PEDIATR RESPIR J Vol. 2(4), 152-161, 2024

RESEARCH ARTICLE

Experiences and opinions of cystic fibrosis patients and their families about their inability to access modulator treatments in Turkey: a qualitative study

Özge **Keniş-Coşkun** [1, *], Gürkan **Sert** [2], Perihan **Dikili** [3], Evrim **Karadağ-Saygi** [1], Pinar **Ergenekon** [4], Yasemin **Gökdemir** [4], Ela **Erdem-Eralp** [4], Bülent **Karadağ** [4]

[*] **Correspondence to:**
ozgekenis@gmail.com. ORCID: https://orcid.org/0000-0002-3004-1992

Doi
10.56164/PediatrRespirJ.2024.55

[1] Department of Physical Medicine and Rehabilitation, School of Medicine, Marmara University, Istanbul, Turkey
[2] Department of Medical History and Ethics, School of Medicine, Marmara University, Istanbul, Turkey
[3] Health Sciences Institute, Marmara University, Istanbul, Turkey
[4] Department of Pediatric Pulmonology, School of Medicine, Marmara University, Istanbul, Turkey

ABSTRACT

Modulator drugs cannot be provided regularly to our patients because they are not reimbursed by the Ministry of Health in Turkey. Patients can access these drugs on a limited basis and with detrimental intervals after a series of legal processes. This study aimed to qualitatively investigate both the clinical effect of intermittent modulator therapy on patients, the difficulties in accessing the drugs, and opinions about the process. Our research was designed as qualitative. It included patients over the age of 18 diagnosed with cystic fibrosis who had access to modulator treatments through legal processes, who may or may not currently use the drugs, and caregivers of patients under the age of 18. A total of 3 patients, 5 caregivers and one attorney has been interviewed. Four themes have emerged from the analyses of patient interviews: before and after the modulator, receiving information about modulators, difficulties in obtaining the drug and hoping for a permanent solution. To the best of our knowledge, our country is the only place where they are obtained through legal processes on a semi-regular basis. This is detrimental for patient well-being and must be addressed immediately.

HIGHLIGHTS BOX

What is already known about this topic? Modulator drugs for cystic fibrosis are not still fully reimbursed in Turkey, causing problems in patient care. **What does this article add to our knowledge?** Currently, patients try to obtain these drugs through complicated legal process which causes unforeseen intervals in treatment and worsening of clinical conditions of the patients. **How does this study impact current management guidelines?** Urgent action is needed to end health inequality and improve drug access for all patients who are not currently have a constant access to modulator drugs.

KEY WORDS
Cystic fibrosis; modulator drug; health inequity.

INTRODUCTION

With the development and approval of treatments that modulate the Cystic Fibrosis Transmembrane Regulator (CFTR) gene by the Food and Drug Administration (FDA) in 2019, important progress was made in the treatment of patients

with cystic fibrosis (CF) who are eligible to receive these drugs (1). These treatments can correct the protein synthesis disorder caused by the particularly common F508del mutation by improving the synthesis of the CFTR protein, thus significantly improving the function of the CFTR protein and the function of the sodium channel (2). Studies have shown that the use of modulator drugs provides clinically significant improvement in CF patients (3).

These treatments cannot be provided regularly to our patients because they are not reimbursed by the Ministry of Health in our country and are costly. However, after a series of legal processes, patients can access these drugs on a limited basis and with intervals that are detrimental to the treatment process. Despite the benefits provided by modulator drugs, these drugs are not yet included in the scope of reimbursement in Turkey. For this reason, individuals living with CF, who are medically thought to benefit from the drug and whose condition is determined by their health reports, cannot obtain modulator drugs within the scope of social security and have to apply for legal processes after documenting their improvements. There is no data in the world literature on intermittent use of modulator drugs in this way, and there is no data on the experiences of patients and families during this process. When talking about the obstacles in accessing medicine in rare diseases, it is pointed out that medicines are expensive and are often sold at prices that patients cannot pay. Although orphan drugs improve patients' health status and quality of life, the cost of these drugs limits patients' access to these drugs (4-6). Life-threatening health conditions and the lack of treatment alternatives can create an inelastic demand for orphan drugs, leading to high prices in a market where competition is already limited (6).

This study aimed to qualitatively investigate both the clinical effect of intermittent modulator therapy on patients, the difficulties in accessing the drugs, and opinions about the process.

METHODS

Our research was designed as qualitative and was conducted between March 2023-December 2023. It was planned to include patients over the age of 18 diagnosed with cystic fibrosis who had access to modulator treatments through legal processes, who may or may not currently use the drugs, and caregivers of patients under the age of 18. Cystic Fibrosis Assistance and Solidarity Association facilitated the meetings. To gain insight about the legal processes of obtaining these drugs, one attorney was also interviewed. A questionnaire containing demographic and personal information, which the participants will fill out before the interviews, and semi-structured one on one interviews were used as data collection methods. The questions that are asked in the semi-structured interviews are given in **Table 1.**

Informed consent for participation in the study was obtained from participants before the interviews.

A descriptive case study approach with single in-depth interviews was employed. The descriptive case study approach was employed because we aimed to investigate a contemporary phenomenon in depth and within its real-life context, in which the boundaries between phenomenon and context were not clear and as investigators we had no control over events, as described by Yin (7, 8). Interviews were conducted using online platforms to decrease the risk of infection in these patients. The interviews were conducted by a researcher who is not working in the study clinic and not involved in the decision for modulator drugs and follow-up process and has a 15-year of experience in qualitative study interviewing. Observer notes were kept, and audio recordings were made during these interviews. The interview with each participant lasted

Table 1. *Questions of the semi-structured interview.*

Semi-structured interview's questions
1. How did you first learn about the existence of modulator drugs?
2. Are you currently using your medication? When was the last time you used it? If you are not currently using it, how long have you been off it?
3. What is the most difficult aspect of obtaining your medication?
4. What are the differences you see when you compare your state of using the medication to your state of not using it?

approximately 50-60 minutes. After each interview, the voice recordings were converted into transcripts with notes taken and were coded independently by at least 3 researchers without waiting for the next interview (9). Conventional content analysis method is used for the data analysis of this qualitative study (10). A thematic map – a visual representation of the relationship between various codes – was employed in our study to organize the codes under categories and understand the relationship between various codes and categories and overarching themes (11, 12).

All interviews were audiotaped and transcribed and all participant identifiers were removed from transcripts. All Authors independently reviewed a selection of transcripts, familiarized themselves with the data, and generated initial codes using inductive coding. Codes were the starting points and the concepts in the transcripts about the experiences and perspectives of the participants. A new list of codes was produced, and each code included illustrative quotes. The codes generated from the data separately by the researchers were discussed together with the help of the clinical stories of the patients and the families to build categories at first. The codes are placed under the categories which were built after comparing, contrasting, combining, splitting, or renaming through consensus. After using discussions, analysis, matrices, and flowcharts to prompt deeper thinking, researchers described the related categories and put them together, and refined themes as the frame of the results (13). The themes were integrated into a meaningful conceptual framework to adequately tell the story of the data and answer the research questions. Excerpts from the data were used to support the themes and illustrate patterns in the experiences of both the children and parents (14).

The themes were then reviewed to ensure that they adequately captured the details of all the coded transcripts. An effort was made to ensure that the themes were representative of the range of views expressed by all the participants and that the ideas from one participant or theme were not over-represented or under-represented (15).

RESULTS

A total of 9 participants were interviewed. Their characteristics are given in **Table 2.**

THEMES

In our study, four main themes were created as a result of the thematic analysis conducted in line with the questions asked to the participants. These are: 1) the situation before the modulator drug; 2) information about the modulator drug and access to the drug; 3) the situation after the use of the modulators; 4) the legal process and thoughts and recommendations for the authorities.

Before the modulator

Under this theme, the difficulties faced by the participants before using modulator drugs are included. The patients and parents stated that they had significant problems in performing daily living activities: «Before the medication, he wasn't active, (…) He was immobile because he couldn't breathe. He was sleeping a lot because his lungs were not working. He was out of breath the moment he walked (...) There was no water or food (patient 4)».

***Table 2**. The characteristics of the participants in the study.*

Participant	Gender and age	Current FEV_1 level of the patient	Pre modulator FEV_1 level of the patient
Participant 1	female, 33	63%	55%
Participant 2	male, 36	44%	40%
Participant 3	male, 19	52%	48%
Participant 4 and Caregiver 1	female, 35	94%	94%
Participant 5 and Caregiver 2	female, 42	75%	65%
Participant 6 and Caregiver 3	male, 51	81%	67%
Participant 7 and Caregiver 4	female, 41	73%	53%
Participant 8 and Caregiver 5	female, 45	89%	85%

«I'm just going to sit at the table, mom», he says, «I can't expectorate my phlegm after the meal». He says, «Let's expel my phlegm thoroughly before the meal», and we try. Now he's really passing out thinking he's going to cough up phlegm (patient 1)».

Patients and their families were forced to live with above-normal restrictions in their home lives and stated these in their interviews: «Of course, we took it under more protection. After that we started paying attention to everything. We have been experiencing the pandemic for 6 years that people experienced in 2 years and a half. We do not receive many guests at our home. When we come out of the house, we change completely and take a shower. We do the same routine when my other two children come home from school (participant 4)».

«So, it is very difficult to accept the existence of the disease and to live with it. It was like we were in a bowl. «The people who come home should not have any diseases, that is, I do not meet with people who have the flu or something (patient 5)». Difficulties in the social life of the patient and his family: «He didn't go to nursery or school anywhere (patient 5)»; «He said he would not receive a high school education at home (patient 1)»; «So, we don't have the chance to have a social life anyway. We cannot even take two children to the wedding to prevent our children from getting infected. If we go alone. This time, we always have to leave it unfinished and come back because the child is left alone at home. It is necessary to follow his medications, he needs to do respiratory therapies. Unfortunately, it constantly reduces our quality of life because it is necessary to keep it under constant surveillance (patient 3)»; «The child was at home with his mother and father. He had an individual environment without much human contact, mostly with adults, not children (patient 5)»; «Before the medication, I could not go into crowded places. Because there are people who cough, sneeze, *etc.* I was more likely to stay at home and not be able to engage in social circles. When a person is masked like this, I don't hug or kiss him from afar (patient 7)».

The patients and parents stated that they had to endure frequent and long hospitalization periods for exacerbations, which disrupted the normal flow of their daily life: «The first 6 years were very difficult. There were constant hospitalizations. We were afraid of losing him in intensive care twice. It was pseudomonas. Pseudomonas is our greatest enemy (patient 3)»; «I was in the hospital once a week and every 15 days (patient 1); «I didn't take my bag and ID when I went to the hospital. I was packing a small suitcase. I was leaving with that suitcase because I knew I wouldn't be able to come back (patient 4)».

Getting informed about the modulators

After the participants obtain information from the association, the nurse or physician in the health institution or organization they apply to, about the existence of the drug, the benefits it will provide to the patient, and the possibility of accessing the drug through a lawsuit, they try to reach the attorneys interested in the subject. Participants stated that they were informed by the relevant health professionals about the reports and documents that needed to be submitted to the court and that they received support from these people regarding the documents.

A significant portion of the interviewees stated that they received their first information about the drug from a physician or nurse during hospitalization: «So, when the drug started coming out, they looked at our genes. Doctor, this medicine suits you», he said, «You know, file a lawsuit and get the medicine». «So, I said let me wait a little bit. Then, as I waited, it started to get worse. My bronchi are starting to burst or something. My cough started to get worse. I started vomiting blood. The doctor said, let's apply for medicine, come and use it, it will be good for you too. That's how we applied (patient 7)»; «When we contacted our nurses during the hospitalization, they gave directions: 'Actually, if your genetic result matches, you can do it'. We applied immediately. (patient 4); «How did I first find out? This is from our professors. They are already following the research beforehand. We were aware of the studies (patient 8); «We were in the hospital, while Dr. gave information about the medicine. We decided to apply (patient 2)».

Participants stated that physicians also provide information about modulator drugs from the patients' association. Individuals/families living with CF also stated that since the disease affects every moment of their lives, they actively use internet resources and follow foreign publications and opportunities in order to obtain information about developments and treatment opportunities. However, it appears that patients learn

about the modulator drug from social groups and social media: «In the association, in the family information meetings, in the information given by our professors, *etc.* We first learned about medicine when we were 3-4 years old, but our professors constantly said that there were studies, and this was good news for the future. We need to bring this to Turkey, we need to work for it (…) (patient 3)»; «I heard about a group of them via W….app. What did they say? Is it compatible or not? We looked and went to the nurses. From there, our nurses said: 'Let's see'. After that they said it is compatible with the medicine. How do we do it, how do we proceed? Thanks to our nurses who helped us, our doctors helped us (patient 1)»; «We are already connected to the association on Facebook. We were also following the processes regarding the drugs that were released. You know, abroad, long before this. Before modulator therapy was used in Turkey, we heard that it was happening abroad, that they had started it, their treatments, *etc.* We were getting excited too. We were following it to see if it would happen in Turkey as well (patient 6)»; «I first became aware of the modulator drug from international articles. I knew that such a medicine existed, but we were not old enough yet. When we reach the age of 6, our doctors already advise us to start this treatment. They said the mutations were compatible (patient 5)».

After the modulator

All participants stated that there was an improvement in the patient's health and a noticeable improvement in their quality of life after the modulator drug: «We see 98-99 when using medication. During the periods when we were not using medication, we were mostly hospitalized due to this low saturation. It drops as low as 92, when we are at home it is 95-96, but when we are on medication, we can see even 99%. But it drops a lot when there is no medicine (patient 4)»; «Since breathing becomes easier while using the medicine, both he feels more at ease. He's not having any trouble (patient 3)»; «Participants said that there were positive changes such as increased appetite, weight gain, and increase in physical activity along with relief in breathing. While using the medicine, he even eats his meals comfortably because he does not have phlegm and does not get stuck while eating. Weight gain is easy (patient 3)»; «So, I can say that he may have been sick less than normal children while using (…) (patient 5)»; «So, you're getting a little more comfortable in terms of weight», «My cousins, brother, I saw you very well, you know (patient 8)».

Participants pointed out that the patient's adaptation to social life increased when using modulator drugs: «He went on trips with his uncle. He never stayed at home (patient 1)»; «Of course, after the modulator drug, he relaxed a lot, he can play with his friends», «He calls me home, makes me play, he becomes more social (patient 4)»; «Right now, M… is going to school while everyone is on holiday. They opened a special class for university preparation. He joined a group of 50 people and enjoys going back and forth (patient 3)»; «Their physical activity has increased. Most importantly, he started first grade. While using this medicine. We handled the school process very smoothly (patient 5)»; «At that time, my cousin was having an engagement party. It was a very closed, airless area. You know, I've never felt such a blockage, tightness, or cough. Other than that, in general, I don't cough at all at work (patient 8)».

They stated that patients and their families felt psychologically relieved due to the benefits of the modulator drug: «We felt more relaxed as a family, both psychologically and physically. So, for example, when you send T… to school when it is not being used, will there be anyone sick in the classroom, will anyone sneeze, will anything happen? Will the child be infected with anything? You send it out of fear, but when you receive T…, we are like the same as the others (patient 5)»; «Yes, sir, it would mean the world to me for him to go somewhere alone. For the first time, we stayed away from our son for 15 days», «I have never been apart even for a day (patient 1)».

All of the interviewees stated that during periods when they could not access medicine due to the negativities experienced in the court and drug procurement processes. Their medical situation, which improved while using medication, became worse when they did not use medication. They experienced decrease in oxygen saturation, a decrease in physical activity in a short time, malnutrition, and weight loss: «When the medicine is finished and when the body starts to produce phlegm, it becomes difficult to breathe because it causes shortness of breath even from the food it eats due to the phlegm (H3)»; «When the medicine does not arrive,

after 20-25 days, their movements slow down and their steps slow down. Phlegm and cough begin (patient 2)».

Legal processes and recommendations for authorities

Since CF modulator drugs are not produced domestically and are not covered by reimbursement, patients file lawsuits with the Social Security Institution (SSI) to access the drug. All of the interviewees who participated in our study were patients or their relatives who had access to medicine by applying to the judiciary. The legal process of one participant was concluded in his favor, and the process of the others is still ongoing. According to the data we obtained from the interviewees, patients generally resort to litigation in line with the information of healthcare professionals and carry out the processes with attorneys specialized in healthcare law: «We reached (the attorney) from Ankara. He guided us. You will prepare the following documents and send them to us. We went to the notary. We gave him power of attorney, then he filed the lawsuit (patient 6)». They specifically stated that it takes a long time for the payment of the medicine to depend on the court decision. One participant made a comparison with a drug within the scope of payment: «So normally, let me tell you in comparison to medicine. At least the doctor writes the prescription directly, and we inform the pharmacy of the prescription. And what happens is that the delivery time for the medicine is 4-6 weeks, during which time the medicine comes to me. But after we get the prescription written, we provide SSI documents. SSI is given by court decision, and these are examined. These then go to the Turkish Association of Pharmacists, where they are reviewed and ordered again, and this process inevitably takes a long time. Since it was taken by judicial decision, it is not within the scope of payment. The process is getting slower (patient 5)». The interviewees pointed out that many documents had to be prepared before starting the litigation process and that the patient had to have some examinations re-done. The interviewees also stated that healthcare professionals provide support with the necessary documents when initiating the legal process: «We photocopied our file (in the hospital), no matter how long we had been treated there at that time, our entire file (in the hospital) was around 600 pages, and we turned it into a file and handed it over. They were also presented to the court (patient 6)»; «During the court process, they asked us for (the patient's) disability report and documents. Of course, they asked for additional examinations, eye examination, sweat tests, stool tests. They asked for our routine medical check-up, that is, our cystic fibrosis hospital doctor, diagnoses and lung function tests. We prepared these. Then as I remember. Yes, we sent an attorney to an attorney one on one. We waited, we waited for a long time (patient 4)». Some of the participants said that the courts issued an interim injunction at the beginning of the trial, ensuring that the cost of the medicine was paid to the patient. However, during this process, participants also pointed out that there were interruptions in access to medicine due to court decisions and other procedures: «We waited, we waited for a long time. We even got rejected. We objected again and received a rejection. We applied again and had trouble in court, but it did not come directly. You know, we applied right away, but it didn't come right away. It took almost 9 months for us to gain indefinite time in court. We won it back. But before that, for the third month, our medication was indefinite (patient 4)».

Before starting the modulator drug, all examinations are performed again, and the drug is started to be used with the approval of the doctors. One month after using the medication, the tests are repeated and sent to the court. These tests are repeated every three months to prove the effectiveness of the drug: «When the drugs start arriving, examinations are renewed every 3 months. How did this happen with drugs? The hospital prepares a report saying that the child is feeling better or something like that. We photocopy those hospital files 3-4 times. We send it to an attorney every 3 months with the epicrisis report and expert decision. Then the attorney applies to the court on our behalf. And after 3 months, the medicine comes again. It always takes 3 months. At these intervals, usually every 3 months, 3 boxes of medicine come to us. We renew the tests not as soon as they arrive, but before the first box is finished. Because it takes a long time for the documents to come out. Then we send it to the Court. After these cases, we got hopeful (patient 2)».

Although patients have access to modulator drugs during the trial, they are concerned that the case may end against them: «Yes, we are supplying the medicine

right now, but they have come up with a different process related to the litigation process. In other words, we won the big case, but now our files are in appeal, so when the appeal is rejected, you will apply to the Constitutional Court. You have to go one step further, but of course there will be times when we will be without medication during this process. There will be times when our child may deteriorate rapidly. Their concerns are definitely high (patient 5)»; «After winning another case, an injunction decision is taken, which is confusing. You take the dose for 3 months. You can object the decision. Meanwhile, if the injunction is lifted, the litigation process becomes longer. You request again as the case continues. For example, if you run out of medicine between the hearing and the date when the injunction order is lifted, you cannot take the medicine (patient 8)».

One interviewee stated that after the lawsuit was filed during the legal process, they went drug-free for a period after using it regularly for nine months: «I don't remember what the problem was exactly. We were without medication for almost three months. We had one hospitalization in those three months. Afterwards, we live, of course, we can go without medication for a week or 10 days, of course we experience problems. But this one week and 10 days may seem too short for others, but as soon as we stop taking the drug, we go back to the old situation (patient 4)».

Participants are of the opinion that the legal process is quite detailed and long due to the procedures. Interviewees pointed out the difficulties in accessing medicine in a timely manner while the judicial process continues: «Taking the drug by judicial decision is a really bad thing. We receive our right to health, that is, one of our medicines, by a judicial decision, and inevitably, the drugs taken by judicial decision are more stuck in the procedure. So, for example, we apply to SSI. Then, the delivery of these documents from TEB is delayed and SSI first reviews the court decisions. The period after that is really challenging and prolongs our access to medicine (patient 5)»; «We apply while taking the medicine for a month. We are left with 2 months of medication. Are we supposedly told to have 4 or 6 weeks? It's been 6 weeks for me and I'm still waiting for it to arrive. We always wander around in such uncertainty, that is, in such chaos regarding medicine. Let's see, there's a cycle going on saying 'Let's hope our children are well'. Let's see what happens (patient 1)»; «The most challenging thing is that it does not reach us quickly. Thanks to our attorneys, they can reach us, but I wish we had not gone to the attorney and the state would have reimbursed us and all children would have benefited. Nobody hears our children's voices anyway. Let me say as a state. Our doctors are trying hard, and they are very caring (patient 2)»; «In out first attempt were rejected. We had a hard time accepting that decision. We have waited for so long. Then we used the medication for 2 months. Then we faced with a third rejection (patient 4)».

However, some interviewees also pointed out that the process of drug procurement has accelerated with the increase in the number of cases. He emphasized that the institutions responsible for this issue also gained experience: «I used one dose; it made a difference. I waited another month and a half for the second doses. I don't know, there was a problem here and there, there weren't many people filing lawsuits back then. You know, this case process was not widely spread. For example, medicines are now becoming easier to obtain. I am waiting very little; we are waiting for a maximum of 10 days (patient 7)».

Doctors and patients have developed some solutions to overcome the difficulties they experience when they cannot access medicine through the legal process and are left without medication. In order not to lose the duration of the drug's effect, they use it in half doses or every other day: «So, the doctors said to use the medicine in the morning and evening, never in half. That's how they made me use it. But many patients, those who are followed up from other hospitals; you know, when the medicine is almost finished, they break it in half and take it. But I don't do anything like that. At least, I say, I can take it in the evening and morning, but the effects still remain. Also, during the waiting period, I started to give the nebulized medications even more (patient 7)».

DISCUSSION

In this study, we aimed to document the hardships that the patients face during the obtaining of modulator drugs in a country that does not reimburse this treatment. For this purpose, we interviewed a variety of patients and their parents that have been through this process. To increase diversity, we tried to include both

adult patients that are handling their own process and parents who care for and handle for these processes. We reached the patients with the help of the patients' association that are helping the patients guide through these processes and we included patients that have been through this process both just once and a couple of times to diversify the statements.

The patient association makes significant contributions to ensuring individuals' right to access health and the right to be informed about innovations by informing patients about new drugs and developments regarding the treatment of the disease by physicians and nurses. It is important for an association whose all activities can be audited, with the support of physicians who are experts in their fields, to inform patients and their relatives about scientific developments, treatment-related developments, and the current stages of research by experts and competent people, so that patients are not misinformed, have unfounded hopes, are not abused, and are not directed to unnecessary demands. The fact that the interviewees participating in the research were informed about issues such as the fact that the drug will not produce the same results for every patient and that the drug cannot be used in every patient and age also suggests that education and information are beneficial. Main challenge that the patients face is the interruptions during the obtaining of the drug due to complicated legal processes. If the lawsuit regarding the payment of drugs is filed with a request for injunction, the judge may decide to use the drug as a precaution. In this case, shortly after the case is filed, the Social Security Institution begins to pay for the drug purchased. However, a significant risk that this decision poses for the family is that the Social Security Institution may overturn the decision in the appeals court. Then until the case is concluded, the institution will not pay for the medicines the patient.

The scope of interim injunction decisions may also vary. For example, a decision may be made to use a three-month dose of the same modulator drug. In this case, the patient also needs a judicial decision to pay for each subsequent three-month dose. This situation causes consequences such as interruption of the use of doses. In these cases, the health of a patient whose treatment is going well may deteriorate again. Sometimes, the judiciary imposes a precautionary measure for the use of the drug as long as the case continues. In this case, since only applying to the institution for payment is sufficient to pay for the medicine, fewer problems are encountered in timely access to the medicine. The attorney said that in both cases, procedures were restarted a month after the first dose was used so that an application could be made to the court or institution to ensure that the social security institution paid for the next dose. The attorney stated that patients or their families who do not want to take the risks of injunction, can also choose to file the case without requesting injunction. If this method is used, the patient will have to wait for the end of the case to be paid for the medicine, which can be very long.

In this study, patients are caregivers clearly stated that using modulator drugs have improved their quality of life and their trajectories significantly, which is also supported by quantitative data. They also stated that every interval causes significant decrease in their quality of life and nullifies the progress made during the use of the drugs. In this context, it should be accepted that access to medicine through litigation causes significant problems in the patient's access to medicine and in time. It is important to take the necessary steps to ensure patients' access to drugs with proven effectiveness and to include the drugs within the scope of reimbursement. The fact that patients who are not informed about these drugs, even if they have knowledge, are not informed about how to access these drugs, or cannot access support, cannot access the medicine will also cause violations in terms of the right to fair and equal access to healthcare services. Most modern societies consider it an ethical obligation to provide patients with access to medicines for the prevention and treatment of serious and life-threatening diseases (6). The fact that the medicine needed by a child living with a rare disease is not covered by social security is against all international agreements and national legislation in which the right to life is accepted as a fundamental right. In this context, it is not controversial that access to preventive, therapeutic and diagnostic products and services for individuals living with rare diseases is related to the right to life and health recognized by international agreements and domestic legislation of countries (6). Therefore, it is imperative for the health authorities in Turkey and all countries

that are not currently reimbursing these medications to start reimbursing them as soon as possible.

CONCLUSIONS

There is an urgent need for modulator costs and reimbursement policies to be revised for patients with CF in Turkey, because we are losing precious time for all CF patients. The current system is not sustainable, causes significant time losses in patients' care and hinders some patients from accessing the drugs.

ACKNOWLEDGMENTS

The Authors thank all the patients, the caregivers and the attorney for being a part of this study.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interests

The Authors have declared no conflict of interests.

Financial support

There was no institutional or private funding for this article.

Author contributions

Literature search, data analysis, writing and editing of the manuscript: OCK, GS, PD, EKS, PE, YG, EEE, BK. Data acquisition: OCK, GS and PD.

Ethical approval

Human studies and subjects

Informed consent for participation in the study was obtained from participants before the interviews and the research has been performed according to the standards of the Declaration of Helsinki.

Animal studies

N/A.

Data sharing and data accessibility

Data are available upon motivated request to the Corresponding Author.

Publication ethics

Plagiarism

Authors declare no potentially overlapping publications with the content of this manuscript and all original studies are cited as appropriate.

Data falsification and fabrication

All the data correspond to the real.

REFERENCES

1. Bell SC, Mall MA, Gutierrez H, Macek M, Madge S, Davies JC, et al. The future of cystic fibrosis care: a global perspective. Lancet Respir Med. 2020;8(1):65-124. doi: 10.1016/S2213-2600(19)30337-6.
2. Elborn JS. Modulator treatment for people with cystic fibrosis: moving in the right direction. Eur Respir Rev. 2020;29(155):200051.doi: 10.1183/16000617.0051-2020.
3. Muilwijk D, Zomer-van Ommen DD, Gulmans VA, Eijkemans MJ, Van der Ent CK, Altenburg J, et al. Long-term effectiveness of dual CFTR modulator treatment of cystic fibrosis. ERJ Open Res. 2022;8(4):00204-2022. doi: 10.1183/23120541.00204-2022.
4. Krajnović D. Ethical and social aspects on rare diseases. Filozofija i drustvo. 2012;23(4):32-48. doi: 10.2298/FID1204032K
5. Kacetl J, Marešová P, Maskuriy R, Selamat A. Ethical Questions Linked to Rare Diseases and Orphan Drugs − A Systematic Review. Risk Manag Healthc Policy. 2020:13:2125-48. doi: 10.2147/RMHP.S260641.
6. Rodriguez-Monguio R, Spargo T, Seoane-Vazquez E. Ethical imperatives of timely access to orphan drugs: is possible to reconcile economic incentives and patients' health needs? Orphanet J Rare Dis. 2017;12(1):1-8. doi: 10.1186/s13023-016-0551-7.
7. Yin, R. K. Case study research: Design and methods (4th Ed.). Thousand Oaks, CA: 2009, Sage.
8. Ebneyamini S, Sadeghi Moghadam MR. Toward developing a framework for conducting case study research. Int J Qual Meth. 2018;17(1):1609406918817954. doi: 10.1177/1609406918817954.
9. Fernández-Ávalos MI, Pérez-Marfil MN, Ferrer-Cascales R, Cruz-Quintana F, Clement-Carbonell V, Fernández-Alcántara M. Quality of life and concerns in parent caregivers of adult children diagnosed with intellectual disability: A qualitative study. Int J Environ Res Public Health. 2020;17(22):8690. doi: 10.3390/ijerph17228690.
10. Hsieh H-F, Shannon SE. Three approaches to qualitative content analysis. Qual Health Res. 2005;15(9):1277-88. doi: 10.1177/1049732305276687.
11. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3(2):77-101. doi: 10.1191/1478088706qp063oa.
12. Vaismoradi M, Turunen H, Bondas T. Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study. Nurs Health Sci. 2013;15(3):398-405. doi: 10.1111/nhs.12048.
13. Elo S, Kyngäs H. The qualitative content analysis process. J Adv Nurs. 2008;62(1):107-15. doi: 10.1111/j.1365-2648.2007.04569.x.

14. Dierckx de Casterlé B, Gastmans C, Bryon E, Denier Y. QUAGOL: a guide for qualitative data analysis. Int J Nurs Stud. 2012;49(3):360-71. doi: 10.1016/j.ijnurstu.2011.09.012.
15. Shenton AK. Strategies for ensuring trustworthiness in qualitative research projects. Ed Inform. 2004;22(2):63-75. doi: 10.3233/EFI-2004-22201.
16. Royce FH, Carl JC. Health-related quality of life in cystic fibrosis. Curr Opin Pediatr. 2011;23(5):535-40. doi: 10.1097/MOP.0b013e32834a7829.
17. Nesser W, Snyder S, Driscoll KA, Modi AC. Factors associated with quality of life for cystic fibrosis family caregivers. Discov Ment Health. 2023;3(1):20. doi: 10.1007/s44192-023-00046-1.
18. DiMango E, Spielman DB, Overdevest J, Keating C, Francis SF, Dansky D, et al. Effect of highly effective modulator therapy on quality of life in adults with cystic fibrosis. Int Forum Allergy Rhinol. 2021;11(1):75-8. doi: 10.1002/alr.22700.