P070

Topline Results of a Prospective Observational Registry of Repository Corticotropin Injection for the Treatment of Multiple Sclerosis Relapse

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Introduction

- Despite advances in the treatment of multiple sclerosis (MS), patients continue to experience relapses
- Effective relapse treatment is critical for minimizing disability[1]
- Repository corticotropin injection (RCI; Acthar® Gel) is approved by the US Food and Drug Administration for the treatment of MS exacerbations in adults[2]
- A trial comparing RCI versus corticosteroids to treat MS exacerbations demonstrated similar marked improvement for both treatments.[3] In addition, RCI demonstrated positive clinical outcomes and lower numbers of adverse events (AEs) for patients who previously failed treatment with methylprednisolone[4]
- Although the use of RCI in MS has increased over the last decade, there is limited information available regarding the relationship between patient demographics, disease characteristics, precise dosing regimens used, and short- and long-term effects of intermittent RCI use for the treatment of MS relapses
- The objective of this multicenter, prospective, observational registry was to characterize the patient population receiving RCI for the treatment of acute MS relapse and describe their treatment patterns, MS exacerbation recovery, and safety outcomes

Methods

Patients and study design

- This was a multicenter, prospective, observational registry that aimed to enroll patients with MS who were being treated with RCI for MS exacerbations. A patient enrollment and data collection overview is presented in **Figure 1**
- Only MS patients deemed appropriate for RCI treatment were entered into the study. Key inclusion and exclusion criteria are presented in **Table 1**
- All treatment decisions were made at the discretion of the patient's healthcare provider and were not mandated by the study design or protocol
- The study drug was not provided free of charge by the Sponsor. RCI was obtained through usual commercial channels for prescription medicines
- Since it was possible for patients to have more than one exacerbation during the follow-up period, the exacerbation at the enrollment visit was defined as the index exacerbation and subsequent exacerbations were defined as relapses. The results presented here pertain only to the index exacerbation

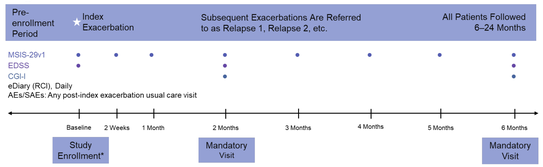
Efficacy and safety assessments

- The primary endpoint was change (from baseline to Month 2) in the MS Impact Scale (MSIS-29v1) physical subscale score
- Patients were also assessed with the Expanded Disability Status Scale (EDSS) and Clinical Global Impression of Improvement (CGI-I) scale
- Safety data (AEs and serious AEs [SAEs]) were collected at each usual care visit and at any relapses

Statistical analyses

- Effectiveness analyses were completed in the intent-to-treat (ITT) population (defined as all patients who received at least 1 dose of RCI and who contributed any data to the study)
- For the MSIS-29v1 and EDSS, tests of the null hypothesis that the mean change from baseline is equal to zero were carried out using two-sided paired t-tests at the alpha=0.05 level of significance (Wilcoxon signed rank test). P-values for the CGI-I are based on the Wilcoxon signed rank test for the null hypothesis of no change (ie, median score=4)
- The number of AEs and SAEs and the number of patients reporting AEs and SAEs were summarized descriptively

Figure 1. Patient Enrollment and Data Collection Overview



*Demographics, medical history, disease modulating therapies (prior 2 years), and concomitant medications collected at study enrollment.
Abbreviations: AE, adverse event; CGI-I, Clinical Global Impression-Improvement; EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; MSIS-29v1, Multiple Sclerosis Impact Scale Version 1; RCI, repository corticotropin injection; SAE, serious adverse event.

Table 1. Key Inclusion and Exclusion Criteria

Key Inclusion Criteria	Key Exclusion Criteria
• Male or Female ≥18 years of age • Has a clinically definite relapsing form of MS according to McDonald Criteria (2010 revision)[5] • Presents with an acute MS exacerbation, as determined by his/her treating clinician • Planning to initiate RCI for the treatment of an acute MS exacerbation • Capable of providing informed consent	• Diagnosis of progressive MS • Requires concomitant corticosteroid therapy • Receiving experimental drug therapy • A history of scleroderma, systemic fungal infections, ocular herpes simplex, or cancer within prior 5 years • Recent surgery or has a history of or the presence of a peptic ulcer within 6 months prior to study entry, congestive heart failure, or sensitivity to proteins of porcine origin

Abbreviations: MS, multiple sclerosis; RCI, repository corticotropin injection

Results

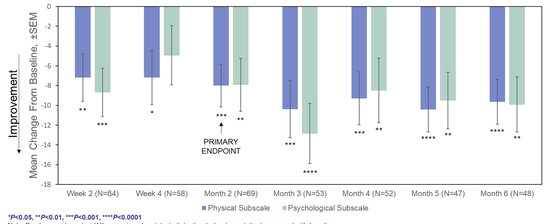
Patient disposition and demographics

- Of 145 patients enrolled, 82 (56.6%) completed the study. The ITT population comprised 125 patients. Mean age was 47 years; 88% of patients were female, and 84% were Caucasian
- The average time since diagnosis of MS was 10.2 years
  - 58.4% of patients had experienced a relapse within the last 2 years
  - 60% had a history of insufficient treatment response, intolerance, or limited intravenous access associated with high-dose corticosteroids

MSIS-29v1 scores

- After treatment with RCI, mean MSIS-29v1 physical subscale scores decreased from baseline (55.69, scaled to 100) by 7.99 at 2 months (P=0.0002) and by 9.64 at 6 months postbaseline (P<0.0001; **Figure 2**)
- A post hoc analysis of MSIS-29v1 physical subscale scores by the number of doses administered was also performed. Numbers were too small for a direct statistical comparison, but there was a clear trend that patients taking >5 doses of RCI had greater improvement in MSIS-29v1 physical subscale scores than patients taking ≤5 doses of RCI (**Figure 3**)

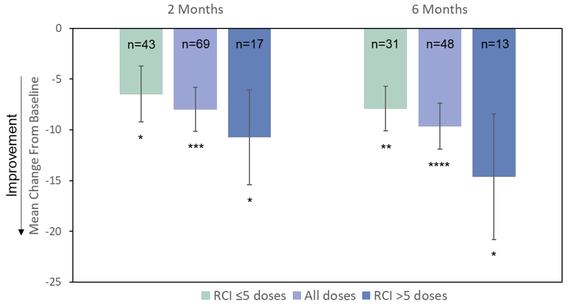
Figure 2. Mean Change From Baseline on the MSIS-29v1 Scale



*P<0.05, **P<0.01, ***P<0.001, ****P<0.0001
Note: P-values are based on Wilcoxon signed rank tests (intention-to-treat population) compared with baseline.
Abbreviations: MSIS-29v1, Multiple Sclerosis Impact Scale Version 1; SEM, standard error of the mean.

Results (cont'd)

Figure 3. Mean Change From Baseline on the MSIS-29v1 Physical Subscale by Number of Doses Administered

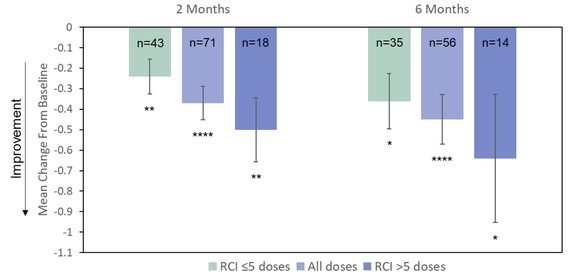


*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001
Note: P-values are based on Wilcoxon signed rank tests (intention-to-treat population) compared with baseline.
Abbreviations: MSIS-29v1, Multiple Sclerosis Impact Scale Version 1; RCI, repository corticotropin injection; SEM, standard error of the mean.

EDSS scores

- Mean EDSS scores decreased from baseline (3.92, scaled to 10) by 0.37 at 2 months (P<0.0001) and by 0.45 at 6 months (P<0.0001; **Figure 4**)
- A post-hoc analysis of EDSS data by the number of doses administered was also performed. N's are too small for a direct statistical comparison, but a clear trend was evident that patients taking >5 doses of RCI had greater improvement in EDSS scores compared to patients taking ≤5 doses of RCI (**Figure 4**)
- The average time since diagnosis of MS was 10.2 years

Figure 4. Mean Change From Baseline on the EDSS Scale by Number of Doses Administered

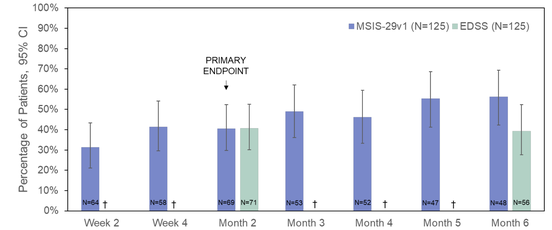


*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001
Note: P-values are based on Wilcoxon signed rank tests (intention-to-treat population) compared with baseline.
Abbreviations: EDSS, Expanded Disability Status Scale; RCI, repository corticotropin injection; SEM, standard error of the mean.

Responders

- By month 2, 40.6% of patients were identified as RCI responders on the MSIS-29v1 Physical Subscale and EDSS, as presented in **Figure 5**

Figure 5. Percentage of Patients Who Were Responders to Treatment (MSIS-29v1 Physical Subscale: ≥8-Points Improvement; EDSS: ≥0.5 Point-Improvement)



†EDSS data collected only at Months 2 and 6.
Abbreviations: CI, confidence interval; EDSS, Expanded Disability Status Scale; MSIS-29v1, Multiple Sclerosis Impact Scale Version 1.

- CGI-I scores indicated improvement in 63.4% of patients at 2 months (45/71, P<0.0001) and 61.4% of patients at 6 months (35/57, P<0.0001)
- Disease-modifying therapies used most often during the study were dimethyl fumarate (20.0%), natalizumab (18.4%), teriflunomide (11.2%), glatiramer acetate (8.8%), ocrelizumab (8.0%), fingolimod (6.4%), and interferon beta-1a (5.6%)
- A total of 83 AEs were reported by 35 (28.0%) patients. A total of 16 SAEs were reported by 11 (8.8%) patients

Conclusions

- Results from this prospective observational study of RCI in patients experiencing an MS exacerbation showed statistically significant and clinically meaningful improvements as early as 2 weeks after the start of treatment on:
  - MSIS-29v1 physical subscale
  - MSIS-29v1 psychological subscale
  - Clinician-rated scales (EDSS and CGI-I)
- Primary objective: MSIS-29v1 physical subscale scores were statistically significant at 2 months postbaseline
- These results are especially relevant because 60% of the patients had a history of insufficient treatment response to corticosteroids. In addition, the patient population in this study was older and had MS longer than is typical for other MS relapse studies
- These results add further evidence supporting the effectiveness and tolerability of RCI as a treatment for MS relapse in a real-world setting

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