A Retrospective Analysis to Assess the Discontinuation of Amikacin Liposome Inhalation Suspension Therapy Among Patients Treated for Refractory Mycobacterium Avium Complex Lung Disease

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Background

Mycobacterium avium complex (MAC) is one of the most common nontuberculous mycobacteria (NTM) pathogen in the U.S.[1] The recommended initial treatment regimen for most patients with MAC lung disease is a three-times-weekly drug regimen including azithromycin or clarithromycin, ethambutol, and rifampicin or rifabutin.[2] The addition of amikacin liposome inhalation suspension (ALIS) to the oral treatment regimen is recommended for patients who have failed guideline-based therapy after at least 6 months.[2] For refractory MAC lung disease patients, guidelines recommend daily azithromycin or clarithromycin, daily ethambutol, daily rifampicin or rifabutin, and daily ALIS or intermittent intravenous aminoglycoside.[2] Guidelines suggest treatment to be administered for at least 12 months after culture conversion.[2]

ALIS is the first and only FDA-approved treatment for adults with refractory MAC lung disease as part of a combination antibacterial drug regimen in adults who did not respond to previous treatment.[3] Treatment options are limited in refractory disease and without completion of the recommended treatment course there is concern the pathogen will not be eradicated. The CONVERT clinical trial gave potential reasons for premature therapy discontinuation.[3] Understanding real-world reasons for discontinuation will be useful in designing interventions to help patients complete therapy.

Objective

The purpose of this study is to assess the discontinuation rate of ALIS therapy and determine the probable reasons.

Methods

A retrospective database analysis of a national rare pharmacy servicing patients receiving ALIS from October 1, 2018 to September 30, 2019 will be conducted. The total population will be defined as patients receiving at least one shipment within the set timeframe. The discontinue population will be defined as patients receiving at least one shipment who also reported discontinuation within the set timeframe. Patient profiles and dispensing databases will be reviewed to obtain all variables. The primary measure of interest is the percent of patients who discontinued therapy. Secondarily, the study will assess the specific reasons for discontinuation, the time to discontinuation, patient characteristics, and prescriber specialty base. Descriptive statistics will be used for the population and to determine the most common reasons for discontinuation.

Results

Figure 1: Total Population Demographics

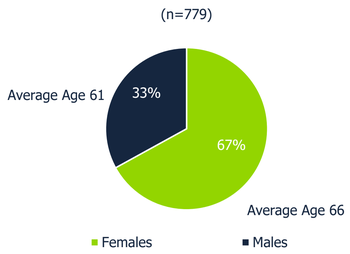


Figure 2: Prescriber Specialty

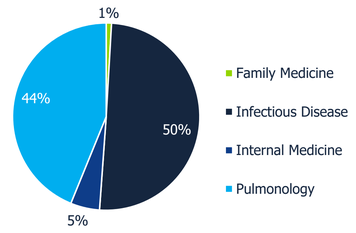


Figure 3: Discontinue Population Demographics

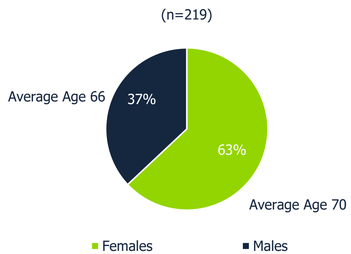


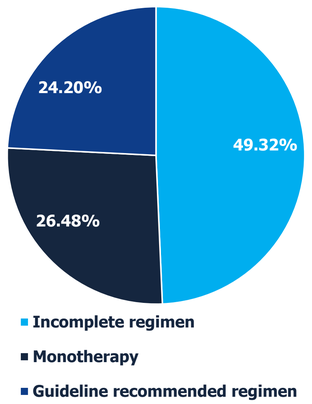
Table 1: Amikacin Liposome Inhalation Suspension Discontinuations

Final Discontinuation Reason	Count	AVG Age	AVG Days to D/C	Discontinuation Rate
Adverse event	135	70	69	17.33%
Discontinued by MD unknown	19	65	134	2.44%
Patient deceased	17	73	97	2.18%
Therapy complete	14	60	146	1.80%
Patient refused	10	75	65	1.28%
Patient unreachable	8	52	167	1.03%
Therapy change	6	60	90	0.77%
No response from MD	3	71	66	0.39%
Patient/MD request to fill at other SP	2	77	99	0.26%
Other	5	50	78	0.64%
Total	**219**	**68**	**86**	**28.12%**

Table 2: Adverse Event Discontinuations

Adverse Event Type	Count	AVG Days to D/C
Bronchospasm	45	59
Cough	33	66
Dysphonia	29	51
Upper airway irritation	14	56
Hospitalization	13	73
Fatigue/asthenia	11	59
Not disclosed	10	81
Ototoxicity	8	130
Chest discomfort	7	68
Not effective	7	74
Nausea	6	85
Pneumonia	6	51
Diarrhea	5	82
Headache	5	34

Figure 4: Antibiotic Background Regimen Use in Discontinue Population



Discussion

In this study, 28.1% of patients discontinued their ALIS therapy prematurely compared to 33.5% and 20.3% seen in two of the clinical trials.[3] Most of the discontinuations, 61.6%, were due to adverse drug events. This study found that 17.3% of patients discontinued due to adverse events, which compares to 17.4% and 14.9% seen in clinical trials.[3] The most common adverse events reported included bronchospasm, cough, dysphonia, and upper airway irritation, with each resulting in an average number of days to discontinuation below 90 days. It is evident that adverse events are a primary barrier to continuation of therapy and appropriate mitigation strategies may be necessary to improve continuation of therapy.

Patients who were noted to have completed therapy had an average number of 146 days of therapy before discontinuation. This is well below the guideline recommendation, suggesting patient and provider education may be warranted. Finally, the study assessed whether the patient's regimen followed treatment guidelines. Only 24.2% of patients who discontinued therapy were on a guideline recommended antibiotic background regimen consisting of a macrolide, a rifamycin, and ethambutol with or without additional antibiotics. Future research analyzing how background regimens correlate with discontinuation of therapy and eradication of infection is still needed. Limitations to this study include patient-reported antibiotic background regimens and reporting of days to discontinuation may not account for therapy holds ultimately leading to discontinuation.

Conclusion

Discontinuation of ALIS was primarily due to adverse events with the most commonly reported adverse events being bronchospasm, cough, dysphonia, and upper airway irritation. Of the patients who discontinued therapy, a majority were not on a guideline recommended antibiotic background regimen.

References

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