

has led some authorities to state that it cannot simultaneously be a dietary supplement and hence the concerns raised by Scharf et al. However, to date, the Food and Drug Administration has not pursued this angle aggressively, and most of the action against CBD manufactures and/or sellers has been in response to unsubstantiated medical claims. The Food and Drug Administration has announced plans to release new guidance in the near future. Pending that announcement, we appear to be in limbo, where CBD remains readily available to consumers while government agencies continue to debate its long-term fate.

The fact that manufactures and sellers of CBD often make unsubstantiated medical claims was noted in our article but bears repeating.

We also noted that the CBD market is crowded with many products that do not contain the ingredients or the amounts found on the label. To help guide patients who choose to use a CBD or hemp oil product, we included in our article a section titled “Finding a Quality Product” to help offer guidance for consumers navigating this burgeoning market.

We also appreciate the added cautionary notes provided by Scharf et al with regard to the extra risks associated with vaping CBD (or any substance). Given space limitations, we were not able to discuss the many forms of CBD in detail and so we are grateful for the opportunity to echo the concerns about vaping in particular.

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1. Scharf EL, Ward AM, Ebbert JO. Commercial cannabinoid caution: a new gold rush. *Mayo Clin Proc.* 2020;95(1):200.

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Amikacin Liposome Inhalation Suspension as a Treatment Option for Refractory Nontuberculous Mycobacterial Lung Disease Caused by *Mycobacterium avium* Complex



To the Editor: We read with much interest the review by Shulha et al.¹ The article is a comprehensive and well-written overview of pharmacological treatment approaches of nontuberculous mycobacterial (NTM) diseases. Table 2 (titled “NTM Medication Dosing, Adverse Effects, and Recommended Monitoring”), however, did not include an approved treatment option for NTM lung disease caused by *Mycobacterium avium* complex (MAC), namely, amikacin liposome inhalation suspension (ALIS; Ari-kayce). Amikacin liposome inhalation suspension is the first Food and Drug Administration (FDA)—approved medication with a specific indication for refractory MAC lung disease (MAC-LD). It was granted accelerated approval by the FDA in September 2018 and is “indicated in adults who have limited or no alternative treatment options, for the treatment of *Mycobacterium avium* complex (MAC) lung disease as part of a combination antibacterial drug regimen in patients who do not achieve negative sputum cultures after a minimum of

six consecutive months of a multidrug background regimen therapy.”^{2(p1)}

The accelerated FDA approval was based mainly on the results of the phase 3 CONVERT study (clinicaltrials.gov Identifier: NCT02344004),³ which reported a more than 3-fold increase in culture conversion rates by month 6 when ALIS was added to a background multidrug regimen compared with those treated with their continued background regimen alone (n=65/224, [29.0%] vs n=10/112 [8.9%]; $P < .001$).³ It should be noted that a rigorous definition of *culture conversion* was used in CONVERT in that patients had to have 3 consecutive monthly negative sputum cultures by month 6 to meet the primary end point. Importantly, data from CONVERT presented at American Thoracic Society annual meeting in May 2019 demonstrated that among patients with treatment-refractory disease who received ALIS in addition to a background regimen and met the primary end point of culture conversion by month 6, 80% (n=52) were confirmed culture negative at the end of treatment and 63% (n=41) remained culture negative 3 months after discontinuing all MAC treatments.⁴ Because relapse and reinfection are common in MAC-LD, the durability of sputum conversion reported in CONVERT is particularly encouraging. The most common adverse reactions reported in CONVERT at the month-6 safety analysis were primarily respiratory (ALIS plus background regimen, 87.4%; background regimen alone, 50.0%), predominantly mild to moderate in intensity, and included dysphonia, cough, dyspnea, hemoptysis, and oropharyngeal pain.³

As noted in a 2012 review by Griffith and Aksamit,⁵ “the choices for effective treatment of these patients [with refractory NTM lung disease] are depressingly sparse.”^(p218)

Physicians who manage patients with refractory MAC-LD should have access to information on all potential treatment approaches, as this disease remains quite difficult to treat and is associated with poor outcomes and high mortality.⁵ Amikacin liposome inhalation suspension is currently the only FDA-approved pharmaceutical product with a specific indication in patients with MAC-LD and is an important therapeutic option for some patients with treatment-refractory disease. The CONVERT study, together with the phase 2 study mentioned in Shulha's review,^{1(p1574)} represents the largest body of evidence for antibiotic efficacy and safety in this rare and difficult-to-treat pulmonary disease.

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2. Arikayce [package insert]. Bridgewater, NJ: Insmed Inc; 2018.
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In reply—Amikacin Liposome Inhalation Suspension as a Treatment Option for Refractory Nontuberculous Mycobacterial Lung Disease Caused by *Mycobacterium avium* Complex

We thank Swenson and Del Parigi¹ for their comments on our article.² The article originally submitted on September 6, 2018. This formulation of amikacin inhalation (Arikayce) received Food and Drug Administration approval on September 28, 2018. Although we agreed that liposomal amikacin is an important therapeutic option for refractory mycobacterium avium complex pulmonary disease, at the time of our original submission we had included timely information on pages 1574 to 1575. Unfortunately, we did not have the Food and Drug Administration—approved dosage of Arikayce at the time of submission nor did the reviewers request us to include this information in Table 2 upon editing.

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Potential Competing Interests: The author reports no competing interests.

1. Swenson C, Del Parigi A. Amikacin liposome inhalation suspension as a treatment option for refractory nontuberculous mycobacterial lung disease caused by *Mycobacterium avium* complex. *Mayo Clin Proc.* 2020;95(1):201-202.

2. Shulha JA, Escalante P, Wilson JW. Pharmacotherapy approaches in nontuberculous mycobacteria infections. *Mayo Clin Proc.* 2019;94(8):1567-1581.

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FRIENDS: A Communication Guide for Advance Care Planning

To The Editor: We propose a user-friendly communication tool to guide and routinize Advance Care Planning (ACP) discussions with patients in any care setting. ACP empowers patients to communicate their preferences for medical care in case they become incapacitated. ACP decreases stress for surrogate decision makers,¹ reduces health care costs, and produces positive outcomes at both patient and systems levels.² However, a national survey³ found that almost half (46%) of physicians felt unsure of what to say and less than one third reported having any end-of-life conversation training. Now that Medicare requires its beneficiaries be offered ACP services routinely,⁴ it is critical for physicians to get comfortable having these discussions. We propose FRIENDS as a communication tool to train clinicians on ACP discussions.

1. Familiarize yourself with advance directives forms: An Advance Directive (AD) is the documentation of decisions generated from ACP discussions. Clinicians must educate themselves on different types of ADs, as laws and documentation required vary by state (Table).

2. Routinize the conversation: ACP discussions should be a routine part of the clinical encounter regardless of the patient's age or stage of illness. This normalizes the process for both the patient and clinician.