Nephrotic Syndrome: Patient characteristics, treatment patterns, and related outcomes after treatment with Acthar® Gel or comparable standard of care in a large administrative claims database

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BACKGROUND

- Nephrotic syndrome (NS) is a kidney disease characterized by the loss of large amounts of protein in the urine. The incidence of nephrotic syndrome in adults is approximately 1-3 per 100,000 adults [1]
- About 20-40% of patients with difficult to treat nephrotic syndrome fail to adequately respond to first-line corticosteroids, classified as steroid-dependent (SDNS) or steroid-sensitive (SSNS). Patients that are steroid-dependent have a high corticosteroid (CS) burden and experience frequent relapses, and combined with patients who are steroid resistant, alternative steroid-sparing treatment options are needed [2]
- Patients who don't respond to CS may require more aggressive treatment with other medications, such as calcineurin inhibitors (CNIs) or other alternative treatments (azathioprine, chlorambucil, cyclophosphamide, mycophenolate mofetil, or rituximab) [3]
- Patients who are steroid dependent (SD) or steroid sensitive (SS) with high relapse rates have significantly higher risk of developing end stage renal disease (ESRD) and renal replacement therapy [4]
- Acthar Gel is indicated for Inducing a diuresis or a remission of proteinuria in nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus [5]

OBJECTIVE

- This real-world evidence (RWE) study objective is to characterize NS patients who initiated Acthar Gel or similar comparators used after early line treatment with CS and/or CNIs, and to compare changes in CS use and other NS-related treatments and outcomes, using a large administrative claims database (Symphony Health)

METHODS

- This study is a retrospective, observational cohort comparison of NS patients who initiate treatment with Acthar Gel or similar later line standard of care (SOC) comparators (azathioprine, chlorambucil, cyclophosphamide, mycophenolate mofetil, or rituximab) in a large commercial claims database (Symphony Health)
- **Inclusion criteria**:
  - Patients had a confirmed NS ICD-10-CM diagnosis (**NS cohort index date**; N02.8, N04) with either ≥1 inpatient or ≥2 outpatient claims during the study period (01/01/2016 to 12/31/2022)
  - Patients were ≥18 years old and had 12 months of continuous enrollment pre- and post-index
  - Patients must have at least one record with any activity (diagnosis, medication, procedure or surgery) in the database >180 days before AND >180 days after the index treatment claim
  - Patients were excluded if they had a contraindication to Acthar Gel in the 12-month baseline including adrenocortical hyperfunction, systemic fungal infections, congestive heart failure, ocular herpes simplex, osteoporosis, peptic ulcers, primary adrenocortical insufficiency, and scleroderma
- **Cohort criteria and index dates**:
  - **Acthar Gel cohort**: Patients with any Acthar Gel claim during the study intake period (01/01/2017 to 12/31/2021), with the first Acthar Gel claim as **Acthar index date**
  - **SOC comparator cohort:** Patients with any claim for a comparable later line therapy used after CS and/or CNIs, similar to Acthar Gel during the study intake period, with first claim as **SOC index date**
  - **FSGS, iMN, and IgAN sub-cohorts:** For both Acthar Gel and SOC comparator cohorts, a confirmed diagnosis of the subtype was required before treatment index
- Statistical testing using Chi-square test or Fisher exact test for categorical variables (Acthar Gel cohort vs. SOC cohort in each period), Welch's t-test for continuous variables (Acthar Gel cohort vs. SOC cohort in each period) and McNemar test for categorical variables (Follow-up period vs. Baseline period in each cohort), paired sample t-test for continuous variables (Follow-up period vs. Baseline period in each cohort).

Table 1. Patient baseline demographics, insurance, and clinical characteristics

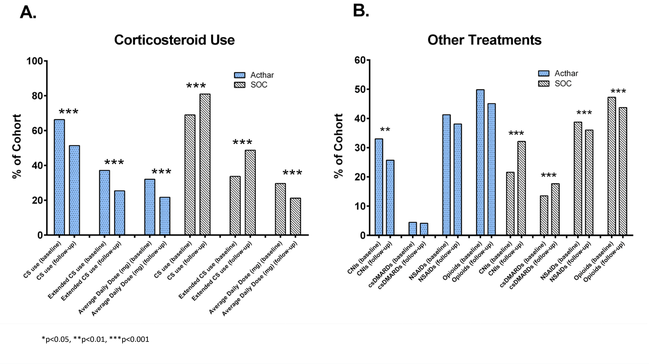
	Full Cohort					FSGS cohort				iMN cohort				IgAN cohort			
	Acthar Gel (n = 315)		SOC comparator (n = 6,812)		p-value**	Acthar Gel (n = 72)		SOC comparator (n = 1,077)		Acthar Gel (n = 72)		SOC comparator (n = 852)		Acthar Gel (n = 36)		SOC comparator (n = 792)	
Baseline* characteristics																	
Age, (mean, sd)	49.4	18.2	46.1	17.9	**0.002**	46.0	19.4	45.7	17.0	54.4	16.7	52.6	16.6	44.1	16.6	46.8	15.4
Male, (n, %)	173	55%	3,306	49%	**0.031**	40	56%	607	56%	43	60%	480	56%	20	56%	433	55%
Ethnicity, (n, %)					0.265												
Black/African American	55	17%	934	14%		13	18%	174	16%	12	17%	132	15%	3	8%	35	4%
White/Caucasian	123	39%	2,660	39%		18	25%	394	37%	39	54%	382	45%	16	44%	344	43%
Hispanic	29	9%	666	10%		8	11%	106	10%	6	8%	85	10%	4	11%	74	9%
Other/Unknown	108	34%	2,552	37%		33	46%	403	37%	15	21%	253	30%	13	36%	339	43%
Region, (n, %)					**<0.001**												
Northeast	64	20%	1,359	20%		11	15%	193	18%	16	22%	168	20%	10	28%	173	22%
Midwest	76	24%	1,839	27%		15	21%	260	24%	14	19%	231	27%	7	19%	227	29%
South	151	48%	2,463	36%		42	58%	463	43%	36	50%	341	40%	16	44%	253	32%
West	24	8%	1,113	16%		4	6%	151	14%	6	8%	110	13%	3	8%	133	17%
Other	0	0%	38	1%		0	0%	10	1%	0	0%	2	0%	0	0%	6	1%
Insurance type, (n, %)					**<0.001**												
Commercial	47	15%	2,372	35%		11	15%	356	33%	13	18%	303	36%	8	22%	268	34%
Medicaid	38	12%	1,143	17%		6	8%	153	14%	5	7%	117	14%	3	8%	98	12%
Medicare	68	22%	1,087	16%		16	22%	207	19%	21	29%	186	22%	5	14%	110	14%
Multiple	37	12%	512	8%		11	15%	104	10%	8	11%	52	6%	3	8%	86	11%
Other/Unknown	125	39%	1,698	24%		27	40%	222	24%	24	35%	177	22%	14	48%	212	29%
CDMF-Charlson comorbidity index, (mean, sd)	2.3	1.8	2.5	2.0	**0.005**	2.7	1.8	2.9	1.8	2.2	1.8	2.3	1.8	2.3	1.9	2.7	1.9
Individual CDMF Charlson comorbidity, (n, %)																	
Myocardial infarction	3	1%	188	3%	**0.049**	0	0%	31	3%	0	0%	26	3%	0	0%	15	2%
Congestive heart failure	26	8%	523	8%	0.666	5	7%	64	6%	10	14%	65	8%	4	11%	37	5%
Peripheral vascular disease	13	4%	475	7%	0.052	7	10%	96	9%	2	3%	63	7%	1	3%	62	8%
Cerebrovascular disease	18	6%	247	4%	0.066	5	7%	35	3%	6	8%	48	6%	1	3%	17	2%
Chronic pulmonary disease	46	15%	873	13%	0.345	5	7%	131	12%	11	15%	124	15%	4	11%	97	12%
Rheumatic disease	23	7%	1,691	25%	**<0.001**	2	3%	87	8%	7	10%	173	20%	3	8%	108	14%
Liver disease (mild)	20	6%	404	6%	0.715	7	10%	49	5%	5	7%	49	6%	2	6%	56	7%
Diabetes without chronic complication	33	10%	479	7%	**0.025**	9	13%	84	8%	6	8%	77	9%	8	22%	51	6%
Renal disease (mild, moderate)	192	61%	3,052	45%	**<0.001**	41	57%	397	37%	48	67%	521	61%	21	58%	296	37%
Diabetes with chronic complication	50	16%	930	14%	0.276	10	14%	154	14%	14	19%	118	14%	6	17%	111	14%
Any malignancy (excluding skin)	12	4%	435	6%	0.073	4	6%	32	3%	5	7%	57	7%	0	0%	25	3%
Liver disease (moderate or severe)	0	0%	77	1%	0.050	0	0%	8	1%	0	0%	7	1%	0	0%	8	1%
Renal disease (severe)	67	21%	2,012	30%	**0.001**	27	38%	573	53%	9	13%	139	16%	9	25%	359	45%

FSGS = Focal segmental glomerulosclerosis, iMN = idiopathic membranous nephropathy, IgAN = IgA nephropathy

*Baseline period: [index date - 365, index date)

**p-value calculated using Chi-square test or Fisher exact test for categorical variables (Acthar Gel cohort vs. SOC cohort in each period), Welch's t-test for continuous variables (Acthar Gel cohort vs. SOC cohort in each period) and McNemar test for categorical variables (Follow-up period vs. Baseline period in each cohort), paired sample t-test for continuous variables (Follow-up period vs. Baseline period in each cohort).

Figure 1. Treatments used at baseline compared to follow-up



*p<0.05, **p<0.01, ***p<0.001

Table 2. Treatment patterns and outcomes in follow-up

	Acthar Gel (n = 315)		SOC comparator (n = 6,812)		p-value***	Acthar Gel (n = 315)		SOC comparator (n = 6,812)		p-value***	Acthar Gel	SOC comparator
Outcomes: Treatment pattern and NS related procedures	**Baseline period***					**Follow-up period****					**Baseline vs. Follow-up** p-value***	
Corticosteroid (CS)												
# of patients with ≥1 fills of corticosteroids (n, %)	209	66%	4,702	69%	0.347	162	51%	5,516	81%	**<0.001**	**<0.001**	**<0.001**
Corticosteroids dosing group, (n, %)												
Intermittent, < 60 days of continuous corticosteroid use	75	24%	2,088	31%	**0.012**	62	20%	1,657	24%	**0.069**	0.228	**<0.001**
Extended, ≥60 days of continuous corticosteroid use	117	37%	2,293	34%	0.224	80	25%	3,319	49%	**<0.001**	**<0.001**	**<0.001**
Corticosteroid dosing strength, (n, %)												
low (≤7.5 mg/day)	19	6%	510	7%	0.380	25	8%	1,037	15%	**<0.001**	0.210	**<0.001**
medium (>7.5 to 15 mg/day)	16	5%	377	6%	0.899	19	6%	755	11%	**0.004**	0.678	**<0.001**
high (>15 mg/day)	82	26%	1,406	21%	**0.023**	36	11%	1,527	22%	**<0.001**	**<0.001**	**0.006**
Averaged daily dose (ADD), (mean, sd)	32.1	21.3	29.6	24.1	0.229	21.7	21.1	21.2	20.3	0.846	**0.001**	**<0.001**
NS background therapies, (n, %)												
# of patients with >= 1 fill, (n, %)	279	89%	5,427	80%	**0.000**	281	89%	5,683	83%	**0.006**	0.860	**0.000**
ACEI/ARBs	213	68%	3,755	55%	**0.000**	219	70%	3,842	56%	**0.000**	0.561	**0.042**
Anticoagulants	37	12%	695	10%	0.392	50	16%	915	13%	0.207	**0.019**	**0.000**
Beta blockers	79	25%	1,689	25%	0.894	89	28%	1,850	27%	0.698	0.184	**0.000**
Calcium channel blockers	52	17%	827	12%	**0.028**	54	17%	1,018	15%	0.294	0.868	**0.000**
Diuretics	209	66%	3,471	51%	**0.000**	212	67%	3,363	49%	**0.000**	0.813	**0.010**
Statins	173	55%	2,593	38%	**0.000**	173	55%	2,867	42%	**0.000**	1.000	**0.000**
# of unique NS background therapies, (mean, sd)	2.4	1.3	1.9	1.4	**0.000**	2.5	1.4	2.0	1.4	**0.000**	0.072	**0.000**
# of claims for NS background therapies, (mean, sd)	12.4	10.7	8.4	9.1	**0.000**	14.2	11.7	10.5	10.3	**0.000**	**0.000**	**0.000**
Calcineurin inhibitors (CNI)												
# of patients with ≥1 fill, (n, %)	104	33%	1,472	22%	**<0.001**	81	26%	2,188	32%	**<0.001**	**0.008**	**<0.001**
# of claims for CNIs, (mean, sd)	2.0	4.3	1.3	3.4	**0.005**	1.6	4.0	2.8	5.4	**<0.001**	0.079	**<0.001**
Conventional synthetic DMARDs (csDMARD)												
# of patients with ≥1 fills of csDMARDs (n, %)	14	4%	923	14%	**<0.001**	13	4%	1,204	18%	**<0.001**	1.000	**<0.001**
# of claims for csDMARDs, (mean, sd)	0.2	1.1	0.6	2.0	**<0.001**	0.2	1.3	1.0	2.7	**<0.001**	0.131	**<0.001**
Nonsteroidal anti-inflammatory drugs (NSAIDs)												
# of patients with ≥1 fill, (n, %)	130	41%	2,641	39%	0.406	120	38%	2,455	36%	0.495	0.312	**<0.001**
# of claims for NSAIDS, (mean, sd)	1.5	3.2	1.3	2.9	0.171	1.5	3.2	1.3	2.9	0.145	0.867	0.716
Opioids												
# of patients with ≥1 fill, (n, %)	157	50%	3,220	47%	0.403	142	45%	2,979	44%	0.679	0.199	**<0.001**
# of claims for opioids, (mean, sd)	1.9	3.8	1.7	4.5	0.410	2.0	3.9	1.8	4.2	0.342	0.564	0.096
NS related procedures												
# of patients with ≥1 NS related procedure, (n, %)	244	77%	5,617	82%	**0.028**	235	75%	5,013	74%	0.739	0.368	**<0.001**
Dialysis	20	6%	1,105	16%	**<0.001**	45	14%	823	12%	0.251	**<0.001**	**<0.001**
Renal transplant	30	10%	1,315	19%	**<0.001**	32	10%	1,475	22%	**<0.001**	0.774	**<0.001**
Renal biopsy	78	25%	1,814	27%	0.514	15	5%	500	7%	0.094	**<0.001**	**<0.001**
Complications of kidney transplant	18	6%	547	8%	0.164	19	6%	681	10%	**0.020**	1.000	**<0.001**
Proteinuria (including Proteinuria test)	225	71%	4,704	69%	0.383	206	65%	4,338	64%	0.549	0.061	**<0.001**

*Baseline period: [index date - 365, index date)

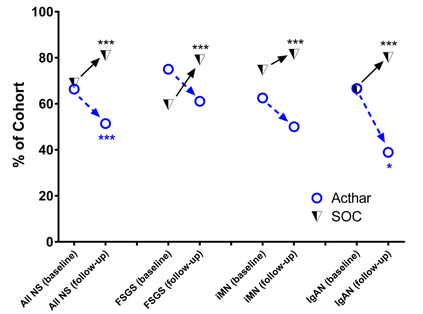
**Followup period: [index date, index date + 365)

***p-value calculated using Chi-square test or Fisher exact test for categorical variables (Acthar Gel cohort vs. SOC cohort in each period), Welch's t-test for continuous variables (Acthar Gel cohort vs. SOC cohort in each period) and McNemar test for categorical variables (Follow-up period vs. Baseline period in each cohort), paired sample t-test for continuous variables (Follow-up period vs. Baseline period in each cohort).

RESULTS

- Patients treated with Acthar Gel were older (49 vs. 46 years, p=0.002), with less commercial coverage (15% vs. 35%), similar racial makeup, and lower comorbidity index score (2.3 ± 1.8 vs. 2.5 ± 2.0, p=0.005) compared to the SOC comparator
- The Acthar Gel cohort had a significant reduction during follow-up in patients taking CS (66% vs. 51%, p<0.001), patients on extended use CS (≥60 days) (37% to 25%, p<0.001), and average daily dose (ADD) (32.1 ± 21.3 to 21.7 ± 21.1, p=0.001), compared to baseline (Fig. 1A)
- Patients in the SOC comparator had a significant increase in the follow-up for patients on CS overall (69% to 81%, p<0.001) and extended use CS (34% to 49%, p<0.001), compared to baseline (Fig. 1A)
- The Acthar Gel sub-cohorts for FSGS (n=72), iMN (n=72), and IgAN (n=36) had a similar trends to the overall cohort, with 15%, 13%, and 18% (p=0.033) reduction in proportion of patients on CS therapy, respectively (Fig. 2)
- The SOC comparator had significant increases of CS use overall and across all three sub-cohorts (Fig. 2)
- The Acthar Gel cohort had an increase in patients on dialysis in the follow-up (6% to 14%, p<0.001), but no change in renal transplants (10% to 10%, p=0.774) or transplant complications (6% to 6%, p=1.000), while the SOC comparator had fewer patients on dialysis (16% to 12%, p<0.001), but an increase in renal transplants (19% to 22%, p<0.001) and transplant complications (8% to 10%, p<0.001)
- In addition to CS use, the Acthar Gel cohort had significant reductions in CNI use (7%), overall reduction of NSAIDs and opioids, while the SOC comparator had significant increase of use for CNIs and csDMARDS, and significant decreases for NSAIDs and opioids (Fig. 1B)

Figure 2. Change in corticosteroid use with Acthar Gel compared to SOC by NS subtype



*p<0.05, **p<0.01, ***p<0.001; FSGS=focal segmental glomerulosclerosis, iMN=idiopathic membranous nephropathy, IgAN=IgA nephropathy

CONCLUSION

- Real-world evidence of nephrotic syndrome patients initiating later line therapy with Acthar Gel had significant reductions in proportion of patients on CS overall, proportion of patients on extended use (>60 days), and average daily dose, while the SOC comparator cohort had significant increases in patients on CS and patients on extended use CS (Table 2)
- There was reduction in CS use across the FSGS, iMN, and IgAN sub-cohorts, like the NS cohort overall (Fig. 2)
- Acthar Gel patients had a significant increase in proportion of patients on dialysis, with no change in renal transplant or complications, while the SOC comparator had a significant reduction of patients on dialysis, but significant increases in patients with transplants or transplant complications (Table 2)
- Acthar Gel is a viable treatment option for patients that don't respond to CS and/or CNIs. Treatment with Acthar Gel shows a steroid-sparing effect and less need for renal transplant compared to the SOC comparator.

LIMITATIONS AND REFERENCES

- This study is limited by the small sample size for patients that initiate Acthar Gel therapy among all NS patients. Due to the small sample size, no exclusion criteria, outside of limiting the data to only adult patients (≥ 18 years old) and patients with contraindicated conditions, was applied before analysis. Other indications for Acthar Gel usage among those diagnosed with NS may also be included in this analysis. Lack of detailed lab values and detailed kidney pathology reports in the claims data prevents true clinical assessment of disease improvement by proteinuria levels and renal glomerular function. This study is limited to commercially insured or Medicare Supplemental health plan members, and as such, results may not be generalizable to government-sponsored health insurance members or those uninsured or underinsured who may not have access to the healthcare resources of interest. This analysis uses claims data which may be limited in the amount of patient information available.

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