European virtual roundtables on SIMEOX therapy

“Experience in clinical practice with the use of Simeox therapy at each stage of the care of the CF patient”

In the period of May 20th - 27th, 3 online meetings were held in the cycle of European virtual roundtables, during which experts from 8 university or research centers for treatment of cystic fibrosis from 5 countries shared their clinical experience of use of Simeox therapy in patients with cystic fibrosis.

Participants:

Dr Rebecca Hamidfar, Dr Boubou Camara – **France**
Dr Philipp Utz, Barbara Räwer physiotherapist – **Germany**
Dr Dorit Fabricius, Dr Hanna Schmidt – **Germany**
Dr Jörg Grosse-Onnebrink, Christina Krämer physiotherapist - **Germany**
Dr Justyna Milczewska, Natalia Jeneralska physiotherapist - **Poland**
Dr Karolina Gwoździewicz, Katarzyna Warzeszak physiotherapist - **Poland**
Dr Tereza Doušová, Anna Chmelařová physiotherapist - **Czech Republic**
Dr Raj Jayaraj, Claire Lord physiotherapist - **United Kingdom**

Preparation of the presentation of cases and discussion:

Dr Justyna MILCZEWSKA, MD, PhD, Ph.D.

Introduction

Bronchopulmonary disease in patients with cystic fibrosis develops from the first months of life. Retention of thick secretion in the respiratory tract leads to emergence of mucus plugs, respiratory tract infections with pathogenic bacteria, which results in bronchiectasis and destruction of the lung parenchyma.

Bronchial drainage using Simeox combines different mechanisms of action, which are aimed to drain the respiratory tract secretions, which are particularly difficult to remove in patients with cystic fibrosis. These mechanisms include mobilization, liquefaction and evacuation of secretions.

This may contribute to slowing down or even stopping of progression of the bronchopulmonary disease, which results in such clinical effects as reduction of cough intensity and the quantity of sputum, reduction in the frequency of exacerbations, stabilization or improvement of function tests and imaging examinations, and ultimately, improvement in the quality of life of patients.

Effective chest physiotherapy is thus necessary both to support treatment of exacerbations in the bronchopulmonary disease and in long-term management of patients with cystic fibrosis in the home environment.

First meeting of 20.05.2021

Reinforcement of intravenous antibiotic therapy by sessions with SIMEOX during bronchopulmonary treatment.

The clinical benefit for the patient.

Participants:

Dr Philipp Utz, Pediatric pulmonologist and
Barbara Räwer, physiotherapist

Tübingen University Hospital Center for Treatment of Cystic Fibrosis in Germany,

Dr Raj Jayaraj, Pediatric pulmonology consultant and
Claire Lord, physiotherapist

James Cook University Hospital Cystic Fibrosis Center in Middlesbrough, United Kingdom

Dr Karolina Gwoździewicz and
Katarzyna Warzeszak, physiotherapist

Institute of Tuberculosis and Lung Diseases in Rabka-Zdrój, Poland.

Dr Philipp Utz, Barbara Räwer physiotherapist

Dr Philipp Utz presented a case of a 14-year-old girl with cystic fibrosis (genotype F508del/N1303K), with a chronic respiratory tract infection with Staphylococcus aureus and Escherichia coli, hepatic steatosis. The patient's nutritional status is acceptable. She is receiving a standard chronic treatment for the underlying disease (hypertonic salt inhalations, Dornase alfa, physiotherapy of the respiratory tract, supplementation of pancreatic enzymes).

Exacerbations of the bronchopulmonary disease emerge in the patient approximately 3 times per year.
In test functions of the respiratory tract, symptoms of pulmonary hyperinflation (in body plethysmography RV 193% of predictable value) and pseudorestriction have been observed. In imaging examinations, there are features of advanced bronchopulmonary disease (pulmonary parenchyma consolidations, air traps, bronchial wall thickening). The patient started periodic chest physiotherapy using Simeox in October of 2019, and for the first time Simeox was used simultaneously with IV antibiotic therapy (Cetofaxime + Tobramycin IV) in December of 2019.

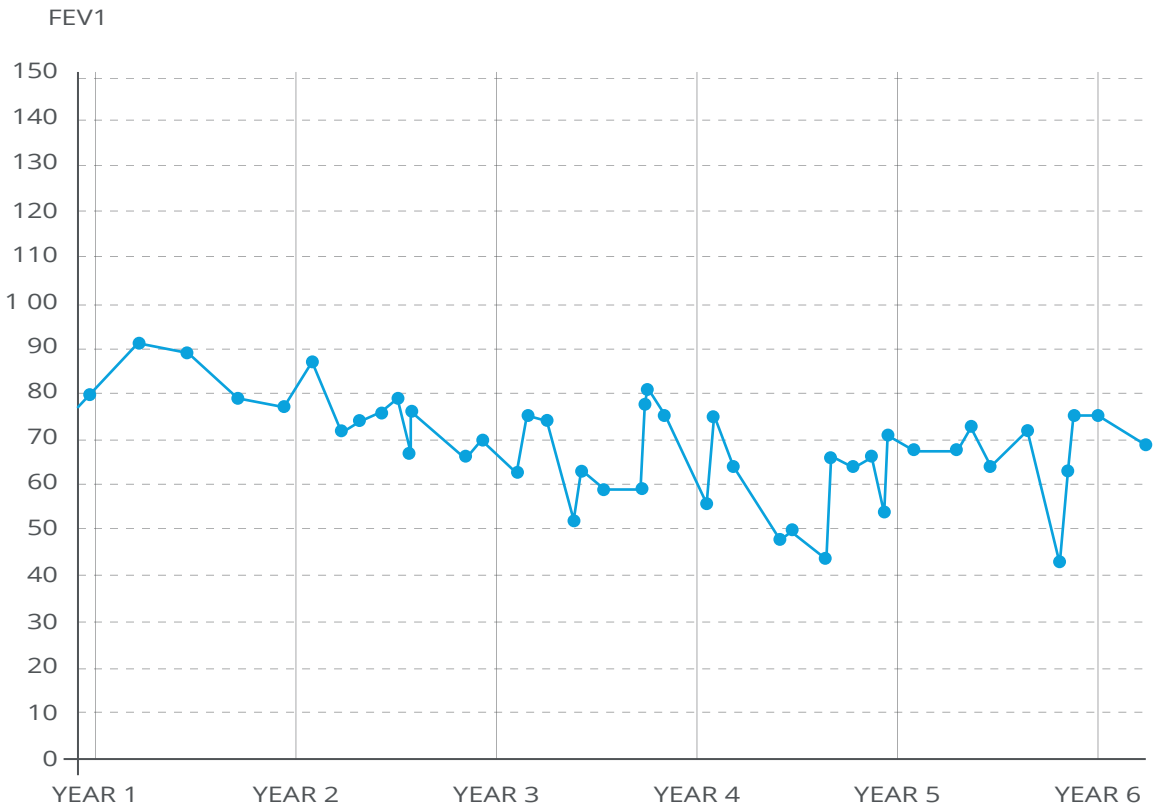


Fig. 1. A change in the percentage of FEV1 predictable value in 5 years in a 14-year-old female patient, presented by the German team.

Prior to commencement of this combined therapy, FEV1 was 54% of predictable value, RV was 193% of predictable value and RV%TLC was 194% of predictable value. Physiotherapy using Simeox was performed 3 x daily during intravenous antibiotic therapy.
On the 8th day of treatment, significant improvement was observed (increase in FEV1 to 71% of predictable value and decrease in RV to 169% and RV%TLC to 154% of predictable value).

After release from the hospital, the patient continued chest physiotherapy with the Simeox device in the home environment (it was rented from the hospital), and during an outpatient clinic visit 6 weeks later, further decrease in the parenchymal hyperinflation (air trap) parameters was observed RV 141%, RV%TLC 141% of predictable value.

Summary of the case presented:

- even in the era of effective treatment with CFTR protein modulators, intensive treatment of bronchopulmonary disease remains a necessity for a group of selected patients with cystic fibrosis
- in cystic fibrosis, combination of intensive chest physiotherapy and IV antibiotic therapy is of great significance in treatment of exacerbation of bronchopulmonary disease
- **in order to shorten the hospitalization time**, good effects are attained by two-phase treatment:
  1st phase: combining of IV antibiotic therapy and intensive physiotherapy using Simeox in the course of hospitalization (this phase also includes a training in the most effective operation of the device)
  2nd phase: continuation of IV antibiotic therapy in the home environment, combined with continuation of intensive drainage of the respiratory tract (Simeox)
- drainage devices such as Simeox play an important role in supporting intravenous antibiotic therapy
- in documenting of efficacy of treatment, body plethysmography and nitrogen multiple breath washout (N2MBW) testing can be considered
- it is very important to stay in touch with the physiotherapist managing the patient under home conditions to jointly choose the best therapeutic options.

Afterwards, **Barbara Räwer, a renowned and respected respiratory physiotherapist of Germany,** pointed out that thanks to chest physiotherapy using Simeox, the quantity of sputum evacuated from the most distal parts of the lungs increased, while some of the previously inactive lung areas were recruited to participate in gaseous exchange.
Prior to commencement of Simeox treatment, some observations were made regarding the patient's respiratory pattern. Intensive activity of additional respiratory muscles was observed even at rest, muscular clavicles and upper ribs, decreased mobility of the lower parts of the chest.

Physiotherapy sessions of the patient start by administering inhaled Salbutamol and a hypertonic salt inhalation. Afterwards, stretching exercises are performed, and then - drainage of the bronchi using Simeox (usually, 3 cycles of 10 breaths each, device power 50%), in a sitting position, so that the diaphragm and the chest are optimally positioned, and drainage is associated with the least effort possible.
At the beginning of treatment, the patient reported lesser effort while breathing and being able to breathe more deeply.
During the first few Simeox sessions, the patient expectorated large quantities of bronchial secretion, which had been retained for a long time. In the subsequent sessions, the quantity of sputum expectorated was significantly reduced. A decision was then made to introduce other drainage positions (lying on both sides), which resulted in mobilization of secretions from other parts of the lungs.
The patient also used the Simeox mouthpiece for autogenic drainage, which also greatly improved its quality.
At present, the patient is receiving CFTR protein modulators and there is less secretion retained in her respiratory tract; however, the role of bronchial drainage remains very significant, as the secretion is present mainly in the smallest distal bronchi.

Physiotherapy using Simeox is very effective, particularly in the peripheral parts of the lungs. This kind of physiotherapy is recommended in patients with cystic fibrosis, receiving causal treatment.

Summary

- Simeox enables mobilization of bronchial secretion, particularly in the first period of its use
- Simeox makes it possible to change the breathing pattern to a deeper one, thus facilitating breathing
- Simeox reduces hyperinflation of the pulmonary parenchyma

Recommendations

- Simeox therapy should be considered in treatment of exacerbation of bronchopulmonary disease in combination with IV antibiotic therapy
- Simeox therapy should not replace other components of chest physiotherapy
- the patient's individual preferences should always be taken into consideration
- reduction of lung hyperinflation should be documented by body plethysmography and N2MBW (sensitivity of spirometry can turn out to be too low to prove the effects of use of the device).

Dr Raj Jayaraj and Claire Lord, physiotherapist

Dr Raj Jayaraj and Claire Lord presented 2 clinical cases. The first is the case of a 17-year-old male patient with cystic fibrosis (genotype F508del/F508del), diagnosed right after birth - in the 2nd day of life, the patient underwent a surgery due to meconium ileus. The patient has suffered from a chronic infection of the respiratory tract with Staphylococcus aureus and Pseudomonas aeruginosa and colonization by Mycobacterium abscessus. He has been diagnosed with CFRD diabetes, and, due to highly insufficient body mass increase, he is fed via a PEG tube. Due to the necessity of regular planned IV antibiotic therapies every 3 months, he has a PortaCath installed. The patient is a high school student; however, due to his poor health condition, he is frequently absent, which is a source of frustration for him. His socio-economic status is low, compared to the British standards. During hospitalization, he is very rarely visited by his family. A list of the patient's regular medications has been presented:

- ivacaftor/ lumacaftor (included before it was registered in Great Britain), recently replaced with ivacaftor/tezacaftor/elexacaftor
- doxycycline
- tobramycin, colistin inhaled in alternating cycles
- inhaled Dornase alfa
- inhaled 7% NaCl
- inhaled Salbutamol
- inhaled Beclomethasone
- Mometasone nasal spray
- insulin
- ursodeoxycholic acid
- Omeprazole
- vitamins
- pancreatin

Patient's physiotherapy prior to inclusion of Simeox

- Oscillating Positive Expiratory Pressure device (O-PEP)
- Active Cycle of Breathing Technique, increased exhalation technique
- postural drainage, manual techniques
- physical activity (as much as possible)
- non-invasive mechanical ventilation in biPAP mode

Due to infection of the respiratory tract with multi-resistant pathogens and a significant weight deficiency, the patient was disqualified from lung transplantation. In the recent period prior to inclusion of Simeox, he required intravenous antibiotic therapy more than every 3 months, his weight decreased, his ability to engage in physical activity kept deteriorating, he expectorated very significant amounts of thick purulent sputum, which provoked vomiting, his FEV1 was about 30% of predicted value, FVC 48% of predicted value, MEF25-75 10% of predicted value, and body plethysmography indicated significant features of pulmonary hyperinflation.

The patient cooperated poorly in terms of physiotherapy, sometimes he avoided it and he suppressed coughing, as once started, it usually lasted a very long time and was very exhausting, provoking vomiting. During one of the IV antibiotic therapies, it was found that due to intensified symptoms of lung hyperinflation, use of positive expiratory pressure drainage devices was not recommended for the patient. At the time, the decision was made to include physiotherapy using Simeox to support IV antibiotic therapy.

The patient was trained to use the device and willingly started to use it. During drainage in sitting position, 25-50% of the device power was applied, 6-10 breathing cycles per series depending on the patient's condition, 2 x daily. The patient reported feeling discomfort due to the tongue being sucked in by the mouthpiece, which was solved by adapting the mouthpiece accordingly.

After his discharge from the hospital, the patient eagerly used Simeox at home. The main advantage of this device, in his opinion, was the fact that it allowed him to cough up sputum, and he found drainage much less exhausting in comparison with conventional chest physiotherapy methods. Moreover, he felt more comfortable, and physiotherapy using Simeox took him less time than before. In 6 weeks of using the device, FEV1 increased from 30% to 39% of the predicted value, FVC increased from 48% to 59% of the predicted value, and MEF25-75 increased from 10% to 18% of the predicted value (almost a twofold increase).

According to the physiotherapist, the patient was able to control bronchial drainage better than before inclusion of Simeox, he was much more committed and able to conduct physiotherapy on his own at home. He was no longer vomiting purulent secretion from the respiratory tract, and the process of expectoration of sputum became much easier.

Table 1. The selected spirometry parameters in a 17-year-old patient presented by the British team prior to and after commencement of Simeox treatment.

	FEV1	%	FVC	%	FEF25-75	%
Admission	1.21	30%	2.23	48%	0.46	10%
Discharge	1.47	37%	2.63	57%	0.47	10%
Week 3	1.51	38%	2.61	57%	0.61	14%
Week 4	1.54	39%	2.66	58%	0.71	16%
Week 6	1.56	39%	2.68	59%	0.81	18%

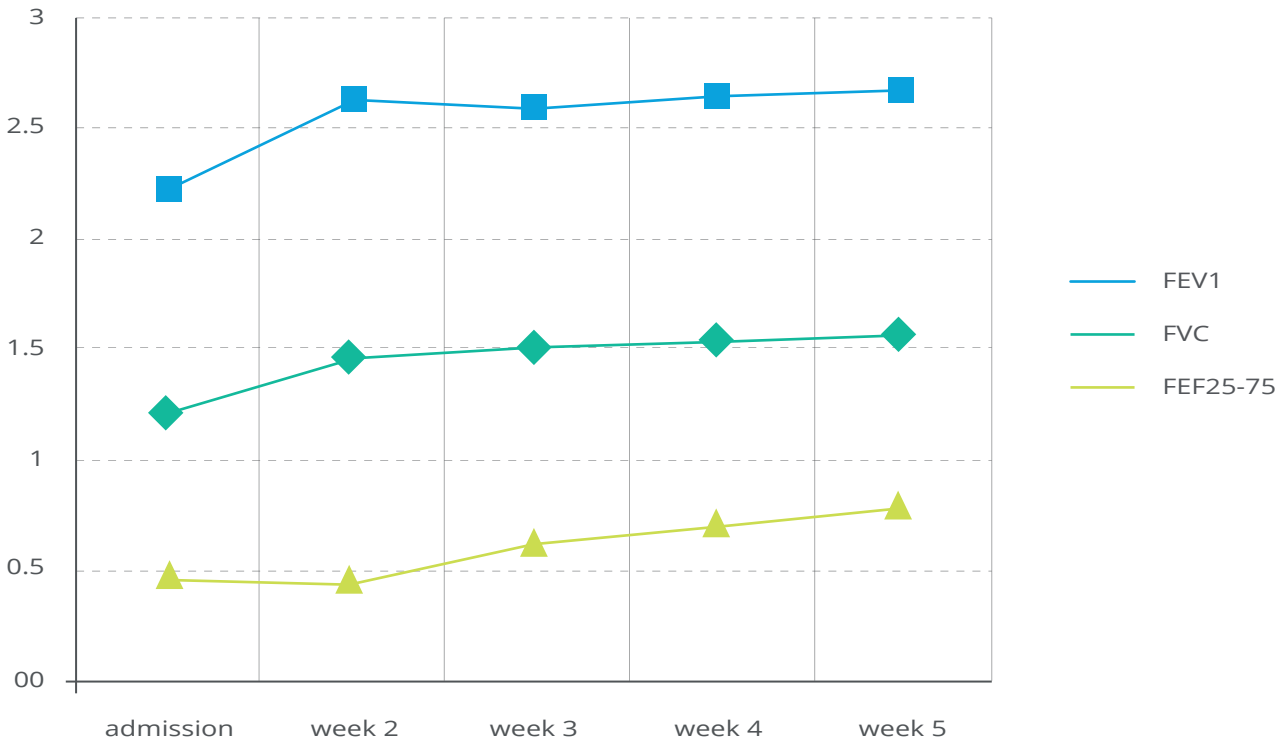


Fig. 2. The selected spirometry parameters in a 17-year-old patient presented by the British team prior to and after commencement of Simeox treatment.

The second case was of a 16-year-old female with cystic fibrosis (genotype F508del/F508del). She had been diagnosed with exocrine pancreatic insufficiency, a chronic infection of the respiratory tract with Pseudomonas aeruginosa and CFRD diabetes (very poorly controlled). The girl attends a school, she comes from a family of a very low socio-economic status, she hardly follows any recommendations and is a typical rebellious teenager. During medical appointments, she declares to follow all doctor's recommendations; however, on the basis of her test results, the medical team believes she performs them very irregularly. A list of the patient's regular medications has been presented:

- ivacaftor/tezacaftor/elexafactor
- flucloxacillin
- inhaled colistin
- inhaled Dornase alfa
- inhaled 7% NaCl
- inhaled Salbutamol
- Mometasone nasal spray
- insulin therapy using a personal pump
- ursodeoxycholic acid
- vitamins
- pancreatin

Patient's physiotherapy prior to inclusion of Simeox

- Oscillating Positive Expiratory Pressure device (O-PEP)
- the active cycle of breathing technique, the increased exhalation technique
- postural drainage, manual techniques
- physical activity (running, gymnastics)

Table 2. The selected spirometry parameters in a 16-year-old patient presented by the British team prior to and after commencement of Simeox treatment.

	IVAB'S at home with Simeox		
	FEV1	FVC	FEF25-75%
Start	1.4	1.66	1.36
Mid	1.52	1.81	1.58
End	1.65	1.87	1.81

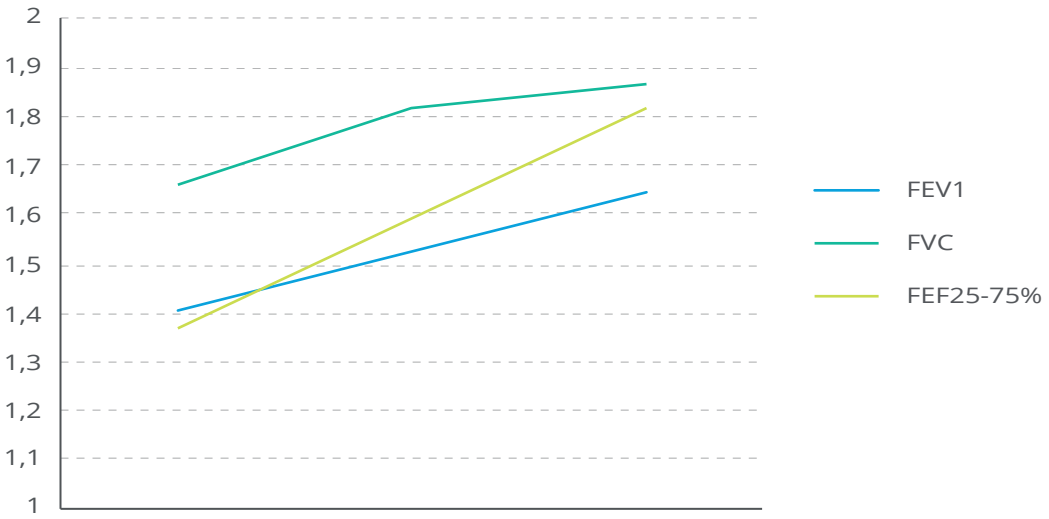


Fig. 3. The selected spirometry parameters in a 16-year-old patient presented by the British team prior to and after commencement of Simeox treatment.

The results obtained were compared to the earlier hospitalization (IV antibiotic therapy + conventional techniques of physiotherapy of the respiratory tract), when FEV1 increased from 1.56 to 1.71 l, FVC - from 1.85 to 2.07 l, MEF25-75 - from 1.56 to 1.62 l. In particular, improvement in MEF25-75 (parameter proving patency of the smallest bronchi) only after supporting IV antibiotic therapy with Simeox was spectacular.

Table 3. A change in the selected spirometry parameters after IV antibiotic therapy combined with Simeox therapy in the home environment in a 16-year-old female patient presented by the British team

	IVAB'S at home with Simeox		
	FEV1	FVC	FEF25-75%
Start	1.4	1.66	1.36
Mid	1.52	1.81	1.58
End	1.65	1.87	1.81

Table 4. A change in the selected spirometry parameters after IV antibiotic therapy combined conducted in the hospital, combined with conventional physiotherapy of the respiratory tract, in a 16-year-old female patient presented by the British team

	IVAB'S in Hospital with other ACT		
	FEV1	FVC	FEF25-75%
Start	1.56	1.85	1.56
Mid	1.69	2.08	1.59
End	1.71	2.07	1.62

The patient reported that physiotherapy using Simeox was in her case more effective and easier in comparison with conventional physiotherapy of the respiratory tract. The patient was very happy that IV antibiotic therapy and intensive chest physiotherapy could take place at home. In the opinion of the physiotherapist, introduction of the new drainage method, accepted by the patient, improved cooperation in terms of compliance with the recommendations. Secretions from the respiratory tract were better evacuated. Improvement in the MEF25-75 spirometry parameter is a very positive phenomenon. In the summary of the 2 clinical cases, it was stated that the key advantages of using Simeox to support IV antibiotic therapy included: improvement in the MEF25-75 spirometry parameter, easy evacuation of secretions from the respiratory tract (particularly the small bronchi), lack of risk of barotrauma/hyperinflation of the lungs and the fact that the device could be used both in the hospital and at home.

Dr Karolina Gwoździewicz and Katarzyna Warzeszak, M.Sc.

Dr Karolina Gwoździewicz and Katarzyna Warzeszak, M.Sc. presented the case of a 17-year-old boy with cystic fibrosis, genotype F508del/F508del, diagnosed in the 1st year of life, with exocrine pancreatic insufficiency, malnutrition (BMI 16.56 kg/m2; fed enterally via PEG tube) and a moderately progressing bronchopulmonary disease. Since 06.2019, the patient has been under care of the Institute of Tuberculosis and Lung Diseases in Rabka-Zdrój due to progression of the disease - exacerbation of the bronchopulmonary disease, requiring hospitalization and IV antibiotic therapy on the average twice a year. Moreover, the patient was diagnosed with CFRD diabetes, polyposis of the paranasal sinuses and the nose (condition after endoscopy of the paranasal sinuses in 2015), Asperger syndrome, anxiety and obsessive-compulsive disorders. Radiological examination of the chest indicates general bronchiectasis, thickening of the bronchial walls, some minor peribronchial consolidations, hyperinflation of lung fields. As for the respiratory tract, a chronic infection with Staphylococcus aureus has been diagnosed. Infection of the respiratory tract with Pseudomonas aeruginosa occurred for the first time in May 2020, and it was effectively eradicated at the time. Moreover, the patient has suffered from periodic infections with Stenotrophomonas maltophilia and Acinetobacter baumannii. Between 06.2019 and 11.2020, the patient suffered from a very significant deterioration in the lung function – FEV1 decreased from 94% to 68% of the predicted value, FVC – from 117% to 90% of the predicted value. During this period, the patient required IV therapy and intensive nutritional treatment three times. At the time, physiotherapy of the patient's respiratory tract was as follows:

- 2 x daily inhaled formoterol, followed by inhalation with 5% NaCl
- 2 x daily Dornase alfa inhalation
- 2 x daily drainage of the respiratory tract (about 30 minutes) using a Positive Expiratory Pressure device (PEP) and an Oscillating Positive Expiratory Pressure device (O-PEP).
- Moreover, physical activity: mountain climbing, cycling.

In 02.2021, the boy required hospitalization due to yet another exacerbation of the bronchopulmonary disease. Presented below are results of a physical examination and additional tests:

- Symptoms: loss of appetite and decrease in demand for insulin, body mass reduction by 2.5 kg (current weight 46 kg), weakness, difficulty in coughing up retained bronchial secretion
- Upon hospitalization: moderate general condition, slight dehydration symptoms, no dyspnea, SpO2 93%, ineffective coughing, on auscultation - bilateral crackles, particularly in the upper parts of the lungs, depressed mood, substantial anxiety and helplessness
- Laboratory test results: CRP 74,01 mg/L, WBC 15.44 thousand/μL, neutrophilia 83.8 %, fibrinogen 6.88 g/L (N to 4.0), acid–base homeostasis within limits
- Sputum smear: Staphylococcus aureus (MSSA)
- Ultrasound of the lungs: in the right upper lobe, in the posterior region, atelectasis 11 mm, in the anterior region - atelectasis 13 mm; in the lower part of segment 3, atelectasis 24 mm; in the left upper lobe, small focal consolidations
- Spirometry: further, very substantial decrease in FEV1 to 51% of the predicted value (by 17% of the expected value), FVC to 76% of the predicted value (by 14% of the predicted value).

IV antibiotic therapy was commenced, using piperacillin-tazobactam combined with tobramycin. Moreover, due to the first episode of such severe exacerbation of the bronchopulmonary disease in the patient's life, problems with coughing up secretion and a poor prognosis due to the observed trend in the spirometry parameters, despite concerns with regard to cooperation of the patient (diagnosed with Asperger syndrome), the decision was made to introduce chest physiotherapy using Simeox.

Physiotherapy

- During the first day of hospitalization, Simeox was included (2 x daily 20 minutes, preceded with nebulization using 5% NaCl), combined with a positive expiratory pressure device,
- Device settings: power of 25-50%, 4 cycles,
- Initially, drainage in a sitting position,
- Despite his anxiety disorders, the patient tolerated the device well and was eager to work with it, and he quickly mastered the proper technique,
- Initially, he coughed up increased quantities of secretion without any effort,
- Initially, for the first time, he ceased to experience problems with coughing up sputum.

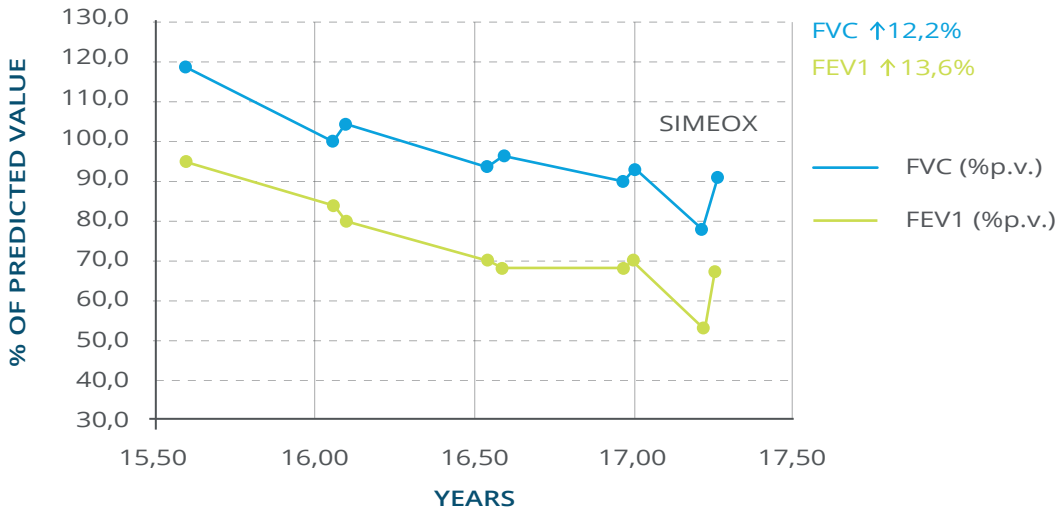


Fig. 4. A change in the percentage of the predicted value of FEV1 in 2 years in a 17-year-old patient presented by the Polish team (the most recent values after application of Simeox therapy in the course of IV antibiotic therapy).

Table 5. The selected spirometry parameters in a 17-year-old patient presented by the Polish team prior to and after commencement of Simeox treatment in the course of IV antibiotic therapy

Spirometry (05.02.2021)			Spirometry (17.02.2021)		
FVC	3,37 [L]	76% p.v.	**FVC**	4,09 [L]	92% p.v.
FEV1	1,96[L]	51% p.v.	**FEV1**	2,56 [L]	66% p.v.
FEV1/FVC	58,33 %	67% p.v.	**FEV1/FVC**	62,42 %	72% p.v.
PEF	5,16 [L/s]	77% p.v.	**PEF**	6,82 [L/s]	101% p.v.
MEF75	2,45 [L/s]	42% p.v.	**MEF75**	3,35 [L/s]	57% p.v.
MEF50	1,17 [L/s]	27% p.v.	**MEF50**	1,73 [L/s]	39% p.v.
MEF25	0,41 [L/s]	19% p.v.	**MEF25**	0,58 [L/s]	27% p.v.

Results achieved

- Improvement in the overall condition, mood and wellbeing of the patient,
- Noticeable effects of drainage of the bronchial system, with no additional effort,
- Concentration during drainage,
- Willingness, commitment, motivation of the patient to perform drainage of the bronchial system.
- Subsiding of auscultatory changes above the lung fields,
- Return of appetite and increased demand for insulin, increase in weight,
- Normalization of inflammatory parameters and leukocytes in the blood count,
- Improvement in spirometry parameters (FEV1 and FVC values became close to those prior to the exacerbation, of 70% and 90% of the predicted value, respectively).

During a check-up visit 2 months later, the spirometry parameters of the date of completion of the IV antibiotic therapy was observed, as well as increase in body weight by 3 kg. Moreover, at present, the patient is able to cough up sputum retained in the respiratory tract without any problems, and bronchial drainage is much more effective.

Table 6. Maintaining of spirometry parameters as recorded on the date of finishing of IV antibiotic therapy 2 months later in a 17-year-old male patient presented by the Polish team

Spirometry (17.02.2021)			Spirometry (21.04.2021)		
FVC	4,09 [L]	92% p.v.	**FVC**	4,03 [L]	89% p.v.
FEV1	2,56 [L]	66% p.v.	**FEV1**	2,69[L]	69% p.v.
FEV1/FVC	62,42 %	72% p.v.	**FEV1/FVC**	66,81%	76% p.v.
PEF	6,82 [L/s]	101% p.v.	**PEF**	7,36 [L/s]	112% p.v.
MEF75	3,35 [L/s]	57% p.v.	**MEF75**	3,39 [L/s]	57% p.v.
MEF50	1,73 [L/s]	39% p.v.	**MEF50**	1,62 [L/s]	36% p.v.
MEF25	0,58 [L/s]	27% p.v.	**MEF25**	0,54 [L/s]	24% p.v.

After the three presentations of the first meeting, there was an extensive discussion, which included the following problems:

- the role of Simeox in patients with autism spectrum disorders (such as Asperger syndrome); work with the device is very systematic and, in the opinion of physiotherapists, makes it easier for patients with significant concentration difficulties caused by their disorder to focus on drainage; in these patients, another problem is caused by their lack of willingness to establish communication with other people (usually in conventional physiotherapy), while work with Simeox does not require such communication
- assessment of efficacy of physiotherapy using Simeox: parameter MEF25-75 proves patency of the small bronchi, and its increase was spectacular in both patients presented by the UK team; it would be advisable to conduct an examination to assess this parameter in patients, who do not require IV antibiotic therapy, as well as research to assess the LCI values after the Simeox therapy
- during therapy with Simeox, it is not necessary to use a specific breathing pattern; it is sufficient for the patient to breathe calmly and be relaxed
- it is beneficial to use the device in different drainage positions, depending on the lesions found in the lung parenchyma, especially in small children, who are often irritated by having to remain in the same position
- the device is microbiologically safe when used in different patients, as the air flow always takes place from the patient to the device only; for the purpose of microbiological control

Conclusions based on the first meeting:

- Simeox quickly brings benefits in terms of improvement of the pulmonary function and making it easier to cough up sputum, when introduced at the beginning of the IV therapy in the daily protocol of the chest physiotherapy.
- Drainage using Simeox in combination with other therapies (CFTR protein modulators, other bronchial drainage techniques) results in decreased hyperinflation of the lung parenchyma.
- Patients claim to require little time to get familiar with the device and to learn to use it. Only a short time is required to feel comfortable with Simeox.
- Simeox is a good alternative to other techniques of airway clearance in order to increase motivation for CPT among patients with poor compliance or low commitment, especially young patients with cystic fibrosis
- Patients in a poor general condition of suffering from substantial fatigue can use Simeox therapy without an additional effort and with good tolerance, and the device is particularly recommended for patients, who find it difficult to cough up secretion.

Second meeting of 25.05.2021

Mobilization of mucus in the bronchial tree with SIMEOX in patients with cystic fibrosis

The benefits of planned hospitalization

Participants

Dr Justyna Milczewska, pediatric pulmonologist

Cystic Fibrosis Treatment Center of the Independent Complex of Public Health Care Institutions of the Children of Warsaw in Dziekanów Leśny, the Clinic and Unit of Cystic Fibrosis of the Institute of Mother and Child in Warsaw and **Natalia Jeneralska**, physiotherapist, Cystic Fibrosis Treatment Center of the Independent Complex of Public Health Care Institutions of the Children of Warsaw in Dziekanów Leśny, Poland

Dr Tereza Doušová, pediatric pulmonologist and
Anna Chmelařová, physiotherapist

University Hospital of Motol and the Charles University in Prague, the Czech Republic

Dr Hanna Schmidt the Cystic Fibrosis Treatment Center of the Ulm University Hospital, Germany.

Dr Tereza Doušová and Anna Chmelařová

Dr Tereza Doušová and Anna Chmelařová presented a case of a 11-year-old boy, diagnosed with cystic fibrosis (genotype F508del/F508del) at the age of 5 months (at the time, infant screening tests were not performed in Czech Republic). At the time, the symptoms already included chronic productive cough, inflammatory lesions in the lower right lung and substantial signs of malnutrition. The concentration of chloride in sweat was 88.8 mmol/l, activity of pancreatic elastase in stool was indeterminable. Exocrine pancreatic insufficiency was diagnosed.

At present, the patient suffers from chronic infection of the respiratory tract with Staphylococcus aureus and Pseudomonas aeruginosa, as well as periodic infections of the respiratory tract with Stenotrophomonas maltophilia, Exophiala dermatidis and Aspergillus fumigatus.

In 2019, the patient was diagnosed with allergic bronchopulmonary aspergillosis (glucocorticosteroids and an antifungal drug have been administered orally). In this period, the patient also had some very severe symptoms of malnutrition (BMI 15 (-1.5 SD)). In CT of the lungs, the patient showed exacerbated symptoms in form of mucus plugs, bronchiectasis and atelectasis in the lower right lobe. The patient chronically coughs up quite substantial amounts of sputum.

In years 2018-2020, progressive deterioration of the lung function was observed in the spirometry tests (decrease of FEV1 from 92% to 74% of the predicted value). When FEV1 decreased to 74% of the predicted value, chest physiotherapy using Simeox was commenced. At the time, the patient's chronic treatment included supplementation of pancreatic enzymes and vitamins, probiotics administered orally, as well as Dornase alfa, hypertonic salt (6%), long- and short- acting beta-2-mimetics, glucocorticosteroids administered by inhalation.

In 02.2021, a CFTR protein modulator was included - a combination of ivacaftor and lumafactor.

Physiotherapy sessions usually start with irrigation of the nasal cavities. Afterwards, following use of the bronchodilator, inhalations are performed, in which particular emphasis is put on the proper inhalation technique and body posture. The respiratory tract drainage device used chronically is the Oscillating Positive Expiratory Pressure device (O-PEP). The airway clearance device Simeox was introduced in the patient's treatment for the first time in 02.2020 during exacerbation of the bronchopulmonary disease under hospital conditions, after which the patient borrowed the device to use it at home. One month of work with the device produced excellent results.

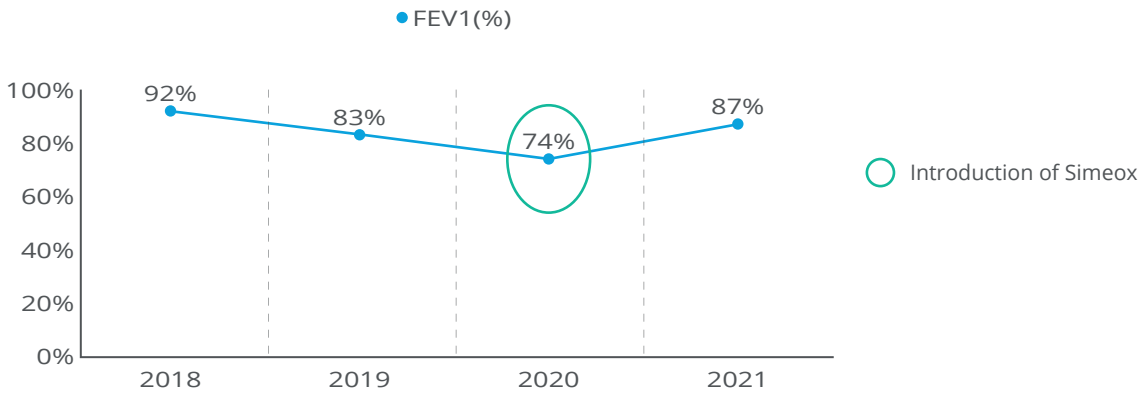


Fig. 5 A change in the percentage of FEV1 predictable value in 3 years in a 11-year-old male patient, presented by the Czech team.

Afterwards, in 08.2020, the patient underwent a 10-day planned hospitalization, during which Simeox was used in chest physiotherapy. Drainage using the device was conducted twice a day, in a sitting, semi-sitting, lying position on both sides and on the stomach. The patient was trained to exhale properly while working with the device. The device power was set to 25-100% (decreased gradually during exhalation to include drainage in the parts of the respiratory tract characterized by the lowest caliber). The patient tolerated therapy well.

Moreover, he was trained to develop his inhalation technique and to perform breathing exercises to stretch his chest muscles. Motor rehabilitation was also included (posture exercises, exercises to improve muscle tension).

A significant improvement in spirometry parameters was achieved in 10 days of hospitalization: FEV1 79% –> 104% p.v., FVC 92% –> 114% p.v., MEF75 74% –> 110% p.v., MEF50 46% –> 81% p.v., MEF25 29% –> 41% p.v. Improvement was also observed in terms of coughing up of secretion retained in the respiratory tract, as well as improvement in the boy's body posture: reduction of shoulder anteflexion, normalization of tension of the chest and stomach muscles, reduction of chest kyphosis.

Table 7. The selected spirometry parameters in a 11-year-old patient presented by the Czech team prior to and after commencement of Simeox treatment.

	17.08.2020	27.08.2020
FVC	92%	114%
IRV	0,97 l	1,10 l (+0,13 l)
ERV	0,44 l	0,71 l (+0,27 l)
FEV1	79%	104%
MEF 75	74%	110%
MEF 50	46%	81%
MEF 25	29%	41%
PI max	105%	115%
PE max	82%	109%

Dr Justyna Milczewska and Natalia Jeneralska, M. Sc.

Dr Justyna Milczewska and Natalia Jeneralska, M. Sc. presented a case of a 13-year-old boy with cystic fibrosis (genotype W356X/R553X) diagnosed in the course of infant screening tests, with slight symptoms of the bronchopulmonary disease (FEV1 75-88% of the predicted value), and a chronic infection of the respiratory tract with Staphylococcus aureus.

Since 2017, the patient has recorded a significant increase in the concentration of total IgE (1000-2500 u), treated for toxocariasis, under observation due to suspicion of allergic bronchopulmonary aspergillosis.

From 10.2018 until 01.2020, treated with itraconazole, and then with voriconazole for infection of the respiratory tract with Aspergillus fumigatus (due to lesions typical for a fungal infection in the LDCT). The boy is under observation due to suspicion of cirrhosis of the liver and has polyposis of the paranasal sinuses. Moreover, there are behavioral problems, and the boy cooperates poorly in terms of physiotherapy of the respiratory tract.

In the late 2019/ early 2020, he was treated due to exacerbation of the bronchopulmonary disease (amikacin, ceftazidime IV), later - due to atelectatic lesions with a pleural reaction, this treatment was replaced with meropenem and clindamycin IV and colistin administered by inhalation.

During exacerbation of the bronchopulmonary disease, there was a significant reduction in the spirometry parameters (up to 70% of the predicted value), which after treatment returned to their previous levels.

In December of 2020, the patient underwent a planned hospitalization for the purpose of check-up tests, during which he was trained in using the Simeox device in chest physiotherapy (sitting position, 10 exhalations per series, 6-8 series per session depending on the quantity of retained secretion, device power of 25% in the first 2 series, followed by 50%) and the boy was encouraged to perform inhalation-drainage treatment on a regular basis.

In March 2021, the patient underwent a check-up at the Cystic Fibrosis Treatment Center. After more than 2 months of physiotherapy using Simeox 2 x daily in the home environment, his general wellbeing and physical capability improved, coughing during the day subsided, and the patient's motivation to engage in chest physiotherapy increased.

According to his parents, after introduction of the Simeox drainage device, the patient started to perform the physiotherapy recommendations eagerly, on a regular basis. A significant improvement was also recorded in function tests of the respiratory tract (increase in FEV1 from 88% to 105% of the predicted value, FVC from 96% to 110% of the predicted value).

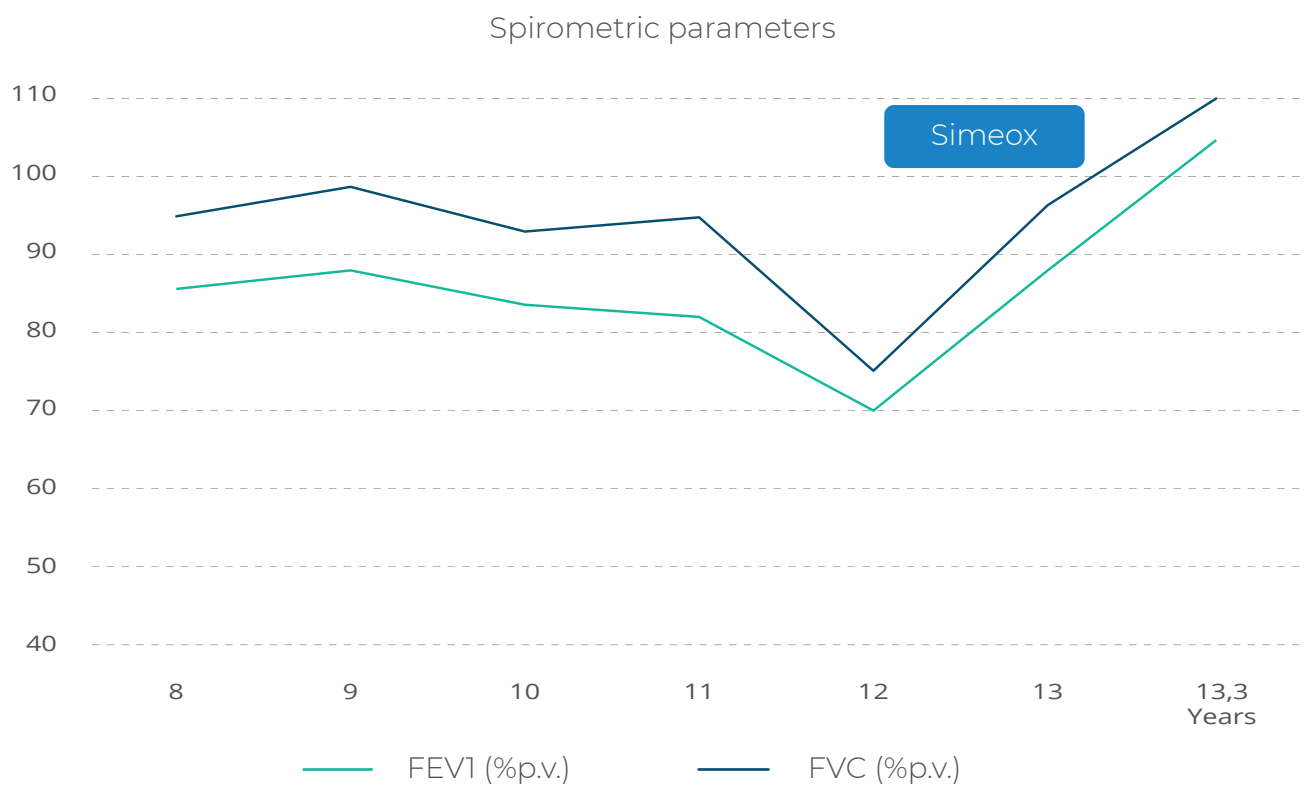


Fig. 6. A change in the percentage of FEV1 predictable value in 5 years in a 13-year-old male patient, presented by the Polish team.

The presentation was summarized as follows:

- Optimally, introduction to physiotherapy using the Simeox device should take place during an individual physiotherapy training during several days of hospitalization.
- This allows for introduction of personalized - "tailored" therapy (selection of an optimum set of parameters for a given patient).
- The proper drainage technique (maximum use of the device capacity, avoiding of typical mistakes) produces better results, which are translated to enhanced wellbeing and encourages the patient to continue working with the device.

Dr Hanna Schmidt

Dr Hanna Schmidt presented results of a pilot research project conducted in adult patients with cystic fibrosis to assess short-term effects of chest physiotherapy using the Simeox device. The aim of this work was to assess the positive results of physiotherapy using Simeox in these patients. 3 research hypotheses were made:

- 1. Mobilization of bronchial secretion using Simeox would lead to improvement of the lung function (improvement of spirometry parameters)
- 2. Mobilization of bronchial secretion using Simeox would lead to better mobility of the diaphragm (improvement visible in the ultrasound examination).
- 3. Simeox therapy would influence the characteristics of secretion expectorated spontaneously (viscosity, DNA concentration).

The project encompassed 21 adult patients with cystic fibrosis in a clinically stable period of the disease. Basic clinical data:

- age 30.1 ± 9.26 years (21-53)
- 11 men, 10 women
- BMI 21.62 ± 2.07 kg/m2 (18.0-25.1)
- FEV1 2.75 ± 1.20 L (1.23-6.29)
- FEV1 71.55 ± 20.47 % of the predicted value (35-106)
- FVC 3.921 ± 1.23 L (2.33-6.44)
- FVC 88.55 ± 21.96 % of the predicted value (54-126)

The criteria of exclusion from the project were as follows:

- acute infection, exacerbation of the bronchopulmonary disease
- unstable disease of the lungs or cardiovascular system
- recent pneumothorax
- recent significant hemoptysis
- pregnancy

Procedures included in the scope of the research project:
- patient recruitment, informed written consent in participation in the research
1st session:

- ultrasound of the diaphragm, spirometry, collection of sputum samples
- followed by a physiotherapy session using Simeox assisted by a physiotherapist
- another ultrasound of the diaphragm, spirometry, collection of sputum samples

2nd session after several (3-6) weeks following the first one:

- ultrasound of the diaphragm, spirometry, collection of sputum samples
- followed by a physiotherapy session using Simeox assisted by a physiotherapist
- another ultrasound of the diaphragm, spirometry, collection of sputum samples
- the patient fills out the device assessment questionnaire

Results:

- Spirometry:

no statistically significant differences were found in terms of FEV1, FVC, MEF75, MEF50, MEF25 in the spirometry tests performed before and after the physiotherapy session using the Simeox device

- Ultrasound of diaphragm mobility :

- the method is used to assess efficacy of chest physiotherapy e.g., in patients with chronic obstructive pulmonary disorder or patients requiring intensive care
- diaphragm inclination, assessed during the examination, is correlated with severity of the disease, and it increases (indicating improvement in diaphragm mobility) in the course of use of effective forms of chest physiotherapy
- data on use of this method in patients with cystic fibrosis is limited
- during the examination, patients are in a semi-lying position, breathing freely
- diaphragm mobility is assessed in B and M mode
- the maximum amplitude of diaphragm inclination was measured
- in ultrasound examinations performed after the physiotherapy session with Simeox, it was shown that the diaphragm inclination amplitude increased significantly in comparison with examinations performed prior to the Simeox physiotherapy session

Sonographic assessment of diagphragm mobility

Lying position,
breathing at rest

B-mode

M-mode

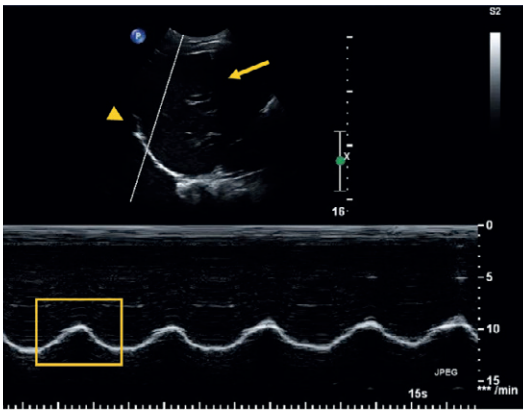


Fig. 7. Imaging of diaphragm mobility in the ultrasound examination in B and M mode

Sputum viscosity and DNA concentration

- in vitro research indicated dilution of sputum after using oscillating devices, which, however, was not confirmed by in vivo research
- in the present research project, it was shown that sputum coughed up after the Simeox session was more viscid in comparison to samples collected before the session
- a slightly greater concentration of DNA in the sputum was observed after the Simeox session in comparison with the sputum samples collected before (DNA in the sputum of patients with cystic fibrosis comes mainly from neutrophils, and its concentration is correlated with viscosity)
- the most probable reason for obtaining results of this kind: as a result of intensive and highly effective drainage of the small bronchi, as well as parts of the lungs subject to intensified inflammation, secretions containing large numbers of inflammatory cells emerge, which are more viscous and have a higher DNA concentration of neutrophils

Results of questionnaires assessing the method, filled out by patients:

- the device is effective in terms of drainage of bronchial secretion (median of 8 points on a 10-point scale)
- in comparison with other physiotherapy methods, the device removes secretions from deeper parts of the lungs (median of 6 points on a 10-point scale)
- the device is easy to use (median of 10 points on a 10-point scale) and to handle (median of 9 points on a 10-point scale)
- "I could use the device on my own" (median of 9.5 points on a 10-point scale)
- drainage wasn't painful (median 9 point on a 10-point scale)
- drainage wasn't exhausting (median 8 points on a 10-point scale)
- 66.7% patients would recommend Simeox to other patients

What the patients found most important:

- better sputum mobilization immediately after drainage or within the next hours (5 responses)
- "I find it easier to breathe" (4 responses)
- the technique does not require much effort (3 responses)
- the device is easy to use (2 responses)

Asked about weaknesses of the device, the patients answered it was rather loud and big (cumbersome)

Conclusions

- no adverse events (high level of safety of Simeox therapy)
- no short-term impact of Simeox therapy on spirometry results was shown
- improvement in diaphragm mobility after therapy was observed
- after the physiotherapy session with Simeox, sputum viscosity and neutrophil DNA concentration increased, which may prove that use of the device contributes to activation of sputum from other lung parts in comparison with other physiotherapy methods; probably, the inflammation was more intensive in these regions
- work with Simeox was well tolerated and easy after a proper training
- in order to assess long-term clinical benefits of use of Simeox, it is necessary to perform further research

After three presentations of the second meeting, there was an extensive discussion, which included the following topics:

- accessibility of the device - the Cystic Fibrosis Treatment Center in Dziekanów Leśny has 2 Simeox devices, which are used by patients during hospitalization, when they undergo trainings on use of the device. Moreover, doctors and physiotherapists cooperate with the patient to assess whether the patient would benefit from use of the device in the course of chronic treatment at home. So far, the device is not subject to refund by the National Health Fund, so its availability in the home environment has been significantly limited. There is a possibility of receiving grants e.g., from rehabilitation funds or private charity collections on behalf of individual patients. The Cystic Fibrosis Treatment Center in Dziekanów Leśny has some experience in terms of efficiency of home physiotherapy using Simeox, which has been very good. It includes improvement in patients' motivation to perform drainage of the respiratory tract (interest in the physiotherapy method, which the patients find to be modern, interesting and effective), which is of great significance in the case of cystic fibrosis. Improvement of the lung function thanks to Simeox therapy oftentimes results in significant improvement of the physical capacity. Similar experiences and observations were shared by the team of the University Hospital of Motol and Charles University in Prague in Czech Republic.

- more precise information was provided on the research project presented by dr Hanna Schmidt: only about 60% of patients participating in the study were able to cough up secretions; some patients had coughed up no secretion prior to the intervention, while they did after the Simeox physiotherapy, which proves to be a very efficient drainage; patients who coughed up before and after the intervention were in a more advanced stage of the bronchopulmonary disease; a study on long-term efficacy of the device has been planned

- one of the participants asked how patients were selected to be offered to attempt drainage using Simeox:

- the Czech team: Simeox is usually proposed to patients, in which conventional physiotherapy brings no results, usually with worse results of function tests of the lungs, in a worse overall condition; in these patients, we expect more spectacular results; proper cooperation is also of great importance.
- the team of Dziekanów Leśny: invitations to cooperate are addressed to all patients, however, priority is given always to those in a worse overall condition; the number of patients asking about the possibility of trying to work with Simeox even before they are proposed a trial is increasing.
- Dr H. Schmidt of Germany: the center treats adults and children, and in the first place, adults are offered the possibility of trying to work with the device; in Germany, the device can be refunded or lent,

- another question: how Simeox can be helpful in patients with deterioration of their lung function and what tools can be used to assess the efficacy of the therapy:

- dr H. Schmidt of Germany: the most important tool is spirometry, while N2MBW is not performed
- the team of Dziekanów Leśny and the Czech team: spirometry, N2MBW and other function tests of the respiratory tract are performed; the measure of efficacy of physiotherapy in patients, who have suffered from deterioration of their lung function, is restoration of the primary lung function parameters, that is, "making up for the loss", which, unfortunately, is not always possible

- another question: can Simeox be used in patients with increased breathing effort - reply (team of Dziekanów Leśny, the Czech team, dr H. Schmidt of Germany): it can be used by patients with increased breathing effort - moreover, it is recommended for such patients, as drainage takes place during exhalation, which is a passive process and thus less exhausting; Simeox can also be used successfully in patients using passive oxygen therapy, as well as patients with cystic fibrosis and allergic bronchopulmonary aspergillosis; in the case of e.g. hyperreactivity of the bronchi, the possibility of individual setting of the device parameters (such as power) has turned out to be very useful

- a question to dr H. Schmidt of Germany: how can we explain the correlation between increased mobility of the diaphragm and improved lung function ?- reply: one of the hypotheses is that improvement of the lung function is related to reduction of hyperinflation of lung fields, which translates to better mobility of the diaphragm; moreover, it can contribute to reduction in the quantity of secretions in the respiratory tract and removal of mucus plugs

- the following question regarded combination of Simeox with other drainage techniques: according to all participants, Simeox should always be used in combination with other physiotherapy methods to produce optimum results

Conclusions based on the second meeting:

- Simeox slows down (or even brings to a halt) progression of the bronchopulmonary disease, if used in the long-term perspective on a regular basis in chronic treatment, and a planned hospitalization for several days is a good method of introducing this therapy
- Drainage of the bronchial system using Simeox is a safe and effective therapeutic option, particularly if the results of standard chest physiotherapy are not sufficient (mobilization of only a part of secretion retained in the respiratory tract)
- Simeox allows for a more thorough drainage of bronchi in the lung regions subject to inflammatory condition and distal parts of the respiratory tract while causing less irritation of the respiratory tract in comparison with standard physiotherapy of the chest
- Work with the device contributes to improved cooperation with patients regarding chest physiotherapy
- Optimum results are obtained by combining bronchial drainage using Simeox with other methods of physiotherapy of the respiratory tract

Third meeting of 27.05.2021

Observations of medical teams in patients using SIMEOX in their home rehabilitation.

Personalized medicine.

The clinical benefit for the patient

Participants

Dr Justyna Milczewska, pediatric pulmonologist

Cystic Fibrosis Treatment Center of the Independent Complex of Public Health Care Institutions of the Children of Warsaw in Dziekanów Leśny, the Clinic and Unit of Cystic Fibrosis of the Institute of Mother and Child in Warsaw and **Natalia Jeneralska**, physiotherapist, Cystic Fibrosis Treatment Center of the Independent Complex of Public Health Care Institutions of the Children of Warsaw in Dziekanów Leśny, Poland

Dr Jörg Grosse-Onnebrink, pediatric pulmonologist and **Christina Krämer**, physiotherapist of the Cystic Fibrosis Treatment Center at the University Hospital in Münster, Germany

Dr Boubou Camara and **Dr Rebecca Hamidfar**, pulmonologists of the Cystic Fibrosis Treatment Center (CRCM) in Grenoble, France.

Dr Boubou Camara

Dr Boubou Camara presented the assumptions applied to the clinical study being currently conducted by his center on the efficacy and safety of the Simeox device used on their own by patients with cystic fibrosis as a part of home chest physiotherapy. It is a prospective, randomized, multi-center study (5 pulmonology centers in France).

The control group consists of patients with cystic fibrosis engaged in conventional physiotherapy (without the Simeox device).

The study duration is 3 months, and it is aimed at assessing respiratory symptoms and lung capacity in function tests in patients with cystic fibrosis, engaged in physiotherapy using Simeox. The primary outcome measures are:

- respiratory symptoms (change in the score of respiratory symptoms CFQ-R in 3 months of the study duration)
- spirometry parameter of the lung function (FEV1 changes in the 3 months of the study)

The secondary outcome measures are:

- quality of life assessment (CFQ-R)
- safety of use of Simeox device
- assessment of the method by patients
- impact on the lung function
- assessment of the overall quality of life
- assessment of the quality of sleep
- assessment of tiredness after the physiotherapy session
- necessity to use antibiotic therapy
- time until first exacerbation of the bronchopulmonary disease
- possibility of remote control of the therapy

The inclusion criteria include:

- patient with diagnosed cystic fibrosis
- in a stable period of the disease (at least 4 weeks have passed since the last exacerbation of the bronchopulmonary disease)
- age above 14
- patient requiring at least 1 session of drainage of the respiratory tract per week (using any technique)
- patient understanding the significance of procedures exercised in the study, able to give their informed consent in participation in the study

The study exclusion criteria include:

- pneumothorax or exacerbated hemoptysis (above 30 ml in 24h) in 6 weeks prior to inclusion in the study
- patient on an active lung transplantation list
- any contraindications for bronchial drainage using mechanical devices
- patient already using Simeox at home
- patient unable to attend check-up visits included in the study protocol
- patient participating in any other clinical study
- pregnancy, postnatal period, breastfeeding

Procedures included in the scope of the research project:

- inclusion in the study (patient recruitment, informed written consent in participation in the research, randomization in the study or control group, collecting of sputum sample)
- initial visit (anthropometry, CFQ-R, spirometry, 7-day actimetry, in the case of patients randomized to be included in the Simeox group, a training on use of the device - 5 meetings, possibly remote)
- phone-call based visits every month (information on adverse events)
- visit after 3 months of the study (anthropometry, CFQ-R, spirometry, 7-day actimetry, collection of data on exacerbations of the bronchopulmonary disease requiring hospitalization or not, antibiotic therapy, adverse events; only for the Simeox group: questionnaires of assessment of the device by the patient).

70 patients are to be included in the study. In this group, a sub-group of 56 patients has been identified, who are to be subjected additionally to body plethysmography with RV assessment.

As of the presentation date, 23 patients had been randomized in the study, including 12 to be included in the Simeox group. In this sub-group, the patients quickly learned to use the device, they experienced no difficulties related to using it, reported a subjective of improvement of their lung function, a feeling of more effective drainage of the bronchi, related to smaller effort in comparison with conventional physiotherapy. They reported the big size of the device to be inconvenient. We expect the full results of the study to be delivered after its completion.

Dr Boubou Camara also presented a case of a 39-year-old male patient, diagnosed with cystic fibrosis at 37 (genotype G85E/D1152H). Diagnostics for suspected cystic fibrosis commenced due to recurring infections of the respiratory tract, infertility, infection of the respiratory tract with Pseudomonas aeruginosa and diagnosing of allergic bronchopulmonary aspergillosis. The patient was also diagnosed with a chronic infection of the respiratory tract with Staphylococcus aureus and Aspergillus fumigatus.

The patient performed chest physiotherapy 2 x per week, he periodically suffered from effort dyspnea resulting from bronchial obstruction. In March 2020, chest physiotherapy involving Simeox was commenced. Prior to treatment, FEV1 was 93% of the predicted value, and FVC - 96% of the predicted value; after 3 months of therapy, these values increased to 113% and 104% of the predicted value, respectively. Residual volume (RV) decreased significantly. After 3 months, the score on the scale of respiratory symptoms CFQ-R increased from 55 to 72 per 100 points. The patient reported that physiotherapy sessions were not related to effort or fatigue. The patient reported better quality of sleep and improvement in overall wellbeing.

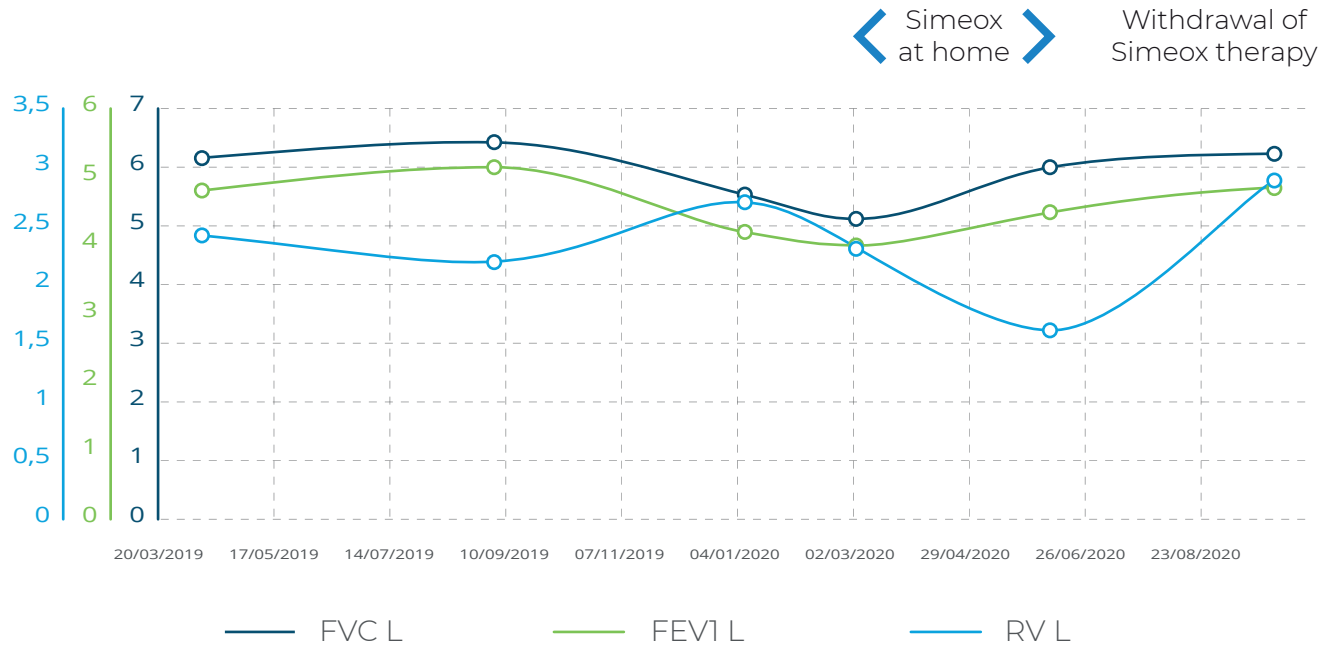
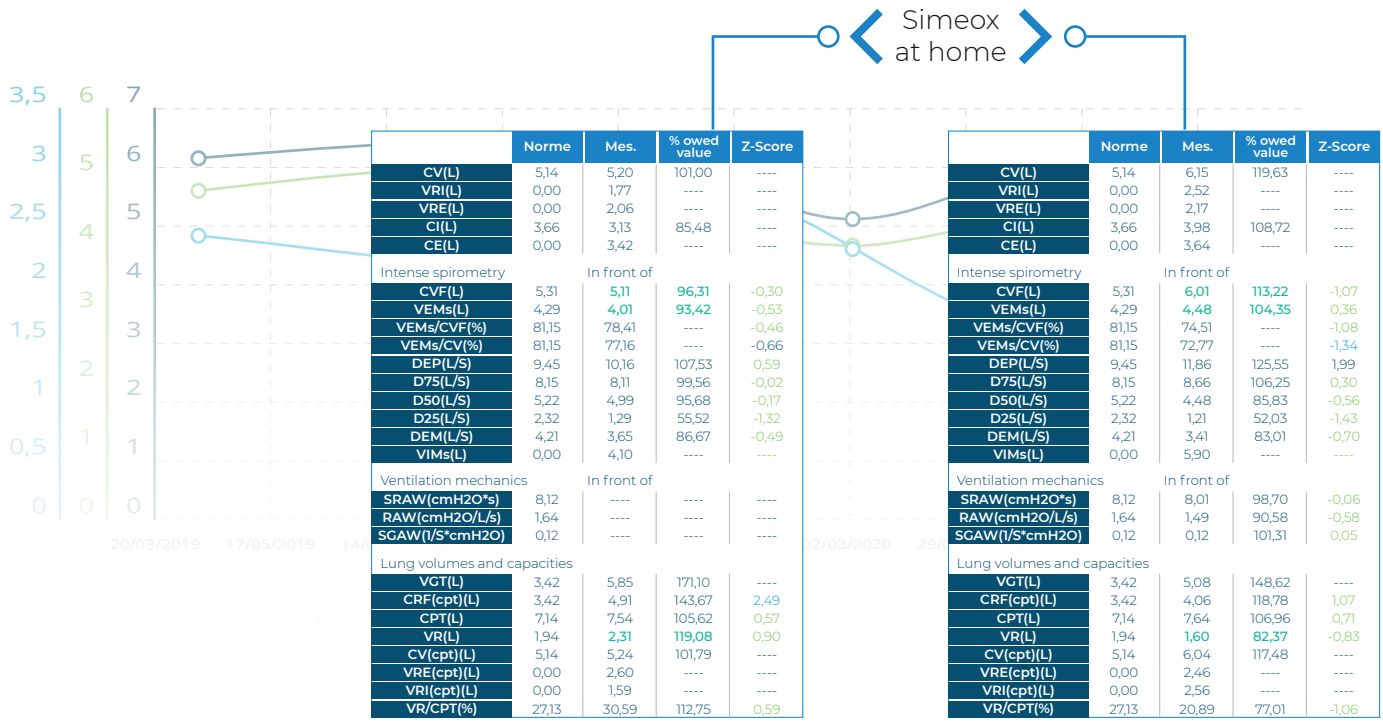


Fig. 8. Selected spirometry parameters in a 39-year-old patient prior to and after inclusion of Simeox treatment and after its cessation

Tab. 8. Selected spirometry parameters in a 39-year-old patient presented prior to and after commencement of Simeox treatment



	Norme	Mes.	% owed value	Z-Score
CV(L)	5,14	5,20	101,00	----
VRI(L)	0,00	1,77	----	----
VRE(L)	0,00	2,06	----	----
CI(L)	3,66	3,13	85,48	----
CE(L)	0,00	3,42	----	----
Intense spirometry		In front of		
CVF(L)	5,31	5,11	96,31	-0,30
VEMs(L)	4,29	4,01	93,42	-0,53
VEMs/CVF(%)	81,15	78,41	----	-0,46
VEMs/CV(%)	81,15	77,16	----	-0,66
DEP(L/S)	9,45	10,16	107,53	0,59
D75(L/S)	8,15	8,11	99,56	-0,02
D50(L/S)	5,22	4,99	95,68	-0,17
D25(L/S)	2,32	1,29	55,52	-1,32
DEM(L/S)	4,21	3,65	86,67	-0,49
VIMs(L)	0,00	4,10	----	----
Ventilation mechanics		In front of		
SRAW(cmH2O*s)	8,12	----	----	----
RAW(cmH2O/L/s)	1,64	----	----	----
SGAW(1/S*cmH2O)	0,12	----	----	----
Lung volumes and capacities				
VGT(L)	3,42	5,85	171,10	----
CRF(cpt)(L)	3,42	4,91	143,67	2,49
CPT(L)	7,14	7,54	105,62	0,57
VR(L)	1,94	2,31	119,08	0,90
CV(cpt)(L)	5,14	5,24	101,79	----
VRE(cpt)(L)	0,00	2,60	----	----
VRI(cpt)(L)	0,00	1,59	----	----
VR/CPT(%)	27,13	30,59	112,75	0,59

	Norme	Mes.	% owed value	Z-Score
CV(L)	5,14	6,15	119,63	----
VRI(L)	0,00	2,52	----	----
VRE(L)	0,00	2,17	----	----
CI(L)	3,66	3,98	108,72	----
CE(L)	0,00	3,64	----	----
Intense spirometry		In front of		
CVF(L)	5,31	6,01	113,22	-1,07
VEMs(L)	4,29	4,48	104,35	0,36
VEMs/CVF(%)	81,15	74,51	----	-1,08
VEMs/CV(%)	81,15	72,77	----	-1,34
DEP(L/S)	9,45	11,86	125,55	1,99
D75(L/S)	8,15	8,66	106,25	0,30
D50(L/S)	5,22	4,48	85,83	-0,56
D25(L/S)	2,32	1,21	52,03	-1,43
DEM(L/S)	4,21	3,41	83,01	-0,70
VIMs(L)	0,00	5,90	----	----
Ventilation mechanics		In front of		
SRAW(cmH2O*s)	8,12	8,01	98,70	-0,06
RAW(cmH2O/L/s)	1,64	1,49	90,58	-0,58
SGAW(1/S*cmH2O)	0,12	0,12	101,31	0,05
Lung volumes and capacities				
VGT(L)	3,42	5,08	148,62	----
CRF(cpt)(L)	3,42	4,06	118,78	1,07
CPT(L)	7,14	7,64	106,96	0,71
VR(L)	1,94	1,60	82,37	-0,83
CV(cpt)(L)	5,14	6,04	117,48	----
VRE(cpt)(L)	0,00	2,46	----	----
VRI(cpt)(L)	0,00	2,56	----	----
VR/CPT(%)	27,13	20,89	77,01	-1,06

Dr Justyna Milczewska and Natalia Jeneralska, M.Sc.

Dr Justyna Milczewska and Natalia Jeneralska, M.Sc. presented a case of a 16-year-old male patient with cystic fibrosis, genotype 2143delT/delPr-3, and with mild bronchopulmonary disease (FEV1 105-116%).

In March 2018, the patient was subjected to eradication of the first-time infection of the respiratory tract with Burkholderia gladioli. He has been found to have a periodic infection of the respiratory tract Pseudomonas aeruginosa (the last positive smear test result in 08.2019). Moreover, the patient suffers from a chronic inflammation and polyposis of the paranasal sinuses (in 2017 and 2019 he underwent endoscopic surgeries of the sinuses), hepatic steatosis and a bicuspid aortic valve. In March 2019, he was diagnosed with diabetes related to cystic fibrosis (CFRD).

In January of 2020, the patient's condition was stable, without symptoms of exacerbation of the bronchopulmonary disease, in spirometry: FEV1 116% of the predicted value, FVC 114% of the predicted value, MEF25 119% of the predicted value. The next routine visit was planned 3 months later - in April 2020, however, the parents of the patient cancelled it due to the pandemic. Until July 2020, they failed to visit the Cystic Fibrosis Treatment Center or to ask for another visit to be arranged. Moreover, at the time, the boy displayed significant behavioral problems - due to teenage rebellion phase, cooperation deteriorated greatly, and the patient almost completely ceased to perform any inhalation-drainage procedures. The cause of urgent hospitalization in July 2020 was severe exacerbation of the bronchopulmonary disease (without effect of outpatient treatment with oral ciprofloxacin).

Upon admission, the patient's overall condition was moderate, with periodical wheezing, intensive wet cough, tachypnea, tachycardia, saturation drops to 88-90%. On auscultation, multiple rhonchi and wheezing were observed above the lung fields, and in laboratory tests - elevated inflammation indicators, while the radiology of the chest revealed a visibly thickened parenchymal opacity in the lower and middle field of the right lung, hyperinflation of the left lung along the perimeter, thickening of the bronchial walls in the lower and medial fields of both lungs. Moreover, there was a substantial deterioration in the spirometry parameters: FEV1 75% of the predicted value (reduction by 41% of the predicted value), FVC 74% of the predicted value (reduction by 40% of the predicted value), MEF25 71% of the predicted value (reduction by 48% of the predicted value).

Treatment included:

- cefepime, amikacin IV
- salbutamol was replaced with formoterol
- additional second inhalation with Dornase alfa after the morning drainage
- passive oxygen therapy 1-2 l/min for the first 3 days of hospitalization
- as massive growth of Aspergillus fumigatus was observed in the culture of the sputum smear, itraconazole was introduced p.o., combined with amphotericin B administered by inhalation
- Simeox in the second part of the stay (previously the device was not accessible in the ward)

The results obtained:

- improvement in the overall condition, stabilization of life parameters, reduction of cough
- withdrawal of auscultatory changes
- regression of lesions in the radiology of the chest
- slight improvement/ deterioration of spirometry parameters FEV 81% of the predicted value, FVC 98% of the predicted value, MEF25 55% of the predicted value.

Continuation of physiotherapy with Simeox was recommended under home conditions 2 x daily. During the two subsequent visits to the Cystic Fibrosis Treatment Center, the patient was in a good overall condition, without exacerbation symptoms, and he reported complete withdrawal of everyday cough. Very significantly, the patient's motivation to perform chest physiotherapy increased substantially. He liked to work with the device very much; he believes that thanks to drainage of the respiratory tract with Simeox, his lung capacity and overall physical condition has improved very much. Thanks to these positive treatment results, he is very eager to perform physiotherapy sessions, more importantly, on a regular basis. A spectacular improvement has also been observed in the lung test function: increase in the spirometry parameters and decrease in the LCI value (fig. 1, 2).

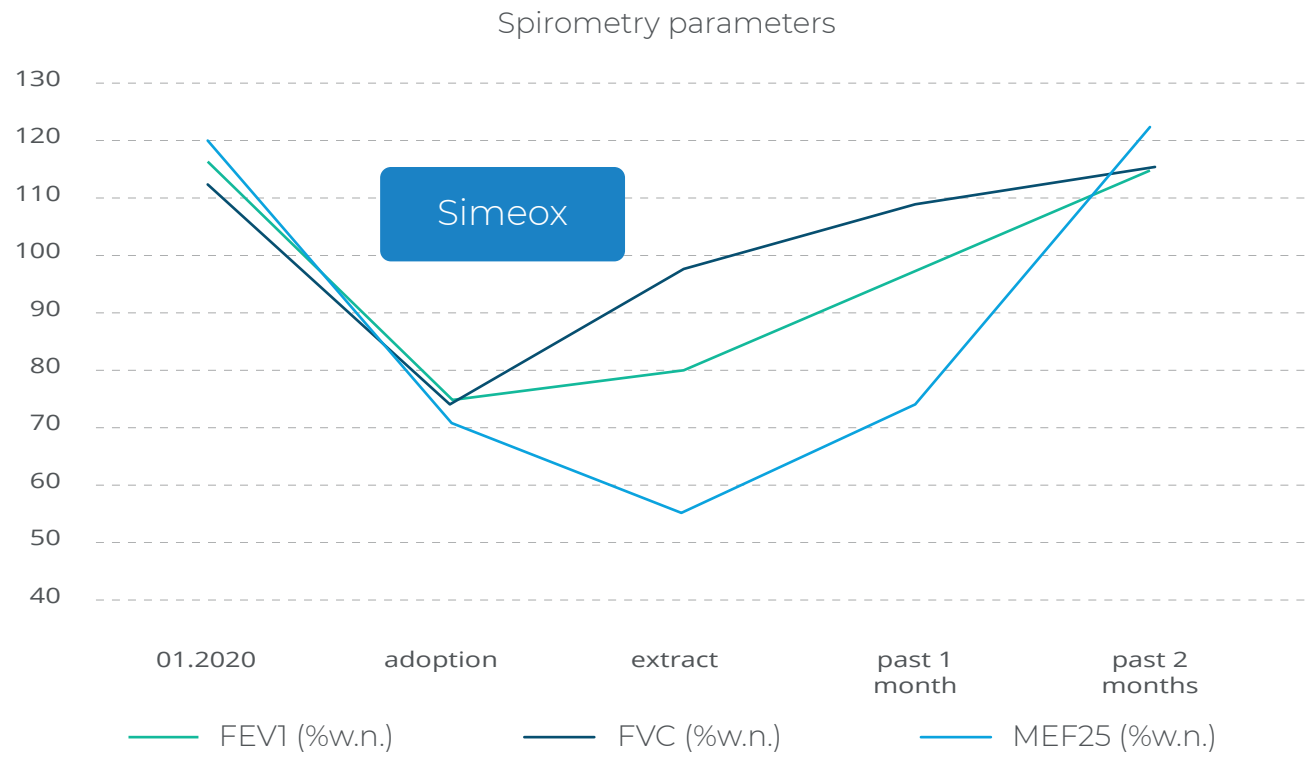


Fig. 1. Values of selected spirometry parameters discussed for the patient.

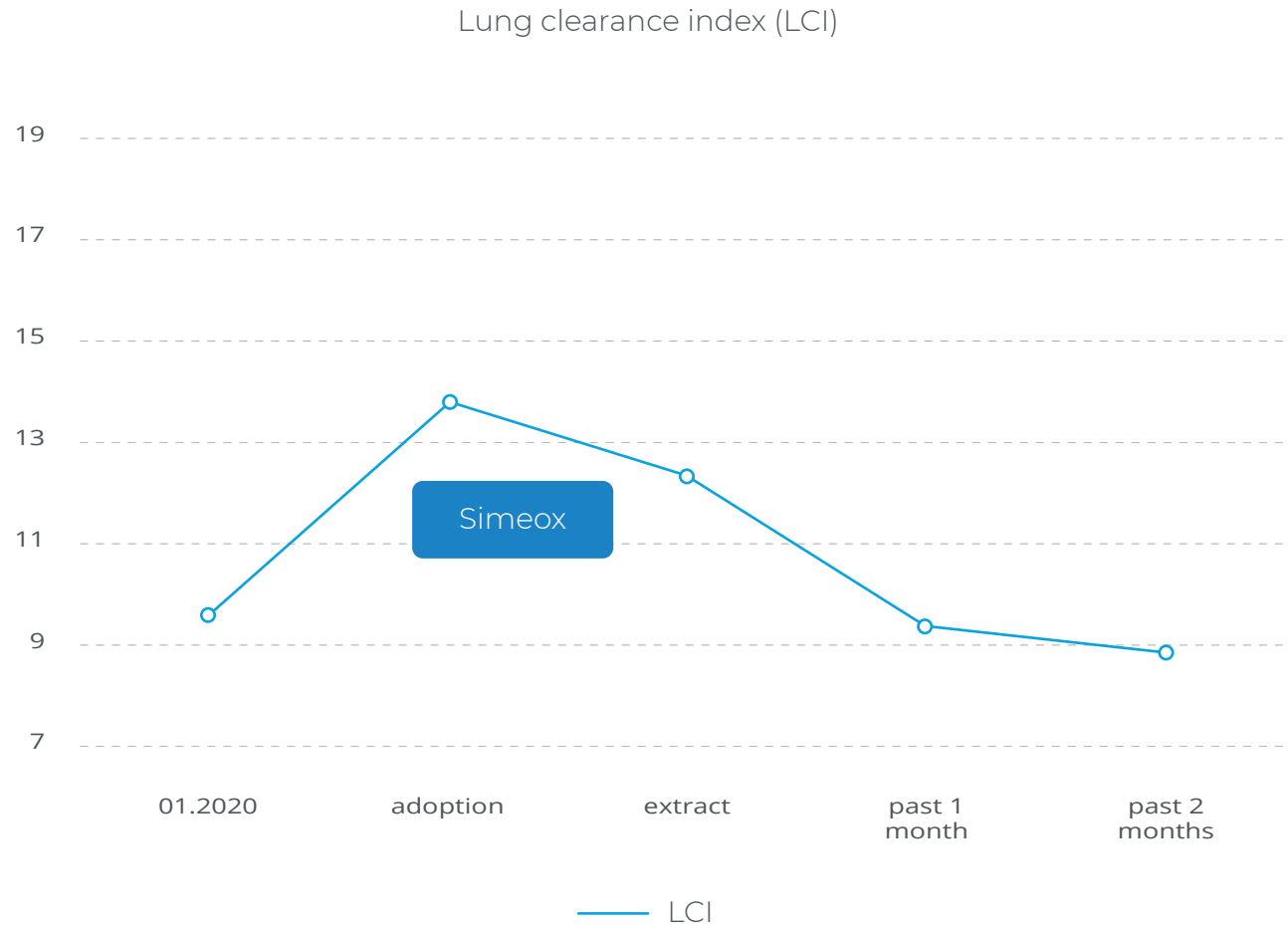


Fig. 2. Values of the lung clearance index in the patient under discussion.

The presentation was summarized as follows:

- better effects of physiotherapy using Simeox in terms of mobilization, liquefaction and evacuation of secretion in comparison with other methods
- independent performance of drainage by the patient without assistance of a physiotherapist, which is particularly important under the conditions of COVID-19
- shortened drainage time in some patients
- patients tired with many years of use of earlier drainage methods are willing to try out innovative methods of respiratory tract clearing, and the possibility of chronic use of Simeox at home increases motivation for systematic work

Dr Jörg Grosse-Onnebrink and Christina Krämer

Dr Jörg Grosse-Onnebrink and Christina Krämer presented their experience in respiratory tract drainage using Simeox in patients with cystic fibrosis.

Since 2018, more than 50 patients performed drainage using the device at their clinic, while 21 of these patients used Simeox at home. There are 2 devices available in the hospital ward. A training for use of the device takes 1 to 3 physiotherapy sessions. A prerequisite for recommending physiotherapy with Simeox is good cooperation with the patient and readiness to use the device at least 3-5 x per week (assuming it is complementary to conventional physiotherapy). The results of a short study of 2019 were presented, comparing efficacy of physiotherapy using a drainage vest (The Vest) with Simeox. Results:

- 9 out of 10 patients preferred Simeox to the drainage vest
- 86% patients would recommend Simeox to other patients

Simeox therapy is refunded in Germany. It is necessary to get a pulmonologist's prescription. In some cases, the insurer requires additional clarifications. The German team underlined very good cooperation with the device manufacturer.

Next was a presentation of a clinical case of a 17-year-old female patient with cystic fibrosis (genotype F508del/F508del), at a very advanced stage of the bronchopulmonary disease.

It is a well-cooperating, intelligent patient. Since 2009, she has been diagnosed with chronic infection of the respiratory tract with Pseudomonas aeruginosa (she requires IV antibiotic therapy on a regular basis), and in 2018 she was treated due to infection with Mycobacterium abscessus. She has a nutritional gastrostomy (PEG tube) and a PortaCath.

Since 2017, her FEV1 has remained below 40% of the predicted value, and in 2019, it was 32% of the predicted value. In imaging examinations, the patient had very severe lesions typical for the primary disease (bronchiectasis, air traps), as well as for pulmonary mycobacteria (many small-nodule-type lesions).

In 2019, the patient commenced Simeox therapy at home 2 x daily. During the COVID-19 pandemic, visits at the physiotherapist, formerly taking place once a week, became impossible. At the time, she benefited most from home Simeox therapy. It has been underlined that in the case of this patient (as well as others), proper training and customization of parameters of the device allows them to obtain maximum benefits from use of the device. The patient adjusts the device power (from 100% to 25%) to evacuate secretion from the small bronchi.

During her therapy with Simeox, the patient's FEV1 increased from 32% to 37% of the predicted value in several months. Thanks to use of the device, she started to cough up sputum retained in the bronchial system, which had been a problem to her. Afterwards, in 2020, her treatment was extended to include a combination of ivacaftor/tezacafto/relexacaftor (CFTR protein modulators), after which FEV1 increased further by more than ten percent of the predicted value. Physiotherapy using Simeox was continued by the patient (2 x daily). The patient has reported that since commencement of CFTR protein modulator treatment, the bronchial secretion has been diluted, however, it is still present and Simeox does much to facilitate its evacuation.

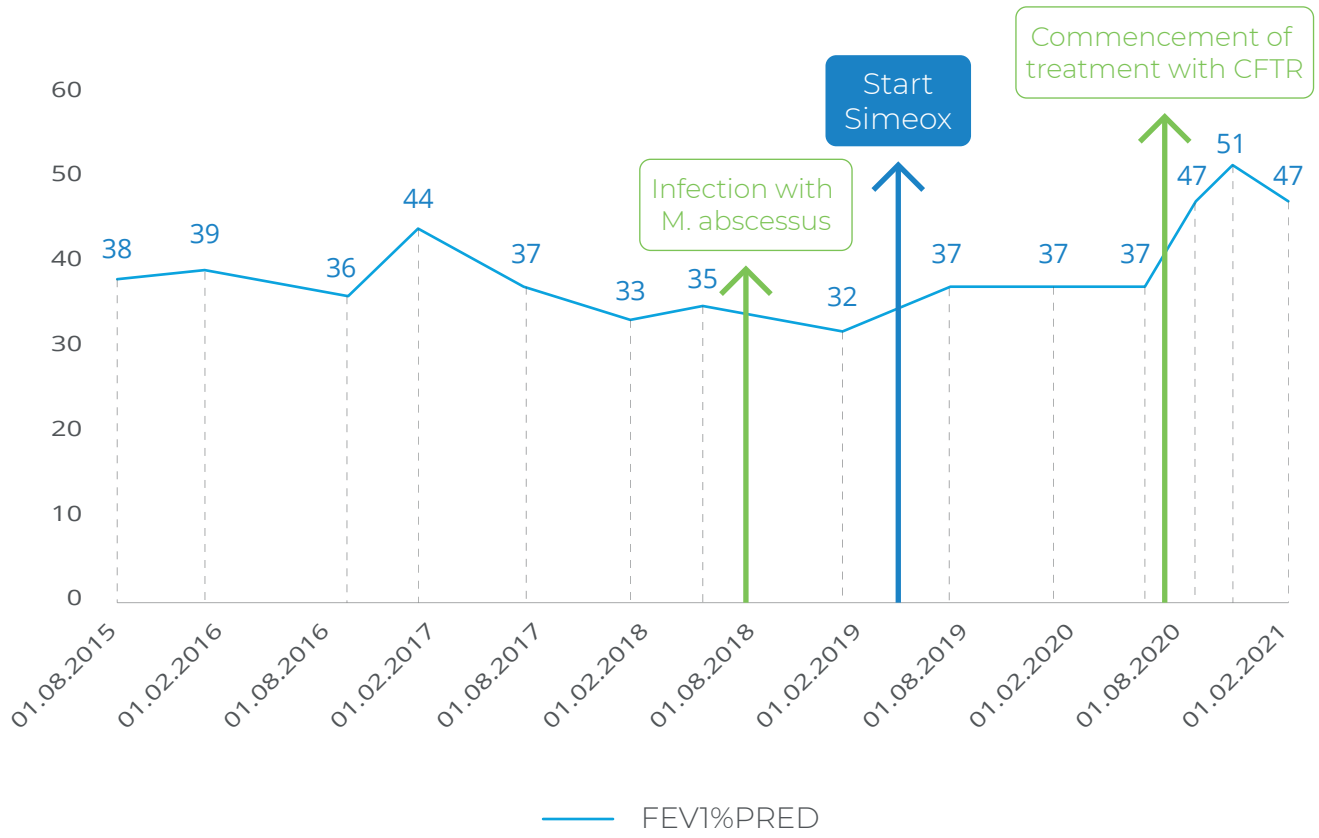


Fig. 11. Change in the percentage of due FEV1 over 5 years in a 17-year-old patient presented by a German team.

Experiences of another German cystic fibrosis center in Essen have also been presented: prior to start of CFTR protein modulator treatment, thanks to Simeox device, the quantity of thick bronchial secretion, difficult to evacuate, was drained; after inclusion of ivacaftor/tezacaftor/elexacaftor, and when Simeox is not used, patients cough up very small quantities of secretion; however, after inclusion of Simeox, they start to cough up moderate quantities of much more liquefied sputum, which proves it is present in the bronchial system, but very difficult to evacuate. It was therefore concluded that a combination of physiotherapy using Simeox with treatment using CFTR protein modulators provides optimum therapeutic effects.

After the three presentations of the third meeting, there was an extensive discussion, which included the following topics:

- underlining of the positive effect of chest physiotherapy on lung capacity of patients with cystic fibrosis, related to general physical condition of the patient, indicating at the same time that the benefits were bidirectional, as high level of physical activity is a form of drainage of the respiratory tract, which exerts a very positive impact on the condition of these patients

- asked how the treating team convinced patients to use the device: the team of the CF center in Dziekanów Leśny replied that a great majority of patients took the initiative to ask about the possibility of using the device during their hospitalization, after which some of them decided to use it long-term under home conditions; some patients are proposed to try the device and get familiar with it; patients, who are tired with the previously used drainage techniques (especially teenagers in the rebellion period), who experience a deterioration in cooperation with physiotherapists, are often very eager to try Simeox, which is something new for them - a modern, interesting and also effective device

- it was underlined that in the era of the COVID-19 pandemic, many clinical trials had to be discontinued due to the necessity to isolate patients; luckily, in the case of studies concerning home care (including Simeox physiotherapy in home conditions), the pandemic did not have such great effect, as most interventions take place at home; experiences on remote training of operation of Simeox were described; a remote training will never replace the physiotherapist being with the patient, however, remote training and supervision of physiotherapy is possible and successful in an increasing number of patients, especially under the conditions of the COVID19 pandemic; in many cases, the training is commenced at the cystic fibrosis treatment center and then it is continued and supervised remotely

- experiences in use of CFTR protein modulators were described (triple therapy) in combination with Simeox: dr Grosse-Onnebrink presented the view that the greatest benefits of use of these medications were experienced by those patients, who have undergone very small permanent lesions in their respiratory tract, in whom the bronchial walls have remained intact or undergone lesions to a very small extent; in these patients, CFTR protein modulator treatment results in normalization of physical properties of the bronchial secretion, which becomes very easy to cough up spontaneously; however, in patients with aggravated lesions of the bronchial walls (bronchiectasis, weakening of the walls) and chronic infections of the respiratory tract with pathogenic bacteria (such as Pseudomonas aeruginosa), even secretions with physical properties that are normal can be difficult to remove (this applies, in particular, to the most distal parts of the bronchial system), and in these patients, inclusion of physiotherapy using the Simeox device (intermittent negative pressure in the respiratory tract) produces optimum effects: the team from the CF center in Dziekanów Leśny shared its experience related to a patient, in whom the combination of Simeox and the triple therapy improved FEV1 by 40%

- the next topic discussed was the very significant and difficult problem of motivating patients (with the disease requiring chronic time- and energy-consuming treatment for the rest of their life) to properly follow recommendations of the treatment team and the modes of verification of whether these recommendations are followed.

The treatment team from Dziekanów Leśny stated that none of the patients performed 100% of the recommendations; however, on the basis of experience of physicians and physiotherapists in managing patients with cystic fibrosis, they could state, on the basis of progressing of the primary disease, as well as observations of the way of performance of chest physiotherapy by the patient, whether they followed the recommendations in almost 100% or only to a small extent.

Dr Grosse-Onnebrink said that the team usually did not ask the patients directly whether they followed all recommendations, but e.g. asked: “was the physiotherapy equipment working properly?”, “did the patient encounter any problems?”, or “how many times during the week did the patient manage to perform chest physiotherapy accurately and properly?” - thanks to this, the patients feel less pressured, and it is more probable that they will answer the questions asked honestly; patients who benefit from use of Simeox in terms of their improved wellbeing, better physical capacity, lesser number of exacerbations etc. follow the recommendations, and they often perform drainage using the device even more frequently than recommended. It should also be noted that in the case of patients with cystic fibrosis, the problem of compliance with the recommendations emerges due to the fact that effects of inhalation and drainage treatment in this disease are rarely immediate - usually, they emerge in the perspective of weeks or months, which does much to weaken the motivation to follow the recommendations. In the case of Simeox therapy, the effects are often visible and felt by patients after the first drainage sessions, which may have a very positive effect on their cooperation, motivating them to perform chest physiotherapy on a regular basis

- another question addressed to the team of Dziekanów Leśny concerned use of N2MBW in monitoring of long-term effects of Simeox therapy using the LCI indicator; dr J. Milczewska answered that a study on efficacy of Simeox in chronic treatment under home conditions had been completed several weeks earlier, and the results were being prepared; the team was looking forward to obtaining these (they were presented during the 44th Conference of the European Society of Cystic Fibrosis on 10.06.2021 by Professor Dorota Sands), in their opinion being a very useful and sensitive indicator for long-term monitoring of the lung function, especially in patients with spirometry parameters within the limits. The N2MBW test is easier to perform in the case of small children, as it requires no special breathing maneuvers (like in the case of spirometry), other than regular, quiet breathing and remaining in a sitting position

Conclusions based on the third meeting

- A training in use of Simeox to allow the patient to use it at home is short, which is perceived by patients as a great advantage.
- Bronchial drainage using Simeox is very effective, especially in the peripheral parts.
- This kind of physiotherapy is recommended in patients with cystic fibrosis, receiving causal treatment, as in their case, combination of physiotherapy using Simeox with CFTR protein modulators produces optimum therapeutic results.
- Simeox can be successfully used to optimize management of home-based patient care, especially during the COVID-19 pandemic.
- The observable short-term benefits of use of Simeox at the cystic fibrosis center leads to a positive impact on compliance with the recommendations at home, as they motivate patients to continue regular work with the device.
- Regular supervision of patients under home care, performing chest physiotherapy with Simeox, is recommended (optimally once a month) via phone calls or other remote communication tools.
- Efficacy of home-based Simeox therapy can be monitored over time using a nitrogen multiple breath washout (N2MBW) test (including a lung clearance index assessment), especially in children.

List of abbreviations used

- FEV1 – forced expiratory volume in 1 second
- FVC – forced vital capacity
- FEV1/VC – forced expiratory volume in one second / vital capacity ratio
- MEF25 – maximal expiratory flow at 25% of FVC
- MEF50 – maximal expiratory flow at 50% of FVC
- MEF75 – maximal expiratory flow at 75% of FVC
- IC – inspiratory capacity
- TV – tidal volume
- ERV – Expiratory reserve volume
- IRV – inspiratory reserve volume
- N2MBW – nitrogen multiple breath washout
- LCI - lung clearance index
- RV/TLC – residual volume expressed as percent of TLC
- FRC – Functional residual capacity
- CFQ-R - the Cystic Fibrosis Questionnaire-Revised

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CNB04_EN01_0721

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