objectives: To present interim data after 100% enrollment from the initial 12-week open-label phase of a multicenter, 2-part study evaluating the efficacy, safety, and appropriate duration of RCI therapy in patients with persistently active RA despite receiving 1 or 2 DMARDs and/or CSs.

Methods: In the open-label period (Part 1, Weeks 0–12), all enrolled patients received RCI 1 mL (80 U SC) twice weekly for 12 weeks. Patients who achieved low disease activity (LDA; DAS28-ESR score <3.2) at Week 12 continued in the double-blind, randomized maintenance phase of the trial (Part 2) for an additional 12 weeks. The primary endpoint was the proportion of patients who achieved LDA at Week 12. Secondary endpoints included assessment of the safety and tolerability of RCI. Disease activity was also assessed by the proportion of patients who achieved ACR 20%, 50%, and 70% (ACR20, 50, 70) responses and patient reported outcomes at Week 12. Bone turnover markers were assessed as an exploratory endpoint.

Results: 259 patients had enrolled, 235 had completed and 24 had discontinued the 12-week open-label period of the study; 88.9% were female and mean age was 51 years. RCI treatment resulted in 62.5% of patients achieving LDA at Week 12; results for this interim analysis are presented in the **Table**. Bone turnover markers were stable from baseline

to Week 12, indicating no effect of RCI on bone metabolism. 98 (37.8%) patients reported adverse events (AEs) with 3 (1.2%) patients reporting serious AEs (ie, non-cardiac chest pain, pneumonia, and craniocerebral injury). The most common AEs were urinary tract infection (n=10), headache (n=9), and pharyngitis (n=7).

Abstract THU0170 – Table 1.

Table. Results for Patients Who Completed the Open-label Period (mITT; N=259)

Endpoints	Baseline	Week 4	Week 8	Week 12
LDA (DAS28-ESR <3.2; Primary Endpoint)	-	6.6%	14.3%**	62.5%**
ACR20	-	48.6%**	69.9%**	79.5%**
ACR50	-	12.0%**	35.9%**	62.2%**
ACR70	-	4.6%	8.5%	31.7%**
DAS28-ESR score, mean	6.3	4.9*	4.4*	3.6*
Tender joint count, mean	14.6	7.7*	5.7*	3.9*
Swollen joint count, mean	10.9	5.6*	4.0*	2.8*
Patient global assessment of disease activity (20% improvement)	-	56.0%**	71.8%**	80.3%**
FACIT-F, mean	22.9	17.5*	16.0*	13.9*
HAQ-DI, mean	1.7	1.2*	1.0*	0.8*

FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue Scale; HAQ-DI, Health Assessment Questionnaire – Disability Index; LDA, low disease activity.
 The modified intent to treat (mITT) population includes all subjects who received RCI with any post-treatment efficacy assessments.

*p < 0.001 vs baseline. **p < 0.0001 vs baseline.

Conclusion: In the 12-week open label period of this study, RCI appeared to be generally safe and effective in patients with persistently active RA who were nonresponsive to DMARDs and CSs. This was demonstrated by improvement in multiple measures of disease activity. Further results will be evaluated in Part 2 of the study.

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THU0171

TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN THE TREATMENT OF RHEUMATOID ARTHRITIS – THE RESULTS OF RUSSIAN NATIONAL REGISTER OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB

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Background: Tofacitinib (TF) is an oral Janus Kinase inhibitor for the treatment of rheumatoid arthritis (RA).

Objectives: To evaluate the one-year effectiveness of tofacitinib as first-line therapy in RA conventional synthetic (cs) DMARDs non-responders.

Methods: Data from 415 patients from Russian national register of patients with RA treated with TF were analyzed. 119 RA patients, who had complete clinical and laboratory data from 4 consecutive visits after baseline with an interval of 3 months between the visits and who used the TF as first-line therapy after failure of cs DMARDs, were included. Treatment with any biologics ever was an exclusion criteria.

Demographical (age, sex) and RA activity data (DAS28, SDAI, number of tender and swollen joints (NTJ, NSJ), erythrocytes sedimentation rate (ESR), C-reactive protein (CRP), and HAQ. EQ5D were collected, table 1. Statistical analysis performed in SPSS2017. p-value <0.05 considered as significant.

Results: At baseline 12 (10%) were treated with NSAIDs, 15 (12.6) with 5-10 mg/day of prednisolone, 82 (68.9) – with methotrexate (10-25 mg/week), 8 (6.7%) – with sulfasalazine (2.0-3.0 g/day).

Abstract THU0171 – Table 1. Baseline characteristics of the patients with RA (n=119)

Parameter	Characteristics
Male, n (%)	24 (20.16)
Age of disease onset, years (mean ±SD)	41.1±11.5
Symptoms duration, month (mean ±SD)	113.7± 96.61
Positive rheumatoid factor, n (%)	68 (34.17)
Positive antibodies to cyclic citrullinated peptide (anti-CCP), n (%)	82 (68.9)
Erosions of hand joints (X-rays), n (%)	28 (23.5)
BMI, kg/m ² (mean ±SD)	21.82±5.37
Smokers (current and in the past), n (%)	42 (35.3)

Changes in the disease activity in patients with RA, treated with tofacitinib after csDMARD are presented in Table 2

Abstract THU0101 –Table 1. Efficacy outcomes in patients with RA treated with tofacitinib

	NTJ 28	NSJ 28	Patients' Global	ESR, mm/h	CRP, mg/l	DAS28	HAQ	EQ- 5D
Baseline	8.48	3.68	52.48	29.32	19.10 ±	4.56	1.61	0.58
	±6.53	±5.02	±19.22	±22.69	37.4	±1.32	±0.63	±0.2
Month3 [#]	6.29	1.0	39.29	22.29	8.43	3.84	1.08	0.71
	±5.64*	±3.52*	±20.41*	±19.51*	±27.5*	±1.33*	±0.7	±0.17
Month 6 [#]	4.69	2.34	37.51	27.12	10.86	3.85	1.02	0.68
	±4.6*	3.2*	±20.22*	±20.54	±17.47*	±1.3*	±0.7	±0.18
Month 9 [#]	4.61	2.28	36.23	26.85	10.91	3.80	1.0	0.68
	±5.51*	±3.56*	±20.6*	±19.96	±20.96*	±1.3*3	±0.68	±0.16
Month12 [#]	3.64	1.6	30.92	24.54	9.18	3.55	0.82	0.71
	±4.21*	±2.41*	±18.12*	±18.94*	±14.11*	±1.15*	±0.58*	±0.16

*difference with baseline is significant (p<0.05). # – ±1 month

At visit 3 DAS28 <3.2 achieved 80 (67.22%) of the patients: 71 patients on 20 mg of TF (59.66%) and 9 patients on 10 mg of TF 11 (9.24%) patients at visit 3 had DAS28 ≥5.1.

Conclusion: Treatment with TF may provide good response rates in RA patients, refractory previous cs DMARDs.

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THU0172

UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGICAL DMARDs: RESULTS AT 60 WEEKS FROM THE SELECT-BEYOND STUDY

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Background: In patients (pts) with active rheumatoid arthritis (RA) and inadequate response or intolerance to bDMARDs, treatment with upadacitinib (UPA), a JAK1-selective inhibitor resulted in significant improvements over 24 weeks (wks).¹

Objectives: We assessed UPA safety and efficacy through Wk60 in an ongoing extension of the phase 3 SELECT-BEYOND study.

Methods: SELECT-BEYOND enrolled a population of patients with active RA who had failed at least one prior biologic therapy.¹ Pts received UPA 15mg or 30mg once daily (QD) or placebo (PBO) on top of background csDMARD treatment for 12 wks. From Wk12, pts randomized to UPA at baseline (BL) continued their assigned doses while pts initially randomized to PBO received UPA 15mg or 30mg QD per pre-specified assignment at BL. Patients who completed Wk 24 entered the blinded long-term extension. Dose adjustments to UPA were not allowed. Adverse events (AE) per 100 pt years (PY) are summarized based on a cut-off date of 16 April 2018. Efficacy data up to the Wk60 visit are reported "As Observed".

Abstract THU0172 –Table 1.

Any Adverse Event	UPA 15 MG vs 30 MG	
	UPA 15 MG vs 30 MG	UPA 30 MG vs 30 MG
	Pts=283.7	Pts=283.7
	E/100PYs	E/100PYs
Any Adverse Event	353.3	435.8
Serious AE	17.9	29.2
AE Leading To Study Drug D/C	9.5	15.1
Serious Infection ^a	3.0	8.3
Herpes Zoster ^a	4.6	8.9
Hepatic disorder ^a	4.5	8.3
Any Malignancy (incl. NMSC) ^b	1.7	1.0
MAE (adjudicated) ^c	1.0	0.3
YTE (adjudicated) ^d	2.3	0.7
Deaths ^e	0.7	1.0

E, events; Pts, patient-years; E/100PYs, events per 100 patient-years; NMSC, non-melanoma skin cancer; MAE, major adverse cardiovascular event (cardiovascular death, non-fatal myocardial infarction (MI), non-fatal stroke); YTE, venous thromboembolism (DVT, deep vein thrombosis, pulmonary embolism).

^aMost frequently reported serious infections were pneumonia, HZ, influenza, and respiratory tract infections.

^bHZ: most involved 1 or 2 dermatomes. No meningococcal/septicemic/noncutaneous involvement. Two HZ events were reported as opportunistic.

^cMalignancy (excluding NMSC): UPA15: 1 malignant melanoma in situ, 1 bladder cancer, 1 pancreatic carcinoma Stage IV, 1 colon cancer, 1 non-small cell lung cancer metastatic; UPA30: 2 prostate cancers, 1 rectal cancer metastatic.

^dMAE (adjudicated): UPA15: 1 CV death, 1 non-fatal MI, 1 non-fatal stroke; UPA30: 1 pt with 2 concurrent events (non-fatal MI and acute congestive heart failure) adjudicated to non-fatal MI.

^eDeaths: UPA15: 1 pt with PE, 1 pt with DVT, 1 pt with PE and DVT, 1 pt with non-assessable thrombotic event; UPA30: 1 pt with PE, 1 pt with PE and DVT; no dose relationship in the rates of YTE or patterns in the time to onset of the events, were observed.

^fDeaths: UPA15: 1 due to other CV causes, 1 due to cardiac arrest; UPA30: 1 pt with cardiac decompensation, 1 pt with presumed MI, 1 pt with rectal cancer metastatic to liver.

Results: 418/498 (84%) pts were randomized, completed 24 wks and entered the extension on study drug. By the safety data cut-off date, 19% pts discontinued study drug: 5% due to AE, 4% due to lack of efficacy, 3% withdrew consent, 2% were lost to follow-up, and 5% discontinued due to other reasons. Cumulative exposures to UPA15 and UPA30 were 301.7 and 290.7 PYs, respectively. Rates (Events/100PYs) of treatment-emergent AEs are reported (Table 1), and were numerically higher in the UPA30 vs UPA15 arm for serious AEs, AEs leading to discontinuation, serious infections, herpes zoster and hepatic disorders. Based on As Observed analysis, for pts completing Wk60 on UPA15 [172/216 (80%)] and UPA30 [168/202 (83%)], clinical and functional outcomes continued to improve compared to Baseline, or were maintained from Wk24 onwards¹ in pts initially randomized to UPA15 or 30; Remission by CDAI≤2.8 at Wk60 was achieved by 20% and 32%, respectively, and DAS28-CRP<2.6 was achieved by 53% and 52%. Pts who were switched to UPA from PBO at Wk12 had comparable efficacy to pts initially randomized to UPA (Table 2).

Abstract THU0172 –Table 2.

Efficacy Endpoints at Week 60 (as observed): Responses compared to Baseline, n/N (%)	PBO → UPA		UPA 15 MG		UPA 30 MG	
	PBO → UPA	UPA 15 MG	PBO → UPA	UPA 15 MG	PBO → UPA	UPA 30 MG
ACRO	40/59 (68)	52/62 (84)	102/133 (77)	97/116 (84)	102/133 (77)	97/116 (84)
ACRO	36/60 (60)	40/61 (66)	70/134 (52)	71/117 (61)	70/134 (52)	71/117 (61)
ACRO	20/60 (33)	24/61 (39)	45/135 (33)	49/118 (41)	45/135 (33)	49/118 (41)
DAS28-CRP≤2.6	37/59 (63)	46/64 (72)	92/133 (69)	86/117 (74)	92/133 (69)	86/117 (74)
DAS28-CRP≤2.6	31/59 (53)	36/64 (56)	70/133 (53)	61/118 (52)	70/133 (53)	61/118 (52)
CDAI≤2.8	42/60 (70)	45/63 (72)	91/132 (69)	74/117 (63)	91/132 (69)	74/117 (63)
CDAI≤2.8	18/60 (30)	17/63 (27)	26/132 (20)	37/117 (32)	26/132 (20)	37/117 (32)
SDAI≤3.3	19/59 (32)	20/63 (32)	26/161 (20)	36/114 (32)	26/161 (20)	36/114 (32)
HAQ-DIC≤0.22	40/60 (67)	49/63 (78)	91/130 (70)	87/118 (74)	91/130 (70)	87/118 (74)
Change from BL in HAQ-DIC	-0.52	-0.61	-0.52	-0.65	-0.52	-0.65

Conclusion: The benefit:risk of upadacitinib treatment in this refractory population remains favorable. No new safety signals were identified. Some AEs were numerically higher for UPA30 vs 15; however the clinical significance of this, the assessment of rare safety events in this study, and the overall benefit:risk of upadacitinib 15mg and 30mg in the treatment of RA are best evaluated in an integrated analysis across the phase 3 program. UPA15mg and 30mg continued to be effective in treating RA signs and symptoms, and in improving physical function.

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