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The Royal Marsden NHS
NHS Foundation Trust

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PATIENT INFORMATION SHEET AND CONSENT FORM

Full Title

Prospective randomised controlled trial to investigate the effectiveness of inhalers for the relief of breathlessness in patients with lung cancer and COPD

Short Title

Airways Disease-Optimisation of Pharmaco-Therapy in lung cancer (ADOPT)

Dear Patient

You are being invited to take part in a clinical research study. This leaflet gives you some information about the study, why it is being done, what it will involve, and what the potential benefits and risks may be. It is important that you read and understand this information leaflet before you decide whether or not to take part. If you have any questions about this study, you should ask your hospital doctor. You may wish to discuss the study with friends and relatives.

- Part 1 tells you the purpose of this study and what will happen to you if you take part.

- Part 2 gives you more detailed information about the conduct of the study

Please ask us if there is anything that is not clear or if you would like more information.

Thank you for reading this information leaflet

PART 1

What is the purpose of the study?

Breathlessness is a major symptom in patients with lung cancer and specific treatments are limited. There are a number of reasons why patients with lung cancer may be breathless. One reason is that they may have a condition called 'COPD'. COPD stands for **C**hronic **O**bstructive **P**ulmonary **D**isease. This is a term used for a number of conditions; including chronic bronchitis and emphysema. COPD is common in patients with lung cancer.

Patients who have COPD have narrowed airways which makes it hard for them to get air in and out of their lungs. Therefore they may develop breathlessness. Other symptoms of COPD may include cough, wheeze, and increased sputum production.

Patients with COPD may benefit from an inhaler. Inhalers contain medicines which help to make the airways wider and improve breathlessness. There are different types of inhalers which work in different ways and they can be of benefit if they are used together. Ventolin$_{TM}$Evohaler$_{TM}$, Spiriva®, and Seretide® are common inhalers used in patients with COPD.

A large proportion of patients with lung cancer also have COPD. However, the COPD may have not been diagnosed and therefore they will not be receiving appropriate treatment such as inhalers.

We know that treating patients with COPD with inhalers is very effective at improving breathlessness. However, as yet, it is unclear if treating patients with COPD and lung cancer with inhalers is also effective at improving

breathlessness. Therefore we plan to conduct a study to assess if the use of inhalers in patients with COPD and lung cancer improves breathlessness.

Why have I been invited to take part in the study?

You have been invited to take part in the study because the doctors who have been treating you for lung cancer believe that you also have a condition called COPD and may benefit from inhalers to improve your breathlessness. Therefore, if you meet all other study requirements, you may be eligible to join in the research study to test if the use of inhalers in patients with lung cancer and COPD improves breathlessness.

Do I have to take part?

Your participation in this study is entirely voluntary. We will describe the study and go through this information sheet with you. If you agree to take part, you will be given this information sheet and we will then ask you to sign a consent form. By signing the consent form, you agree to take part, but you are free to withdraw at any time without giving a reason. If you decide not to take part or to withdraw from the study, the decision will not affect the level of care that you receive and your doctor will continue to treat you with the best means available.

What will happen to me if I take part and what will I have to do?

The study will run alongside any regular appointments that you have with your medical team. If you decide to take part, any regular appointments, investigations and future treatments planned for you by your doctor will not change.

If you decide to take part then you will be put randomly into 1 of 2 groups. Neither you nor the study doctors will have an influence on which group that you are put in.

Group 1 (Intervention arm), patients in this group will be given inhalers

Similar to participants in Group 2, participants in this group will have their breathlessness managed according to best supportive care (see below). In addition participants in this group will be given 2 inhalers, a Ventolin® inhaler and a Spiriva® inhaler. The 2 inhalations of the Ventolin inhaler is taken 4 times a day and one inhalation of the Spiriva inhaler is taken once a day. Some patients may also be given a 3rd inhaler called Seretide® this will depend on how severe the COPD is thought to be. 1 inhalation of the Seretide inhaler is used twice a day. These inhalers are used widely to improve breathlessness and other symptoms of COPD such as wheeze and cough. You will be shown how to use the inhalers by a doctor, specialist nurse or pharmacist/pharmacy technician. You will receive the first dose of each inhaler in hospital under supervision so that the doctors can ensure that you are able to use the inhalers properly.

The study will last for 4 weeks and you will be required to visit the Royal Marsden Hospital for 3 visits. Each visit will last for approximately 2 hours and some will coincide with your normal routine clinic visit to see your doctor. During your first study visit, you will be provided with the inhalers and will be shown how to use them properly. We will perform a chest X-Ray and an ECG to exclude other causes of breathlessness. In addition we will perform a routine blood test and may ask to take a further sample which will be stored and may be used in future research studies (this however is entirely optional). We will also want you to perform some breathing tests and a walking test. You will also be required to complete 2 questionnaires which will allow us to determine how your breathlessness is affecting your quality of life and your activity levels. We will ask to perform a urine pregnancy test if appropriate as if it is positive, you will not be eligible for this study.

Your second visit will occur 2 weeks after your first visit. On this visit, your doctors will ensure that your breathing has not become any worse since starting the inhalers. You will be required to perform some breathing tests

and a walking test but you will not be required to complete the questionnaires that you completed during your first visit.

Your last study visit will occur 4 weeks after your first visit. This visit will be very similar to your first visit and you will be required to perform some breathing tests and a walking test. You will also be required to complete the same 2 questionnaires that you completed during your first visit. The purpose of performing these breathing tests and questionnaires is so that we can find out if the inhalers have improved your breathing, your quality of life and your activity levels. The extra visits should last no longer than 2 hours.

Your involvement in the study will finish 4 weeks from when you were given the inhalers. There will be no extra study visits after this and you will not be required to perform any more breathing tests or to complete any more questionnaires. However, if you found that the inhalers helped your breathing then we would recommend to your G.P that you should continue using them.

Group 2 (Best supportive care arm), patients in this group will not be given inhalers

Patients in this group will not be given any inhalers. Your breathlessness will be managed in consultation with your doctor who will decide what the most appropriate treatment is to improve your breathlessness. Breathlessness is sometimes treated with a drug called Oramorph (oral morphine solution). If you and your doctor feel that you may benefit from having Oramorph then it will be prescribed for you.

The study will last for 4 weeks and you will be required to visit the Royal Marsden Hospital for 3 visits. Each visit will last for approximately 2 hours and some will coincide with your normal routine clinic visit to see your doctor. During your first study visit we will want you to perform some breathing tests and a walking test. We will perform a chest X-Ray and an ECG to exclude other causes of breathlessness. In addition we will perform a routine blood test and may ask to take a further sample which will be stored and may be

used in other research studies in the future (this however is entirely optional). You will also be required to complete 2 questionnaires which will allow us to determine how your breathlessness is affecting your quality of life and your activity levels. We will ask to perform a urine pregnancy test if appropriate as if it is positive, you will not be eligible for this study.

Your second visit will occur 2 weeks after your first visit. On this visit, your doctors will ensure that your breathing has not become any worse over the previous 2 weeks. You will be required to perform some breathing tests and a walking test but you will not be required to complete the questionnaires that you completed during your first visit.

Your last study visit will occur 4 weeks after your first visit. This visit will be very similar to your first visit and you will be required to perform some breathing tests and a walking test. You will also be required to complete the same 2 questionnaires that you completed during your first visit. The purpose of performing these breathing tests and questionnaires is so that we can find out if the inhalers have improved your breathing, your quality of life and your activity levels.

When you are assessed at the 2 week visit, if your breathing is found to have deteriorated since you started the study, you will be offered inhalers (the same as the patients in the other group) to see if they can improve your breathing.

Your involvement in the study will finish 4 weeks from when you were given the inhalers. There will be no extra study visits after this and you will not be required to perform any more breathing tests or to complete any more questionnaires.

What is Ventolin Evohaler ® and what are the possible risks?

Ventolin Evohaler contains a medicine called salbutamol. Salbutamol is not a new drug and it is currently used widely to treat patients with COPD. Salbutamol belongs to a group of medicines called bronchodilators. Bronchodilators help the airways in your lungs to stay open. This makes it easier for air to get in and out of the lungs may improve breathlessness, chest

tightness, wheezing and cough. The side effects of normally used inhaled doses of salbutamol are mild and they usually disappear with continued treatment. Serious side effects are very rare. The side effects described below have been experienced by people taking this medicine and they are listed according to frequency.

Common side effects (occur in between 1 in 10 patients and 1 in 100 patients)

Feeling shaky, headache

Uncommon side effects (occur in between 1 in 100 patients and 1 in 1000 patients)

Mouth and throat irritation, muscle cramps

Rare side effects (occur in between 1 in 1000 patients and 1 in 10,0000)

A low level of potassium in your blood, increased blood flow to your extremities (peripheral dilatation)

Very rare side effects (occur in less than 1 in 10,000 patients)

Allergic Reactions swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing, itchy rash, feeling faint and light headed, and collapse. Changes in sleep patterns and changes in behaviour, such as restlessness and excitability.

Not Known

The following side effects can also happen but the frequency of these are not known:

Chest pain due to heart problems such as angina.

What is Spiriva® and what are the possible risks?

Another name for Spiriva® is Tiotropium. Spiriva is not a new drug and it is currently used widely and helps people who have chronic obstructive pulmonary disease (COPD) to breathe more easily. Spiriva is a long-acting bronchodilator that helps to open airways and makes it easier to get air in and out of the lungs. Regular use of Spiriva can also help breathlessness and it can help to minimise the effects that breathlessness has on everyday life. It also helps patients with COPD and breathlessness to be active longer. Daily use of Spiriva can also prevent sudden, short-term worsening of COPD symptoms which may last for several days. The effects of Spiriva lasts for 24 hours, so you only need to take it once a day.

The side effects described below have been experienced by people taking this medicine and they are listed according to frequency.

Common side effects (occur in between 1 in 10 patients and 1 in 100 patients)

Dry mouth: this is usually mild

Uncommon side effects (occur in between 1 in 100 patients and 1 in 1000 patients

Dizziness, headache, taste disorders, blurred vision, irregular heart beat (atrial fibrillation), sore throat (pharyngitis), hoarseness (dysphonia), cough, inflammation of the mouth (stomatitis), heart burn (gastrooesophageal reflux disease), constipation, feeling sick (nausea), rash, difficulty passing urine (urinary retention), painful urination (dysuria)

Rare side effects (occur in between 1 in 1000 patients and 1 in 10,0000 patients)

Difficulty in sleeping (insomnia), seeing halos around lights or coloured images in association with red eyes (glaucoma), increase of the measured eye pressure, irregular heart beat (supraventricular tachycardia), faster heart beat (tachycardia), feeling your heartbeat (palpitations), tightness of the chest, associated with coughing, wheezing or breathlessness immediately after

inhalation (bronchospasm), nosebleed (epistaxis), inflammation of the larynx (laryngitis), inflammation of the sinuses (sinusitis), blockage of intestines or absence of bowel movements (intestinal obstruction including ileus paralytic), inflammation of the gums (gingivitis), inflammation of the tongue (glossitis), fungal infections of the oral cavity and throat, (oropharyngeal candidiasis), difficulties swallowing (dysphagia), allergic reactions (hypersensitivity), including immediate reactions, nettle rash (urticaria), itching (pruritus), infections of the urinary tract

Not Known

The following side effects can also happen but the frequency of these are not known:

Depletion of body water (dehydration), tooth decay (dental caries), serious allergic reaction which causes swelling of the face or throat (angioneurotic oedema), infections or ulcerations of the skin, dryness of the skin, swelling of joints

What is Seretide® and what are the possible risks?

Seretide is not a new drug and it is currently used widely to treat patients with COPD. Seretide contains two medicines, salmeterol and fluticasone propionate. Salmeterol is a long-acting bronchodilator. Bronchodilators help the airways in the lungs to stay open. This makes it easier for air to get in and out. The effects last for at least 12 hours. Fluticasone propionate is a corticosteroid which reduces swelling and irritation in the lungs.

Seretide reduces the number of flare ups of COPD symptoms such as breathlessness.

The side effects described below have been experienced by people taking this medicine and they are listed according to frequency.

Very common side effects (occur in more than 1 in 10 patients)

Headache - this usually gets better as treatment continues, increased number of colds

Common side effects (occur in between in 1 in 10 patients and 1 in 100 patients)

Thrush (sore, creamy-yellow, raised patches) in the mouth and throat, also sore tongue, throat and hoarse voice, feeling shaky and fast or uneven heartbeat, palpitations, muscle cramps, pneumonia and bronchitis (lung infection), bruising and fractures, Inflammation of sinuses (a feeling of tension or fullness in the nose, cheeks and behind the eyes, sometimes with a throbbing ache), a reduction in the amount of potassium in the blood (may get result in an uneven heartbeat, muscle weakness, cramp).

Uncommon side effects (occur in between 1 in 100 patients and 1 in 1000 patients)

Very fast heartbeat (tachycardia), rash

Very rare side effects (occur between 1 in 1000 patients and 1 in 10,0000)

Bronchospasm (breathing difficulties or wheezing that get worse straight after taking Seretide), slowing of growth in children and adolescents, thinning of the bones, cataract and glaucoma, weight gain, rounded (moon shaped) face (Cushing's Syndrome), uneven heartbeat or heart gives an extra beat (arrhythmias), increases in the amount of sugar (glucose) in blood (hyperglycaemia), feeling worried, disturbed sleep and behavioural changes, such as being unusually active and irritable (these effects mainly occur in children), aching, swollen joints and muscle pain.

What will be the benefits to me if I take part?

We cannot promise the study will help you, but the information we get from this study may help improve the future management of breathlessness in people with lung cancer and COPD. This will be useful as breathlessness is a very common symptom in patients with lung cancer and at the moment there are not many treatments to offer these patients.

What happens when the research study stops?

After the 4 week period of the study, your care will continue as planned by your doctor. The frequency of appointments, the investigations required and any treatments will be decided by your doctor. If you were in the group that didn't receive inhalers, following discussion with your doctor you may be started on some.

What if there is a problem?

Any complaint about the way you have been treated during the study or any possible harm you might suffer will be addressed. More detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

Thank you for taking time to read this leaflet and considering taking part in this study. This completes Part 1. If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

PART 2

What if relevant new information becomes available?

If we receive any new information that might influence your continued willingness to take part in the study you will be informed without delay. If you decide not to carry on you can withdraw from the study. Your normal planned treatment, investigations and appointments with your doctor will continue as normal.

What will happen if I do not want to carry on with the study?

You are free to leave the study at any time. In a clinical study like this one it is usually important to retain data already collected but we will not collect any new data from you. Your normal planned treatment, investigations and appointments with your doctor will continue as normal.

What if there is a problem?

If you are harmed by taking part in this study there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action but may have to pay for this. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints procedure mechanisms will be available to you. Your doctor will give you further information as necessary.

Will my taking part in this study be kept confidential?

All your details will be treated as confidential. All information about you which leaves the hospital will refer to you only by a unique study number allocated to you, or by your initials to preserve your anonymity.

Occasionally we may need to check your medical records to make sure that the information provided about you was accurate. This will be done by clinical staff (doctors and nurses) or designated study personnel. A government body called the Medicines and Healthcare products Regulatory Agency (MHRA) may also require access to your medical records to ensure that the study is being run in accordance with UK law.

The results of these studies may be used for medical and scientific publications, but you will not be identified by name in any presentations or reports dealing with this research. Under no circumstances will you be identified in any way in any report arising from the study.

Involvement of the General Practitioner/Family doctor (GP)

With your consent, your GP will be informed that you wish to take part in the study.

Private medical Insurer

If you have private medical insurance you should inform your insurer that you are taking part in this study

What will happen to the results of the research study?

The results will be presented at scientific meetings and it is also planned to publish the results in scientific journals. You will not be personally identifiable in any presentation of this research. If you wish we will provide you with a summary of the results.

Who is organising and funding the research?

This study is being sponsored by The Royal Marsden NHS Foundation Trust.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed by the South East Research Ethics committee on 13th October 2010 and given a favourable opinion.

What if I want more information?

You will be given a copy of this information sheet and the signed copy of the consent form for you to keep. Please feel free to ask any further questions of the doctors and nurses looking after you before deciding to take part in the trial or at any time during the study. Before you make a decision, you may want to discuss the study with your family and friends and/or with your GP.

Doctor ..... **Telephone No**: .....

Study Nurse ..... **Telephone No:** .....

24 hour contact number: 020 8642 6011

The 24 hour contact number can be used out of working hours (9am – 5pm) in the event where you need to contact a hospital doctor immediately.

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Consent Form

Prospective randomised controlled trial to investigate the effectiveness of inhalers for the relief of breathlessness in patients with lung cancer and COPD (ADOPT)

CCR:3480

Study number_____

Name of Principal Investigator……

Please initial each box	Please initial
1. I confirm that I have read and understand the information sheet dated……. version…….for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without my medical care or legal rights being affected.	☐
3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from The Royal Marsden or from regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	☐

4. I agree to my GP being informed of my participation in the study. ☐

5. I agree to take part in the above study. ☐

Optional Blood Samples

6. I agree to an extra blood test being performed at the start of the study which will be stored and may be used for future research (this is optional and you may still take part in this study if you refuse). *Please tick as appropriate* ☐ YES ☐ NO ☐

Name of patient	Date	Signature
Name of person taking consent (If different from researcher)	Date	Signature
Name of researcher	Date	Signature

When completed, Consent original to be kept in Site Master File, 1 copy for patient, and 1 copy for medical notes.