Cost-Effectiveness of Acthar Gel versus Standard of Care for the Treatment of Advanced Symptomatic Sarcoidosis

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BACKGROUND

- Sarcoidosis is a chronic granulomatous disease of unknown etiology that primarily affects the lungs and may involve multiple organs[1-4]
  - Prevalence of sarcoidosis is estimated to be 60 per 100,000 adults in the United States (US), with over 25,000 patients diagnosed annually[5]
  - Sarcoidosis has a broad spectrum of clinical manifestations that vary in severity and impair the patient's mental and physical functioning[6]
- Sarcoidosis-related disability can result in a considerable economic burden on patients[6,7]
- Pharmacological treatment is aimed at the reduction of granulomatous inflammation and averting irreversible organ damage while preventing toxicity from medications[8]
  - Oral glucocorticoids are the first-line treatment approved by the US Food and Drug Administration (FDA) for pulmonary sarcoidosis
    - However, persistent glucocorticoid use over the long term is associated with an elevated risk of adverse events and increased healthcare resource burden[9,10]
  - Despite the current standard of care (SoC), there is an unmet need for the treatment of advanced symptomatic sarcoidosis
- Acthar® Gel (repository corticotropin injection) is another treatment approved by the US FDA for symptomatic sarcoidosis[11]
  - Existing literature suggests that Acthar Gel may be a viable treatment option for advanced symptomatic sarcoidosis[12-15]
- No study has examined the economic benefits of Acthar Gel in this patient population
  - Evaluation of interventions integrating data on clinical facets, healthcare resource use and costs, and patient's quality of life to support decision-making for clinicians and payers

OBJECTIVE

To estimate the cost-effectiveness of Acthar Gel versus SoC in patients with advanced symptomatic sarcoidosis from the US payer and societal perspectives over 2 and 3 years

METHODS

Model Overview

- A probabilistic cohort-level state-transition approach was used for this analysis (**Figure 1**)
- Patients were monitored at the end of a 3-month cycle for attainment of partial or complete response (PR/CR)
  - Patients in PR, CR, or no response (NR) state could transition to each of these states at 3-month cycles
  - Following attainment of response, patients could have durable response or relapse to a NR state
  - Patients in NR state received treatment and could transition into a response state or NR based on the probability of treatment success with the respective treatment

Model Inputs

- Clinical parameters and utilities were derived for the modified intent-to-treat population from double-blind randomized phase 4 trial of the Acthar Gel in Participants with Pulmonary Sarcoidosis (PULSAR) trial (NCT03320070) **[Table 1]**
  - Clinical response was based on composite sarcoidosis treatment score (STS), derived from the following measures – pulmonary function tests (percentage predicted forced vital capacity and percentage predicted diffusing capacity of the lungs for carbon monoxide), high-resolution computed tomography and chest x-rays, patient-reported quality of life outcomes (King's Sarcoidosis Questionnaire and Fatigue Assessment Scale), and extent of steroid tapering
- Healthcare utilization, direct costs, and disutilities were sourced from the published literature **(Tables 2 and 3)**
  - All unit costs were inflated to 2023 US Dollars (USD) utilizing the historical Consumer Price Index for medical care from the US Bureau of Labor Statistics

Analyses

- **Model outcome**: Incremental cost-effectiveness ratio (ICER), defined as the difference in total costs divided by the difference in quality-adjusted life-years (QALYs) of Acthar Gel and SoC
- **Base case:** ICER was assessed from both payer and societal perspectives over 2 and 3 years
- **Sensitivity analyses:** Assessed for the time horizon of 2 years from a payer perspective

Figure 1. Schematic of the probabilistic cohort-level state-transition model

Note: Response was assessed based on sarcoidosis treatment score (STS)

Table 1. Clinical parameters among patients with symptomatic pulmonary sarcoidosis

Parameter	Proportion of patients		
Clinical response	**NR**	**PR**	**CR**
Acthar Gel			
3 months	44.4%	37.0%	18.5%
6 months	40.7%	29.6%	29.6%
SoC			
3 months	60.7%	21.4%	17.9%
6 months	53.6%	28.6%	17.9%
FVC% predicted[a]	**NR**	**PR**	**CR**
60.0-69.9	33.3%	20.0%	16.7%
50.0-59.9	16.7%	20.0%	0.0%
Less than 50	11.1%	0.0%	0.0%
Pain[b]	**NR**	**PR**	**CR**
Mild	27.8%	66.7%	75.0%
Moderate	50.0%	13.3%	16.7%
Severe	22.2%	0.0%	0.0%
Depression[c]	**NR**	**PR**	**CR**
Mild	33.3%	26.7%	33.3%
Moderate	33.3%	6.7%	16.7%
Severe	5.6%	6.7%	0.0%
3-month probability[d]	**Acthar Gel**		**SoC**
PR to NR	0.200		0.333
PR to PR	0.400		0.500
PR to CR	0.400		0.167
CR to NR	0.000		0.200
CR to PR	0.600		0.400
CR to CR	0.400		0.400

Abbreviations: CR, complete response; FVC% predicted, forced vital capacity percent predicted; KSQ, King's Sarcoidosis Questionnaire; NR, no response; PR, partial response; SoC, standard of care

[a] Measure for lung function; patients with FVC% predicted ≥70 not included

[b] Pain score was calculated based on pain-related items in KSQ, including joint pain, cough pain, chest pain, and eye pain; patients with "no pain" not included

[c] Depression score was based on the patient's experience with depression as measured on the steroid toxicity questionnaire; patients with "no depression" not included

[d] This only considers the movement of patients between response states and from a response state to a NR state. Probability of transition from a NR state to a response state is based on clinical response probability; patients moving from NR to a response state in any model cycle are assumed to have the same probability of clinical response as that of the first cycle.

Source: Data were derived from the PULSAR trial

Table 2. Health utilities and disutilities

Parameter	Value
Health utility[a]	
NR	0.215
PR	0.612
CR	0.680
Disutilities	
Lung transplant	-0.510
Extrapulmonary organ involvement	
Skin	-0.057
Cardiac	-0.076
Eyes	-0.220
Bone or joint	-0.030
Liver	-0.130
Chronic medication use	
Chronic oral corticosteroid use	-0.023
Substance use disorder	-0.132
Pain	
Mild	-0.170
Moderate	-0.400
Severe	-0.430
Depression	
Mild	-0.130
Moderate	-0.180
Severe	-0.310

Abbreviations: CR, complete response; EQ-5D, EuroQol five-dimension; FVC% predicted, forced vital capacity percent predicted; NR, no response; PR, partial response

[a] EQ-5D health utility score was mapped from the King's Sarcoidosis Questionnaire score, accounting for the disutility based on FVC% predicted [derived from the PULSAR trial]

Table 3. Healthcare resource use and cost inputs

Parameter	Value		
Direct medical costs			
Cost of Acthar Gel; use (12 months)[a]	$42,703; 9.27 packs		
Other Medications	**NR**	**PR**	
Acthar Gel			
Oral corticosteroids	25.5%	12.9%	
Biologics	10.3%	4.3%	
Antimalarial	12.6%	6.0%	
Immunosuppressants	11.9%	6.6%	
SoC			
Oral corticosteroids	95.5%	95.5%	
Biologics	24.0%	24.0%	
Antimalarial	22.7%	22.7%	
Immunosuppressants	63.6%	63.6%	
Cost of medications (12 months)			
Oral corticosteroids	$2,326		
Biologics	$63,694		
Antimalarial	$404		
Immunosuppressants	$2,262		
Sarcoidosis-related healthcare costs			
Inpatient	$28,634		
Physician office	$719		
Laboratory	$182		
Outpatient	$2,049		
Emergency department	$1,027		
Home Health	$3,153		
Durable medical equipment	$1,839		
Other	$3,397		
Respiratory insufficiency			
Lung transplant costs (per transplant)	$496,061		
Extrapulmonary organ involvement costs			
Skin	$9,309		
Cardiac	$12,238		
Eyes	$1,599		
Bones/Joints	$20,845		
Liver	$2,858		
Pain-related costs			
Mild	$13,158		
Moderate	$18,779		
Severe	$17,034		
Sarcoidosis-related opioid abuse	$52,643		
Depression-related costs			
Mild	$7,810		
Moderate	$9,811		
Severe	$13,691		
CS toxicity			
CS dosage group[b]	**NR**	**PR**	**CR**
Intermittent use	5.6%	20.0%	25.0%
Low dose	38.9%	46.7%	50.0%
Moderate dose	38.9%	33.3%	25.0%
High dose	16.7%	0.0%	0.0%
CS-related toxicity costs			
Intermittent use	$40,134		
Low dose	$39,161		
Moderate dose	$43,581		
High dose	$83,995		
Indirect costs[c,d]			
Work-related productivity loss	$4,143		
Caregiving	$4,719		
Work-related training	$23,925		
Substance abuse due to chronic pain	$25,003		

Abbreviations: CR, complete response; CS, corticosteroid; NR, no response; PR, partial response; SoC, standard of care

[a] Using dispensing data from specialty pharmacies, from the last 12 months as of March 29, 2019

[b] Derived from the PULSAR trial

[c] Disability was assumed for patients with moderate-to-severe pain, fatigue, or depression; distribution of patients with a disability was 77.8%, 40.0%, and 25.0% for NR, PR, and CR, respectively

[d] Work-related productivity loss was computed for patients who were employed (41.8%)

Note: All parameter values were sourced from the published literature and all cost presented are annual costs, unless otherwise noted

References for these parameter estimates are available on request

RESULTS

Base case

- From a payer perspective, Acthar Gel versus SoC results in an ICER of $134,796 and $39,179 per QALY over 2 and 3 years, respectively (**Table 4**)
- From a societal perspective, Acthar Gel versus SoC results in an ICER of $117,622 and $21,967 per QALY over 2 years and 3 years, respectively (**Table 4**)

Total costs (Figure 2)

- Acthar Gel versus SoC had lower direct medical and indirect costs over 2 years
- Lower direct medical costs were primarily attributed to reduction in lung transplant and corticosteroid use

Deterministic sensitivity analysis (Figure 3)

- Acthar Gel is a cost-effective strategy over SoC at a threshold of $150,000 per QALY over 2 years from the payer perspective, consistent with the base case
- Efficacy of Acthar Gel, lung transplant cost, the prevalence of pain, the cost related to corticosteroid-related toxicity, and cost of Acthar Gel are major influencers of the ICER

Probabilistic sensitivity analysis (Figure 4)

- Acthar Gel versus SoC is cost-effective for 73.9% of the iterations at a willingness-to-pay threshold of $150,000 per QALY over 2 years from a payer perspective
- Acthar Gel versus SoC results has higher incremental costs but results in gain in QALYs

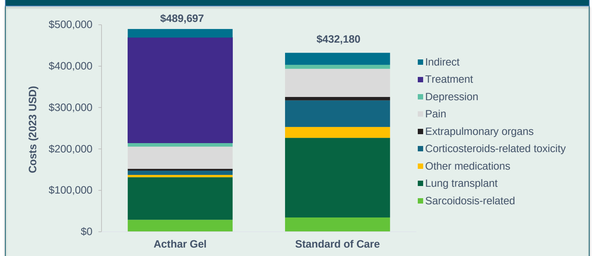
Table 4. Base case incremental cost-effectiveness among patients with symptomatic sarcoidosis

Acthar Gel versus SoC	Incremental costs	Incremental QALYs	ICER (Incremental cost per QALY)
Payer perspective			
2 years	$65,915	0.489	$134,796
3 years	$29,306	0.748	$39,179
Societal perspective			
2 years	$57,517	0.489	$117,622
3 years	$16,431	0.748	$21,967

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life years; SoC, standard of care; USD, United States dollars

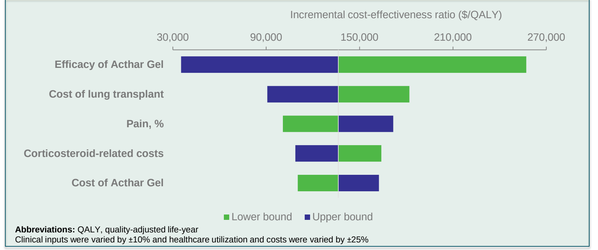
Base case analysis considered ICER over 2 years from the payer perspective; All costs are presented in 2023 USD; Costs and QALYs were discounted at 3.0%; Results are presented on a per-person basis

Figure 2. Base case per patient-year costs among patients with symptomatic sarcoidosis over 2 years



Abbreviations: USD, United States dollars

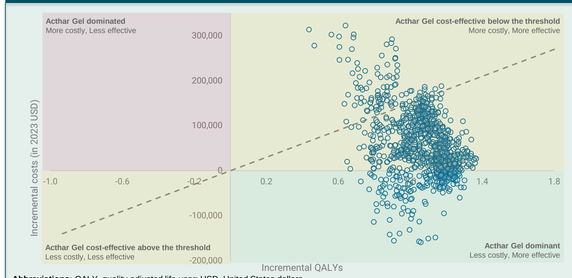
Figure 3. Tornado chart: Deterministic sensitivity analysis comparing Acthar Gel and standard of care



Abbreviations: QALY, quality-adjusted life-year

Clinical inputs were varied by ±10% and healthcare utilization and costs were varied by ±25%

Figure 4. Cost-effectiveness plane comparing Acthar Gel and standard of care



Abbreviations: QALY, quality-adjusted life-year; USD, United States dollars

Performed using 1,000 model iterations

LIMITATIONS

- Clinical, SoC, and health utility data were derived from the PULSAR clinical trial, which may not reflect real-world clinical practice
  - Further, PULSAR clinical trial had a small sample size and may have introduced bias to the findings
- Exact magnitude of sarcoidosis is not well quantified in literature; a simplified care paradigm was applied for the model which may not capture the complexity of sarcoidosis
- Clinical response was based on composite STS; this measure has its strengths and limitations and thus might result in variation in cost-effectiveness estimates
- PULSAR clinical trial examined outcomes at 24 weeks in the randomized phase; the model extrapolated data to assess the cost-effectiveness over 2 and 3 years, which might result in under or over-estimation of the effectiveness of Acthar Gel
- Healthcare utilization, costs, and health disutility were sourced from published literature and may result in under or over-estimation of results
  - Uncertainty in the parameters was accounted for by conducting a sensitivity analysis

CONCLUSIONS

- Findings from this analysis suggest that Acthar Gel is a cost-effective, value-based treatment option for appropriate patients with advanced symptomatic sarcoidosis at a willingness-to-pay threshold of $150,000 over 2 and 3 years from the US payer and societal perspectives
  - Acthar Gel versus SoC results in additional QALYs, thereby improving patients' quality of life which is an important consideration for advanced symptomatic sarcoidosis
  - Initial high cost of Acthar Gel treatment for sarcoidosis is offset by the reduction in disease progression-related medical costs
  - ICER for Acthar Gel was reduced from 2 to 3 years, resulting from a decrease in medical direct and/or indirect costs with improvement in QALYs compared to SoC
- Sensitivity analyses findings were consistent with the base case
  - Efficacy of Acthar Gel, lung transplant cost, prevalence of pain, cost related to corticosteroid-related toxicity, and the cost of Acthar Gel were key drivers of variation in ICER estimates
    - Improved efficacy of Acthar Gel may delay lung damage and corticosteroid-related toxicity, thereby reducing cost burden with improvement in patient quality of life
- Further research is required to examine the long-term clinical effectiveness and cost-effectiveness of Acthar Gel for advanced symptomatic sarcoidosis

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DISCLOSURES

This study was sponsored by Mallinckrodt Pharmaceuticals; George Wan, Kyle Hayes, and John Niewoehner are employees of Mallinckrodt Pharmaceuticals; Ishveen Chopra was a research collaborator and Jas Bindra and Mary Panaccio were paid research consultants for the study