RT01

A Prospective Observational Registry of H.P. Acthar® Gel for the Treatment of Multiple Sclerosis Relapse

Bryan R. Due, PhD[1]; Patricia K. Coyle, MD[2]; Patrice M. Becker, MD[3]; and Timothy Vollmer, MD[4]

[1]Clinical Sciences, Mallinckrodt Pharmaceuticals, Hampton, NJ; [2]Stony Brook University, Stony Brook, NY; [3]Science & Technology, Mallinckrodt Pharmaceuticals, Hampton, NJ; [4]Department of Neurology, University of Colorado Denver, Aurora, CO

Introduction

- During the last several years, there has been tremendous expansion in the range of agents available to treat multiple sclerosis (MS)[1,2]
  - Several disease-modifying therapies (DMTs) are currently available, and several more are under investigation
    - DMTs reduce the occurrence of MS relapses, slow disability worsening, and decrease activity on magnetic resonance imaging
- Despite these advances in treatment, many patients with MS experience relapses
- High-dose corticosteroid therapy (eg, with methylprednisolone) is the mainstay of acute treatment of MS relapses[3,4]
  - Results from randomized, double-blind clinical trials suggest that 19% to 35% of patients may not adequately respond to this therapy[5,6]
- For patients who do not respond to or are unable to tolerate high-dose corticosteroids, options for acute treatment of relapses are limited
- Incomplete recovery from MS relapses may contribute to accrual of disability, highlighting the importance of effective relapse treatment[4,7,8]
- Repository corticotropin injection (RCI; H.P. Acthar Gel) contains a porcine-derived analogue of adrenocorticotropic hormone (ACTH) approved by the US Food and Drug Administration for treatment of MS relapses in adults[9]
  - Anti-inflammatory and immunomodulatory effects of ACTH in MS historically were attributed solely to its ability to stimulate endogenous cortisol, but more recent evidence suggests that corticosteroid-independent melanocortin receptor–mediated activity may contribute[10]
- Study objectives
  - Characterize the population of patients who receive RCI for MS relapses
  - Identify treatment patterns, MS relapse recovery, and safety outcomes
- This interim report summarizes data collected through October 27, 2016

Methods

Study Design

- Ongoing multicenter, prospective, 24-month, observational registry study
- Target enrollment: 260 patients at up to 60 sites (ie, neurology practices in the United States that treat adult patients with MS)

Enrollment and Data Collection

- Potentially eligible patients are recruited during routine care visits at the study sites
  - Those who meet the study eligibility criteria (**Table 1**) and provide informed consent are enrolled

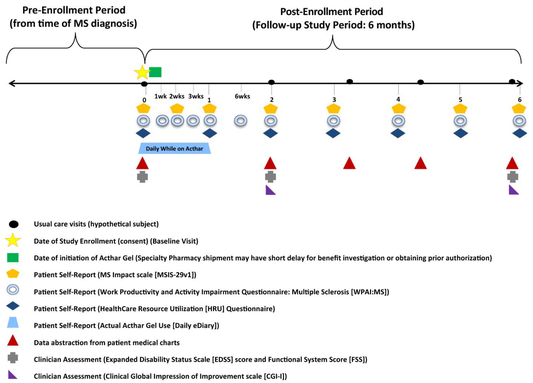
Table 1: Key Inclusion and Exclusion Criteria

Inclusion
Age ≥18 years
Clinically definite relapsing form of MS according to McDonald criteria (2010 revision)[11]
Acute MS exacerbation as determined by treating clinician
Planning to initiate RCI therapy for acute MS exacerbation
Exclusion
Diagnosis of progressive MS
Requirement for concomitant corticosteroid therapy
Receiving experimental drug therapy
History (within 5 years) of scleroderma, systemic fungal infections, ocular herpes simplex, or cancer
Recent surgery or a history (within 6 months) or presence of a peptic ulcer, congestive heart failure, or sensitivity to proteins of porcine origin
Pregnancy, breastfeeding, or (if woman of childbearing potential) unwillingness to use appropriate contraception

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

- Each patient will be followed up for a minimum of 6 months and a maximum of 24 months
- Data will be abstracted from patient medical records at predefined time points (**Figure 1**)
- RCI will be obtained via the usual commercial channels for prescription medications
- While receiving RCI, patients will record data on daily RCI use in electronic diaries (**Figure 1**)
- Patients will also complete the following self-report instruments at the times specified in **Figure 1**
  - 29-item Multiple Sclerosis Impact Scale, version 1 (MSIS-29v1)
  - 6-question Work Productivity and Activity Impairment questionnaire for multiple sclerosis (WPAI:MS)
  - 5-question healthcare resource utilization (HRU) questionnaire
- The clinician assessments below will be administered at the times depicted in **Figure 1**
  - Expanded Disability Status Scale (EDSS) and Functional System Score (FSS)
  - Clinical Global Impression of Improvement (CGI-I) scale

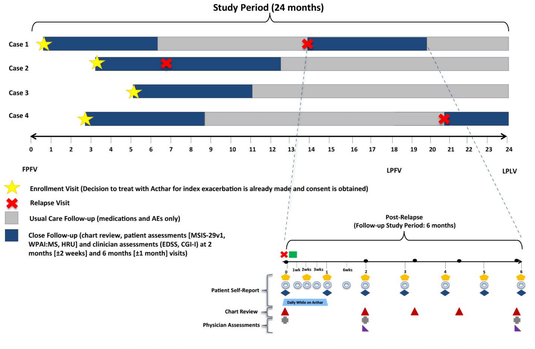
Figure 1. Patient Enrollment and Data Collection Overview[a,b]



[a] Patients who experience post-enrollment relapses while the study is ongoing will be followed up for the relapse as specified for the index exacerbation (ie, for 6 months) or until study close (if the latter occurs before 6 months have elapsed). *Index exacerbation* is defined as the MS exacerbation at study enrollment.
[b] SAEs will be reported within 24 hours of identification, even when outside of usual care visits.
Abbreviations: MS, multiple sclerosis; SAE, serious adverse event.

- Because patients may have >1 MS exacerbation during the follow-up period, the exacerbation at study enrollment is defined as the *index exacerbation*, and subsequent exacerbations are defined as *relapses*
  - Relapses that occur during the study will be followed up as specified for the index exacerbation (ie, for 6 months) or until the study ends (if the latter occurs before 6 months have elapsed) (**Figures 1 and 2**)

Figure 2. Data Collection Schematic With Case Examples



Abbreviations: AE, adverse event; CGI-I, Clinical Global Impression of Improvement; EDSS, Expanded Disability Status Scale; FPFV, first patient first visit; HRU, healthcare resource utilization; LPFV, last patient first visit; LPLV, last patient last visit; MSIS-29v1, 29-item Multiple Sclerosis Impact Scale, version 1; WPAI:MS, Work Productivity and Activity Impairment questionnaire for multiple sclerosis.

Results

Patient Characteristics and Medication Use at Enrollment

- As of October 27, 2016, 45 patients had enrolled in the study and provided data
- Patient characteristics and medication use at enrollment are shown in **Tables 2** and **3**, respectively
- 23 patients (51%) had a history of insufficient treatment response to, intolerance of, or intravenous access problems with high-dose corticosteroid therapy

Table 2. Patient Characteristics at Enrollment

Characteristic	Initial Screening (N=45)
Age,[a] mean (SD), y	50.2 (10.7)
Gender, No. (%)	
Male	5 (11)
Female	31 (69)
Missing	9 (20)
Race, No. (%)	
Black/African American	4 (9)
White	29 (64)
Hispanic	1 (2)
No information/missing	11 (24)
EDSS score,[b,c] mean (SD)	4.4 (1.9)
Previous treatments for MS, No. (%)	
Methylprednisolone	13 (29)
RCI	11 (24)
IV steroids (unspecified)	2 (4)
Prednisone	2 (4)
Glatiramer acetate	1 (2)
Teriflunomide	1 (2)
None	1 (2)
Unknown	1 (2)
No information	12 (27)
MSIS-29v1 physical section score,[d,e] mean (SD)	65.4 (19.4)

[a] Data were available for 36 patients. [b] Data were available for 27 patients. [c] Rated on a scale from 0 (normal neurologic exam) to 10 (death due to MS). [d] Data were available for 35 patients. [e] Scored on a scale from 0 to 100, with 100 representing the worst possible score.
Abbreviations: EDSS, Expanded Disability Status Scale; IV, intravenous; MSIS-29v1, 29-item Multiple Sclerosis Impact Scale, version 1; RCI, repository corticotropin injection; SD, standard deviation.

Table 3. Summary of Medication Use at Enrollment (N=45)

Characteristic	No. (%)
DMT use	
Yes	32 (71)
No	5 (11)
Missing	8 (18)
Specific DMT use[a]	
Dimethyl fumarate	15 (33)
Glatiramer acetate	9 (20)
Natalizumab	8 (18)
Alemtuzumab	5 (11)
Teriflunomide	5 (11)
Fingolimod	4 (9)
Interferon β-1a	2 (4)
Other concomitant medication/supplement use[a,b]	
Cholecalciferol	10 (22)
Ergocalciferol	8 (18)
Baclofen	7 (16)
Fampridine	6 (13)
Gabapentin	6 (13)
Cyanocobalamin	5 (11)
Multivitamins	5 (11)
Amantadine	3 (7)
Levothyroxine sodium	3 (7)
Topiramate	3 (7)

[a] Some patients were receiving >1 medication at time of enrollment. [b] Only medications used by ≥5% of patients are listed.
Abbreviations: DMT, disease-modifying therapy; RCI, repository corticotropin injection.

RCI Use

- Data on RCI use have been collected for 31 patients and are summarized in **Table 4**

Table 4. Summary of RCI Use (n=31)

	Median (IQR)
No. of doses per patient	5.0 (5.0)
Strength per dose, U	80 (0)
No. of days dosed[a]	5.0 (5.0)
Total dose per day, U	80 (0)

[a] RCI dosing was on 5 consecutive days for 22 patients (71%).
Note: RCI was injected subcutaneously in all patients who specified the mode of administration.
Abbreviations: IQR, interquartile range; RCI, repository corticotropin injection.

Safety

- 9 adverse events (AEs), including 3 serious adverse events (SAEs), have been reported (**Table 5**)
- All SAEs were considered not related or unlikely related to RCI, and all patients recovered

Table 5. Summary of AEs

Subject	AE Term	Considered Serious
A	Nausea	No
	Vomiting	No
	Headache	No
B	UTI	Yes
C	Trigeminal neuralgia	No
D	UTI	No
	Acute sinusitis	No
E	Asthenia	Yes
F	MS relapse	Yes

Abbreviations: AE, adverse event; MS, multiple sclerosis; SAE, serious adverse event; UTI, urinary tract infection.

Conclusions

- Data from this ongoing study will expand current understanding of RCI use for the treatment of MS relapses and will provide information regarding
  - Characteristics of patients treated with RCI
  - MS relapse treatment patterns
  - Treatment response and MS relapse recovery
  - RCI safety
  - Characteristics of patients who experience additional MS relapses (ie, following the index exacerbation) during the study period
- The data collected to date suggest that RCI is typically dosed using a regimen of 80 U/d for a period of 5 days
  - Additional data on RCI dosing and therapeutic response collected during the remainder of the study could be used to explore possible clinical implications for the treatment of MS relapses
- Study enrollment is anticipated to conclude by the end of 2017

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