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Adherence to inhaled antibiotics in people with cystic fibrosis: insights from a virtual patient advisory board

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ABSTRACT

Background: Chronic airway infection by *Pseudomonas aeruginosa* significantly impacts the health of people with cystic fibrosis (PwCF), presenting complex treatment challenges.

Research design and methods: To gain insights into PwCF's experiences, a virtual European Patient Advisory Board was convened. Board explored inhaled antibiotic usage, treatment adherence, and associated challenges. Additionally, an online survey was conducted among PwCF to further understand real-life experiences and unmet needs, particularly related to CFTR modulators.

Results: The Advisory Board proved instrumental in collecting valuable real-world perspectives, offering potential avenues for reshaping the care model for complex diseases like cystic fibrosis.

Conclusions: PwCF on CFTR modulators are questioning the necessity of continuing chronic medications and therapies. Physicians are urged to carefully consider the balance between simplifying antibiotic treatment and the risk of clinical deterioration due to bacterial infections when making treatment decisions. Furthermore, the development and global harmonization of diagnostic tools for chronic lung damage and treatment guidelines are crucial to justify the demanding routines that PwCF must endure to manage their condition.

The heterogeneity in patient journeys, diagnostic challenges, treatment complexity, and issues related to adherence highlight the need for patient-centric, personalized care that emphasizes improving and maintaining treatment adherence to optimize cystic fibrosis management.

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Cystic fibrosis; inhaled antibiotics; treatment journey; adherence to therapy; patient advisory board

1. Introduction

There are around 162,000 people estimated to be living with cystic fibrosis worldwide [1], including over 50,000 in Europe [2]. A virtual European Patient Advisory Board and associated online survey were conducted on 20 February 2023 to gain insights from eight people with cystic fibrosis (PwCF) on their experience and treatment journey, inhaled antibiotic usage and adherence, and the challenges and limitations of their treatment. Participants were volunteers aged 22 to 56 years (5/8 female) selected from National Patients Associations in four European countries: Cystic Fibrosis Trust in the UK, Belgian CF Association (BCFA), Belgium, Asociación Madrileña de Fibrosis Quística in Spain, and Lega Italiana Fibrosi Cistica (LIFC) in Italy. Although center-based care led by multidisciplinary teams has become the norm across Europe, adequate and equal access to diagnostics and medication varies between countries and can be challenging.

1.1. Consent to participate

Consent was obtained from participants through their respective patient organizations to participate in the patient advisory board meeting.

1.2. Consent for publication

Consent for the publishing the outcomes of this meeting was obtained from participants through their respective patient organizations.

2. The patient journey

Chronic airway infection with *Pseudomonas aeruginosa* is a major cause of increased morbidity and mortality in PwCF [3], and often cannot be eradicated [4]. The current recommendation is inhaled antibiotic therapy for the treatment of initial or new growth of *P. aeruginosa* from an airway culture [5,6]. All eight PwCF had been diagnosed with *P. aeruginosa* infection at some point; however, three were not currently taking inhaled antibiotics. One of the three participants had undergone double lung transplantation 10 years previously and no longer had *P. aeruginosa* infection, which is unusual as many PwCF experience recolonization after transplantation [7]. *P. aeruginosa* was eradicated in the second participant following treatment with inhaled antibiotics. The third participant is using a CFTR modulator and had been taken off inhaled antibiotics. The number of inhaled antibiotics taken by participants over the previous 6 months varied from 0 to ≥ 2, with continuous treatment more common than cyclical. The

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inhaled antibiotic treatments taken by the participants varied based on factors such as treatment response, tolerance, and availability. Furthermore, paranasal sinuses are potential reservoirs for intermittent colonization by *P. aeruginosa* [8,9], which may have impacted the requirement for the participants to take inhaled antibiotic therapies.

3. The impact of adherence to treatment

The chronic reservoir of infection in the lungs of PwCF who test positive for *P. aeruginosa* requires chronic usage of antibiotic therapy. Adherence to treatment is essential to minimize further lung damage and preserve lung function. More than half the participants (5/8) had difficulties with inhaled antibiotic devices. All participants who took inhaled antibiotics over the previous 6 months reported missed doses, with two participants missing more than 10 doses. Forgetfulness, stemming from repetition of exactly the same process every day, was the most common reason for missed doses (4/8 participants).

Participants described the time needed to take medications as incredibly impactful, with a third daily dose in the middle of the day particularly problematic. The majority pointed out how hard it is to combine inhaled antibiotic regimens with professional activities and travel. One participant, whose co-morbidities include diabetes (a common co-morbidity in PwCF [10]) and heart disease, finds nebulizer treatment a significant burden on top of all their other treatments, stating: 'If I did everything I am supposed to do [for my nebulised treatment], I wouldn't have time to do anything else.'

All participants also emphasized how time-consuming the device cleaning process is, with one noting that: 'The cleaning [of the device] is harder than doing the treatment.' One participant suggested that the information provided on correct use and cleaning of devices 'could be better,' including regular review of inhalation and cleaning techniques and practical demonstrations. Other participants noted that PwCF may not realize they are using their device incorrectly and 'bad habits [in device use and cleaning] are hard to break.'

Tolerance of inhaled antibiotic treatments varied among the participants. Two participants stated that they cannot tolerate nebulized treatment because of ear, nose and throat issues, and this affected their adherence. Switching to dry powder inhalers in cases of nebulizer burden may not always be possible because of access or reimbursement issues.

Factors that participants thought helped improve their adherence to treatment included switching to products that did not require refrigeration, working from home or close to home, setting alarms on mobile devices, and using a pillbox to ensure no doses are missed. However, participants mentioned that if they are feeling better they may delay, or forget to take, their treatment.

4. Heterogeneous approaches to treatment

Three-quarters of participants (6/8) were taking CFTR modulators, with half of those no longer taking inhaled antibiotics. Participants discussed improving on CFTR modulators and questioned whether the inability to produce sputum means there was still lung damage or *P. aeruginosa* infection, what the protocol is for such patients, and whether they need to keep taking their (e.g. tobramycin) treatment. There is no conclusive evidence to indicate that decreased sputum production is associated with decreased lung damage or eradication of *P. aeruginosa* [11], and a protocol should be followed to manage *P. aeruginosa* infection to preserve lung function. There is planned and ongoing research about the impact of reducing inhaled antibiotic treatments for PwCF in the context of CFTR modulators [12,13]. According to Elborn *et al*., studies are needed to determine whether discontinuing maintenance therapy is safe in PwCF receiving CFTR modulators [12]. For now, PwCF are recommended to continue their prescribed medications, including antibiotic therapy [12].

5. Discussion and take home messages

The virtual Patient Advisory Board represented a valuable opportunity to engage with PwCF and gather insights into their real-life experiences and unmet needs surrounding treatment, particularly for *P. aeruginosa* infection in the era of CFTR modulators. The opportunity was embraced fully by the participants, who described living with CF as 'a lonely journey.' The heterogeneity in the patient journey, challenges in chronic *P. aeruginosa* infection diagnosis, complexity of treatment, and issues leading to suboptimal adherence indicate that patient-centric, individualized treatment, with a focus on improving and maintaining treatment adherence, is required to optimize management of CF.

PwCF taking CFTR modulators are questioning the recommendation to continue their chronic medications and therapies [14]. Physicians are urged to weigh the simplification of antibiotic treatment with the risk of clinical deterioration resulting from bacterial infection in decision-making. Also, diagnostic tools for chronic lung damage and treatment guidelines need to be developed and harmonized worldwide to justify the time required for the burdensome routine in which PwCF have to engage to manage their condition.

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Declaration of interests

S Gambazza was a consultant for BGP Products Operations GmbH and V Purohit is an employee of Viatris Inc. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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Author contributions

All authors participated in the Patient Advisory Board, reviewed the draft manuscript, and read and approved the final version for publication.

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