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Improved Patient-Reported Outcomes in Patients With Persistently Active Rheumatoid Arthritis Following Treatment With Repository Corticotropin Injection

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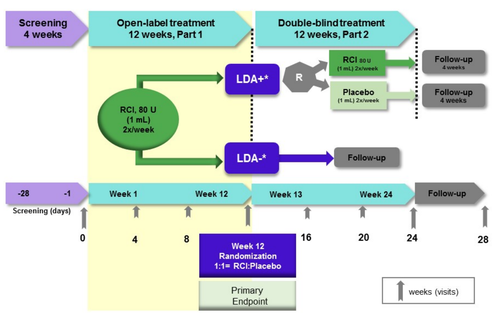
Introduction

- Rheumatoid arthritis (RA) is an autoimmune disorder characterized by progressive inflammation and irreversible joint damage
- Treatment of active disease includes the appropriate use of disease-modifying anti-rheumatic drugs (DMARDs) and possibly short-term corticosteroid (CS) use[1]
- A comprehensive assessment of clinical treatment outcomes should include validated patient-reported outcome (PRO) instruments[2]
- Repository corticotropin injection (RCI) is approved by the FDA for short-term adjunctive use in the treatment of RA[3]
- A naturally sourced complex mixture of purified adrenocorticotropic hormone analogues and other pituitary peptides, RCI stimulates endogenous CS production and is an agonist for all 5 melanocortin receptors (MCRs)[3,4]
- MCR activation by RCI has been shown to have direct and indirect anti-inflammatory and immunomodulatory effects[4,5]
- To explore the effect of RCI treatment on PROs with the greatest impact on quality of life (ie, pain, fatigue, physical functioning, and ability to work) in patients with persistently active RA, a 2-part (open-label followed by double-blind), placebo-controlled, multicenter Phase 4 trial was initiated
- Data presented here are from the open-label period (ClinicalTrials.gov ID: NCT02919761)

Methods

- Adults with active RA (defined as Disease Activity Score with 28 Joint Count score [DAS28] >3.2) despite DMARD and continued CS use received 80 U of RCI subcutaneously twice weekly during a 12-week open-label period (**Figure 1**)
- PRO measurements included the Health Assessment Questionnaire – Disability Index (HAQ-DI), Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scale, Patient Global Assessment of Pain (visual analog scale), and Work Productivity and Activity Impairment (WPAI) scale
- Statistical analyses were conducted by comparing mean change from baseline using one-sample *t* tests

Figure 1. Study Schematic



*The primary efficacy endpoint was the proportion of patients who achieved LDA (DAS28 <3.2) at week 12 in part 1 of the study.
After screening, patients received open-label treatment with RCI subcutaneously twice per week for 12 weeks prior to being evaluated for a treatment response.
Abbreviations: DAS28, Disease Activity Score with 28 joint count; LDA, low disease activity; R, randomization; RCI, repository corticotropin injection.

Results

- Of the 259 patients in the modified intent-to-treat population (mITT), 89% were female and 66% were Caucasian; mean age was 51 years
- Baseline characteristics and PROs are shown in **Table 1**

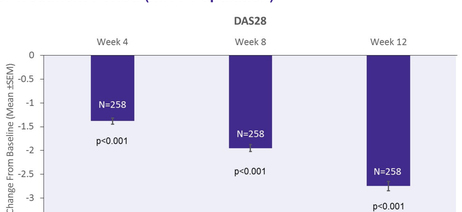
Table 1. Baseline Demographics and PROs (mITT Population)

Demographics and PROs	RCI (N=259)
Age, years, mean (SD)	51 (12.2)
Women, n (%)	231 (89.2)
Height (cm), mean (SD)	158.9 (8.9)
Weight (kg), mean (SD)	72.9 (17.0)
ESR (mm/hr), mean (SD)	43.6 (24.8)
DAS28, mean (SD)	6.3 (1.0)
CDAI, mean (SD)	38.3 (12.3)
FACIT-F, mean (SD)[a]	22.8 (8.4)
HAQ-DI score, mean (SD)[b]	1.7 (0.6)
WPAI: ability to perform work scores[c]	
Percentage work time missed due to RA, n	69
Mean (SD)	24.9 (27.6)
Percentage impairment while working due to RA, n	66
Mean (SD)	50.3 (27.1)
Percentage overall work impairment due to RA, n	66
Mean (SD)	58.1 (28.6)
Percentage activity impairment due to RA, n	259
Mean (SD)	63.2 (24.2)

[a]FACIT-F: scores range from 0 to 52, with lower scores indicating less fatigue. Scores are calculated by using the 13 items in the "additional concerns" section of the FACIT-F form, calculated as follows: sum of the scores from the answered items*13 / number of the answered items; MCID: 3- to 4- point change or 3.563.
[b]HAQ-DI: derived from the 8 sections of the health assessment questionnaire: dressing, arising, eating, walking, hygiene, reach, grip, and activities. Each question is scaled from 0 (item can be performed without any difficulty) to 3 (unable to do). For each section, the score given to that section is the worst score within the section. In addition, if an aid or device is used or if help is required from another individual, then the minimum score for that section is 2. If the section score is already 2 or more, then no modification is made. The formula for calculating the HAQ-DI is the sum of the scores from the 8 sections / number of sections with non-missing score; MCID=0.22.
[c]WPAI: impairments are rated with reference to a specified health problem (arthritis) during the past 7 days and are measured on a scale from 0 to 10, with 0 representing no effect (on work or activity) and 10 as completely preventing the patient from doing work or activity. Impairments at work and activity are calculated as a percentage (of a maximum potential score of 10). The higher the percentage, the greater the impairment; MCID: 7% absolute change in WPAI:RA score.
Abbreviations: CDAI, clinical disease activity index; DAS28, Disease Activity Score with 28 Joint Count; FACIT-F, Functional Assessment of Chronic Illness Therapy–Fatigue; HAQ-DI, Health Assessment Questionnaire Disability Index; MCID, minimum clinically important difference; mITT, modified intent-to-treat; PRO, patient-reported outcome; RA, rheumatoid arthritis; SD, standard deviation; WPAI, Work Productivity and Activity Impairment.

- During the 12-week initial open-label treatment period, 62.9% of patients [163/259] achieved low disease activity by Week 12; improvement in DAS28 scores is shown in **Figure 2**
- Mean improvements from baseline were clinically and statistically significant at all time points for HAQ-DI and FACIT-F for patient-reported global assessments of disease activity and pain (**Figure 3**)

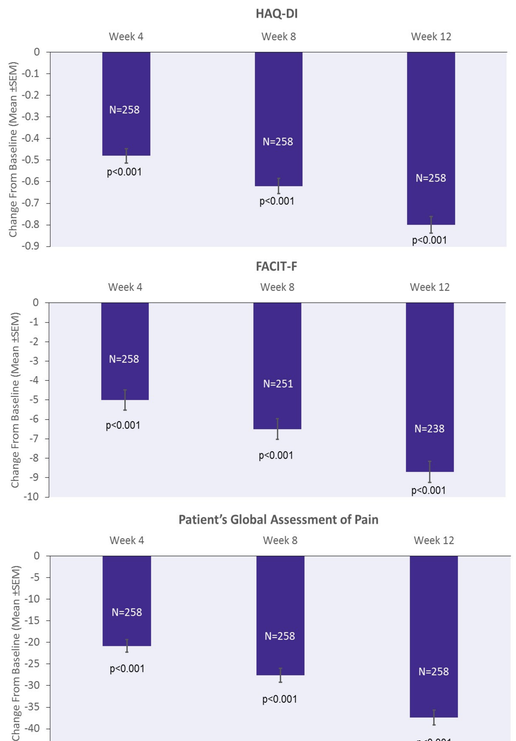
Figure 2. Improvement in the DAS28 From the 12-Week Open-label RCI Treatment Period (mITT Population)



p-values were calculated by one-sample *t* test compared to baseline.
Abbreviations: DAS28, Disease Activity Score with 28 joint count; mITT, modified intent-to-treat; RCI, repository corticotropin injection; SEM, standard error of the mean.

Results (cont'd)

Figure 3. Improvement in PROs (HAQ-DI, FACIT-F, and Patient's Global Assessment of Pain) From the 12-Week Open-label RCI Treatment Period (mITT Population)

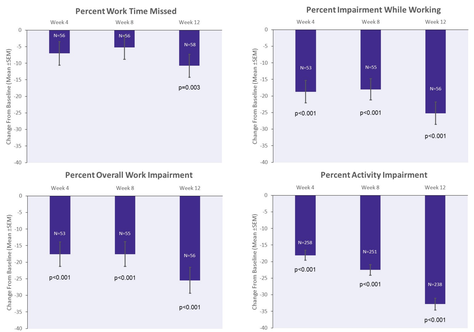


p-values were calculated by one-sample *t* test compared to baseline.
Abbreviations: FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; HAQ-DI, Health Assessment Questionnaire – Disability Index; mITT, modified intent-to-treat; PRO, patient-reported outcome; RCI, repository corticotropin injection; SEM, standard error of the mean.

Results (cont'd)

- Clinically and statistically significant improvements in 3 of 4 WPAI sub-scores—including percent impairment while working, percent activity impairment, and percent overall work impairment—were observed at all time points (**Figure 4**)
  - For percent work time missed, significant improvement was achieved by Week 12

Figure 4. Improvement in PROs (WPAI Questionnaire) From the 12-Week Open-Label RCI Treatment Period (mITT Population)



p-values were calculated by one-sample *t* test compared to baseline.
Abbreviations: mITT, modified intent-to-treat; PRO, patient-reported outcome; RCI, repository corticotropin injection; SEM, standard error of the mean; WPAI, Work Productivity and Activity Impairment Questionnaire.

Conclusions

- RCI treatment resulted in rapid and clinically meaningful improvements in PROs deemed most relevant to quality of life by patients with persistently active RA
- During the 12-week open-label treatment period, RCI significantly improved patient-reported physical functioning, fatigue, pain, and work-related impairment as early as Week 4, with continued improvement over time

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