Retrospective Analysis to Assess the Effect of Targeted Clinical Interventions on the Discontinuation Rate of Amikacin Liposome Inhalation Suspension Therapy among Patients Treated for Refractory *Mycobacterium avium* Complex Lung Disease

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Background

Nontuberculous mycobacteria (NTM) lung disease is most commonly attributed to the development of an infection from the inability to clear the *Mycobacterium avium* complex (MAC) species.[1,2]

Treatments for refractory MAC lung disease remain limited, considering intravenous aminoglycosides are associated with nephrotoxicity and ototoxicity.[1,2] Amikacin liposome inhalation suspension (ALIS), the first approved treatment in the U.S. for refractory MAC lung disease, targets delivery into the lungs to minimize systemic exposure.[2,3] The 2020 NTM Clinical Practice Guidelines strongly recommend that ALIS be added to treatment regimens for patients with refractory MAC lung disease.[4]

Previous research has been conducted to assess the reasons for discontinuation of ALIS using real-world evidence from a national rare pharmacy. Discontinuation was primarily due to adverse events such as bronchospasm, cough and dysphonia. Utilizing this data, targeted clinical interventions were implemented to decrease premature discontinuation of therapy. Patients on ALIS therapy may benefit from additional support, however, there are currently no studies assessing targeted clinical interventions and their effect on ALIS discontinuation.

Objective

To determine if targeted clinical interventions made by a national rare pharmacy change the discontinuation rate of ALIS due to adverse events and the number of days on therapy among patients treated for refractory MAC lung disease.

Methods

This retrospective analysis utilizes a national rare pharmacy's database to identify patients receiving ALIS from April 1, 2020 to February 28, 2021. Targeted clinical interventions were initiated in March of 2020 and continue to be made telephonically to patients to include side effect mitigation strategies for some of the most common side effects. As part of the intervention, clinical pharmacists also review goals of therapy and set expectations of ALIS prior to starting therapy. The total population includes patients receiving at least one shipment of ALIS within the timeframe. The discontinue population is defined as patients receiving at least one shipment who discontinued therapy within the timeframe. Patient profiles and dispensing databases were reviewed to obtain patient demographics, shipments and reasons for discontinuation to assess the percentage of patients who discontinued therapy due to adverse events and persistence on therapy after clinical interventions were initiated.

Figure 1. Study Cohort

PANTHERx Rare patients aged 18 years or older

↓

Patients with at least one initial shipment between April 1, 2020 and February 28, 2021

↓

Patients who are prescribed the standard once daily dosing of ALIS indicated for the treatment of MAC lung disease
n = 344

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Patients with at least one shipment who discontinued ALIS between April 1, 2020 and February 28, 2021
n = 133

Results

Figure 2. Total Population Demographics (n=344)

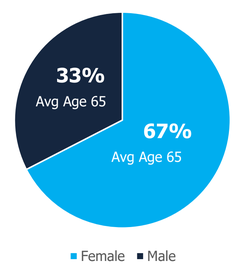


Figure 3. Prescriber Specialty

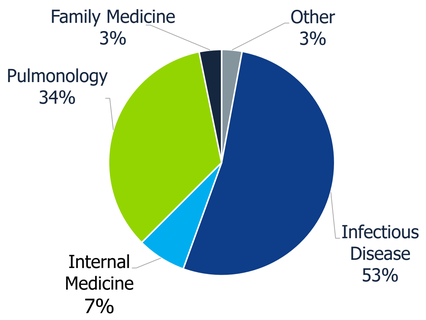


Figure 4. Discontinue Population Demographics (n=133)

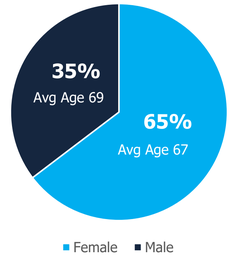


Figure 5. Antibiotic Background Regimen in the Discontinue Population

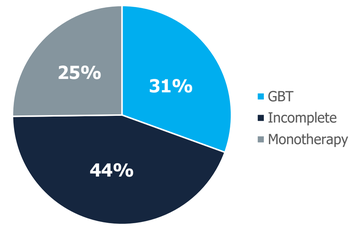


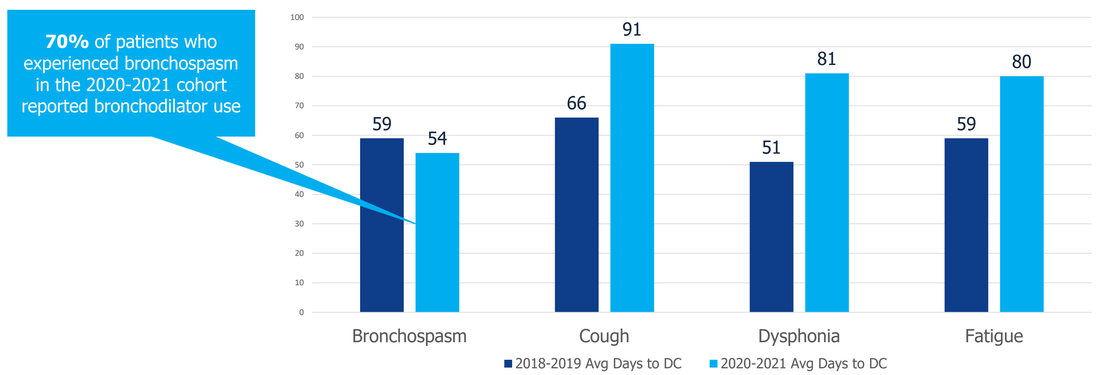
Table 1. Amikacin Liposome Inhalation Suspension Discontinuations

Final Discontinuation Reason	Count	Average Age	Average Days to Discontinuation
Adverse Event	73	70	71
Therapy Complete	13	75	139
Prescriber Choice Unknown	13	66	130
Deceased	12	70	63
Insurance/Cost	5	49	69
Patient Choice Unknown	5	64	167
Patient Unreachable	5	50	90
Therapy Change	5	69	105
Patient Transferred Pharmacy/Provider	2	58	265
Total	**133**	**68**	**91**

Table 2. Adverse Event Discontinuations

Adverse Event Type	Percent of Total Adverse Events	Average Days to Discontinuation
Bronchospasm	37%	54
Cough	19%	91
Dysphonia	14%	81
Fatigue	11%	80
Ototoxicity	10%	106
Hemoptysis	8%	70
Upper Airway Irritation	8%	93
GI Upset	8%	28
Chest Discomfort	4%	61

Figure 6. Comparison of Average Days to Discontinuation due to an Adverse Event



Discussion and Conclusion

In this 11-month, retrospective analysis, the most common reasons for discontinuation of ALIS were adverse events, completion of therapy and prescriber's decision. Among the total study population, 21.2% discontinued due to an adverse event, which compares to the 17.4% of patients who discontinued due to an adverse event in the CONVERT trial.[2] Of the 13 patients who reported completion of ALIS therapy, 4 of those patients reported culture conversions, while 3 of the remaining 9 patients reported improvement in symptoms or lung function.

When comparing the average days to discontinuation due to cough, dysphonia and fatigue to the previously completed study, patients in this study were able to persist on ALIS therapy for approximately 25 days more. This improvement could be attributed to the targeted clinical interventions made by the dispensing rare pharmacy, which included side effect mitigation strategies for cough, dysphonia and fatigue.

Consistent with the previous findings, the leading adverse events contributing to discontinuation were bronchospasm, cough and dysphonia. As bronchospasm continues to be one of the primary adverse events leading to discontinuation, this study showed that approximately 70% of patients who experienced bronchospasm were also using a bronchodilator, which may have caused exacerbation of this side effect.

Considering this patient population being high-risk during the COVID-19 pandemic, the results of this study may have been impacted, however, it is evident that the targeted clinical interventions helped patients who were experiencing the most common side effects persist on ALIS longer.

References

1. Shirley M. Amikacin Liposome Inhalation Suspension: A Review in Mycobacterium avium Complex Lung Disease [published correction appears in Drugs. 2019 Apr 3;:]. *Drugs*. 2019;79(5):555-562.
2. Griffith DE, Eagle G, Thomson R, *et al*. Amikacin Liposome Inhalation Suspension for Treatment-Refractory Lung Disease Caused by *Mycobacterium avium* Complex (CONVERT). *Am J Respir Crit Care Med*. 2018;198(12):1559-1569.
3. ARIKAYCE [prescribing information]. Bridgewater, NJ: Insmed Incorporated; 2018.
4. Daley CL, Iaccarino JM, Lange C, *et al*. Treatment of Nontuberculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline. *Clin Infect Dis*. 2020;71(4):e1-e36.

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