A pilot-scale observational study of self-monitoring of symptoms and spirometry via the patientMpower platform in patients with idiopathic pulmonary fibrosis.

IPF patientMpower 02

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NCT 03104322

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PROTOCOL SUMMARY

PRODUCT	patientMpower platform
CLINICALTRIALS.GOV IDENTIFIER	NCT 03104322
PROTOCOL TITLE	A pilot-scale observational study of self-monitoring of symptoms and spirometry via the patientMpower platform in patients with idiopathic pulmonary fibrosis
CO-ORDINATING INVESTIGATOR	Prof. Anthony O'Regan, Galway University Hospital
NUMBER OF TRIAL SITES	One
CLINICAL PHASE	Not applicable
STUDY OBJECTIVES	Determine the • acceptability of the patientMpower platform from patient and healthcare professional perspective • the impact of active engagement and self-monitoring using patientMpower on Patient Reported Outcome Measures (PROMs) in IPF • impact of patientMpower platform on medication compliance. • correlation between patient-reported measures (PROM, spirometry) and clinical measures and outcomes
METHODOLOGY	Single-centre, prospective, open-label, usual care controlled, open, fixed-order, two-period crossover observational study
NUMBER OF SUBJECTS	Total randomised: 8 Each treatment patientMpower platform followed by usual care observation: 8
DIAGNOSIS	Confirmed diagnosis of IPF
MAIN CRITERIA FOR INCLUSION	Age ≥40 years, daily access to smartphone or tablet device, written informed consent
TEST PRODUCT	patientMpower platform (via smartphone or tablet device)
COMPARATOR PRODUCT	Usual care
DURATION OF OBSERVATION	Sixteen weeks (two periods of eight weeks)

END OF STUDY DEFINITION	Sixteen weeks
PRIMARY ENDPOINTS	Acceptability of the patientMpower platform from patient and healthcare professional perspective.
SECONDARY ENDPOINTS	Impact of active engagement and self-monitoring using the patientMpower platform on PROMs in IPF Impact of using the patientMpower platform on exercise performance (e.g. walking distance) Effect of the patientMpower platform on medication compliance Correlation between patient-reported measures (PROMs, spirometry) and clinical measures and outcomes
INTERIM ANALYSIS	None planned
STATISTICAL METHODS	Descriptive statistics tables will be prepared

FLOW CHART

	Baseline (clinic visit)	Daily (patient -reported)	2 days (telephone call)	14 days (telephone call)	8 weeks (clinic visit)	End of study 12-16 weeks (clinic visit)
	Period 1: patientMpower platform (~8 weeks) + Period 2: usual care (~8 weeks)					
	Period 1				Period 2	
Informed consent and randomisation	X					
Spirometry, dyspnoea[1], 6-minute walk distance	X				X	X
Demographic data (include IPF & medicines history)	X					
Instruction on patientMpower platform, home spirometry and start using platform	X					
Patient training & encouragement	X		X	X		
[2]Record compliance/changes (IPF medicine)	X	X	X	X	X	X
[2]Patient-measured FVC	X	X	X	X	X	
Record impact of IPF (PROM)[3]	X	X	X	X	X	X
[4]Patient-reported outcomes (e.g. oxygen consumption, dyspnoea, pulse oximetry, cough, vital signs)		X				
Stop use of patientMpower platform					X	
Utility & acceptability of platform[5]					X	
Clinic-reported outcomes (e.g. exacerbations)						X
End of study						X

[1] Modified Borg scale used to assess dyspnoea in clinic.
[2] Reported by patient on patientMpower platform every day during Period 1 (up to 8 weeks). Assessed by clinic at end of Period 1 and Period 2.
[3] Impact of IPF on daily life (patient reported outcome measure) to be assessed at clinic at baseline, at the end of Period 1 and and at the end of Period 2 (i.e. end of study) and recorded on the patientMpower platform. Impact of IPF on daily life (patient reported outcome measure) to be reported by the patients on patientMpower platform at start of Period 1 and then every week during Period 1.
[4] Reported by patient as often as possible, ideally each day
[5]Patient and healthcare professional perspective. If patient is withdrawn prematurely, try to capture patient perspective of utility and acceptability of platform at time of withdrawal.

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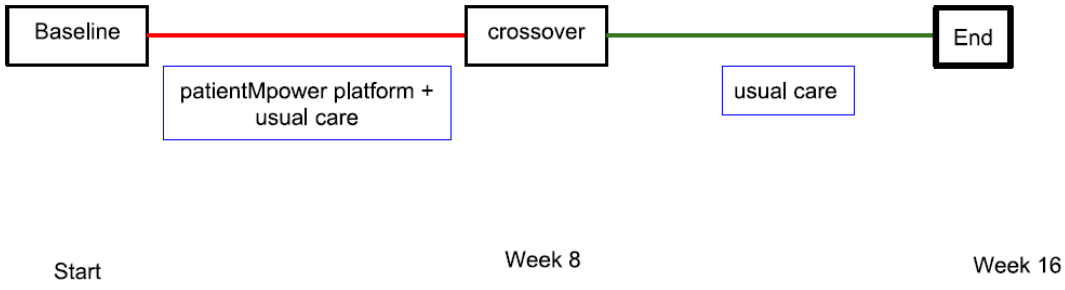


List of Abbreviations

ATS	American Thoracic Society
DLCO	Diffusing Capacity of the Lung for Carbon Monoxide
ERS	European Respiratory Society
FEV_1	Forced Expiratory Volume in 1 second
FVC	Forced Vital Capacity
IP	Internet Protocol
IPF	Idiopathic pulmonary fibrosis
JRS	Japanese Respiratory Society
K-BILD	King's Brief Interstitial Lung Disease Questionnaire
mMRC	modified Medical Research Council
PEF	Peak Expiratory Flow
PROM	patient reported outcome measure
SSH	Secure Shell
SSL	Secure Sockets Layer
TLS	Transport Layer Security

1. Introduction

1.1 Medical background

Idiopathic pulmonary fibrosis (IPF) is an irreversible lung disease leading to progressive dyspnoea and a deterioration of pulmonary function reflected by a progressive decline of forced vital capacity (FVC) and diffusing capacity of the lung for carbon monoxide (DLCO). Progression of the disease results in a serious limitation of physical activities and has a major impact on the patient's quality of life [1].

Digital medicine platforms which directly record patient experiences (e.g. symptoms, impact on daily life, medication compliance) and measurements (e.g. blood pressure, blood sugar levels) have been developed for chronic medical conditions and may be valuable in helping the patients to manage their condition. To date, no digital platform has been specifically developed for patients with IPF.

At the time of writing, there are few simple disease-specific instruments to assess health-related quality of life in patients with IPF. A modified version of the St. George's Respiratory Questionnaire has been developed for IPF [2]. Another group has developed and tested the King's Brief Interstitial Lung Disease Questionnaire (K-BILD) in an interstitial lung disease population [3,4]. The Brompton Hospital, London has recently developed a patient reported outcome measure (PROM) specifically to capture the impact of IPF on the patients' daily life and this is currently being evaluated [5]. This PROM can be used on a very regular basis (e.g. every week) and could provide information on longitudinal trends on the impact of IPF on daily life. It is possible that patient-reported information may be more useful than clinic-reported assessments in characterizing the impact of IPF on quality of life.

1.2 Product profile

The patientMpower platform is a digital medicine platform which has been developed for and is used in providing support to patients with breast cancer, prostate cancer and post-renal transplant. The platform is downloaded as an app to a mobile phone or tablet device and patients can record various parameters (e.g. blood pressure, symptoms, medication compliance, impact of their medical condition on daily life) on a regular basis (sometimes daily). The patient has a permanent health diary of their self-reported measurements available to them on their mobile device. The platform includes a health journal which allows patients to record symptoms at the time they occur. This is helpful for the patient in monitoring their health and in preparing them for appointments with their healthcare professionals, particularly if there is a long interval between clinic visits. If appropriate, certain clinic-derived measurements (e.g. therapeutic drug levels, spirometry data) can be shared with the patient via the platform.

A version of the patientMpower platform has been developed for renal transplant recipients and this is now offered as standard care at the national renal transplantation centre in Ireland. It has been positively received by patients and healthcare professionals and studies of its use are ongoing. However, it is important to recognise that patient demographic factors vary by medical condition and this can have an impact on the utility and acceptability of digital health platforms in the patient user group.

This version of the patientMpower platform has specifically been developed to capture parameters which are relevant for patients with IPF. Examples of measures which can be recorded by the patient include dyspnoea [modified Medical Research Council (mMRC) Dyspnoea Scale], activity (steps/day), vital signs, temperature, oxygen use, type of activity linked to maximum dyspnoea, medication compliance and cough. In addition, patients can report measures linked to the recently developed PROM specifically developed to capture the impact of IPF on patients' daily life [5].

A recent study in patients with IPF has suggested that daily home monitoring of FVC by patients is clinically informative and daily FVC may be of value as a primary endpoint in short proof-of-concept studies [6]. The patientMpower platform can link to home spirometry devices to allow longitudinal collection and upload of long-term patient-measured FVC data to the platform. The Spirobank Smart spirometer (Medical International Research, Via del Maggiolino 125, 00155 Roma, Italy. www.spirometry.com) is one example of a home spirometer which can collect and wirelessly upload FVC and other spirometry data to the patientMpower platform.

This study will capture longitudinal data on home measurement (by the patient) of FVC and patient-reported outcomes within the same cohort of patients. This will enable assessment of the degree of correlation between the two types of measurement.

2. Rationale, objectives and benefit-risk assessment

2.1 Rationale for performing the trial

There are few data on longitudinal trends in patient reported outcomes and patient-measured FVC in IPF. It is possible that these data may be predictive of important health outcomes (e.g. exacerbations). The patientMpower platform provides a tool to collect and share this type of information between patients and their healthcare professionals.

In addition, as no specific digital patient support platform for patients with IPF is available and validated, there is sufficient justification in testing the effectiveness and acceptability of the patientMpower platform in a controlled observational setting.

2.2 Trial objectives

The objectives of this observational study of patientMpower in IPF are:

- Acceptability of the patientMpower platform from patient and healthcare professional perspective
- Impact of active engagement and self-monitoring using patientMpower on PROMs in IPF.
- Impact of patientMpower platform on medication compliance.
- Correlation between patient-reported measures (PROMs, spirometry) and clinical measures and outcomes.

2.3 Benefit-risk assessment

The patientMpower platform has been evaluated in other clinical settings (e.g. prostate cancer, post renal transplant). The renal transplant version of the patientMpower platform is now offered as standard care at the national renal transplantation centre in Ireland. It has been positively received by patients and healthcare professionals and studies of its use are ongoing.

It is not expected that the study or patientMpower platform will create any additional risks for IPF patients.

3. Description of design and trial population

3.1 Overall design and plan

This is an open-label, prospective, usual care controlled, open, fixed-order two-period crossover observational study of a population of IPF patients. Patients who enter the study will be trained in correct use of the patientMpower platform and the Spirobank Smart home spirometer and encouraged to use them on a daily basis. The study will not make any other changes to the therapeutic interventions offered to the patients.

3.1.1 Administrative structure of trial

This is a single centre study at a tertiary centre in Ireland with expertise in the treatment of IPF.

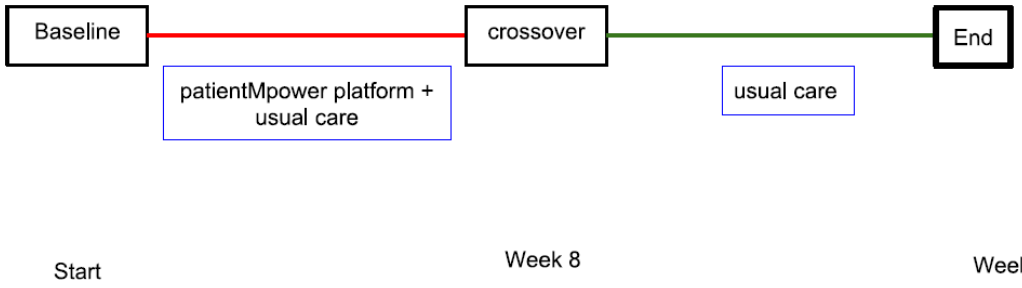
The study is sponsored by an unrestricted research grant from the Quality Innovation Corridor Digital Programme of eHealth Ireland. The patientMpower platform was developed and is owned by patientMpower, Dublin 8, Ireland. The Spirobank Smart home spirometer was developed by Medical International Research, Via del Maggiolino 125, 00155 Roma, Italy. The protocol was designed by patientMpower Ltd. and Prof. Anthony O'Regan, Galway University Hospital, the principal investigator.

3.2 Discussion of trial design, including choice of control group

This is an open-label, prospective, usual care controlled, open, fixed-order two-period crossover observational study of a population of IPF patients.

The treatment sequence is period 1: patientMpower platform and usual care followed by period 2: usual care alone. The design is illustrated in Figure 3.2: 1 below:

Figure 3.2: 1 Diagram of study design



The control treatment is usual care alone. The active treatment is patientMpower platform and usual care.

This design allows comparison of the effect of the patientMpower platform with usual care within the same patient.

Each treatment period is eight weeks. The total observation time is approximately sixteen weeks (i.e. two treatment periods of eight weeks). In routine practice, patients with IPF are seen at the clinic at intervals of approximately sixteen weeks (similar to the duration of the study).

It is not anticipated that there are any carryover effects ofthe patientMpower platform so there is no washout between treatment periods 1 and 2.

Patients enrolled in the study will capture information on relevant health outcomes related to IPF on a regular basis (daily for some parameters) using the patientMpower platform. Patients will also measure FVC at home once per day using the Spirobank Smart spirometer (ideally at approximately the same time each day). The patient measured FVC and other spirometry data will be captured automatically by the patientMpower platform. These data will form the patient-reported outcome database.

Clinical assessments (e.g. FVC, 6-minute walking distance, impact of IPF on daily life) in the same cohort of patients will be assessed at the beginning and end of the study.

This design allows comparison of patient-reported data and their longitudinal trends with clinic reported data in a cohort of patients with IPF. The correlation between the two types of data and the value of patient measurements in predicting health outcomes can be assessed and quantified.

This design will also allow evaluation of the utility and acceptability of the patientMpower in patients with IPF. This will be assessed from both the patient and healthcare professional perspectives.

The patientMpower platform will include key questions derived from a PROM developed specifically for patients with IPF [5] and will help to evaluate the utility of an electronic health diary in capturing PROM data in IPF patients.

3.3 Selection of trial population

3.3.1 Main diagnosis for study entry

Idiopathic pulmonary fibrosis

3.3.2 Inclusion criteria

Aged at least 40 years

Confirmed diagnosis of IPF [according to American Thoracic Society (ATS), European Respiratory Society (ERS) or Japanese Respiratory Society (JRS) criteria] [7].

Has daily unrestricted access to a suitable smartphone or tablet device at home.

Demonstrate understanding of the protocol requirements, and correct use of the Spirobank Smart spirometer and the patientMpower platform.

Able and willing to perform spirometry every day at home.

Willing to give written informed consent.

3.3.3 Exclusion criteria

Significant confusion or any concomitant medical condition which would limit the ability of the patient to record symptoms or use a home spirometer on a regular basis.

New prescription of antifibrotic therapy for IPF (e.g. pirfenidone, nintedanib) within the four weeks before the baseline visit.

Recent exacerbation of IPF or other clinically significant change in the patient's medical condition in the four weeks before the baseline visit.

3.3.4 Removal of patients from study or assessments

3.3.4.1 Removal of individual patients

Patients are free to withdraw from the study at any time without any impact on their ongoing medical care.

The investigator may withdraw a patient from the study at any time if they believe that further participation in the study is not in the best interests of the patient.

3.3.4.2 Discontinuation of the study by the sponsor.

The study sponsor may terminate the study early if recruitment is significantly behind schedule or if for any other reason, it is unlikely that the study can be completed.

4. Treatments

All patients will continue to receive all usual care throughout the study as prescribed by their healthcare professionals.

4.1 Study intervention

4.1.1 Identity of study intervention

The study intervention is a digital medicine platform, patientMpower. This version has been developed specifically for patients with IPF. The platform is an electronic application downloaded to the patient's mobile phone or tablet device. The application is designed to allow the patient to report various parameters relevant to IPF and record these on a regular basis, ideally daily. The information recorded by the patient will be stored in a secure cloud system and will be available to the patient through their phone or mobile device at all times. No personal health data are stored on the phone or mobile device itself.

Patients will be asked to report measurements on the patientMpower platform each day. Patient-reported measures (at a minimum) will include FVC (one reading once/day), dyspnoea, activity (steps/day), distance walked per day and compliance with IPF medication. In addition, the impact of IPF on daily life (as response to PROM questions) should be reported every week.

Additional patient-reported measures which can be reported on the patientMpower platform include vital signs (e.g. heart rate), temperature, pulse oximetry, cough severity, activity causing worst dyspnoea and oxygen consumption. These are optional measurements and will only be recorded where practical for the patients.

4.1.2 Method of assigning patients to study intervention

All patients who give informed consent will be allocated to the treatment sequence described in section 3.2 above.

Patients will be given training on the correct use of the patientMpower platform and Spirobank Smart home spirometer at the start of the patientMpower platform + usual care period and will be encouraged to use them on a daily basis.

4.1.3 Blinding and procedures for unblinding

The study is open-label.

4.2 Concomitant therapy, restrictions and rescue treatment

4.2.1 Rescue medication, emergency procedures and additional treatment

4.2.1.1 Management of acute exacerbations

Any exacerbations of the patient's IPF or any other underlying medical condition(s) should be treated according to standard procedures.

4.2.1.2 Management of other adverse events

Any other adverse events should be treated according to standard procedures.

4.2.2 Restrictions

4.2.2.1 Restrictions on concomitant treatment

There are no restrictions on concomitant treatment. All concomitant treatments as prescribed by the patient's healthcare professionals are allowed. Patients will continue to take all medicines as prescribed by their healthcare professionals.

4.2.2.2 Restrictions on diet and life-style

There are no restrictions on diet or life-style. Patients will continue to follow all instructions on diet, exercise and lifestyle as directed by their healthcare professionals.

4.3 Treatment compliance

Patients will use the patientMpower platform to record daily compliance with medications prescribed for treatment of their IPF.

5 Variables and their assessment

5.1 Efficacy

The objectives of this observational study of patientMpower in IPF are to determine the:

- Acceptability of the patientMpower platform from patient and healthcare professional perspective.
- Impact of active engagement and self-monitoring using patientMpower on PROMs in IPF.
- Impact of patientMpower platform on medication compliance.
- Correlation between patient-reported measures (PROMs, spirometry) and clinical measures and outcomes.

5.1.1 Efficacy endpoints

5.1.1.1 Primary endpoint

The primary endpoint is the acceptability of the patientMpower platform from patient and healthcare professional perspective.

The primary endpoint variables (from the patient perspective) will be assessed by their response to these questions:

- the instructions given in using the patientMpower platform were clearly understandable (strongly agree/agree/disagree/strongly disagree)
- using the patientMpower platform helped me to take the correct dose of my medicines for lung fibrosis every day (strongly agree/agree/disagree/strongly disagree)
- using the patientMpower platform helped me to take my medicines for lung fibrosis at the correct time every day (strongly agree/agree/disagree/strongly disagree)

- using the patientMpower platform helped me to reach my personal exercise goal every day (strongly agree/agree/disagree/strongly disagree)
- using the patientMpower platform helped me to walk further (or exercise more) compared with before (strongly agree/agree/disagree/strongly disagree)
- using the patientMpower platform gave me more confidence/a greater sense of control in managing my lung health (strongly agree/agree/disagree/strongly disagree)
- I found it useful to be able to record the impact of lung fibrosis on my daily life (strongly agree/agree/disagree/strongly disagree)
- using the patientMpower platform encouraged me to look at the informational videos on the platform (strongly agree/agree/disagree/strongly disagree)
- my preference for using the patientMpower platform versus not using it (yes, no preference, no)
- my difficulty rating in using the patientMpower platform (very easy, easy, difficult, very difficult)
- what was the effect of using the patientMpower platform on the impact of lung fibrosis on my well-being and daily life (positive, negative, optional open text field for participant to give opinion)
- I found it tiring or irritating to use the patientMpower platform (strongly agree/agree/disagree/strongly disagree)
- do I want to continue using the patientMpower platform after the end of the study (yes, no)
- I would recommend other people with my condition to use the patientMpower platform (yes/no)
- what other measurements, reminders or information would be useful to have on the patientMpower platform? (optional open text for patient to give opinion)
- describe the benefits and/or disadvantages of using the patientMpower platform (optional open text for patient to give opinion)
- any other comments on the patientMpower platform (optional open text field for participant to give opinion)

The primary endpoint variable (from the healthcare professional perspective) will be assessed by their response to these questions:

- preference for using the patientMpower platform versus not using it (yes, no preference, no)
- difficulty rating in using the patientMpower platform (very easy, easy, difficult, very difficult)
- did using the patientMpower platform help me to help the patient manage their IPF better? (yes, no)
- did using the patientMpower platform help the patient to take their IPF medicines at the correct dose every day (yes, no)
- do I believe the patient should continue using the patientMpower platform after the end of the study (yes, no)

- what other measurements, reminders or information would be useful to have on the patientMpower platform? (Open text for healthcare professional to give opinion)
- describe the benefits and/or disadvantages of using the patientMpower platform (Open text for healthcare professional to give opinion)

5.1.1.2 Secondary endpoints

The secondary endpoints include

- the impact of active engagement and self-monitoring using the patientMpower platform on PROMs in IPF
- the impact of using the patientMpower platform on exercise performance (e.g. walking distance)
- the effect of the patientMpower platform on medication compliance
- the correlation between patient-reported measures (PROMs, spirometry) and clinical measures and outcomes.

The secondary endpoint variables (reported by patients) are:

- FVC (recorded once per day)
- maximum level of dyspnoea each day (ideally linked to description of activity causing maximum dyspnoea)
- activity (number of steps/day)
- distance walked per day
- compliance with medicines prescribed for treatment of IPF
- addition of any new prescribed medicines for treatment of IPF
- impact of their medical condition on their daily life (once per week; questions to be derived from PROM)

Additional secondary endpoint variables which can be recorded (if measurement devices available to the patient) include:

- duration of walking per day
- number of episodes of walking per day
- cough (worst severity each day)
- heart rate (if patient has access to wearable fitness device)
- blood pressure (if patient has access to measurement device)
- temperature (if patient has access to measurement device)
- body weight (once/week)
- oxygen saturation at rest (if patient has access to pulse oximetry device and wishes to record saturation)
- oxygen consumption (cylinders/month)

Patients can also record symptoms using the health journal entry pages on the patientMpower platform at any time.

Patients will assess dyspnoea with the mMRC scale [8] which may be a useful prognostic indicator in IPF [9].

Clinic-derived measurements (for example):

- FVC
- DLCO (if measured)
- 6-minute walking distance
- Dyspnoea (e.g. modified Borg scale) [10]
- Impact of the patient's medical condition on their daily life (using the same PROM questions as for the patient)

Health outcomes (for example):

- Medication adherence
- Change in IPF medication (dose change or new medicine prescribed)
- Oxygen usage
- Exacerbations of IPF
- Hospitalisations due to IPF

5.1.2 Assessment of efficacy

The primary efficacy endpoint data will be assessed by analysis of changes in the patient-reported FVC and health parameters, clinic-derived parameters and health outcomes over time (described above in 5.1.1.1).

The impact of IPF on daily life (i.e. PROM) at the end of each treatment period will be compared with the start of each treatment period. In addition the end of period PROM will be compared between treatment periods.

The longitudinal trend of patient-measured FVC will be compared with the FVC values observed in the clinic at the beginning and end of each treatment period.

The secondary efficacy endpoints will be assessed by analysis of the responses to the patient and healthcare professional questionnaires (described above in 5.1.1.2).

5.2 Safety

It is not anticipated that any safety issues will arise from use of the patientMpower platform or the Spirobank Smart spirometer.

Any adverse events observed with medical treatments should be reported to the manufacturers of those treatments.

5.2.1 Safety endpoints

None.

5.3. Other variables

Demographic data (date of birth, gender, date of IPF diagnosis, other respiratory conditions, medication prescribed for IPF).

Type of smartphone or tablet device (i.e. iPad or Android tablet, iPhone or Android phone)

Engagement of patients with the patientMpower platform will be assessed by analysis of the numbers of

- patients asked to take part in the study
- patients who give informed consent to take part in the study.
- consented patients who download the platform application to their smartphone or tablet device
- patients who use the platform at least once after downloading
- patients who use the platform more than once
- frequency of use by each patient
- date intervals between informed consent, download, first use
- date intervals between first and subsequent uses
- frequency of recording FVC at home
- frequency of recording other measures at home

5.3.2 Other assessments

Data on the air quality and weather conditions at the patients' geographical locations over the duration of the study will be captured. This may be analysed retrospectively to see if there is any correlation between air quality and impact of IPF on patient quality of life, respiratory measurements or exacerbations.

Data on the ultraviolet index at the patients' geographical locations over the duration of the study will be captured. This may be analysed retrospectively to see if there is any correlation between possible ultraviolet exposure and impact of IPF on patient quality of life or possible side-effects of IPF treatment.

5.4 Appropriateness of measurements

The primary endpoint parameters are measurements which are affected by the patient's IPF and respiratory health.

The questionnaires used to assess usefulness and patient acceptability have been used to assess these parameters for other patient support platforms and have been shown to be robust.

6 Investigational plan

Patients who participate in the study will beallocated to the treatment sequence. Patients will follow their usual care programme throughout the study.

During the patientMpower treatment period, patients will be encouraged to use the patientMpower platform and Spirobank Smart spirometer every day to record parameters relevant to their health status (described in section 5.1.1.2 above).

6.1 Visit schedule

The total observation period will be approximately sixteen (16) weeks.

6.2 Details of trial procedures at selected visits

The trial procedures at each visit are summarized in the flow charts on page 6.

6.2.1 Baseline clinic visit

Patients visiting the IPF clinic for diagnosis or routine care will be offered the opportunity to participate in the study.

The study will be explained to the patient and written informed consent obtained before any study-specific procedures. On receipt of written informed consent, a unique identification number will be assigned to the patient.

The patient will be allocated to the treatment sequence:
period 1: patientMpower platform and usual care followed by period 2: usual care alone.

The patient and the investigator site will know the treatment sequence assigned to the patient.

Demographic data, medical history and concomitant therapy for IPF will be recorded.

The following parameters will be assessed and recorded in the clinic records:

- spirometry (to include FVC)
- DLCO (if measured)
- patient's exercise ability (e.g. 6-minute walking distance or other standard measure)
- dyspnoea (e.g. modified Borg scale)
- impact of IPF on daily life (using the same PROM as in the patientMpower platform)

6.2.2 Treatment and observation period

Period 1: patientMpower platform and usual care
Period 2: usual care alone

At the baseline visit, the patientMpower platform will be downloaded to the patient's mobile phone and they will be trained in correct use of the platform. A tablet device will be supplied to the patient if they do not have access to a suitable smart device at home.

The patient will be instructed in the correct use of the Spirobank Smart home spirometer and uploading of data to the patientMpower platform. The patient's understanding of the patientMpower platform, Spirobank Smart home spirometer and the study procedures should be checked before they leave the clinic.

Patients will be encouraged to record the parameters described in section 5.1.1.1 on a regular basis.

The following should be recorded by the patient each day:

- FVC (one spirometry maneuver each day ideally at approximately the same time each day)
- compliance with medication prescribed for IPF
- any changes to medication taken for IPF
- activity (number of steps per day)
- distance walked per day
- maximum level of dyspnoea

Impact of IPF on daily life (PROM) should be recorded by the patients once per week.

Other parameters should be recorded by the patient (if suitable measurement devices are available to the patient and where practical for the patient) frequently. Examples include duration of walking, number of episodes of walking, cough, heart rate, blood pressure, temperature, body weight, oxygen saturation and oxygen usage (cylinders/month).

Two (2) days after starting period 1, the patient will be contacted by telephone to check the following

- patient understanding of the study
- they have started to record medication compliance, activity, dyspnoea and FVC every day
- patient is recording symptoms and other parameters on a regular basis (ideally daily)

Appropriate advice will be given to the patient if needed.

Fourteen (14) days after starting period 1, the patient will be contacted by telephone to check the following

- patient understanding of the study
- patient is continuing to record medication compliance, activity, dyspnoea and FVC every day
- patient is recording impact of IPF on daily life (PROM) every week
- patient is continuing to record symptoms and other parameters on a regular basis (ideally daily)

Appropriate advice will be given to the patient if needed.

The patient will continue using the patientMpower platform until the clinic visit at eight (8) weeks after starting period 1.

6.2.3 8-week clinic visit

At this visit, the following parameters will be assessed and recorded in the clinic records:

- spirometry (to include FVC)
- patient's exercise ability (e.g. 6-minute walking distance or other standard measure)
- dyspnoea (e.g. modified Borg scale)
- impact of IPF on daily life (using the same PROM as in the patientMpower platform)
- medication adherence
- changes in or addition of any new medicines for the treatment of IPF
- exacerbations of IPF since baseline
- hospitalisations due to IPF since baseline

The patient and healthcare professional opinion on the usefulness and acceptability of the patientMpower platform will be assessed and recorded.

The patient will stop using the patientMpower platform and will crossover to the alternative treatment period (usual care only for a further eight weeks). There will be no further interventions until the End of Study visit (at least sixteen weeks after the baseline visit).

6.2.4 End of Study clinic visit (at least 16 weeks)

The following parameters will be assessed and recorded in the clinic records:

- spirometry (to include FVC)
- DLCO (if measured)
- patient's exercise ability (e.g. 6-minute walking distance or other standard measure)
- dyspnoea (e.g. modified Borg scale)
- impact of IPF on daily life (using the same PROM as in the patientMpower platform)
- medication adherence

- changes in or addition of any new medicines for the treatment of IPF
- exacerbations of IPF since previous visit
- hospitalisations due to IPF since previous visit

7. Statistical methods and determination of sample size

This a pilot study to assess the feasibility of patients with IPF using the patientMpower platform including home-based FVC to monitor their health.

7.1 Statistical design and model

Single-centre, prospective, open-label, usual care controlled, open, fixed-order, two-period crossover observational study

7.2 Null and alternative hypotheses

Not relevant.

7.3 Planned analyses

Results will be collected and summarized for descriptive statistical display.

7.3.1 Primary analyses

The primary efficacy endpoints will be assessed by analysis of the responses to the patient and healthcare professional questionnaires (described above in 5.1.1.1).

7.3.2 Secondary analyses

The secondary efficacy endpoints in the two treatment periods will be compared.

7.3.3 Safety analyses

Not relevant.

7.3.4 Interim analyses

None planned.

7.3.5 Health economic analyses

Health outcomes (e.g. exacerbations of IPF) will be recorded.

7.4 Handling of missing data

No imputations of missing data will be made.

7.5. Randomisation

Not relevant.

7.6 Determination of sample size

This is pilot study. The sample size of 8 subjects has been chosen arbitrarily.

8. Informed consent, data protection and trial records

8.1 Study approval, patient information and informed consent

The study will be approved by the relevant ethics committee(s) for the participating centre.

The study will be discussed with each patient and they will be provided with a written document describing the study conditions and procedures.

All patients will give written informed consent before participation.

8.2 Data quality assurance

All endpoint data will be stored on a central database for analysis. The data as reported by the patients will not be queried before descriptive statistical analysis tables are prepared.

8.3 Records

8.3.1 Source documents

The original electronic data will be the source document.

8.3.2 Direct access to source data and documents

Source data verification will not be performed.

8.3.3 Storage of records

Medical data relating to patient care will be stored in the medical records according to the usual procedures of the investigator site.

The endpoint data collected by the participants and recorded on the patientMpower platform will be stored indefinitely in a secure cloud database managed by patientMpower Ltd. These data will be available to patients indefinitely to aid them in self-management of their medical condition. Participants can request deletion of their data from the patientMpower cloud database at any time.

The information on the patientMpower Ltd database for this study may be analysed again as part of other scientific studies in the future.

8.4 Statement of confidentiality

Participants will only be identified by a unique identification number and data will be anonymised on the trial database. The identity of the participants will be known to patientMpower Ltd. All data will be treated as confidential. Each patient's data will linked to their unique identification number on the trial database.

The patientMpower platform is designed with stringent security protocols. The solution is hosted in Google Compute Engine. The security protocols used include:

- platform uses a PostgreSQL database (https://www.postgresql.org/) which is backed up nightly
- platform is patched regularly to ensure it is maintained against security vulnerabilities
- only certain Internet Protocol (IP) addresses can login to the cloud infrastructure using Secure Shell (SSH) with IP whitelists and public/private key access only
- built-in firewalls
- encrypted data storage
- patientMpower staff access to the PostgreSQL database, and content system is restricted and monitored
- a unique username and password for each user.
- audit and accounting of all access to the system is recorded. In the event of any staff looking at data without proper authorisation, there is an audit trail of what data was viewed
- data transfer between the patient mobile device and cloud server is sent securely via Transport Layer Security (TLS) and the platform's cloud infrastructure uses an Extended Validation Secure Sockets Layer (SSL) Certificate issued by Digicert (https://www.digicert.com)

- data on the server is encrypted, only authenticated users can access the server

8.5 Completion of trial

The trial will be complete when 8 patients have completed the 16-week observation period.

If it appears to be unlikely that the target number of patients can be achieved (e.g. because of slow recruitment) a lower target will be set (after discussion and agreement with investigator sites).

8.6 Protocol violations

All data will be analysed on an intention-to-treat basis without regard to protocol violations.

8.7 Compensation available to the patient in the event of trial-related injury

It is not anticipated that any trial-related injury will occur.

9 References

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10 Appendices

10.1 modified Medical Research Council Dyspnoea Scale

Grade	Description of breathlessness
0	I only get breathless with strenuous exercise
1	I only get short of breath when hurrying on level ground or walking up a sight hill
2	On level ground, I walk slower than people of the same age because of breathlessness or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing

None.

10.2 Instructions for performing spirometry at home

Patients will perform one spirometry reading at home once per day (ideally at 12:00 noon + 1:00 hour).

Each patient will be supplied with a Spirobank Smart home spirometer (Medical International Research, Via del Maggiolino 125, 00155 Roma, Italy. www.spirometry.com). This spirometer will automatically upload Peak Expiratory Flow (PEF), Forced Expiratory Volume in 1 second (FEV_1), FVC and FEV1/FVC data directly to the patientMpower platform.

11 Summary of clinical trial protocol modifications

The protocol was revised to Version 2 on 12th July 2017. The design was changed from a randomized, two-period crossover design to a fixed-order two-period crossover design. This change was made due to operational difficulties in implementing the original design. There were no changes to the patient selection criteria or study measurements.