Section of Pulmonary, Critical Care, Allergy and Immunological Diseases

PRELIMINARY STUDY FOR COMPARISON OF TRIPLE THERAPY NEBULIZER VERSUS DRY POWDERED INHALER FOR CARE TRANSITIONS IN COPD

Informed Consent Form to Participate in Research
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INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you have been hospitalized for Chronic Obstructive Pulmonary Disease (COPD) exacerbation (flare). Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of the study is to compare two drug delivery devices for the treatment of COPD: nebulized therapies versus Dry Powered Inhalers (DPI). For the purpose of this study, medications delivered via nebulizer are: Brovana, Pulmicort and Atrovent, and medications delivered via DPI are: Spiriva and Advair. Both drug delivery devices and all medications are approved for use by the U.S. Food and Drug Administration (FDA). As part of this study, we will note and record different lung measurements, patient preference, unscheduled doctor's office visits, emergency room visits and hospital re-admission rates.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

This study wil1 enroll 100 people at this research site.

WHAT IS INVOLVED IN THE STUDY?

You will be randomized into one of two drug delivery devices as described below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in either group. You will receive either:

- Nebulizer Group (Brovana 15mcg twice per day via inhaled nebulizer, Pulmicort 0.5mg twice per day via inhaled nebulizer and Atrovent 0.5mg 3 times per day via inhaled nebulizer)
  or
- Dry Powered Inhaler Group (Spiriva 18mcg once per day via inhalation and Advair 250/50 twice per day via inhalation)

You will be expected to use the assigned drug delivery device as directed until the End of Study visit (approximately 90 days after hospital discharge). Once the study is completed you will resume your prior home respiratory medication regimen, or be prescribed an appropriate COPD

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management regimen.

The study will consist of enrollment during hospitalization and 3 outpatient visits:

Enrollment: You will be identified, qualified, consented and enrolled by the respiratory therapy navigator (RTN).You will receive your assigned drug delivery device (nebulizer or inhaler) and medications free of charge prior to hospital discharge. The RTN will teach you how to take the medications with the assigned drug delivery device.

Visit 1: You will return for a standard of care post hospital discharge visit 3 to 14 days after you are discharged from the hospital. As part of that visit you will be evaluated by both a physician and a respiratory therapist. In addition to the standard of care procedures performed at this visit, the following will be collected for the study: lung volume measurements, questionnaires and evaluation your drug delivery preference. The RTN will also determine and record if you have had an unscheduled physician appointment, urgent care, ER or inpatient visits for COPD or any other condition since discharge.

Visit 2: The 30+/-5 day visit will include lung volume measurement, questionnaires and evaluation of your drug delivery preference. The RTN will also determine and record if you have had an unscheduled physician appointment, urgent care, ER or inpatient visit for COPD or any other condition since the last visit. Study medications will be refilled at this time.

Visit 3: The end of study visit (90+/- 10 days) will include lung volume measurements, questionnaires, evaluation of your drug delivery preference and collection of unused medications and the drug delivery devices. The RTN will also determine and record if you have had an unscheduled physician appointment, urgent care, ER or inpatient visit for COPD or any other condition since the last visit. If you were randomized to the nebulizer arm, you will need to return the study nebulizer machine that was dispensed at the start of the study.

Enrollment	Transitional care visit (3-14 days after leaving hospital)	30+/-5 day visit	End of study visit (90+/- 10 days)
•Obtain informed consent •Questionnaires about your breathing and living with a breathing condition •Randomization to drug delivery device (nebulizer or inhaler) •Medication administration training	•Measure how fast you take a deep breath •Measure lung volumes •Questionnaires about your breathing and living with a breathing condition •Ask your preference of nebulizers or inhalers •Navigator will ask you about all: -Unscheduled MD visits -Urgent Care visits -Emergency Room visits -Hospital admissions for any causes & COPD	•Measure how fast you take a deep breath •Questionnaires about your breathing and living with a breathing condition •Ask your preference of nebulizers or inhalers •Refill medications •Navigator will ask you about all: -Unscheduled MD visits -Urgent Care visits -Emergency Room visits -Hospital admissions for any causes & COPD	•Measure how fast you take a deep breath •Measure lung volumes •Questionnaires about your breathing and living with a breathing condition •Ask your preference of nebulizers or inhalers •Collect medications and equipment •Navigator will ask you about all: -Unscheduled MD visits -Urgent Care visits -Emergency Room visits -Hospital admissions for any causes & COPD

How Long Will I Be in the Study?

You will be in the study for about 100 days.

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. If all medications are discontinued, you are at risk of having increased COPD symptoms and a possible COPD exacerbation.

What Are the Risks of the Study?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the study include: One drug delivery device may be more beneficial to a specific group of people. Therefore, you could experience an

increase in COPD symptoms or exacerbations. The medications you will be randomized to as in this study are considered the standard of care for treatment of COPD. You will likely have been or are currently on some, if not all, of the three medications in an arm of this study. Medication adverse reactions for medications in either the nebulizer arm or dry powder inhaler arm are included in the table below:

Study Arm	Medication	Medication Class	Adverse Reactions
Nebulizer Arm	Aformoterol *(Brovana)*	Long-acting B_2-agnoist	Pain, chest pain, back pain, diarrhea, sinus infection, leg cramps, shortness of breath, rash, flu syndrome, peripheral edema (leg swelling), pulmonary/chest congestion
	Budesonide *(Pulmicort)*	Inhaled corticosteroid	Respiratory infection (thrust, fungal infection), rhinitis (runny/stuffy nose), coughing, otitis media (ear infection), viral infection, , gastroenteritis (stomach flu), vomiting, diarrhea, abdominal pain, ear pain, epistaxis (bloody nose), conjunctivitis (pink eye), rash
	Ipratropium *(Atrovent)*	Short-acting anti-cholinergic	Tachycardia (fast heart rate), palpitations, eye pain, eye dilation, urinary retention, urinary tract infection, urticaria (hives)
Dry Powder Inhaler Arm	Fluticasone propionate and salmeterol *(Advair)*	Long-acting B_2-agnoist/ Inhaled corticosteroid	Pneumonia, oral candidiasis (thrush), thoat irritation, dysphonia (hoarse voice), viral respiratory infections, headache, musculoskeletal pain
	Tiotripium bromide *(Spiriva)*	Long-acting anti-cholinergic	Upper respiratory tract infection, dry mouth, sinusitis, pharyngitis (sore throat), non-specific chest pain, urinary tract infection, dyspepsia (indigestion), rhinitis (runny/stuffy nose)

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

Since there is no possible benefit from participating in this protocol for a pregnant woman, we will exclude pregnant women. Subjects will be excluded if female and are not post-menopausal for at least one year. If a subject is found to be pregnant during the 90-day study period, they will be excluded from the study and their data not used for study purposes.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You are not expected to receive any direct benefit from taking part in this research study. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, you have these options: Continue your current respiratory medications or change to new medications. You could be treated with study treatments/drugs even if you do not take part in the study.

WHAT ARE THE COSTS?

All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

Your first visit is standard of care after hospitalization and it will be billed to you or your insurance company. The 30 day and 90 day visits are for research only and will be paid for by the study. Medications will be provided to you, by the study, for the length of time you are enrolled in the study. The drug delivery device will be provided to you, by the study, for the length of time you are enrolled in the study.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a research study. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people

who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

WILL YOU BE PAID FOR PARTICIPATING?

You will receive a $15.00 Walmart card at the transitional care visit that occurs within 14 days of hospital discharge, $50 if you complete study visit 2 and $50 after you complete study visit 3, for a total of $115.00 to cover expenses incurred by you as a result of the study such as gasoline and/or a meal. If you withdraw for any reason from the study before completion you will not be paid for any visits that are not completed.

To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

Additionally, if you were randomized to the nebulizer arm, you will need to return the study nebulizer machine that was dispensed at the start of the study in order to receive the final $50 check after the End of Study visit.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Sunovion Pharmaceuticals Inc. The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

Dr. Jill Ohar, the Principle Investigator, however is on the advisory board for Sunovion, the makers of Brovana, and the sponsor of the study and receives consulting fees from the company.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted]

If you are injured, the sponsor may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the sponsor is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call [redacted]

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes: medical history**,** questionnaires, lung test results, hospitalizations, doctor visits and patient preference.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any

publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Jill A Ohar that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health

Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm