Dear Healthcare Professional,

Thank you for your unsolicited request for information. Accompanying this letter is the following information you requested on Purified Cortrophin® Gel. If we can be of any further assistance, please contact our Medical Information department at (844) CORT-GEL (844-267-8435) between the hours of 9:00 AM to 7:00 PM ET (6:00 AM to 4:00 PM PT), Monday through Friday or via email at cortrophinmedinfo@anipharmaceuticals.com.

Purified Cortrophin Gel is indicated in the following disorders:

1. Rheumatic disorders:
As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in:
- Psoriatic arthritis.
- Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy).
- Ankylosing spondylitis.
- Acute gouty arthritis.

2. Collagen diseases:
During an exacerbation or as maintenance therapy in selected cases of:
- Systemic lupus erythematosus.
- Systemic dermatomyositis (polymyositis).

3. Dermatologic diseases:
Severe erythema multiforme (Stevens-Johnson syndrome).
Severe psoriasis.

4. Allergic states:
Atopic dermatitis
Serum sickness.

5. Ophthalmic diseases:
Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as:
- Allergic conjunctivitis.
- Keratitis.
- Iritis and iridocyclitis.
- Diffuse posterior uveitis and choroiditis.
- Optic neuritis.
- Chorioretinitis.
- Anterior segment inflammation.

6. Respiratory diseases:
Symptomatic sarcoidosis.

7. Edematous states:
To induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus.

8. Nervous system:
Acute exacerbations of multiple sclerosis.

Purified Cortrophin Gel is contraindicated for intravenous administration.

Purified Cortrophin Gel is contraindicated in patients with scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive heart failure, hypertension, or sensitivity to proteins derived from porcine sources.

Purified Cortrophin Gel is contraindicated in patients with primary adrenocortical insufficiency or adrenocortical hyperfunction.

Please see the enclosed Purified Cortrophin Gel Prescribing Information (PI) for detailed information including Warnings and Precautions and Adverse Reactions as well as the appropriate use of Purified Cortrophin Gel.

Thank you for your inquiry.

Sincerely,

Steve Wu, PharmD
ANI Pharmaceuticals Medical Information

Use of Purified Cortrophin® Gel (Repository Corticotropin Injection USP) 80 U/mL in Patients With Systemic Dermatomyositis or Polymyositis

Abstract

- This document provides summary information pertaining to Purified Cortrophin Gel® (repository corticotropin injection USP) and its indication for use in systemic dermatomyositis or polymyositis.
- The active agent in Cortrophin Gel is porcine-derived adrenocorticotropic hormone (ACTH peptide, amino acids 1-39), which is biologically similar to endogenous, human ACTH, and of the same class as other, FDA-approved natural-product and synthetic ACTH formulations.
- To date, there are no published clinical data available that directly interrogate the clinical efficacy and safety of Cortrophin Gel in patients with systemic dermatomyositis or polymyositis.
- Summarized in this document are the results of a literature search of publicly available, peer-reviewed clinical studies of other natural-product and synthetic formulations of ACTH.
- The included selection is limited to key studies in patients with systemic dermatomyositis or polymyositis, in retrospective or prospective studies, registries, retrospective medical records reviews, and claims database analyses of 10 or more patients. In aggregate, the 6 included studies represent a total of 1026 patients with systemic dermatomyositis or polymyositis.

Note that this document is for information purposes only. Please refer to the Purified Cortrophin Gel (repository corticotropin injection USP) USPI for full prescribing information. ANI Pharmaceuticals does not recommend the use of its products in any manner inconsistent with the FDA-approved labeling.

To report an adverse event for any ANI Pharmaceuticals product, please call 1-800-308-6755 or contact the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Email: drugsafety@anipharmaceuticals.com.

Introduction

Clinical Background[1]

Purified Cortrophin Gel® (repository corticotropin injection USP) is approved by the FDA for use in collagen diseases, during an exacerbation or as maintenance therapy in selected cases of systemic dermatomyositis (polymyositis).

Composition of Purified Cortrophin Gel[1]

Purified Cortrophin Gel is a porcine-derived purified corticotropin, adrenocorticotropic hormone (ACTH), in a sterile solution of gelatin. It is made up of a complex mixture of ACTH, ACTH-related peptides, and other porcine pituitary-derived peptides.

The drug product is a sterile preparation containing 80 USP units per mL and it contains 0.5% phenol (as preservative), 15.0% gelatin (for prolonged activity), water for injection, and the pH is adjusted with hydrochloric acid and sodium hydroxide.

Purified Cortrophin Gel contains the porcine-derived ACTH (1-39) with the following amino acid sequence:

Purified Cortrophin Gel Clinical Pharmacology[1]

ACTH, the active agent in Purified Cortrophin Gel, is the anterior pituitary hormone which stimulates the functioning adrenal cortex to produce and secrete adrenocortical hormones.

Following administration of a single intramuscular (IM) injection of 80 units of Purified Cortrophin Gel to healthy volunteers (n=20) in an open label pharmacodynamic study, the median time (range) to reach peak plasma cortisol concentration was 8 (3 to 12) hours. The baseline corrected geometric mean maximum (CV%) cortisol levels were 34.52 µg/dL (28.2%).

The porcine-derived ACTH (1-39) found in Purified Cortrophin Gel is biologically similar to endogenous human ACTH[2], and of the same class as other natural-product and synthetic ACTH formulations.[3,4]

ANI conducted a study on the pharmacodynamic effect of Purified Cortrophin Gel, including E_{max}, $AUEC_{0-24}$, and TE_{max}, and compared it with the response of the same or similar depot structures from published literature.[5]

Select Clinical Data in Support of Cortrophin Gel in Systemic Dermatomyositis or Polymyositis

Study Selection

ANI Pharmaceuticals is not aware of any other published (or unpublished) randomized clinical trials or adequately designed studies using Purified Cortrophin Gel for the treatment of systemic dermatomyositis or polymyositis that directly interrogate its clinical efficacy and safety.

Below is a selection of peer-reviewed publications of clinical studies that use Acthar Gel, which shares the same porcine-derived active agent, ACTH, as Purified Cortrophin Gel.[6] The summary below provides an overview of the available clinical evidence of in-class ACTH-based therapies, with references to source material.

Based on results of a PubMed search (performed April 2024), the selection is limited to retrospective or prospective studies including 10 or more patients with systemic dermatomyositis or polymyositis.

This summary includes 6 studies (**Tables 1 and 2)** totaling 1026 patients with systemic dermatomyositis or polymyositis that were treated with Acthar Gel.

Table 1: Summary of Select Clinical Data in Support of Purified Cortrophin Gel Use in Patients With Systemic Dermatomyositis or Polymyositis

Study	Study Type	ACTH, n	Comparator, n	Patient Population	Study Treatment	Efficacy	Safety
Repository Corticotropin Injection							
Levine 2016[7]	Registry	24	N/A	Adult male or female patients with refractory DM/PM	80 IU SQ twice weekly; doses adjusted at physician direction	14/24 refractory patients (58.3%) responded to RCI treatment. Patients with DM and PM had a 57% and 59% response rate to RCI, respectively. Use of MMF was associated with RCI treatment responsiveness (5/5, 100%; p=0.053).	Overall, RCI treatments were well tolerated, with 41.7% of patients reporting mild-to-moderate AEs, with worsening of diabetes (12.5%) and edema (12.5%) being reported most frequently. No patient discontinued treatment exclusively due to AEs.
Knight 2017[8]	Administrative claims analysis from 3 databases	132	IVIg: 1,150 Rituximab: 562 IVIg + Rituximab: 123	Patients diagnosed with either DM or PM and were treated with RCI, IVIg, or IVIg and rituximab	RCI on at least one medical or pharmacy claim between July 1, 2010, and May 31, 2014	The RCI cohort had fewer PPPM hospitalizations compared with IVIg (p=0.049) and shorter LOS when hospitalized with IVIg (p=0.004) and IVIg + rituximab (p<0.001). The RCI cohort had fewer PPPM HOPD visits compared with the IVIg cohort (p<0.001), the R cohort (p<0.001), and the IVIg + rituximab cohort (p<0.0001). Fewer PPPM physician office visits were observed among the RCI cohort compared with the IVIg cohort (p=0.035). Other differences were not significant between cohorts.	Not reported
Myung 2017[9]	Administrative health care claims database	606	N/A	Pediatric and adult patients with rheumatologic conditions who newly initiated RCI	RCI treatment with claims 2 years prior to first RCI use and 1 year after last RCI use	Prednisone and DMARD use (but not biologics) significantly decreased from the 6 months prior to RCI use to the 6 months after RCI use (p<0.05). Mean prednisone dose was not significantly different in the 12 weeks prior to RCI vs the 12 weeks after RCI.	Not reported

MED-US-CG-2200033 05/2024.

Study	Study Type	ACTH, n	Comparator, n	Patient Population	Study Treatment	Efficacy	Safety
Nelson 2017[10]	Retrospective, medical record review	254	N/A	Patients with rheumatologic disease (RA, PsA, DM or PM, or SLE) who had received RCI therapy	≥1 course of RCI therapy 3-24 months before medical record review	In the 3 months before and after RCI therapy initiation, hospital admissions, hospital days, and outpatients visits were significantly reduced post-RCI vs pre-RCI ($p<0.05$).	Not reported
Aggarwal 2018[11]	Prospective, open-label	10	N/A	Patients at least 18 years of age or older with a diagnosis of definite or probably DM/PM that was refractory to glucocorticoids or ≥1 immunosuppressive agent	80 IU SQ twice weekly	70% (7/10) of patients met the DOI[a] 90% (9/10) of patients had minimal improvement using the 2016 ACR-EULAR myositis response criteria. 20%, 30%, and 40% of patients achieved major, moderate, and minor improvements, respectively. Mean dose of prednisone was significantly reduced at 6 months of RCI therapy ($p=0.01$).	RCI was generally safe and well tolerated over the 24-week study period. SAEs: 5 total in 3 patients. AEs: 22 total in 8 patients, with the most common being injection site bruising and rash (n=4), hyperglycemia (n=3), and calcinosis, hypertension, infection, and insomnia (n=2 each).
Saygin 2020[12]	Longitudinal follow-up from Aggarwal et al.	8	N/A	All patients with refractory DM or PM who were enrolled in the 6-month open-label RCI trial[11]	80 IU SQ twice weekly	50% (4/8) remained stable, whereas the remaining 4 patients had a flare, with 3 requiring an increase in prednisone dose. Among the 4 stable patients, 2 had no significant change in all 6 CSMs. During the 6-month follow-up period, 3 patients who were off prednisone remained off prednisone, 1 patient maintained the same dose of prednisone, 1 flared and restarted prednisone, and 2 patients flared and increased prednisone. 75% (6/8) met the DOI at 12 months.	1 patient was restarted on RCI and reported dizziness that improved with dose reduction. This same patient developed segmental sigmoid colitis and two upper respiratory tract infections while on RCI. Another patient developed avascular necrosis of the femoral head 6 months after the RCI trial. 2 patients reported worsening calcinosis, 2 and 5 months after completion of the trial. 1 patient had two URTIs, 3 and 6 months after the RCI trial. 1 patient had shingles 3 months after completion of the RCI trial. No patient developed diabetes, hypertension or cushingoid features during the follow-up period.

MED-US-CG-2200033 05/2024.

[a]Defined as any 3 of the 6 CSMs improved by ≥20%, with no more than 2 CSMs worsening by ≥25% (worsening measure cannot include MMT).

ACR-EULAR, American College of Rheumatology-European League Against Rheumatism; ACTH, adrenocorticotropic hormone; AE, adverse event; CSM, core set measure; DM, dermatomyositis; DMARD, disease-modifying antirheumatic drug; DOI, definition of improvement; HOPD, hospital outpatient department; IMACS, International Myositis Assessment and Clinical Studies; IU, international unit; IVIg, intravenous immunoglobulin; LOS, length of stay; MMF, mycophenolate mofetil; MMT, Manual Muscle Testing; MRU, medical resource utilization; PM, polymyositis; PPPM, per-patient per-month; PsA, psoriatic arthritis; QW, weekly; RA, rheumatoid arthritis; RCI, repository corticotropin injection; SAE, serious adverse event; SLE, systemic lupus erythematosus; SQ, subcutaneous; URTI, upper respiratory tract infection.

MED-US-CG-2200033 05/2024.

Table 2: Prior and Concomitant Medications for Systemic Dermatomyositis or Polymyositis

Study	Prior therapy	Concurrent therapy to ACTH
Levine 2016[7]	Corticosteroids (n=24)	Prednisone (n=12), methotrexate (n=9), IVIg (n=7), MMF (n=5), azathioprine (n=1), and cyclosporine (n=1)
Knight 2017[8]	Corticosteroids (n=110), methotrexate (n=53), azathioprine (n=38), IVIg (n=30), MMF (n=29), and rituximab (n=7)	Not reported
Myung 2017[9]	Corticosteroids (76%), DMARD (64%), and biologics (1%)	Corticosteroids (68%), DMARD (61%), and biologics (1%)
Nelson 2017[10]	Mean of 2.9 medications prior to initiation of RCI therapy	Not reported
Aggarwal 2018[11]	Prednisone (n=11), methotrexate (n=10), MMF (n=7), azathioprine (n=5), IVIg (n=3), tacrolimus (n=2), and rituximab (n=1)	Prednisone (n=11), methotrexate (n=5), MMF (n=5), azathioprine (n=3), hydroxychloroquine (n=2), and tacrolimus (n=1)
Saygin 2020[12]	Reported in Aggarwal 2018[11] Reported in Aggarwal 2018[11]	Reported in Aggarwal 2018[11] Reported in Aggarwal 2018[11]

ACTH, ACTH, adrenocorticotropic hormone; DMARD, disease-modifying antirheumatic drug; IVIg, intravenous immunoglobulin; MMF, mycophenolate mofetil; RCI, repository corticotropin injection.

MED-US-CG-2200033 05/2024.

Study Details Supporting Use of Cortrophin Gel in Patients With Systemic Dermatomyositis or Polymyositis

The following information encompasses the studies listed in **Table 1** and **Table 2**.

Levine 2016 et al[7]

Levine et al, 2016 was the peer-reviewed publication of registry data presented at the American Association of Neurology.

This registry sought to study the demographics and determine the effect of RCI treatment on the clinical outcomes (dosing, efficacy, and safety) of patients with dermatomyositis (DM) or polymyositis (PM).

Eligible patient population

All adults aged 18 to 85 years, with a clinical/pathological diagnosis of DM or PM refractory to first- and second-line therapies, confirmed by muscle biopsy, were eligible for this registry study.

Patient demographics

Eighteen (75%) patients were female, and 6 (25%) were male. Twenty-four patients had a confirmed diagnosis of DM (n=7) or PM (n=17), with a median age of 58.5 (range 26 to 77). Twenty-two patients received concomitant therapy of prednisone (n=12), methotrexate (n=9), intravenous immunoglobulin (IVIg; n=7), mycophenolate mofetil (MMF; n=5), azathioprine (n=1), and cyclosporine (n=1).

Dosing

Almost all patients (n=22) received 80 IU RCI SC twice weekly. One patient received 40 IU RCI twice weekly while another patient received 80 IU RCI once weekly.

Response to ACTH

Fourteen (58.3%) patients responded to RCI treatment, with a response rate of 57% in patients with DM and 59% in those with PM. Response to treatment occurred frequently in patients with disease activity at baseline ($p<0.0001$), but no association was observed between responsiveness and class of myositis or disease duration prior to RCI treatment. Responders also had a higher mean duration of RCI treatment (9.7 months) vs nonresponders (3.5 months; $p<0.0001$). Concomitant MMF was associated with RCI therapy response; all 5 patients who received concurrent MMF achieved a response, while 47.4% of the remaining patients prescribed an immunosuppressant responded to combination RCI therapy.

Safety

Overall, RCI treatments were well tolerated, with 41.7% of patients reporting mild-to-moderate adverse events (AEs), with worsening of diabetes (12.5%) and edema (12.5%) being reported most frequently. Other AEs reported included gastric reflux, headache, increased blood pressure, nausea, vertigo, and weight gain (4.2% each). No patient discontinued treatment exclusively due to AEs.

Treatment duration and patient follow-up

RCI was administered for a median duration of 6 months, ranging from 2 to 18 months. Patients were followed for 12 months.

Knight et al, 2017[8]

This retrospective observation study sought to compare real-world medical resource utilization (MRU) and associated costs between patients with DM or PM treated with RCI and those treated with IVIg and/or rituximab.

Eligible patient population

Patients included in this administrative claims database study were diagnosed with either DM or PM and were treated with RCI, IVIg, and/or rituximab.

Patient demographics

Of the patients identified, 132 received RCI, 1150 received IVIg, 562 received rituximab, and 123 received IVIg + rituximab. Prior to initiating RCI therapy patients received corticosteroids (n=110), methotrexate (n=53), azathioprine (n=38), IVIg (n=30), MMF (n=29), and rituximab (n=7). Concurrent therapies were not reported.

Dosing

Patients receiving RCI on ≥1 medical or pharmacy claim between July 1, 2010 (1 year post-start of study observation period) and May 31, 2014 (1 month prior to the end of study observation period). Patients receiving IVIg and/or rituximab had ≥1 medical or pharmacy claim between July 1, 2010, and May 31, 2014 and no claim for RCI over the entire study observation period (from July 1, 2009 to June 30, 2014). The IVIg cohort included patients with an IVIg product on at least 1 claim; for rituximab, it was those with rituximab on at least 1 claim. The IVIg + rituximab cohort was patients with at least 1 claim for both an IVIg product and rituximab (this cohort is a subset of those in the IVIg and rituximab cohorts).

Response to ACTH

On average in the postindex period, the RCI cohort had less MRU than the other 3 cohorts. The RCI cohort had fewer per-patient per-month (PPPM) hospitalizations compared with IVIg ($p=0.049$) and shorter length of stay (LOS) when hospitalized compared with IVIg ($p=0.004$) and IVIg + rituximab ($p<0.001$). The RCI cohort had fewer PPPM hospital outpatient department (HOPD) visits compared with the IVIg cohort ($p<0.001$), the rituximab cohort ($p<0.001$), and the IVIg + rituximab cohort ($p<0.0001$). Fewer PPPM physician office visits were observed among the RCI cohort compared with the IVIg cohort ($p=0.035$). The average PPPM total visit costs associated with hospitalizations and nonhospitalizations were also lower than the other 3 cohorts.

Safety

Safety data were not reported in this study.

Treatment duration and patient follow-up

Treatment duration was not calculated in this study, but patients were followed for 5 years from July 1, 2009, to June 30, 2014.

Myung et al, 2017[9]

This study sought to analyze prescription patterns of RCI in patients with rheumatologic conditions and to examine the trend of other prescription medication use, especially prednisone, after RCI administration.

Eligible patient population

This study used the Symphony Health Solutions Claims database (2008-2015) that captures 85% of health events in the United States, including Medicare and Medicaid. Pediatric and adult patients with newly initiated RCI therapy for rheumatologic conditions were included; only patients with claims 2 years prior to first RCI and 1 year after the last RCI were included in the analysis.

Patient demographics

Six hundred six patients with either DM or PM were identified who met the criteria for inclusion in the study. In the 6 months prior to initiation of RCI therapy, 76% of patients received corticosteroids, 64% a disease-modifying antirheumatic drug (DMARD) and 1% biologics; during RCI use, patients also received corticosteroids (68%), DMARD (61%), and biologics (1%), respectively.

Dosing

Most patients received 80 IU twice weekly (68%), with 16% receiving 200 IU per week.

Response to ACTH

Prednisone and DMARD use (but not biologics) were significantly decreased from the 6 months prior to RCI use to the 6 months after RCI use ($p<0.05$). The mean prednisone dose was not significantly different in the 12 weeks prior to RCI vs the 12 weeks after RCI.

Safety

Safety data were not reported in this study.

Treatment duration and patient follow-up

Patients with either DM or PM received RCI for a mean of 157 days. Patients were followed longitudinally for ≥3 years, for the 2 years prior to first RCI use and 1 year after last RCI use.

Nelson et al, 2017[10]

This study sought to describe patient characteristics, RCI treatment patterns, and barriers to RCI use in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), DM or PM, or systemic lupus erythematosus (SLE), and to compare MRU before and after RCI treatment in a large patient population.

Eligible patient population

This study was a national, retrospective, observational study of patients with rheumatologic disease, including RA, PsA, either DM or PM, or SLE. Physicians eligible to participate in the study were those with at least 1 patient who had received RCI therapy. For inclusion, patients had a diagnosis of DM or PM and completion of at least 1 course of RCI therapy in ≤24 months and ≥3 months before medical record review.

Patient demographics

Four hundred forty-nine physicians participated in the study and identified 254 patients with DM or PM. Median age was 50.26 years, and 53% of patients were female. For patients with DM or PM, 75% were identified as receiving their first use of an RCI regimen, with 16% a second-time use and 9% a third-time use. A mean of 2.9 medications had been used prior to initiation of RCI therapy. Other prior therapies and concurrent medications were not reported.

Dosing

Patients received at least 1 course of RCI therapy 3-24 months before medical record review.

Response to ACTH

In the 3 months before and after RCI therapy initiation, hospital admissions, hospital days, and outpatient visits were significantly reduced post-RCI vs pre-RCI ($p<0.05$).

Safety

Safety data were not reported in this study.

Treatment duration and patient follow-up

Treatment duration was not captured in this study. The maximal follow-up time of 24 months was limited by the inclusion criteria.

Aggarwal et al, 2018[11]

The primary end point for the study was the International Myositis Assessment and Clinical Studies (IMACS) definition of improvement (DOI): 3 of any of the 6 core set measures (CSMs) improved by ≥20%, with no more than 2 CSMs worsening by ≥25% (worsening measure cannot include the Muscle Manual Testing [MMT]).

Eligible patient population

Patients were adults with a diagnosis of definite or probable DM or PM (PM either possessed a myositis-associated autoantibody or underwent adjudication to confirm PM diagnosis by another myositis expert). Patients were also refractory and had active disease defined as failing ≥2 months of high-dose glucocorticoids or intolerance to this therapy, and/or ≥1 conventional immunosuppressive agent at near maximal doses for ≥3 months (eg, methotrexate, azathioprine, tacrolimus, cyclosporin, MMF, tumor necrosis factor [TNF] inhibitor, or rituximab).

Patient demographics

Of the 11 patients (6 with DM and 5 with PM) who began the study, 10 completed the 24-week course of RCI therapy without dose modification. At baseline, patients had received the following prior therapies: prednisone (n=11), methotrexate (n=10), MMF (n=7), azathioprine (n=5), IVIg (n=3), tacrolimus (n=2), and rituximab (n=1). Concomitantly with RCI therapy, patients received prednisone (n=11), methotrexate (n=5), MMF (n=5), azathioprine (n=3), hydroxychloroquine (n=2), and tacrolimus (n=1).

Dosing

Patients self-injected 80 IU subcutaneously twice weekly for 24 weeks.

Response to ACTH

Seven of 10 patients met the DOI by a median of 8 weeks. Minimal improvement, using the 2016 ACR-EULAR myositis response criteria, was observed in 90% of patients, with 20%, 30%, and 40% of patients achieving major, moderate, and minor improvements, respectively. Mean dose of prednisone was significantly reduced at 6 months of RCI therapy (p=0.01), with 50% of patients off prednisone.

Safety

RCI was generally safe and well tolerated over 24 weeks. Five serious AES (SAEs) were recorded in 3 patients and 22 AEs in 8 patients, of which 3/5 SAEs were treatment-related as were all of the AEs. The most common AEs were injection site bruising and rash (n=4), hyperglycemia (n=3), and calcinosis, hypertension, infection, and insomnia (n=2 each).

Treatment duration and patient follow-up

Ten of 11 patients completed and were followed during the 24-week course of RCI therapy without dose modification.

Saygin et al, 2020[12]

This study is the extended follow-up from Aggarwal et al, and had the same primary and secondary end points used in the primary trial.

Eligible patient population and patient demographics

All patients with refractory PM or DM who completed the 6-month open-label study[11] were eligible to participate (n=10) in this 6-month extended follow-up study. The diagnoses and baseline characteristics were previously reported for all patients, and 8 patients, PM (n=3) and DM (n=5), were enrolled in this long-term follow-up study.

Dosing

Patients received 80 IU twice weekly for 24 weeks, with study visits every 4 weeks.

Response to ACTH

Of the 8 patients, 50% (4/8) remained stable, whereas the remaining 4 patients had a flare, with 3 requiring an increase in prednisone dose. Among the 4 stable patients, 2 had no significant change in all 6 CSMs. During the 6-month follow-up period, 3 patients who were off prednisone remained off

prednisone, 1 patient maintained the same dose of prednisone, 1 flared and restarted prednisone, and 2 patients flared and increased prednisone; 75% (6/8) met the DOI at 12 months.

Safety

One patient was restarted on RCI and reported dizziness that improved with dose reduction. This same patient developed segmental sigmoid colitis and 2 upper respiratory tract infections while receiving RCI. Another patient developed avascular necrosis of the femoral head 6 months after the RCI trial. Two patients reported worsening calcinosis, 2 and 5 months after completion of the trial. One patient had 2 upper respiratory tract infections, 3 and 6 months after the RCI trial. Finally, 1 patient had shingles 3 months after completion of the RCI trial. No patient developed diabetes, hypertension, or cushingoid features during the follow-up period.

Patient follow-up

Patients were followed for 6 months, with rheumatologist visits every 2 months.

Citations

1. Purified Cortrophin Gel (Repository Corticotropin Injection USP). Published online 2023. Accessed February 9, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/008975s012lbl.pdf

2. Upton GV, Hollingsworth DR, Lande S, Lerner AB, Amatruda TT. Comparison of purified human and porcine ACTH in man. *J Clin Endocrinol Metab*. 1970;30(2):190-195. doi:10.1210/jcem-30-2-190

3. *Acthar Gel (Repository Corticotropin Injection), for Intramuscular or Subcutaneous Use. Prescribing Information*. Mallinkrodt ARD LLC; 2021. Accessed November 12, 2023. https://acthar.com/Static/pdf/Acthar-PI.pdf

4. *Synacthen Depot Ampoules 1 Mg/Ml. Summary of Product Characteristics (SmPC)*. Atnahs Pharma UK Ltd; 2021. Accessed November 12, 2023. https://www.medicines.org.uk/emc/product/10823/smpc/

5. ANI Pharmaceuticals, Inc. Clinical monograph. Data on file.

6. Gong R. The renaissance of corticotropin therapy in proteinuric nephropathies. *Nat Rev Nephrol*. 2011;8(2):122-128. doi:10.1038/nrneph.2011.190

7. Levine T, Malone J. H.P. Acthar® Gel in Dermatomyositis and Polymyositis Treatment Registry: An Interim Analysis. *J Neurol Disord*. 2016;4(5). doi:10.4172/2329-6895.1000292

8. Knight T, Bond TC, Popelar B, et al. Medical resource utilization in dermatomyositis/polymyositis patients treated with repository corticotropin injection, intravenous immunoglobulin, and/or rituximab. *Clinicoecon Outcomes Res*. 2017;9:271-279. doi:10.2147/CEOR.S130992

9. Myung G, Nelson WW, McMahon MA. Effects of Repository Corticotropin Injection on Medication Use in Patients With Rheumatologic Conditions: A Claims Data Study. *Journal of Pharmacy Technology*. 2017;33(4):151-155. doi:10.1177/8755122517709825

10. Nelson WW, Philbin MJ, Gallagher JR, Heap K, Carroll S, Wan GJ. A Retrospective Medical Record Review of Utilization Patterns and Medical Resource Use Associated with Repository Corticotropin Injection among Patients with Rheumatologic Diseases in the United States. *Rheumatol Ther*. 2017;4(2):465-474. doi:10.1007/s40744-017-0087-x

11. Aggarwal R, Marder G, Koontz DC, Nandkumar P, Qi Z, Oddis CV. Efficacy and safety of adrenocorticotropic hormone gel in refractory dermatomyositis and polymyositis. *Ann Rheum Dis*. 2018;77(5):720-727. doi:10.1136/annrheumdis-2017-212047

12. Saygin D, Oddis CV, Marder G, et al. Follow-up results of myositis patients treated with H. P. Acthar gel. *Rheumatology (Oxford)*. 2020;59(10):2976-2981. doi:10.1093/rheumatology/keaa076

13. Nelson WW, Philbin MJ, Gallagher JR, Heap K, Carroll S, Wan GJ. A Retrospective Medical Record Review of Utilization Patterns and Medical Resource Use Associated with Repository Corticotropin Injection among Patients with Rheumatologic Diseases in the United States. *Rheumatol Ther*. 2017;4(2):465-474. doi:10.1007/s40744-017-0087-x