Reduction in Hospitalizations Following Initiation of Amikacin Liposome Inhalation Suspension: A Retrospective Cohort Study of Patients in Real-World Settings

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RATIONALE

- *Mycobacterium avium* complex (MAC) lung disease (LD) is a rare infectious disease associated with worsening lung condition, increased mortality, and high rates of hospitalizations[1,2]
  - MAC-LD is difficult to treat; 20% to 40% of patients do not respond to conventional guideline-based therapy[3]
- In 2018, amikacin liposome inhalation suspension (ALIS) became the first therapy to receive accelerated approval by the US Food and Drug Administration for adult patients with refractory MAC-LD who have limited or no alternative treatment options
  - In clinical trials, addition of ALIS to guideline-based therapy showed evidence of MAC infection elimination in sputum by month 6, which was maintained in most patients through the end of treatment (up to 12 months post-conversion)[4,5]
- The global treatment guidelines for nontuberculous mycobacterial (NTM) lung disease (updated in 2020) recommend addition of ALIS as part of a combination antibacterial drug regimen in patients with MAC-LD who have failed therapy after at least 6 months of guideline-based therapy[6]

OBJECTIVE

- To assess changes in hospitalizations among patients initiating ALIS in the real-world setting

METHODS

Study Design

- A noninterventional retrospective cohort study

Data Source

- The All-Payer Claims Database (APCD) was used to identify patients receiving ALIS from October 2018 to April 2020
  - Data in the APCD are sourced directly from claims clearinghouses responsible for managing claims transactions for Commercial, Medicaid, Medicare Fee Schedule, and Medicare Advantage; more than 300 million unique patients across all US geographic locations are included

Study Population

- Eligibility criteria included age ≥18 years, ≥1 pharmacy claim for ALIS, and ≥12 months of continuous enrollment in health plans both before and after ALIS initiation

Study Outcomes

- Hospitalizations, including inpatient stays plus hospital emergency department visits during the 12 months before and 12 months after initiation of ALIS therapy for both all-cause and respiratory disease–related utilization
- Respiratory disease–related hospitalizations were ascertained using *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)* codes for respiratory diseases

Analysis

- Baseline characteristics, including age, sex, insurance plan type, geographic region, and comorbidities were identified during the 12 months before ALIS initiation and summarized using descriptive statistics (mean [standard deviation; SD] for continuous variables, and frequency [%] for categorical variables)
- All-cause and respiratory disease–related hospitalizations (including inpatient stays and hospital emergency department visits leading to hospitalizations) were compared for the 12 months before and after ALIS initiation
  - Hospitalizations were reported for every 6-month interval of the study period; the 6 months before ALIS initiation was the reference period for statistical comparisons
- To account for the nonindependence of this pre-post analysis, McNemar χ^2 tests were used to compare the proportion of patients with hospitalizations in the baseline period with the proportion of patients with hospitalizations in the follow-up period; Wilcoxon signed rank tests were used to compare the number of healthcare resource utilization outcomes per patient and lengths of stay per hospital admission before and after treatment
- Data analyses were conducted using SAS, version 9.4

RESULTS

- A total of 1542 patients had ≥1 pharmacy claim for ALIS between October 2018 and April 2020
- Of the eligible study population, 331 patients with continuous health plan enrollment before and after ALIS initiation formed the analysis population (**Table 1**)

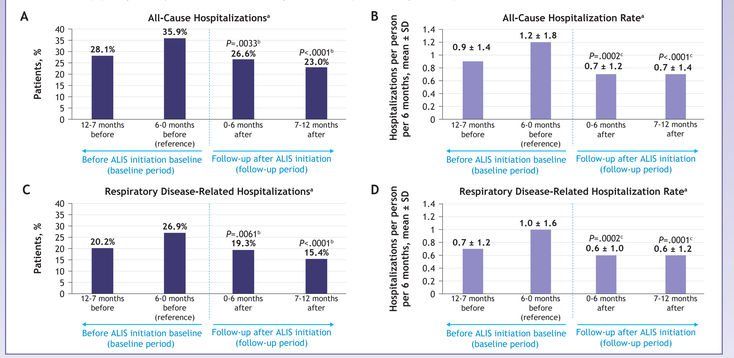
Table 1. Attrition Table

ALIS Cohort		
Inclusion Criteria	**Number of Patients Remaining**	**Percentage of Originally Identified Population Remaining**
1. ≥1 Claim for ALIS during identification period *(restrict to adjudicated/approved claims)*	1542	100%
2. Age ≥18 years on index date	1516	98%
3. Continuous capture (≥1 medical/pharmacy claim record) of patient's health plan 12 months before and after the index date	331	21%
Final sample size: patients with approved ALIS claims	**331**	**21%**

Patient Demographics and Clinical Characteristics

- Patient demographics and common comorbidities are presented in **Table 2**
- Patients were predominantly female (77.9%) and aged ≥55 years (84.0%), reflective of the population of patients with MAC in the real world; most patients (93.4%) had respiratory diseases

Figure 1. Proportion of patients with hospitalizations and hospitalization rates before and after ALIS initiation (A) all-cause and (C) respiratory disease-related hospitalizations. Hospitalization rate per 6 months before and after ALIS initiation for (B) all-cause and (D) respiratory disease-related hospitalization (total 331 patients).



[a] Hospitalizations include inpatient stays as well as hospital emergency department visits leading to inpatient admission.
[b] McNemar χ^2 test.
[c] Wilcoxon signed rank test.

Table 2. Demographic and Clinical Characteristics of Patients During the Period of 12 Months Before ALIS Initiation

Characteristic	ALIS cohort (N=331)
Age, mean (SD), years	64.6 (16.0)
Age category, n (%)	
18-24 years	17 (5.1)
25-34 years	10 (3.0)
35-44 years	12 (3.6)
45-54 years	14 (4.2)
55-64 years	71 (21.5)
65-74 years	115 (34.7)
75+ years	92 (27.8)
Sex, n (%)	
Female	258 (77.9)
Male	73 (22.1)
Health insurance, n (%)	
Commercial	92 (27.8)
Medicare	218 (65.9)
Medicaid	21 (6.3)
US geographic region, n (%)	
Northeast	74 (22.4)
North Central	42 (12.7)
South	152 (45.9)
West	63 (19.0)
CCI, mean (SD)	2.2 (2.0)
Diseases of the respiratory system, n (%)	309 (93.4)
NTM lung disease, n (%)	263 (79.5)
Other pulmonary comorbidities and symptoms, n (%)	311 (94.0)
Aspergillosis	28 (8.5)
Asthma	74 (22.4)
Bronchiectasis	189 (57.1)
COPD	151 (45.6)
Cough	125 (37.8)
Cystic fibrosis with pulmonary manifestations	33 (10.0)

Table 2 (Cont'd). Demographic and Clinical Characteristics of Patients During the Period of 12 Months Before ALIS Initiation

Characteristic	ALIS cohort (N=331)
Diffuse panbronchiolitis	8 (2.4)
Dyspnea	132 (39.9)
Emphysema	51 (15.4)
Hemoptysis	44 (13.3)
Idiopathic interstitial lung disease	19 (5.7)
Idiopathic pulmonary fibrosis	27 (8.2)
Lung transplant	6 (1.8)
Malignant neoplasm of bronchus and lung	15 (4.5)
Pneumonia	2 (0.6)
Pulmonary TB	7 (2.1)
Simple and mucopurulent chronic bronchitis	15 (4.5)
Smoking history	64 (19.3)
Nonpulmonary comorbidities, n (%)	274 (82.8)
Cardiovascular disease	195 (58.9)
Chronic heart failure	15 (4.5)
Chronic kidney disease	30 (9.1)
Dementia	1 (0.3)
Diabetes mellitus	59 (17.8)
Gastroesophageal reflux	97 (29.3)
Hypertension	138 (41.7)
HIV/AIDS	2 (0.6)
Malnutrition	38 (11.5)
Osteoporosis	60 (18.1)
Other cancers	42 (12.7)
Overweight and obesity	11 (3.3)
Rheumatoid arthritis	10 (3.0)
Sjögren syndrome	5 (1.5)
Transplant of kidney or liver	7 (2.1)
Underweight	39 (11.8)
Other NTM disease[a]	24 (7.3)

[a] Other NTM disease includes cutaneous mycobacterial infection and disseminated mycobacterium avium-intracellulare complex (DMAC).

Impact on Hospitalizations

Both all-cause and respiratory disease–related hospitalizations were significantly reduced in the 12 months following ALIS initiation (**Table 3** and **Figure 1**)

- All-cause hospitalizations occurred in the highest proportion of patients in the 6 months immediately preceding ALIS initiation (35.9%)
- A significant reduction in the proportion of patients with all-cause hospitalizations was observed after receiving the first 6 months of ALIS treatment, from 35.9% in the 6 months immediately before ALIS initiation (reference period) to 26.6% (*P*=.0033) in the first 6 months after ALIS initiation
- These significant reductions in the all-cause hospitalizations continued during the follow-up period of 7 to 12 months after ALIS initiation, from 35.9% in the 6 months before ALIS initiation (reference period) to 23.0% (*P*<.0001) in the 7 to 12 months after ALIS initiation
- The mean ± SD number of all-cause hospitalizations per person per 6 months decreased significantly from 1.2 ± 1.8 in the 6 months before ALIS initiation to 0.7 ± 1.2 (*P*=.0002) and 0.7 ± 1.4 (*P*<.0001) in the 0 to 6 months and 7 to 12 months after ALIS initiation, respectively
- For respiratory disease–related hospitalizations, statistically significant reductions were observed in both proportion of patients and number of hospitalizations per person per 6 months in the 0 to 6 months and 7 to 12 months after ALIS initiation, respectively
- Similar statistically significant reductions were also observed for lengths of stay for both all-cause and respiratory disease–related hospitalizations in the 0 to 6 months and 7 to 12 months after ALIS initiation, respectively

Table 3. Hospitalizations Before and After ALIS Initiation (N=331)

	Baseline (before ALIS initiation)		Follow-up (after ALIS initiation)			
Hospitalizations	**7-12 months**	**0-6 months (reference)**	**0-6 months**	***P* value**	**7-12 months**	***P* value**
Proportion of patients with hospitalizations						
All-cause, n (%)	93 (28.1)	119 (35.9)	88 (26.6)	.0033[a]	76 (23.0)	<.0001[a]
Respiratory disease-related, n (%)	67 (20.2)	89 (26.9)	64 (19.3)	.0061[a]	51 (15.4)	<.0001[a]
Number of hospitalizations per person per 6 months						
All-cause, mean ± SD	0.9 ± 1.4	1.2 ± 1.8	0.7 ± 1.2	.0002[b]	0.7 ± 1.4	<.0001[b]
Respiratory disease-related, mean ± SD	0.7 ± 1.2	1.0 ± 1.6	0.6 ± 1.0	.0002[b]	0.6 ± 1.2	.0001[b]
Length of stay (per hospital admission), days						
All-cause, mean ± SD	4.7 ± 4.1	6.2 ± 4.9	3.9 ± 3.8	.0004[b]	4.9 ± 5.6	.0055[b]
Respiratory disease-related, mean ± SD	4.9 ± 4.1	6.2 ± 4.5	4.4 ± 4.0	.0116[b]	5.2 (5.7)	.0209[b]

Hospitalizations include inpatient stays as well as hospital emergency department visits leading to inpatient admission.
[a] McNemar χ^2 test.
[b] Wilcoxon signed rank test.

STRENGTHS AND LIMITATIONS

- The APCD provides comprehensive data inclusive of Medicaid, Medicare, and commercial insurance plans for a nationwide US sample
- There are several study limitations inherent to claims data analysis
  - Pharmacy claims for dispensed ALIS prescriptions were used to identify the patients who initiated ALIS; because there is no *ICD-10-CM* diagnosis code specific to MAC-LD, the study cohort could not be limited specifically to MAC-LD by *ICD-10-CM* diagnosis codes; however, the time stamp on pharmacy claims was used to remove rejected and abandoned claims that were not consistent with the ALIS label indications; therefore, the claims for ALIS prescriptions that were retained for the analysis were consistent with ALIS label
  - Claims data lack the clinical detail of medical charts or prospectively collected data; therefore, the rate of sputum conversion, signs, symptoms, and discontinuation reason could not be assessed; pharmacy claims only capture medication dispensing, which may not reflect actual real-life drug usage
  - The findings may not be generalizable to patients different from the study population, with insurance types not included in the database or with no insurance coverage

CONCLUSIONS

- Significant reductions in both all-cause and respiratory disease–related hospitalizations were observed in the 12 months after ALIS initiation in real-world settings
- The results of this study provide resource utilization related economic information to better understand the impact of initiating ALIS treatment

ABBREVIATIONS

AIDS, acquired immunodeficiency syndrome; ALIS, amikacin liposome inhalation suspension; APCD, All-Payer Claims Database; CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; *ICD-10-CM*, *International Classification of Diseases, Tenth Revision, Clinical Modification*; LD, lung disease; MAC, *Mycobacterium avium* complex; MAC-LD, *Mycobacterium avium* complex lung disease; NTM, nontuberculous mycobacterial; SD, standard deviation; TB, tuberculosis.

DISCLOSURES

- JW, MH, and A Chatterjee are employees of Insmed Incorporated.
- A Cyhaniuk and EA are employees of STATinMED Research, Plano, TX.

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