Participant Information Sheet

Project title: Monitoring intermittent vs Regular inhaled corticosteroids in asthma: MIRSA

Chief investigator: Assoc. Prof John Brannan

You have been invited to participate in a research study. Before agreeing to participate in the study, it is important for you to thoroughly read and understand the following explanation of the study and the procedures. This form describes the purpose, procedures, benefits, and risks associated with this study. If you choose to participate in this study, **you have the right to withdraw at any time.**

What is the study?

Regular use of inhaled steroids, or preventers, have been the most common way to reduce asthma symptoms, and potentially abolish active asthma. Recently, new guidelines have recommended that preventers can be used 'as-needed' instead. Our study will look at comparing different steroids with these two methods to see if active asthma can be abolished, and which method is a more effective treatment for asthma. This study's funding has been provided to the Chief Investigator through GlaxoSmithKline (GSK) via their Supported Collaborative Study program. The drugs provided in this study are provided free of charge by GSK.

Who can be involved?

You are invited to participate because you are aged between **18 and 60 years and** have **mild asthma. You either treat your asthma by taking only a reliever (i.e. Ventolin, Asmol) or dual purpose reliever (i.e. Symbicort) as you need to when you experience symptoms, or a regular preventer containing an inhaled corticosteroid (i.e. Arnuity, Flixotide, Pulmicort) plus a reliever as you need to.** Before beginning the study, you will be asked to complete a few questionnaires either over the phone, in person or online to determine if this study is suitable for you. It is important that women participating in this study are not pregnant or

breast feeding and do not become pregnant during the course of the study. If you are a woman of child-bearing potential and there is any possibility that you are pregnant, the researchers will perform a pregnancy (urine) test before you start in the study. Acceptable contraceptive measures (such as oral or implanted contraception, an IUD or have had a tubal ligation) are recommended for fertile women participating in this study. If at any time you think you may have become pregnant, it is important to let the researchers know immediately.

What does the study involve?

The study will take place within the Adult Respiratory Laboratory located either within the John Hunter Hospital in Newcastle, Australia or East Maitland Pulmonary Function Laboratory, Australia (private clinic). It will involve **6-7 visits** over the course of 22 weeks (most visits are every 4 weeks). Each visit will be approximately **45mins-1hr**.

Visit 1: On your first visit, we will discuss the study with you and check the suitability of the study for you. We will ask you which medications you are currently using. If you are happy to participate in the study, you will be asked to sign the information and consent form.

Note that this visit can be done in person or over the phone.

Visit 2: You will be asked to fill in the ACQ and AQLQ and perform standard lung function testing to characterise your asthma and general lung health (see below for a more detailed description). This will include measuring your blood pressure and heart rate.

We will then ask you to only take a reliever (i.e. Ventolin) as much as you need for the next 4 weeks. If you are usually taking a dual-purpose reliever or preventer medication, we will ask you to withhold from using this medication during this time. This is to make sure that these medications are cleared from your body before we provide you with either a preventer or dual purpose reliever on your next visit (visit 3).

We will also provide you with an electronic monitor known as the Hailie Remote Patient Management (RPM) solution that fits your reliever. This device attaches to your reliever inhaler and connects to your phone via Bluetooth. This device will count how many times and

when you use your reliever and send this information to us for daily monitoring. If we notice that you are using more than 12 puffs of your reliever in a day, we will contact you for safety reasons. Excessive reliever use can suggest that your asthma has become unstable.

You will also be given another ACQ questionnaire to take home and we will contact you by phone 2 weeks into this 4-week reliever only period to ask you to complete this questionnaire.

Note that this visit can be at the same time as Visit 1.

Visit 3: You will be asked to fill in the ACQ and AQLQ and perform standard lung function testing to determine your asthma and general lung health. We will then, like tossing a coin, randomise you into 1 of 3 groups and give you commonly prescribed treatments that have been approved in Australia for the treatment of mild asthma:

- Group 1 – Flixotide Junior Accuhaler as a twice-daily preventer, and Ventolin reliever taken as needed
- Group 2 – Arnuity Ellipta as a once daily preventer, and Ventolin reliever taken as needed
- Group 3 – Symbicort Turbuhaler taken as needed as a dual purpose reliever

The reason we allocate participants to a treatment group randomly (by chance) is to ensure that the results are clear and the researchers cannot influence the outcomes of the study.

These inhalers will also be fitted with Hailie RPM electronic dose counters similar to the ones used on the reliever, so that we can monitor the dose of medication you are taking.

Visit 4-6: You will be asked to take your medication assigned at Visit 3 for the next 3 months. We will monitor your lung function and ACQ + AQLQ at 2, 6 and 12 weeks using the standard tests listed below.

On the 6th visit (Week 12), we will adjust your medication slightly. Group 1 – There will be no changes to your treatment.

- Group 2 – Rather than using the Arnuity Ellipta preventer daily, we will ask you to only take it 3 days per week. Note you will still have Ventolin as a reliever as needed during this period.

- Group 3 - Rather than using the Symbicort Turbuhaler as needed, we will switch you to Pulmicort Turbuhaler) as a twice-daily preventer, and Ventolin reliever taken as needed

Visit 7: After another 6 weeks, we will again monitor your lung function and ACQ +AQLQ. This is the final stage of the study. You may return to your regular medication and exit from the study.

Before each visit to test your lung function, you will be asked to not take any inhaler medication prior to each visit for either 12 hrs (Pulmicort or Flixotide) or 24hrs Symbicort or Arnuity), however, you may take Ventolin up to 8hrs before the visit). You will also be asked to abstain from ingesting caffeine- or xanthine-containing products (e.g., coffee, tea, cola drinks, and chocolate) for 6 hours before the start of lung function testing. You will be sent reminders prior to each visit.

The lung function tests will include:

- ***Fractional exhaled nitric oxide (FeNO)*** **analyser**

This device is a breathalyser-like device that detects nitric oxide in your lungs. This gas is always present in the lungs, although with asthmatics it can be raised and may indicate active inflammation. You will need to blow out through your mouth slowly and steadily for 10s into this device. This test takes less than 5 minutes to complete.

- ***Spirometry***

Spirometry tells us how open the airways of the lung are. This test requires you to take a deep breath and then blow out as quickly as you can, until you're empty, into a mouthpiece. The more air you are able to get out, in a shorter amount of time, the more open the airways. This test will be used to monitor how the airways narrow during the bronchial provocation test.

- ***Bronchial provocation test (BPT)***

This is a diagnostic tool for active asthma that involves inhaling a dry powder of mannitol. In asthmatics, this powder can dry-out the airways and cause the airways to contract slightly. This can cause symptoms common with asthma which include wheeze, chest tightness and cough. After each dose of the powder, we will monitor your airways using spirometry. If the airways contract by 15% then the test is over. This amount can be associated with a wheeze you may or may not take a reliever to reverse.

There are 9 levels to the test and how active your asthma is, depends on how far you make it through the test. i.e., If your asthma is very active your airways will contract quicker and the test ends sooner.

This test takes approximately 25 minutes to complete; however, this time may be shorter depending on how far you make it through the test. Following the test, we will give you Ventolin the reliever medication so that your airways recover back to normal.

<u>The following table outlines all the questionnaires.</u>

Note: that times listed in the table are just a guide; they may take a longer or shorter time.

Questionnaire	*What does it measure?*	*Max duration*
Confidential demographic and general health questionnaire	Your demographics (e.g., age, height, education level, employment), and your general health.	10 minutes
Asthma Control Questionnaire	How often you experience symptoms of asthma	2 minutes
Asthma Quality of life Questionnaire	Does your asthma impact your quality of life	5 minutes

Visit (Week)	*What takes place at the visit which will last for approximately 1 hr (or less)*

Visit 1	Understanding of the study procedures and providing consent by signing Patient Information & consent form. Can be in person or over the phone. You will have time to consult your consenting with others or with your GP if desired and more time can be given to do so.
Visit 2 *(-4 wks)*	Complete questionnaires. Perform spirometry and reversibility with bronchodilator. Perform exhaled nitric oxide test. Commence monitoring period using dose monitor on Ventolin inhaler.
Visit 3 *(0 wks)*	Complete questionnaires. Perform spirometry & exhaled nitric oxide test. Perform mannitol challenge test. If you have airway hyperresponsiveness you are randomised to one of three maintained treatments using an inhaled corticosteroid.
Visit 4 *(2 wks)*	Complete questionnaires. Perform spirometry & exhaled nitric oxide test. Perform mannitol challenge test.
Visit 5 *(6 wks)*	Complete questionnaires. Perform spirometry & exhaled nitric oxide test. Perform mannitol challenge test.
Visit 6 *(12 wks)*	Complete questionnaires. Perform spirometry & exhaled nitric oxide test. Perform mannitol challenge test. For Group 1 treatment stays the same, for Group 2 & 3 the treatment changes for the remaining 6 wks.
Visit 7 *(18 wks)*	Complete questionnaires. Perform spirometry & exhaled nitric oxide test. Perform mannitol challenge test.

Are there any risks involved?

- Any secondary findings that suggest a change in your medical condition (e.g., identification of a previously undiagnosed respiratory disorder) will be communicated to your family doctor and the release of this information to you will be at the discretion of your GP.
- During the study you are asked to perform breathing tests that may cause mild light-headedness. In very rare circumstances spirometry and the BPT can reveal undiagnosed fainting; a condition with which forceful blowing out can cause loss of consciousness (Black out). You may experience a mild cough, wheeze, chest tightness, and

breathlessness although inhaler medication will be available. Your recovery will be closely monitored and experienced medical staff are readily available should you need them.

- All medications have potential side effects. Inhaled corticosteroids can cause a sore throat that can be avoided by gargling with water after each inhalation. Low doses of inhaled corticosteroids are being used in this study, however with high inhaled doses over many months to years are known to have potential side effects of bruising and weight gain. Bronchodilator medications (e.g., Ventolin) can in some cause peripheral tremor (e.g., minor shaking of the hands), however the likelihood of this is reduced over time. We will provide you with product information leaflets that contain further information.

What if I don't want to take part in this study, or if I want to withdraw?

Before deciding whether to take part in this study, you are free to discuss the matter with a relative, friend, or your local doctor. Please note your participation in this study is **voluntary**. You are free to withdraw from the study at any stage without having to give a reason and your information will be deleted. You can notify the contact person at your local site or the chief investigator either by phone or email detailed below. Your decision to take part, not to take part, or to withdraw, will not affect your routine medical treatment or your relationship with those treating you. Your data collected in this study can be deleted at your request.

What are the benefits of participating in this study?

Whilst you may not directly benefit from this study it is predicted that the data from this study will provide a model with which to better treat asthma and potentially abolish active asthma in the presence of preventer therapy.

There is no monetary compensation other than reimbursement for travel expenses, food and parking where applicable.

How will your privacy be protected?

Information collected from you during this study, including any personal information will remain confidential in which only the research staff, ethics committee, and regulatory authorities will have access to your test results. Personal information will be accessed and

stored under the Commonwealth Privacy Laws and the NSW Health Records and Information Privacy Act 2002.

Any information collected during the study will be kept up to 7 years and reassigned under a code that cannot be linked to any of your details (i.e., name, date of birth). Should you wish to withdraw from the study, your information can also be withdrawn at your request.

Ethics:

This research has been approved by the Hunter New England Human Research Ethics Committee of Hunter New England Local Health District, Reference **2020/ETH12142.**

Governance:

The conduct of this research has been authorised by the Hunter New England Local Health District to be conducted at the John Hunters Hospital and East Maitland Respiratory and Sleep Clinic.

Complaints about this research:

Should you have concerns about your rights as a participant in this research, or you have a complaint about the manner in which the research is conducted, it may be given to the researcher, or, if an independent person is preferred, please contact the HNE Research Office, Hunter New England Local Health District, Level 3, POD, HMRI, Lot 1 Kookaburra Circuit, New Lambton Heights NSW 2305.

Telephone: 02 4921 4140. Email: HNELHD-ResearchOffice@health.nsw.gov.au and quote the reference number: **2020/ETH12142.**

How do I become a participant?

If you are interested in the above study and wish to participate or if you simply have any further questions, please contact Dr. John Brannan on: 0435206232 or john.brannan@health.nsw.gov.au or contact Rachel Neal (research coordinator) on 0403600430 or email: rachel.neal@uon.edu.au.

If you wish to participate, you may begin filling out the questionnaires here [hyperlink to be inserted].

This information sheet is for you to keep

Participant Consent Form

Project title: Monitoring intermittent vs Regular inhaled corticosteroids in asthma: MIRSA

Primary investigator: Dr. John Brannan

I,..... (Name) of

..... (Address)

I have read the Information Sheet, a copy which I have retained, and the nature and the purpose of the research project has been explained to me.

I have had the opportunity to have questions regarding the study answered to my satisfaction.

I have been made aware of the procedures involved in the study, including any known or expected inconvenience, risk, discomfort, or potential side effects and of their implications as far as they are currently known by the researchers.

I understand that I may not directly benefit from taking part in the study.

I understand that while the information gained during the study may be published, I will not be identified, and my results will remain confidential.

I understand that participation in the study is voluntary and that I can withdraw from the study at any stage without providing a reason.

I permit the researchers to use the data collected for future research purposes. I permit to be contacted after the study to give my consent to use the data for future related research purposes in de-identified form only. In this circumstance, I understand that I will not be identified, and my results will remain confidential.

NOTE: This permission is optional, and you must notify study investigators if you do not consent for the use of your data for future research purposes and this will be noted in your data records.

☐ I wish to receive a publication of the results via email (optional). Please provide your email address below (optional):

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I confirm that I am between 18-60 years of age.

I hereby agree to participate in this research study.

Name of Participant: …….

Signature: ……. Date: ……. / ……. / …….

If Applicable:

Name of Participant's legal guardian: …….

Signature: ……. Date: ……. / ……. / …….

I have explained the study to the participant and consider that they have understood what is involved.

Researcher: .....

Signature: ……. Date: ……. / ……. / …….