Introduction

- Incomplete recovery from multiple sclerosis (MS) relapses may contribute to accrual of disability, highlighting the importance of effective relapse treatment¹⁻³
- Although disease-modifying therapies (DMTs) are used to reduce the occurrence of MS relapses, relapses still occur^{4,5}
- High-dose corticosteroid (CS) therapy is the mainstay of acute treatment of MS relapses^{2,6} • Results from clinical trials suggest that up to 55% of patients may not adequately respond to intravenous or oral CS⁷⁻¹⁰
- Older age and disease severity are positive predictors of nonresponse to CS therapy¹¹
- Repository corticotropin injection (RCI, H.P. Acthar[®] Gel; Mallinckrodt ARD Inc., Bedminster, NJ, USA) contains a porcine-derived analogue of adrenocorticotropic hormone approved by the US Food and Drug Administration for treatment of MS relapses in adults¹²
- Historically, the effects of RCI in MS were attributed to stimulation of endogenous cortisol production; more recent evidence suggests that CS-independent properties potentially contribute¹³
- RCI is an alternative to high-dose CS in patients with MS relapse¹⁴
- In a study of patients who had previously failed CS therapy and experienced an acute exacerbation, physicians rated the clinical status of a majority of patients as good, very good, or excellent after RCI treatment¹⁵
- There is limited data describing the demographics and disease characteristics of patients treated with RCI for relapses of MS

Study Objectives

- To characterize patients receiving RCI for treatment of acute MS relapse, identify treatment patterns, and examine the efficacy and safety of RCI treatment in MS relapse
- This interim report summarizes preliminary data collected through August 30, 2017

Methods

Study Design

- Ongoing multicenter, prospective, 24-month, observational registry study
- Target enrollment: up to 160 patients at approximately 50 sites (ie, neurology practices in the United States that treat adult patients with MS)

Interim Enrollment and Data Collection

- Potentially eligible patients were recruited during routine care visits
- Those who met the study eligibility criteria (**Table 1**) and provided informed consent were enrolled (Figure 1)

Table 1. Key Inclusion and Exclusion Criteria

Inclusion

Age ≥18 years

Relapsing form of MS according to the McDonald criteria (2010 revision)¹⁶

Acute MS exacerbation as determined by treating clinician Planning to initiate RCI therapy for acute MS exacerbation

Exclusion

Diagnosis of primary progressive MS

Requirement for concomitant CS therapy

Receiving experimental drug therapy

Recent surgery or a history (within 6 months) or presence of a peptic ulcer, congestive heart failure, or sensitivity to proteins of porcine origin

Abbreviations: MS, multiple sclerosis; RCI, repository corticotropin injection; CS, corticosteroid.

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A Prospective Observational Registry of Repository Corticotropin Injection for the Treatment of Multiple Sclerosis Relapse: Baseline Characteristics and Interim Results

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- The instrument includes 2 subscales that measure the physical and psychological impacts of MS
- The Expanded Disability Status Scale (EDSS) was administered by the clinician at baseline (**Figure 1**)
- Adverse events (AEs) were documented at usual care visits and serious AEs (SAEs) were reported within 24 hours
- Data were abstracted from patient medical records at predefined time points (Figure 1)

Efficacy and Safety Assessments

- Baseline characteristics and efficacy were assessed in the intent-to-treat (ITT) population
- AEs and SAEs were assessed in the safety population (ie, any patient who received at least 1 dose of RCI, N=62)
- Efficacy was defined as an improvement (ie, decrease) in MSIS-29v1 score from baseline at 2 weeks and 1, 2, 3, 4, 5, and 6 months
- Treatment responders were defined as patients who had a ≥ 8 point reduction in MSIS-29v1 score from baseline

Statistical Analysis

- The mean changes from baseline of MSIS-29v1 physical subscores were compared over time with a two-sided paired t-test
- The proportion of treatment responders were reported as percentages

Results

Patient Characteristics and Medication Use

- As of August 30, 2017, 80 patients had enrolled in the study
- Patient characteristics and DMT use at enrollment are shown in Table 2
- Thirty-seven patients (60%) reported a history of insufficient treatment response to, intolerance of, or intravenous access problems with high-dose CS therapy

Table 2. Patient Characteristics at Enrollment

Characteristic	ITT Population ^a (N=62)	
Age, mean (SD), y	48.3 (10.9)	
Gender, No. (%) Male Female	6 (10) 56 (90)	
Race, No. (%) Black/African American White Other No information/missing	6 (9.7) 53 (85.5) 1 (1.6) 2 (3.2)	
MSIS-29v1 physical subscore, ^b mean (SD)	55.8 (24.1)	
EDSS score, ^c mean (SD)	4.2 (2.0)	
Time since initial MS diagnosis, mean (SD), y	11.7 (9.4)	
Time since onset of most recent relapse, mean (SD), mo	7.7 (5.8)	
DMT use ^d Yes No	52 (83.9) 11 (17.7)	

^a Baseline characteristics at enrollment in the ITT population (N=62).

Scored on a scale from 0 to 100, with 100 representing the worst possible score

Rated on a scale from 0 (normal neurologic exam) to 10 (death due to MS).

Some patients were receiving >1 medication within the previous 2 years at the time of enrollment. bbreviations: DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; ITT, intent-to-treat; MS, multiple sclerosis; MSIS-29v1, 29-item Multiple Sclerosis Impact Scale, version 1; SD, standard deviation.

- The median dose of RCI was 80 U daily for 5 days, with most patients dosing on consecutive days
- DMTs were used concomitantly with RCI in over 70% of patients; DMTs used are shown in Table 3

Table 3. Summary of Concomitant DMT Use

Characteristic	ITT Population ^a N=62 No. (%)
Any concomitant DMT use ^b	45 (72.6)
Specific DMT use Dimethyl fumarate Natalizumab Glatiramer acetate Teriflunomide Fingolimod Ocrelizumab Interferon β-1a Alemtuzumab	$\begin{array}{c} 15 \ (24.2) \\ 13 \ (21.0) \\ 7 \ (11.3) \\ 7 \ (11.3) \\ 6 \ (9.7) \\ 4 \ (6.5) \\ 2 \ (3.2) \\ 1 \ (1.6) \end{array}$

^a Assessed in the ITT population (N=62).

^b Any DMT taken at any time during the study period. Abbreviations: DMT, disease-modifying therapy; ITT, intent-to-treat.

Interim Efficacy Results

RCI treatment significantly decreased mean MSIS-29v1 physical subscores at 2 and 6 months, both p<0.05 (Figure 2)

Figure 2. Change from Baseline in MSIS-29v1 Physical Subscores at 2 and 6 Months



Assessed in the ITT population (N=62). Data represents the mean + SEM. * p<0.05; *** p<0.001; paired t-test.

Abbreviations: ITT, intent-to-treat; MSIS-29v1, 29-item Multiple Sclerosis Impact Scale, version 1; SEM, standard error of the mean.

At 6 months, up to 56% of patients treated with RCI were responders based on MSIS-29v1 scores (Table 4)







Table 4. Treatment Responders Based on Changes in MSIS-29v1 Physical Subscores from Baseline

Visit	Responders Based on MSIS-29v1 Score ^{a,b} No. (%)
2-month	16 (40.0)
6-month	19 (55.9)
	•

Responders were patients with a score change of ≥8 points on the MSIS-29v1 physical subscore

breviations: ITT, intent-to-treat; MSIS-29v1, 29-item Multiple Sclerosis Impact Scale, version 1

Safety

- A total of 42 AEs were reported; the most common AEs were nausea (n=2), urinary tract infection (n=2), headache (n=2), and rash (n=2)
- Nine SAEs were experienced by 8 patients; the most common of 12 AE terms reported were MS exacerbation (5) and weakness (2)
- Only one SAE, which included the terms dyspnea and atrial fibrillation, was reported as potentially related to RCI treatment and led to discontinuation from the study

Conclusions

- In this interim analysis of an observational study, RCI was effective in reducing MS relapse symptoms on the basis of MSIS-29v1 scores
- The AE and SAE profiles of RCI were similar to those observed in other RCI clinical trials; safety signals will continue to be assessed in future analyses of this trial
- Age and a higher MSIS-29 physical subscore at the time of relapse have been shown to be predictors of poor patient response to CS therapy,¹¹ which highlights the need for additional treatment options
- In addition to age at disease onset, longer disease duration and higher annualized relapse rates are predictors of poor response to relapse treatment with DMTs¹⁷
- Patients were considerably older in the current study (mean age 48) than in most previous reports on relapse recovery (mean ages in the mid 30s); therefore, the population in this study may be expected to experience greater rates of treatment resistance than previous
- Ongoing disease activity and exacerbations early in the course of MS relapse may prevent full remission with CS treatment,¹⁴ and limited data from previous studies showed that patients who previously failed CS therapy may benefit from RCI treatment¹⁵ In this interim analysis, 60% of patients with MS relapse had previous
- nonresponse/failure/intolerance to high-dose CS therapy
- An ongoing controlled study will examine the efficacy of RCI in this subpopulation (ClinicalTrials.gov Identifier: NCT03126760)

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