ClinicoEconomics and Outcomes Research

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Adherence to Acthar Gel (RCI) and Outcomes in Patients with Membranous Nephropathy: A Claims Database Analysis

Kyle Hayes[1], Mohammed Fahim[2], Feng Sheng Hu[2], Mary P Panaccio[1], George J Wan[1]

[1]Mallinckrodt Pharmaceuticals, Bridgewater, NJ, USA; [2]KMK Consulting, Morristown, NJ, USA

Correspondence: George J Wan, Mallinckrodt Pharmaceuticals, 440 Route 22 East, Bridgewater, NJ, USA, Email george.wan@mnk.com

Purpose: To describe real-world patient characteristics and outcomes after initiation of Acthar Gel (repository corticotropin injection, RCI) in the management of nephrotic syndrome (NS). This real-world study characterized patients with membranous nephropathy (MN) who initiated RCI therapy and evaluated the impact of higher versus lower adherence to RCI on NS-related outcomes, healthcare resource utilization, and medical costs.

Patients and Methods: We retrospectively analyzed data from the Integrated Dataverse from Symphony Health database. Adult (≥18 years) patients were included if they had ≥1 inpatient or ≥2 outpatient claims for an NS and MN diagnosis (January 1, 2016-December 31, 2022); ≥1 prescription claim for RCI; and continuous eligibility ≥12 months before and ≥12 months following and including the index date. Patients with ≥2 RCI claims and a calculated proportion of days covered (PDC) were included. Those with a PDC above the sample mean were classified as "above-average" adherence and those below the mean as "below-average" adherence in that period.

Results: The analyzed population comprised 28 patients with below-average and 34 with above-average RCI adherence. The above-average adherence cohort showed a noticeable reduction compared with the below-average adherence cohort in corticosteroid use, extended corticosteroid use, opioid use, NS-related renal biopsy procedures, all-cause and NS-related inpatient hospitalizations, and NS-related office visits. From baseline to follow-up, inpatient hospitalization rates were similar in the below-average adherence cohort for all-cause (50.0% vs 53.6%) and NS-related (35.7% vs 28.6%) admissions but markedly lower in the above-average cohort for all-cause (50.0% vs 23.5%) and NS-related (41.2% vs 8.8%) hospitalizations. Despite similar baseline medical costs, all-cause ($131,306 vs $50,048) and NS-related costs ($111,743 vs $29,868) were noticeably higher at follow-up in the below-average adherence cohort than the above-average adherence cohort.

Conclusion: This real-world study shows that greater adherence to RCI during treatment improves overall outcomes studied.

Plain Language Summary:

What do you need to know?

Membranous nephropathy (MN) is a kidney disease that can lead to nephrotic syndrome (NS), causing swelling, high cholesterol, and protein loss in the urine. Some people with NS do not respond to common treatments like corticosteroids or calcineurin inhibitors. Acthar Gel (repository corticotropin injection, RCI) is a prescription drug used for people with NS and other conditions.

Why did we do this study?

We wanted to see how well RCI works for adults with MN and whether taking it as prescribed can improve health outcomes and reduce medical costs.

How did we do this study?

We studied anonymous health insurance claims records from 62 adults with MN treated with RCI from 2016 to 2022. We divided patients into two groups based on medication adherence (how consistently they took RCI). One group had above-average adherence, and the other had below-average adherence. We compared health outcomes and healthcare use between the groups.

What did we find?

People who took RCI more regularly had better outcomes than those who did not. They used fewer corticosteroids, had fewer hospital visits and kidney procedures (like biopsies), used less opioid medication, and had lower overall healthcare costs.

https://doi.org/10.2147/CEOR.S530426
Received: 15 April 2025
Accepted: 3 December 2025
Published: 7 January 2026

What do the findings mean?

RCI may be a treatment option for adults with MN who do not respond to standard therapies. Taking RCI as prescribed can reduce symptoms and reduce the need for other medical care. Treatment adherence is important for achieving the best health results.

Keywords: Acthar® Gel, nephrotic syndrome, membranous nephropathy, repository corticotropin injection

Introduction

Kidney disease—which includes nephritis, nephrotic syndrome (NS), and nephrosis—is the tenth top leading cause of deaths in the United States.[1] NS is a glomerular disorder characterized by edema, hypoalbuminemia, hyperlipidemia, and proteinuria.[2–4] NS has an estimated annual incidence of 3 per 100,000 among adults in the United States.[5] Complications impacting patients with NS include deep vein thrombosis, infections, hypocalcemia and bone abnormalities, hyperlipidemia and atherosclerosis, hypercoagulability, hypovolemia, acute kidney injury, hypertension, edema, respiratory distress, sepsis, peritonitis, and failure to thrive.[2,5,6] As one of the most common causes of NS in adults, membranous nephropathy (MN) accounts for approximately 30% to 35% of diagnoses in adults.[5] Annual incidence rates per 100,000 range from 1.0 to 1.2 for MN in North America.[7]

According to the Kidney Disease Improving Global Outcomes (KDIGO) 2021 clinical practice guidelines for the management of glomerular diseases, patients should be initially treated with optimized supportive care that includes blood pressure management (eg, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, diuretics), lifestyle modifications, and, if needed, medications to address cardiovascular risk (eg, statins).[8] Depending on the specific NS diagnosis, patients with risk of progression despite maximal supportive care may receive corticosteroids, calcineurin inhibitors, and/or rituximab.[8] Approximately 50% of patients with NS who achieve remission with corticosteroids experience a subsequent relapse of proteinuria.[9,10] Treatment with calcineurin inhibitors has been associated with good remission rates in clinical trials but high relapse rates upon treatment discontinuation.[10–13] The combination of mycophenolate mofetil and corticosteroids offers an alternative to calcineurin inhibitors, but treatment with this combination has been associated with low remission rates in clinical trials.[14] Consequently, a subset of patients with MN depend on second-line and later therapies to induce further remission and prolong progression to end-stage renal disease. Because of complications, resistance, or relapse, patients need alternative treatment options.

Acthar® Gel (repository corticotropin injection [RCI]; Mallinckrodt Pharmaceuticals)—a naturally sourced complex mixture of adrenocorticotropic hormone analogs and other pituitary peptides—is indicated for use to induce diuresis or remission of proteinuria in nephrotic syndrome without uremia of the idiopathic type or due to lupus erythematosus.[15] Treatment with RCI has been shown to reduce proteinuria in patients with NS.[16–21] In a retrospective case series of 11 patients with MN (mean 2.3 prior immunosuppressive therapies) treated with RCI for at least 6 months, Bomback et al[22] reported complete remission in 3 (27%) patients and partial remission in 6 (55%). Similarly, Madan et al[23] reported 2 (18.2%) complete remissions, 4 (36.4%) partial remissions, and proteinuria reduction ≥50% in 8 (72.7%) of 11 patients with MN.

While prior studies have demonstrated the clinical benefits of RCI in reducing proteinuria and achieving remission in MN, real-world evidence on how adherence to RCI influences clinical and economic outcomes remains limited. Treatment adherence is a critical determinant of therapeutic success, particularly in chronic kidney diseases such as MN. Understanding the relationship between adherence to RCI and subsequent healthcare outcomes can inform strategies to optimize treatment effectiveness, reduce healthcare burden, and improve long-term management of MN in real-world settings. We performed a retrospective claims database analysis to characterize patients with MN who initiated RCI therapy and to evaluate how differences in adherence, categorized as below-average versus above-average, affect NS-related outcomes, healthcare resource utilization (HCRU), and medical costs.

Materials and Methods

Study Design and Data Source

Using January 1, 2016, to December 31, 2022, data from a large commercial open-source claims database (Integrated Dataverse from Symphony Health), we performed a retrospective cohort analysis of patients with MN who received RCI

treatment. This database provides a representative sample of the US population by encompassing data from pharmacy point-of-service, claim adjudication services, and direct prescription, medical, and hospital feeds for approximately 168 million longitudinally tracked patients. The database has deidentified patient information from many different types of payers in the United States, including Managed Medicaid, Medicare Advantage, commercial payers, and cash payers.

Relevant methodological details and reporting elements, including study design, participant selection, variables, data sources, and study limitations, were aligned with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement guidelines[24] for observational research to ensure transparency and rigor in study conduct and presentation.

This study used preexisting fully deidentified data, with no direct involvement of human subjects or access to identifiable private information. Based on the authors' determination and in accordance with the US Department of Health and Human Services (45 CFR 46.102) and FDA (21 CFR 56.102) regulations, this work does not meet the definition of human subjects research. Therefore, approval from an institutional review board or ethics committee was not required. This study complies with the Declaration of Helsinki.

Study Population Identification

For inclusion in the analysis, patients had to have: ≥1 inpatient or ≥2 outpatient claims for any NS diagnosis identified using International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) diagnosis code N04 (nephrotic syndrome) between January 1, 2016, and December 31, 2022; ≥1 prescription of medical claim for RCI, identified using National Drug Code (NDC) and Generic Product Identifier drug codes and/or Current Procedural Terminology (CPT) and Healthcare Common Procedure Coding System (HCPCS) procedure codes between January 1, 2016, and December 31, 2022; ≥1 inpatient or ≥2 outpatient claims for confirmed diagnosis of MN based on ICD-10-CM code (N04.2); age ≥18 years at index date, defined as the date of first RCI claim after confirmed MN diagnosis; and continuous eligibility ≥12 months before the index date and ≥12 months following and including the index date. Patients were excluded for having a contraindicated diagnosis for RCI during the 12 months before the RCI index date.

We included in the adherence analysis patients with MN if they had ≥2 claims for RCI in the 1-year follow-up period and a calculated proportion of days covered (PDC) of RCI in the 1-year follow-up period. To calculate PDC of RCI, days drug supplied was divided by days of follow-up (365 days). If the same patient had a fill date with multiple NDC claims for RCI, we only kept the largest days-supplied. Then, we used mean PDC to stratify the adherent patients into 2 RCI adherence cohorts: above-average adherence (defined as adherent patients with > average overall PDC of each cohort's PDC) and below-average adherence (defined as adherent patients with ≤ average overall PDC of each cohort's PDC). While the study was not designed to evaluate outcomes using a strict clinical adherence threshold (eg, PDC ≥80%) given the small sample size and estimated PDC values, a sensitivity analysis was performed. The mean PDC for the overall cohort was 0.711, with 0.4274 for the below-average adherence group and 0.9445 for the above-average group.

Variable and Outcome Measures

We analyzed patient baseline (index) demographic characteristics (ie, age, sex, race/ethnicity, region in the United States, and insurance type) and clinical characteristics (preexisting conditions) assessed using the Charlson Comorbidity Index (CCI).[25,26] We compared all-cause and NS-related background therapies and outcomes, HCRU, and medical costs in the RCI below-average and above-average adherence cohorts before (baseline) and after initiation of RCI (follow-up). NS-related was defined as any claim with an NS diagnosis at any position and/or NS-related procedure/medication, which included drugs in the class of RCI, NS background therapies, corticosteroids, and conventional synthetic disease-modifying antirheumatic drugs. Analysis of NS-related background pharmacotherapies included patient claims for corticosteroids, calcineurin inhibitors, nonsteroidal anti-inflammatory inhibitors (NSAIDs), and opioids. Proportion of patients receiving therapies at baseline and follow-up were compared between the adherence cohorts. Corticosteroid treatment was evaluated by comparing the average daily dose before therapy and in the follow-up. NS-related medical therapies included patient claims for dialysis, renal transplant, or renal biopsy. HCRU included patients with all-cause and NS-related claims for inpatient hospitalization, emergency department (ED) visit, office visit, and visit other than ED or office (henceforth referred to as "other outpatient visits"). Medical costs associated with HCRU claims for inpatient, ED, office, and other non-ED/office claims were compared between baseline and follow-up for the MN adherence cohorts.

Statistical Analyses

This study was designed as an exploratory and descriptive analysis to assess the impact of higher versus lower adherence to RCI on NS-related outcomes, HCRU, and medical costs. No formal statistical hypothesis testing or sample size calculations were performed due to the exploratory nature. Instead, data were summarized using descriptive statistics, including measures of central tendency (eg, mean, standard deviation [SD]) for continuous variables, and number and percentages for categorical variables, as appropriate.

Subgroup trends and patterns were explored qualitatively and quantitatively using graphical representations and summary statistics. The comparisons between groups were presented descriptively, and no inferential statistical tests were conducted to avoid overinterpretation of findings. Statistical analyses were performed using RStudio version 2022.02.0 (Posit, Boston, MA, USA).

Results

Study Population Selection

Among 87,466 patients identified with claims for an NS diagnosis during the study period, 418 (0.5%) patients had an RCI claim, including 91 with an MN diagnosis (Figure 1). After exclusions for age, certain diagnoses, and not having records with activity 365 days before and after the index RCI treatment claim, a total of 72 patients with MN remained. The finalized study population of RCI adherent patients with ≥2 NDC claims for RCI resulted in 62 patients with MN. Using PDC, we stratified RCI-adherent patients with MN into a below-average adherence cohort (n = 28) and an above-average adherence cohort (n=34).

Baseline Characteristics

With some exceptions, most baseline demographic characteristics were similar in the MN below-average and above-average RCI adherence cohorts (Table 1). The below-average adherence cohort versus above-average cohort had numerically lower proportions of patients with Black/African American (14.3% vs 20.6%) or Hispanic (3.6% vs 8.8%) race/ethnicity and Medicare insurance (17.9% vs 41.2%) and a higher proportion of patients with White/Caucasian race/ethnicity (64.3% vs 47.1%) and pharmacy benefit manager insurance (42.9% vs 8.8%).

The baseline claims-based disease-specific refinements CCI mean scores were slightly higher in the below-average adherence cohort versus the above-average cohort (2.46 ± 1.86 vs 1.94 ± 1.79, NS) (Table 1). Individual comorbidities were generally similar between cohorts, although the above-average cohort had a greater proportion of patients with congestive heart failure (7.1% vs 20.6%) and a lower proportion of patients with any malignancy (2.9% vs 10.7%) compared with the below-average cohort.

Acthar Gel (RCI) Treatment

There were more RCI fills and longer duration of treatment in the MN above-average adherence cohort than the below-average adherence cohort (Table 2). The RCI mean (±SD) treatment duration was 114.8 ± 59.9 days in the below-average adherence cohort and 275.0 ± 71.6 days in the above-average cohort. In the 12-month follow-up, patients had an average of 5.04 ± 2.46 fills for RCI in the below-average adherence cohort and 9.94 ± 3.29 fills for RCI in the above-average adherence cohort.

Treatment Patterns

We analyzed corticosteroid treatment patterns in terms of percentages of patients with pharmacy claims for corticosteroids and for extended use of corticosteroids (defined as ≥60 days continuous use with pharmacy claims) before (baseline) and after RCI treatment (follow-up) for the MN below-average and above-average RCI adherence cohorts. The percentages of patients with fills for corticosteroids remained steady from baseline to follow-up in the below-average adherence cohort (57.1% vs 57.1%) and declined in the above-average adherence cohort (67.6% vs 38.2%) (Figure 2A). The percentage of patients receiving prescriptions fills for the extended-use corticosteroid decreased from baseline to follow-up in both cohorts. The below-average adherence group had a 37.4% decrease (28.6% to 17.9%), while the above-

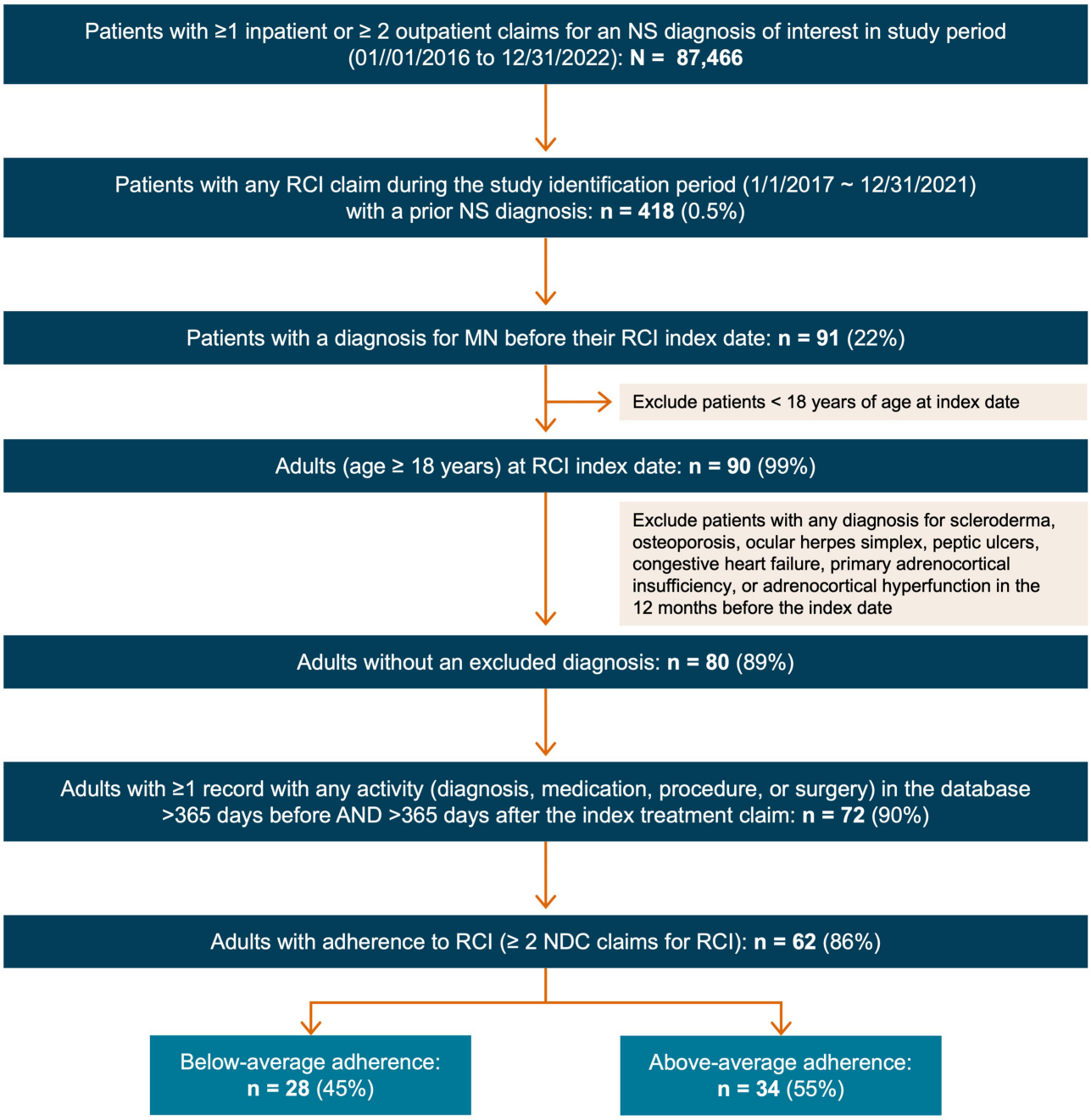

Figure 1 Selection of study population. Flow diagram of the selection process used to form the study cohorts.
Abbreviations: MN, membranous nephropathy; NS, nephrotic syndrome; RCI, repository corticotropin injection.

average adherence group had an 87.7% decrease (23.5% to 2.9%). (Figure 2B). The average daily dose for corticosteroids was similar at baseline and follow-up for the below-average adherence cohort (23.0 ± 12.3 to 23.8 ± 24.1) but was reduced in the above-average adherence cohort (32.3 ± 19.8 to 4.9 ± 0.0).

We analyzed patterns of use of background pharmacotherapies in terms of percentage of patients with claims for calcineurin inhibitors, NSAIDs, and opioids before and after RCI treatment for the MN below-average and above-average RCI adherence cohorts. The percentage of patients with claims for calcineurin inhibitors from baseline to follow-up decreased in both the below-average adherence (35.7% vs 25.0%) and above-average adherence (20.6% vs 14.7%) cohorts (Figure 3A). From baseline to follow-up, the percentage of patients with claims for NSAIDs remained unchanged

https://doi.org/10.2147/CEOR.S530426

Table 1 Patient Demographics and Clinical Characteristics for Below-Average and Above- Average Acthar Gel (RCI) Adherence Cohorts

Characteristics	Below Average Adherence (n = 28)	Above Average Adherence (n = 34)
Age at index date, mean ± SD	53.1 ± 17.2	57.1 ± 15.8
Gender, n (%)		
Female	12 (42.9)	14 (41.2)
Male	16 (57.1)	20 (58.8)
Race/ethnicity, n (%)		
Black/African American	4 (14.3)	7 (20.6)
Hispanic	1 (3.6)	3 (8.8)
White/Caucasian	18 (64.3)	16 (47.1)
Other	2 (7.1)	1 (1.9)
Unknown	3 (10.7)	7 (20.6)
Region in United States, n (%)		
Northwest	6 (21.4)	7 (20.6)
Midwest	6 (21.4)	5 (14.7)
South	13 (46.4)	20 (58.8)
West	3 (10.7)	2 (5.9)
Insurance type, n (%)		
Cash	0	1 (2.9)
Commercial	3 (10.7)	6 (17.6)
Medicaid	1 (3.6)	4 (11.8)
Medicare	5 (17.9)	14 (41.2)
Multiple	4 (14.3)	2 (5.9)
PBM	12 (42.9)	3 (8.8)
Other/unknown	3 (10.7)	4 (11.8)
CDMF CCI, mean ± SD	2.46 ± 1.86	1.94 ± 1.79
Individual CDMF-CCI comorbidities in > 5% of patients in any group, n (%)		
Congestive heart failure	2 (7.1)	7 (20.6)
Peripheral vascular disease	1 (3.6)	1 (2.9)
Cerebrovascular disease	3 (10.7)	2 (5.9)
Chronic pulmonary disease	4 (14.3)	5 (14.7)
Rheumatic disease	4 (14.3)	2 (5.9)
Liver disease (mild)	4 (14.3)	1 (2.9)

(*Continued*)

Table 1 (Continued).

Characteristics	Below Average Adherence (n = 28)	Above Average Adherence (n = 34)
Diabetes without chronic complication	4 (14.3)	1 (2.9)
Renal disease (mild, moderate)	20 (71.4)	22 (64.7)
Diabetes with chronic complication	6 (21.4)	7 (20.6)
Any malignancy, except malignant neoplasm of skin	3 (10.7)	1 (2.9)
Renal disease (severe)	3 (10.7)	3 (8.8)

Abbreviations: CCI, Charlson Comorbidity Index; CDMF, claims-based disease-specific refinements; MN, membranous nephropathy; PBM, pharmacy benefit manager; RCI, repository corticotropin injection.

Table 2 Acthar Gel (RCI) Treatment Duration and Patterns During Follow-Up Period

Characteristics	Below-Average Adherence (n = 28)	Above-Average Adherence (n = 34)
RCI fills, Mean ± SD	5.0 ± 2.5	9.9 ± 3.3
Duration from RCI initiation to last RCI fill in patients with ≥ 2 RCI fills, Mean ± SD	114.8 ± 59.9	275.0 ± 71.6

Abbreviations: MN, membranous nephropathy; RCI, repository corticotropin injection.

in the below-average adherence cohort (46.4% vs 46.4%) and decreased in the above-average adherence cohort (44.1% vs 20.6%) (Figure 3B). Further, at follow-up, NSAID claims were lower among the above-average adherence cohort versus below-average adherence cohort (20.6% vs 46.4%). From baseline to follow-up, the percentage of patients with opioid fills remained steady in the below-average adherence cohort (53.6% vs 50.0%) and decreased in the above-average adherence cohort (58.8% vs 26.5%) (Figure 3C).

We analyzed use of NS-related procedures as the percentage of patients with claims for dialysis, renal transplant, and renal biopsy procedures before and after RCI treatment for both of the MN RCI adherence cohorts. The percentage of patients with dialysis claims increased from baseline to follow-up in the below-average adherence cohort (3.6% vs 21.4%) but remained steady in the above-average adherence cohort (2.9% vs 5.9%) (Figure 4A). None of the patients in either adherence cohort had renal transplant procedure claims at baseline and both cohorts had similar percentages of

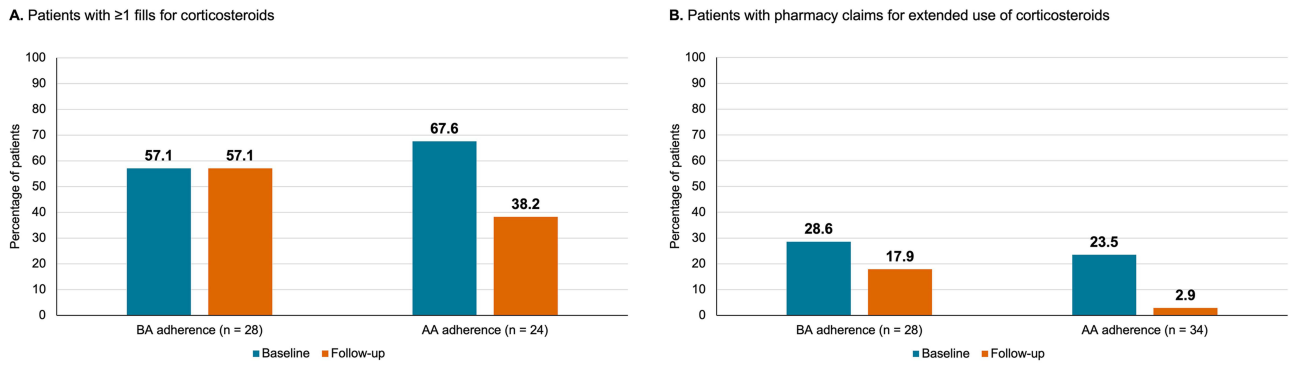

Figure 2 Bar graphs of percentage of patients with MN with ≥1 fills for corticosteroids (**A**) or extended-use corticosteroids (≥60 days continuous use with pharmacy claims) (**B**) before and after Acthar Gel (RCI) treatment for below-average and above-average Acthar Gel (RCI) adherence cohorts.
Abbreviations: AA, above-average adherence; BA, below-average adherence; MN, membranous nephropathy; RCI, repository corticotropin injection.

https://doi.org/10.2147/CEOR.S530426

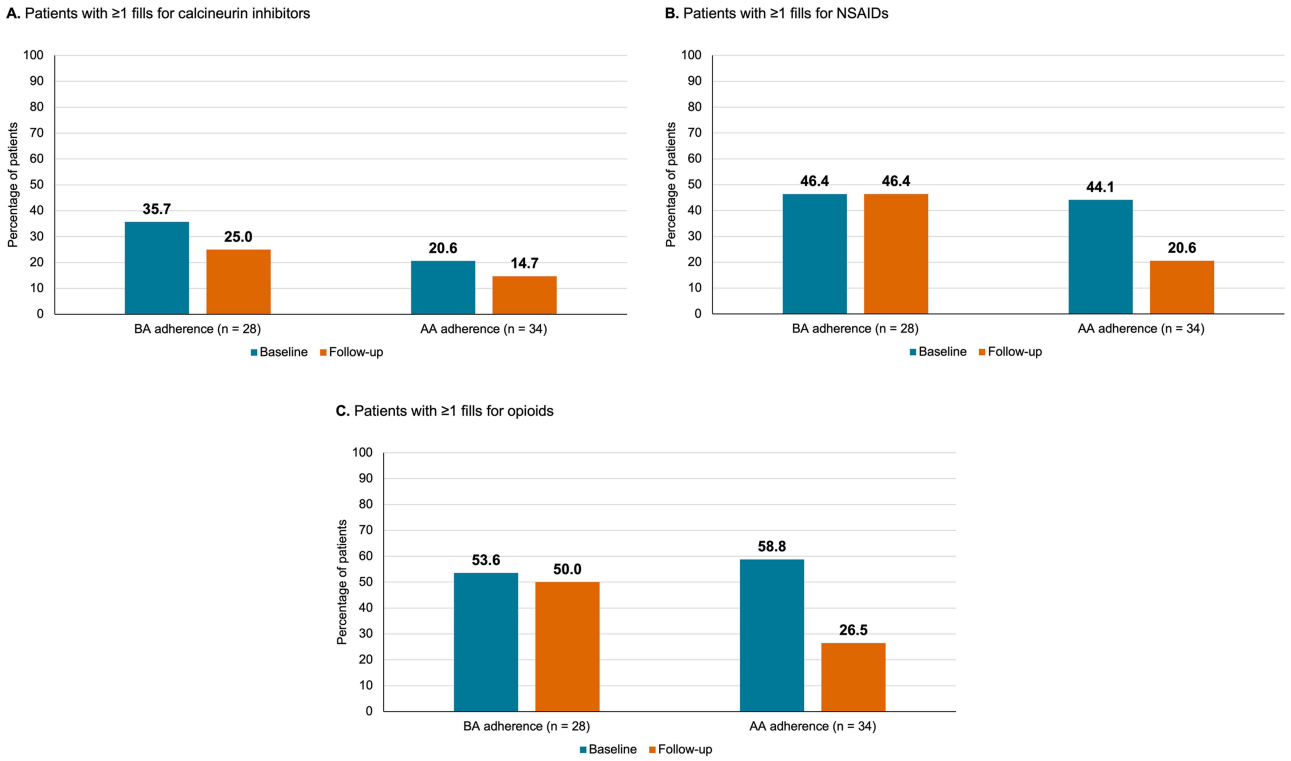

Figure 3 Bar graphs of percentage of patients with MN with ≥1 fills for calcineurin inhibitors (**A**), NSAIDs (**B**), or opioids (**C**) before and after Acthar Gel (RCI) treatment for below-average and above-average Acthar Gel (RCI) adherence cohorts.
Abbreviations: AA, above-average adherence; BA, below-average adherence; MN, membranous nephropathy; NSAID, nonsteroidal anti-inflammatory drug; RCI, repository corticotropin injection.

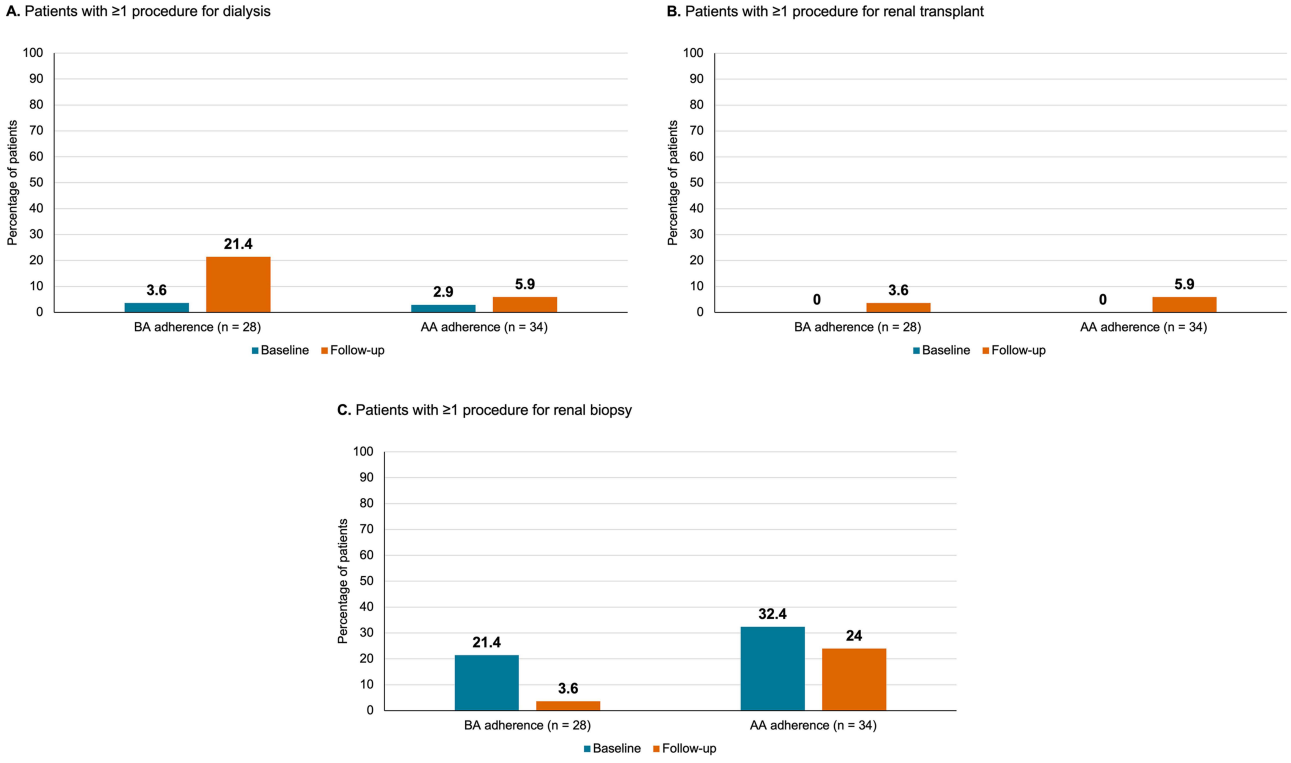

Figure 4 Bar graphs of percentage of patients with MN and with ≥1 procedures for dialysis (**A**), renal transplant (**B**), or renal biopsy (**C**) before and after Acthar Gel (RCI) treatment for below-average and above-average Acthar Gel (RCI) adherence cohorts.
Abbreviations: AA, above-average adherence; BA, below-average adherence; MN, membranous nephropathy; RCI, repository corticotropin injection.

https://doi.org/10.2147/CEOR.S530426

patients with such claims at follow-up (3.6% vs 5.9%) (Figure 4B). From baseline to follow-up, there was a lower percentage of patients with claims for renal biopsy procedures in the below-average adherence cohort (21.4% vs 3.6%) and a marked reduction in the above-average cohort (32.4% vs 2.9%) (Figure 4C).

Healthcare Resource Utilization and Medical Costs

We analyzed all-cause and NS-related HCRU in terms of percentage of patients with claims for inpatient hospitalization, ED visit, outpatient office visit, other outpatient visits, and medical costs before and after RCI treatment for the below-average and above-average MN RCI adherence cohorts. From baseline to follow-up, the percentage of patients with claims for inpatient hospitalization was similar in the below-average adherence cohort for all-cause (50.0% to 53.6%) and NS-related (35.7% vs 28.6%) admission, with noticeable reductions in inpatient hospitalization in the above-average adherence cohort for all-cause (50.0% vs 23.5%) and NS-related (41.2% vs 8.8%) (Table 3). From baseline to follow-up, the percentages of patients with claims for ED use increased in the below-average adherence cohort for all-cause (32.1% vs 50.0%) and NS-related utilization (17.9% vs 21.4%), while there was a reduction in utilization for above-average adherence cohort for all-cause (32.3% vs 20.6%) and no change for NS-related (17.6% vs 17.6%). Results were similar for office visits and other outpatient visits for all-cause and NS-related utilization (Table 3).

Healthcare costs were higher in the below-average adherence cohort than the above-average adherence cohort, which aligns with their higher HCRU. Despite similar baseline costs, follow-up medical costs were noticeably higher in the below-average

Table 3 Comparison of All-Cause and NS-Related HCRU and Medical Costs Before and After Acthar Gel (RCI) Treatment for Below-Average and Above-Average Acthar Gel (RCI) Adherence Cohorts

Comparison	All-Cause		NS-Related	
	Below-Average Adherence (n = 28)	Above-Average Adherence (n = 34)	Below-Average Adherence (n = 28)	Above-Average Adherence (n = 34)
Inpatient hospitalization[a], n (%)				
Baseline	14 (50.0)	17 (50.0)	10 (35.7)	14 (41.2)
Follow-up	15 (53.6)	8 (23.5)	8 (28.6)	3 (8.8)
ED visit[a], n (%)				
Baseline	9 (32.1)	11 (32.4)	5 (17.9)	6 (17.6)
Follow-up	14 (50.0)	7 (20.6)	6 (21.4)	6 (17.6)
Outpatient office visit[a], n (%)				
Baseline	24 (85.7)	28 (82.4)	20 (71.4)	24 (70.6)
Follow-up	24 (85.7)	25 (73.5)	17 (60.7)	17 (50.0)
Other outpatient visit[a,b], n (%)				
Baseline	21 (75.0)	28 (82.4)	16 (57.1)	20 (58.8)
Follow-up	24 (85.7)	22 (64.7)	15 (53.6)	15 (44.1)
Medical cost, USD, mean ± SD				
Baseline	59,265 ± 110,149	65,094 ± 125,059	39,978 ± 83,036	41,380 ± 111,889
Follow-up	131,306 ± 247,984	50,048 ± 114,208	111,743 ± 246,559	29,868 ± 96,533

Notes: [a]Patients with ≥1 claim. [b]Other than ED or office visit.
Abbreviations: ED, emergency department; HCRU, healthcare resource utilization; NS, nephrotic syndrome; RCI, repository corticotropin injection; USD, US dollars.

https://doi.org/10.2147/CEOR.S530426

adherence cohort than the above-average adherence cohort. This difference was observed for both all-cause costs ($131,306 ± $247,984 vs $50,048 ± $114,208) and NS-related costs ($111,743 ± $246,559 vs $29,868 ± $96,533) (Table 3).

Discussion

In this real-world descriptive study, we analyzed claims data from a large representative sample of the US population to characterize MN patients treated with RCI and to examine the impact of RCI adherence on NS-related outcomes. With some exceptions, most baseline demographic characteristics were similar in the below-average and above-average adherence cohorts for patients with MN. Mean RCI treatment duration was over twice as long among the above-average adherence cohort than the below-average adherence cohort. Comparisons of percentages of patients with claims for NS background medications and NS-related procedures from the baseline period to the post-RCI treatment follow-up period revealed interesting and potentially clinically important trends.

In the MN adherence population, we found trends toward reduced percentages of patients with claims for extended-use corticosteroids, calcineurin inhibitors, NS-related renal biopsy procedures, NS-related in-patient hospitalization, and NS-related office visit in both the above- and the below-average RCI adherence cohorts. The percentages of patients with claims for corticosteroids, NSAIDs, opioids, all-cause and NS-related inpatient, ED, and office visits showed decreases from baseline to follow-up in the above-average adherence cohort and remained unchanged in the below-average adherence cohort. Notably, the above-average adherence cohort showed a marked reduction compared with the below-average adherence cohort in corticosteroid use, extended corticosteroid use, opioid use, NS-related renal biopsy procedures, all-cause and NS-related inpatient hospitalizations, and NS-related office visits. The percentage of patients with claims for dialysis procedures showed an increase in the below-average adherence cohort and remained unchanged in the above-average adherence cohort. Improved outcomes in the above-average adherence cohort, such as noticeable reductions in all-cause and NS-related inpatient hospitalization from baseline to follow-up (50.0% vs 23.5% and 41.2% vs 8.8%, respectively) and fewer patients moving to dialysis, were associated with lower medical costs in the follow-up compared with the below-average adherence cohort.

Treatment with RCI has been shown to reduce proteinuria in patients with NS.[16–19,21–23] Furthermore, RCI has also been shown to have a better cost-per-response among patients with proteinuria in NS due to MN compared with other common treatments among adults with refractory proteinuria.[27] The present study is the first real-world analysis to examine adherence to RCI and its association with clinical and economic outcomes among patients with MN. By categorizing adherence into above- and below-average cohorts, our analysis provides novel evidence that consistent RCI use may be linked to lower corticosteroid and opioid utilization, reduced HCRU, and lower overall medical costs. These findings add to the nascent body of literature on RCI and help bridge a critical gap in understanding how adherence influences outcomes in rare kidney diseases such as MN. Future research should build upon these results by incorporating larger longitudinal datasets, applying advanced statistical and survival analyses to confirm associations, and integrating clinical measures (eg, proteinuria reduction, kidney function trajectories) to better elucidate causal pathways between RCI adherence, disease progression, and healthcare utilization.

Reductions in corticosteroid and opioid utilization among patients with above-average adherence to RCI suggest a potential improvement in disease control and symptom management. Corticosteroids are commonly used in MN to manage inflammation and proteinuria, but prolonged use is associated with significant adverse effects such as osteoporosis, metabolic disturbances, and immunosuppression.[28,29] Lower claims for corticosteroids in adherent versus nonadherent patients may reflect stabilization of disease activity with RCI therapy, reducing reliance on broad immunosuppression. Similarly, decreased opioid fills may indicate better symptom management, particularly regarding pain and fatigue often associated with chronic kidney disease. Collectively, these findings suggest the potential clinical value of maintaining consistent RCI adherence to mitigate the long-term burden associated with chronic corticosteroid and opioid exposure.

The reduction in renal biopsy procedures among patients with above-average RCI adherence may indicate fewer disease relapses or less diagnostic uncertainty, potentially reflecting improved disease stability. In contrast, the increase in dialysis procedures in the below-average adherence cohort suggests more frequent progression toward renal dysfunction or end-stage kidney disease. These trends imply that adherence to RCI may contribute to delaying renal deterioration and reducing the need for invasive or resource-intensive interventions. Although causal inference cannot be made due to the descriptive study design, these findings underscore the importance of adherence as a modifiable factor that could influence renal outcomes.

The marked reduction in all-cause and NS-related hospitalizations and office visits among the above-average adherence cohort suggests a broader healthcare benefit associated with consistent RCI use. Fewer hospitalizations might reflect better outpatient disease management and fewer acute complications, while reduced office visits may indicate clinical stabilization and a decreased need for frequent monitoring. In chronic conditions like MN, minimizing hospital-based care not only reduces patient burden but also signals improved health maintenance in real-world practice. These findings align with prior evidence that better treatment adherence in chronic kidney disease correlates with improved clinical stability and fewer acute events.[30]

The lower follow-up medical costs observed in the above-average adherence cohort are consistent with the reductions in hospitalizations, invasive procedures, and pharmacologic burden. While RCI is a specialized therapy, improved adherence appears to yield downstream cost offsets by reducing HCRU and acute care needs. These findings emphasize that consistent adherence to RCI may have economic as well as clinical benefits, offering potential value to both patients and healthcare systems. Continued adherence-focused management strategies could therefore play a key role in optimizing resource use and cost effectiveness in the treatment of MN.

Interpretation of these results must consider study limitations. First, administrative claims data can be incomplete, inaccurate, or missing, and these data may lack clinical details on individual patients. Diagnosis, procedures, and outcomes are based on ICD-10, CPT, and/or HCPCS codes and do not directly measure the conditions. As a retrospective analysis, this study is also subject to inherent biases, including potential data inaccuracies, miscoding, and unmeasured confounders that cannot be fully controlled. The absence of detailed clinical information, such as laboratory values or disease severity, further limits the interpretation of treatment outcomes. Second, our assessments for RCI use, adherence, and outcomes are indirect and based on several assumptions as explained in the Methods section. Although claims data can show that prescription medications have been filled, they cannot confirm that patients have taken the medications. Differences in insurance coverage between the cohorts may impact adherence. Third, the sample size was inherently limited by the rarity of MN[7] and the selective real-world use of RCI. While this constrains the ability to generalize findings broadly, the study provides valuable exploratory insights that can inform future larger-scale evaluations. Finally, while the adherence cohorts had similar baseline characteristics, the below-average cohort had a slightly higher claims-based disease-specific refinements comorbidity index, indicating sicker patients who may not respond as well to treatment. Differences in comorbidity profiles between the adherence cohorts, such as the presence of liver disease or malignancy, may have influenced treatment response, healthcare utilization, and outcomes. These conditions are relatively common in adults with MN and may reflect the heterogeneity of real-world populations rather than true differences in disease etiology This exploratory analysis was not powered to statistically adjust for or isolate the impact of these comorbidities.

Conclusion

This real-world descriptive analysis provides preliminary insights into treatment adherence patterns and associated outcomes among patients with MN treated with RCI. Above-average adherence to RCI was associated with favorable trends in corticosteroid and opioid use, HCRU, and medical costs compared with below-average adherence. Notably, patients with above-average adherence experienced greater improvements in most outcomes than those with below-average adherence. These findings should be interpreted within the exploratory nature of the study and the limited sample size. The results are intended to highlight the potential benefits of consistent RCI use among treated patients. Further research using larger prospective datasets is warranted to validate these observations.

Ethics Approval and Informed Consent

This study used preexisting fully deidentified data, with no direct involvement of human subjects or access to identifiable private information. Based on the authors' determination and in accordance with the US Department of Health and Human Services (45 CFR 46.102) and FDA (21 CFR 56.102) regulations, this work does not meet the definition of human subjects research. Therefore, approval from an institutional review board or ethics committee was not required. This study complies with the Declaration of Helsinki.

Acknowledgments

Monica Nicosia, PhD, and Esther Tazartes, MS, of Global Outcomes Group provided medical writing and editorial assistance, which was funded by Mallinckrodt Pharmaceuticals.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

Funding

Mallinckrodt Pharmaceuticals funded this study and the development of this manuscript. All authors had full access to the data used in this study and take responsibility for the integrity of the data and accuracy of the data analysis.

Disclosure

Kyle Hayes and George J. Wan are employees of Mallinckrodt Pharmaceuticals. Mary P. Panaccio is a paid independent consultant for Mallinckrodt Pharmaceuticals. Mohammed Fahim and Feng Sheng Hu are employees of KMK Consulting Inc., Morristown, NJ, USA, and are paid analysts for Mallinckrodt Pharmaceuticals. At the time of this writing, all the authors declare that they have no other potential conflicts of interest.

References

1. Curtin SC, Tejada-Vera B, Bastian BA. Deaths: leading causes for 2021. *Natl Vital Stat Rep*. 2024;73(4):1–116.
2. Hull RP, Goldsmith DJ. Nephrotic syndrome in adults. *BMJ*. 2008;336(7654):1185–1189. doi:10.1136/bmj.39576.709711.80
3. Kodner C. Nephrotic syndrome in adults: diagnosis and management. *Am Fam Physician*. 2009;80(10):1129–1134.
4. Königshausen E, Sellin L. Recent treatment advances and new trials in adult nephrotic syndrome. *Biomed Res Int*. 2017;2017:7689254. doi:10.1155/2017/7689254
5. Kodner C. Diagnosis and management of nephrotic syndrome in adults. *Am Fam Physician*. 2016;93(6):479–485.
6. Tapia C, Bashir K. *Nephrotic Syndrome*. Treasure Island (FL): StatPearls LLC.; 2024. *StatPearls*.
7. Ronco P, Beck L, Debiec H, et al. Membranous nephropathy. *Nat Rev Dis Primers*. 2021;7(1):69. doi:10.1038/s41572-021-00303-z
8. KDIGO. KDIGO 2021 clinical practice guideline for the management of glomerular diseases. *Kidney Int*. 2021;100(4s):S1–S276. doi:10.1016/j.kint.2021.05.021
9. Ponticelli C, Villa M, Banfi G, et al. Can prolonged treatment improve the prognosis in adults with focal segmental glomerulosclerosis? *Am J Kidney Dis*. 1999;34(4):618–625. doi:10.1016/s0272-6386(99)70384-7
10. Chávez-Mendoza CA, Niño-Cruz JA, Correa-Rotter R, Uribe-Uribe NO, Mejía-Vilet JM. Calcineurin inhibitors with reduced-dose steroids as first-line therapy for focal segmental glomerulosclerosis. *Kidney Int Rep*. 2019;4(1):40–47. doi:10.1016/j.ekir.2018.08.010
11. Ponticelli C, Rizzoni G, Edefonti A, et al. A randomized trial of cyclosporine in steroid-resistant idiopathic nephrotic syndrome. *Kidney Int*. 1993;43(6):1377–1384. doi:10.1038/ki.1993.194
12. Cattran DC, Appel GB, Hebert LA, et al. A randomized trial of cyclosporine in patients with steroid-resistant focal segmental glomerulosclerosis. North America Nephrotic Syndrome Study Group. *Kidney Int*. 1999;56(6):2220–2226. doi:10.1046/j.1523-1755.1999.00778.x
13. Segarra A, Vila J, Pou L, et al. Combined therapy of tacrolimus and corticosteroids in cyclosporin-resistant or -dependent idiopathic focal glomerulosclerosis: a preliminary uncontrolled study with prospective follow-up. *Nephrol Dial Transplant*. 2002;17(4):655–662. doi:10.1093/ndt/17.4.655
14. Gipson DS, Trachtman H, Kaskel FJ, et al. Clinical trial of focal segmental glomerulosclerosis in children and young adults. *Kidney Int*. 2011;80(8):868–878. doi:10.1038/ki.2011.195
15. Mallinckrodt. Acthar Gel (repository corticotropin injection). Prescribing information. Mallinckrodt Pharmaceuticals. 2024. Available from: https://www.acthar.com/pdf/Acthar-PI.pdf. Accessed March 27, 2024.
16. Bomback AS, Canetta PA, Beck LH Jr, Ayalon R, Radhakrishnan J, Appel GB. Treatment of resistant glomerular diseases with adrenocorticotropic hormone gel: a prospective trial. *Am J Nephrol*. 2012;36(1):58–67. doi:10.1159/000339287
17. Tumlin J, Galphin C, Santos R, Rovin B. Safety and efficacy of combination Acthar Gel and tacrolimus in treatment-resistant focal segmental glomerulosclerosis and membranous glomerulopathy. *Kidney Int Rep*. 2017;2(5):924–932. doi:10.1016/j.ekir.2017.05.015
18. Alhamad T, Manllo Dieck J, Younus U, et al. ACTH gel in resistant focal segmental glomerulosclerosis after kidney transplantation. *Transplantation*. 2019;103(1):202–209. doi:10.1097/tp.0000000000002320
19. Chakraborty R, Mehta A, Nair N, et al. ACTH treatment for management of nephrotic syndrome: a systematic review and reappraisal. *Int J Nephrol*. 2020;2020:2597079. doi:10.1155/2020/2597079
20. Zand L, Canetta P, Lafayette R, et al. An open-label pilot study of adrenocorticotrophic hormone in the treatment of IgA nephropathy at high risk of progression. *Kidney Int Rep*. 2020;5(1):58–65. doi:10.1016/j.ekir.2019.10.007
21. Wan GJ, Niewoehner J, Hayes K. Acthar Gel (RCI): a narrative literature review of clinical and economic evidence. *Clinicoecon Outcomes Res*. 2023;15:499–512. doi:10.2147/ceor.S410082

22. Bomback AS, Tumlin JA, Baranski J, et al. Treatment of nephrotic syndrome with adrenocorticotropic hormone (ACTH) gel. *Drug Des Devel Ther*. 2011;5:147–153. doi:10.2147/dddt.S17521
23. Madan A, Mijovic-Das S, Stankovic A, Teehan G, Milward AS, Khastgir A. Acthar gel in the treatment of nephrotic syndrome: a multicenter retrospective case series. *BMC Nephrol*. 2016;17:37. doi:10.1186/s12882-016-0241-7
24. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med*. 2007;147(8):573–577. doi:10.7326/0003-4819-147-8-200710160-00010
25. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005;43(11):1130–1139. doi:10.1097/01.mlr.0000182534.19832.83
26. Glasheen WP, Cordier T, Gumpina R, Haugh G, Davis J, Renda A. Charlson Comorbidity Index: ICD-9 update and ICD-10 translation. *Am Health Drug Benefits*. 2019;12(4):188–197.
27. Bindra J, Chopra I, Hayes K, Niewoehner J, Panaccio MP, Wan GJ. Cost per response of Acthar® Gel vs standard of care for the treatment of proteinuria in nephrotic syndrome due to idiopathic membranous nephropathy among adults from the US healthcare perspective. *JHEOR*. 2025;12(2):50–61. doi:10.36469/jheor.2025.142078
28. Ponticelli C, Locatelli F. Glucocorticoids in the treatment of glomerular diseases: pitfalls and pearls. *Clin J Am Soc Nephrol*. 2018;13(5):815–822. doi:10.2215/CJN.12991117
29. Fardet L, Peterson I, Nazareth I. Common infections in patients prescribed systemic glucocorticoids in primary care: a population-based cohort study. *PLoS Med*. 2016;13(5):e1002024. doi:10.1371/journal.pmed.1002024
30. Cedillo-Couvert EA, Ricardo AC, Chen J, et al. Self-reported medication adherence and CKD progression. *Kidney Int Rep*. 2018;3(3):645–651. doi:10.1016/j.ekir.2018.01.007