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Participant Information Sheet/Consent Form

[insert hospital name]

CHOOSING BETWEEN BIOLOGICAL AGENTS FOR SEVERE ALLERGIC EOSINOPHILIC ASTHMA

Short Title	Choosebetweenamab
HREC Number	**2019/ETH001231**
Coordinating Principal Investigator	Professor Peter Wark
Principal Investigator	[insert PI name]
Location	[insert hospital address]

What is this study about?

You are being invited to take part in this research study because you have severe asthma that is not well controlled.

Your respiratory specialist has profiled your asthma and has found that you are eligible to trial either of two different treatments to see if one of these will help better manage your asthma. These treatments are Nucala (mepolizumab) and Xolair (omalizumab).

Nucala is prescribed for people with a type of asthma where they have an elevated eosinophil count in their blood. Your blood tests have shown that you have a high blood eosinophil count. Eosinophils are a type of white blood cell in the blood that promote inflammation. Nucala lowers the number of blood eosinophils and has been shown to reduce asthma exacerbations by ~ 50%.

Xolair acts against a molecule in the blood called IgE which is produced by the body in response to allergic stimuli like pollens or animals. Your blood tests have shown that you have IgE levels that are high. This causes your asthma symptoms to always be *turned on*. Xolair reduces this over-reactivity and can reduce asthma symptoms

Because we currently do not know which treatment option is best for you, your doctor has to make an educated guess about which drug to trial you on first.

We are trying to see if there are markers in the blood (or sputum) that will show who is likely to respond best to one treatment or the other so that the best medication can be prescribed first time without having to just pick one and see what happens.

This Participant Information Sheet/Consent Form tells you about the research study we are conducting which will try to find out which of these two treatments is best in people who have your type of asthma where blood eosinophils *and* serum IgE are both high.

This document explains the study-specific tests involved. Knowing what is involved will help you decide if you want to take part in the study.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this study is voluntary.

If you don't wish to take part in this study, you don't have to. You will receive the best possible care whether or not you take part and you will be able to trial a medication regardless of whether you enter the study or not. Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with the **[insert hospital name]** Hospital.

If you decide you want to take part in the study, you will be asked to sign the consent section of this document.

By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the study
- Consent to have the tests that are described
- Consent to the use of your personal and health information as described.
- Consent to your doctor giving your name and contact details to study staff based at the John Hunter Hospital in Newcastle, NSW so that they can contact you to ask questions about your asthma during the study period.

You will be given a copy of this Participant Information and Consent Form to keep.

No study procedures will be performed until you have signed the consent.

Which treatment will I receive if I agree to be in the study?

Rather than your treating doctor choosing which study drug to try first, this study will randomly assign you to one or other drug. 190 people will participate in the study and half (95) will receive Nucala and the other half (95) will receive Xolair. A computer program will be used to determine who receives which drug. You will be told which drug you will be treated with and given the product insert sheet for the medication for your information.

Your respiratory specialist and outpatient nurse will inform you about your outpatient visits, when and how often they will take place and what will take happen at outpatient visits. These are not study visits.

Study tests, Procedures and Visits:

Study visits.

There are 3 study clinic visits that will take place over the 6 month drug trial period if you volunteer for this study: V0, V1 and V3. Research staff will try to coordinate these visits with your outpatient visits where you will be administered with either Nucala or Xolair.

The following table (Table 1) shows you what will happen at the study clinic visits. The table also shows when study staff from the John Hunter Hospital who are coordinating this study will telephone (☎) you to ask how your asthma and general health are going while you are being trialled on the medication. These phone calls will take between 5 and 10 minutes.

Table 1 Study visit activities

	V0	☎1	V1 Treatment start	Optional visits Weeks 4 & 12	☎2	☎3	☎4	☎5	☎6	V2
Week of study relative to your first dose of asthma treatment (V1)	-4 to -2	≤48 hours post-V0	0	4	4	8	12	16	22	24
Asthma History	X									
Comorbidities	X									
ACQ5 & ACQ7 Questionnaires	X	X	X	X	X	X	X	X	X	
Exacerbation occurrence	X	X	X	X	X	X	X	X	X	
Asthma meds	X	X	X	X	X	X	X	X	X	
Prednisone usage	X	X	X	X	X	X	X	X	X	
Spirometry	X		X	X						X
FeNO	X		X	X						X
Blood samples										
Full blood count (5ml EDTA tube)	X			X						X

CRP [1] (4 ml serum tube)	X			X						X
IgE (5ml serum tube) & RAST[2] (10ml serum tube)	X									X[3]
Optional samples										
Sputum induction			X	X						X
PBMCs[4] (3 x 9ml EDTA tubes)			X	X						X
Paxgene tube[5] (2.5 ml blood)			X	X						X
SpiroNOSE[6]	X		X	X						X

1.

1. CRP – to measure the amount of inflammation in your body
2. RAST – to see what you may be allergic to.
3. IgE only – IgE is measured to see what your allergic status is.
4. PBMCs peripheral blood mononuclear cells – are isolated from a blood sample to use in the laboratory testing part of this study.
5. Paxgene – a special blood tube that allows RNA to be isolated for laboratory testing. This is not gene sequencing – no gene sequencing will be done in this study.
6. SpiroNOSE – a breath analysis

What will study staff want me to do that is additional to my outpatient visits?

There may be outpatient-specific activities required when you attend an outpatient visit on the same day as a study visit. There are activities that are part of the study. If you volunteer for the study any of the study activities that are also required for your outpatient visit will only be done once if the study visit coincides with your outpatient visit.

Medical and asthma history: the study staff will ask you about any previous and current medical conditions including the details of your asthma, and the treatments or medications that you are currently taking.

Blood tests: you will be asked to provide blood samples as indicated in Table 1. Your specialist may not always require blood samples during the drug trial itself but for the study these are obtained for the following purposes:

- To check your health status
- To check your allergic status.

Spirometry: this procedure is to check your lung function. This involves blowing forcefully into a tube connected to a machine called a spirometer. This will measure the amount of air you can breathe out in one second, and the total amount of air you can breathe out.

FeNO: This procedure will involve breathing into a device to test the levels of exhaled Nitric Oxide in your breath (FeNO).

What are the costs of taking part?

There are no additional costs associated with taking part in this research study, nor will you be paid.

Is there anything else I have to do?

If you agree to take part in this study, you must:

- Be willing to attend the hospital/clinic at the times agreed with study coordinators and have the relevant tests and procedures done at each study visit.
- Provide accurate and complete information about your medical history and your present condition during the drug trial period.
- Tell the study staff about any other medicines, vitamins or herbal supplements you are taking before and during the study.
- Report any unpleasant, unwanted, or unusual symptoms you experience.
- Avoid eating or drinking anything at least 1 hour prior to taking the FENO test (checking inflammation of your airways).
- Avoid strenuous exercise for at least 30 minutes before your lung function tests.

A description of this clinical study will be available on www.anzctr.org.au (Study ID ACTRN12618000850279). 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 website at any time.

What are the possible benefits of taking part?

There may be no direct benefit for you. Information from this study may help doctors understand asthma and treat asthma better or to develop new tests or drugs to help other patients with asthma.

What are the possible risks and disadvantages of taking part?

This study will take place during an outpatient trial of a drug and will be overseen by your respiratory specialist., There are risks specific to each of the medications that you may be prescribed. These risks will be explained to you by your respiratory specialist. However, it is important to remember that this study is not a trial of either of the medications you may be prescribed, but a trial of which medication is best to choose first to treat people who are eligible to be prescribed either.

What is Nucala (mepolizumab)?

NUCALA is a prescription medicine approved for use in Australia for people with severe asthma and is used with other asthma medicines for the maintenance treatment of asthma in people aged 12 years and older whose asthma is not controlled with their current asthma medicines.

NUCALA helps to prevent severe asthma attacks (exacerbations). Clinical trials have shown that for people with asthma, who continue to have poor control of asthma symptoms despite using asthma preventers or continue to have asthma attacks that require treatment with prednisone and have elevated inflammatory cells (eosinophils) in their blood may benefit from using NUCALA.

NUCALA given once a month as a 100mg subcutaneous (under the skin) injection in people with severe eosinophilic asthma has been shown to reduce asthma attacks that require prednisone by about half and to improve asthma symptoms. While in some people who require regular prednisone or prednisone every day, it allows them under the supervision of their doctor to reduce their prednisone dose.

NUCALA may have side effects.

Very common side effects (this may affect more than 1 in 10 people):

- headache

Common side effects (these may affect up to 1 in 10 people):

- injection-site reaction (pain, redness, swelling, itching, and burning sensation of the skin near where the injection was given)
- eczema (itchy red patches on the skin)
- back pain
- pharyngitis (sore throat)
- lower respiratory tract infection (congestion, cough, discomfort)
- nasal congestion (stuffy nose)
- upper abdominal pain (stomach pain or discomfort in the upper area of the stomach)
- urinary tract infection (blood in urine, painful and frequent urination, fever, pain in lower back)
- fever (high temperature)

What is Xolair (Omalizumab)?

XOLAIR is a prescription medicine approved for use in Australia for people with severe asthma and is used with other asthma medicines for the maintenance treatment of asthma in people aged 12 years and older whose asthma is not controlled with their current asthma medicines.

XOLAIR is given once a month or every 2 weeks by a subcutaneous (under the skin) injection in people with severe allergic asthma and has been shown to reduce asthma attacks that require prednisone. XOLAIR has been shown to improve asthma symptoms and help to prevent severe asthma attacks (exacerbations). While in some people who require regular prednisone or prednisone every day, it may allow them under the supervision of their doctor to reduce their prednisone dose.

XOLAIR may have side effects.

Risks from Xolair (omalizumab):

- bruising, redness or pain at the injection site
- mild skin rash
- headache
- tiredness
- hair loss
- joint swelling
- fever (very common in children)
- sore throat and blocked nose (nasopharyngitis)
- feeling of pressure or pain in the cheeks and forehead (sinusitis and sinus headache)
- upper respiratory tract infection, such as inflammation of the pharynx and common cold
- burning sensation or pain when passing urine and having to urinate frequently (possible symptom of an urinary tract infection)
- pain in upper or lower limbs (arms and/or legs)
- pain in muscles and/or bones and/ or joints (musculoskeletal pain, myalgia, arthralgia)

Risks from study procedures

Some of the study tests have possible risks and discomforts. You may experience none, some or all of those listed below.

- Having blood tests may sometimes cause pain at the site where the blood is taken from, bruising, and occasional light-headedness and, rarely, fainting.
- Performing the breathing tests (spirometry or measurement for exhaled nitric oxide levels) may cause temporary dizziness, may lead to fainting, mild chest tightening and coughing (worsening of asthma symptoms). Reliever medication can be used if necessary to open up your airways and help you breathe better.

What will happen to my test samples?

This research study involves the collection of blood samples. Blood samples will be collected to check your general health and to measure specific substances in the blood (biomarkers) that may help in the treatment of asthma in the future if you provide samples for a sub-study.

How much blood will be taken from me for this study?

The total blood volume collected during the main study (6 months) will be approximately 40 mls (about 2.5 tablespoons).

If you volunteer to participate in sub-study 2 there is an additional 60 mls (about 4 tablespoons) requested and an extra 170 mls over the 6 month trial period will be taken for sub-study 3 (about 10 tablespoons) as indicated in Tables 1 & 2.

ADDITIONAL OPTIONAL SAMPLE COLLECTION (BLOOD AND SPUTUM) FOR SUB-STUDIES:

As indicated above the researchers would also like to collect, with your consent, extra blood and/or sputum samples in addition to those that are required for the main study. These additional samples will allow the researchers to perform experiments to see if the two alternate asthma treatments change how immune cells found in the blood behave when stimulated by triggers of asthma like viruses, dust mite and bacteria.

This extra research may identify specific substances in the blood (biomarkers) that could help in the treatment of asthma in the future.

Some blood will be used to look at RNA (ribonucleic acid) to measure the presence and amount of RNA in your blood. RNA is like DNA (deoxyribonucleic acid) which is what your genes are made of; genes are inherited and affect how we grow and develop. DNA and RNA is different in each person. These differences may affect a person's risk of suffering from a particular disease or the way a person responds to a particular medicine. The samples used in this study cannot be used to see what genes you have or if you could be prone to a particular disease. They will only show how active a gene is relative to others.

Table 2: Optional sample collection – this table shows at what visits additional samples will be taken if you agree to participate in a sub-study.

	V0	☎1	V1 Treatment start	Optional visits Weeks 4 & 12	☎2	☎3	☎4	☎5	☎6	V2
Sputum induction			X	X						X
PBMCs[1] (3 x 9ml EDTA tubes)			**X**	X						**X**
Paxgene tube[2] (2.5 ml blood)			**X**	X						**X**
SpiroNOSE [3]	X		X	X						X

Sub-study 1: sputum induction (V1 and V2) (John Hunter and Princess Alexandra Hospitals only)

Sub-study 2: PBMCs (V1 and V2), PaxGene (V1 and V2), SpiroNOSE (V1 and V2)

Sub-study 3: PBMCs, PaxGene, SpiroNOSE (V1, V2 & Weeks 4 & 12),

1. PBMCs peripheral blood mononuclear cells – isolated from a blood sample to use in the laboratory testing part of this sub-study.
2. Paxgene – a special blood tube that is used to allow RNA to be isolated for laboratory testing. This is not gene sequencing – no gene sequencing will be done in this study.
3. SpiroNOSE – a breath analysis

Sputum Induction:

Sputum induction is a technique that encourages you to produce a sample of sputum or phlegm from deep in your lungs by breathing a nebulised mist of sterile hyper-tonic (4.5%) saline (salty water) solution for up to 16 minutes. You will be asked to do this for periods of 30 seconds, 1 minute, 2 minutes, 4 minutes, 4 minutes and 4 minutes, consecutively. A breathing test (spirometry) will be done at the end of each time period and you will be asked to try to produce a specimen of sputum. All together the sputum induction can take up to 60 minutes.

The test will be stopped at your request or if you experiences increased symptoms. It can cause coughing and wheezing and a temporary fall in lung capacity. You will be given a reliever medication if you develop any problems with your breathing. These effects are quickly and completely reversed by reliever medication if necessary. We will closely monitor your symptoms and breathing throughout the study. The sputum sample collected will be used to look at the types of cells that commonly cause lung inflammation in asthmatics.

SpiroNOSE

The SpiroNOSE is an electronic nose (eNose) for medical application at point-of-care. It performs rapid and efficient analysis of exhaled air, allowing assessment of the most probable diagnosis in individual patients. This test simply requires you to exhale into a mouthpiece connected to a breath analyser.

Can I volunteer for none or some of the sub-studies only?

The sub-studies are additional to the main study and you can opt-out of the sub-studies altogether and still be included in the main study.

Residual samples

With your agreement, we would like to store residual biological samples (i.e. blood, serum, sputum) provided by you for future medical research to learn more about asthma. All the testing done on your biological samples, now and in the future, will be for research purposes only. All samples will be stored in secure areas within the research laboratories of the HMRI with restricted access to designated researchers only. This research may lead to the development of new patents, medications, diagnostics or biological products. At this time we do not know what this future research may be or how it might be done. However, ethics approval will be sought before any samples obtained from you will be used for research in addition to the research tasks described in this document. To agree to the use of your residual samples for future medical research, you must complete the consent form options at the end of this document. If you **do not** agree to future research, your samples will be used only for the purposes of the study described in this document.

Use and Storage of Biological Samples

Your samples will be analysed during the study's operation and will be destroyed on completion of the study analyses. You will not get copies of the results. If you have agreed for your samples to be used for future research, then they will be stored for 15 years after the study ends. At that time any remaining samples will be destroyed or anonymised, i.e. the link between you and your samples will be broken so that the samples, and any data obtained from the anonymised samples, can never be traced back to you.

You may withdraw your consent to the use of your residual sample(s) at any time. If you decide to stop taking part in this study, your personal information and samples that we have already collected will still be used in the ways that you agreed to when you started in the study. You can discuss with your study staff if you do not want this to happen.

If you decide to leave the main study you will also, in addition to that, need to notify the study doctor if you want to withdraw your consent to the use of donated sample(s) for additional research.

What if I withdraw from this research study?

At any time during the course of the study, or a sub-study, you are free to withdraw from study tests. This will not affect the standard of care you receive. You will be asked to complete a separate consent form with options for follow-up after withdrawing. You do not have to complete this if you do not want to.

If you decide to withdraw from the study or a sub-study, please notify your Study Doctor or a member of the Study team before you withdraw.

What happens when the research study ends?

When you have finished taking part in this study, your Doctor will decide how to continue to manage your asthma. If the treatment has been successful, an application will be made by your respiratory specialist for continuation of the treatment from the PBS.

What happens if I fail to respond to the treatment I am given?

If after the 6 month trial you do not have any clinical or perceived benefit from the treatment you may be able to trial the alternate medication.

You will need to undergo a 2-month washout period before you can start the next trial. At the end of this time you may trial the alternative monoclonal antibody for 6 months where the same visit schedule will be followed as was done for the initial randomised treatment.

The supply of the alternate medication will be provided on compassionate grounds from either GSK (Nucala: mepolizumab) or Novartis (Xolair: omalizumab).

If the alternate treatment is successful, an application will be made for continuation of the treatment from the PBS.

What will happen to information about me?

By signing this document you consent to the Study Doctor and relevant research staff collecting and using personal information about you for the Study ("Personal Information"). Personal Information collected for the purposes of this Study will include: your date of birth, your sex, your ethnic origin and personal information on your physical or mental health or condition. Your consent to the use of your Personal Information does not have a specific end date, but you may withdraw your consent at any time by notifying the Study Doctor.

Information about you may be obtained from your health records held at this institution and may be obtained from other health services for the purposes of research. By signing this consent form

you agree to the study team accessing health records if they are relevant to your participation in this research study.

Information about your participation in this research study may be recorded in your health records.

Any information obtained for the purpose of this research study and for the future research if applicable that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

The Study Doctor and relevant research staff will use your Personal Information and Study Data to conduct the Study. The Study Doctor and research staff will comply with relevant data privacy laws.

How can I access my information?

In accordance with relevant Australian privacy and other relevant laws, you have the right to request access to the information collected and stored by the researchers about you. You also have the right to request that any information with which you disagree be corrected. Please contact one of the researchers named at the end of this document if you would like to access your information.

If you withdraw your consent during the Study, the Study Doctor and relevant research staff will not collect additional Personal Information from you, although Personal Information already collected will be retained, to ensure the results of the Study can be measured properly and to comply with law.

If you do not consent to the handling of your Personal Information as described above, the Study Doctor will not be able to enrol you in the Study

Complaints and compensation

If you suffer any injuries or complications as a direct result of this study, you should contact the study doctor as soon as possible, who will assist you in arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public participant in any Australian public hospital.

Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research study have been approved by Hunter New England Human Research Ethics Committee.
This study will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007) – updated March 2014*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query.
If you want any further information concerning this study or if you have any medical problems which may be related to your involvement in the study (for example, any side effects), you should contact your local severe asthma clinic on XXXXXXXXXX or any of the following people:

Clinical contact person

Name	
Position	Study Coordinator
Telephone	
Email	

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	
Position	
Telephone	
Email	

If you have any complaints about any aspect of the study, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC name	*Hunter New England Human Research Ethics Committee*
HREC Executive Officer	Dr Nicole Gerrand
Telephone	4921 4950
Email	Nicole.gerrand@hnehealth.nsw.gov.au
Please Quote	2019/ETH01231

Consent Form - *Adult providing own consent*

CHOOSING BETWEEN BIOLOGICAL AGENTS FOR SEVERE ALLERGIC EOSINOPHILIC ASTHMA

Short Title	Choosebetweenamab
HREC Number	**2019/ETH01231**
Coordinating Principal Investigator	Professor Peter Wark
Principal Investigator	[insert PI name]
Location	[insert hospital address]

Declaration by Participant

- I have read the Participant Information Sheet or someone has read it to me in a language that I understand.
- I understand the purposes, procedures and risks of the research described in the study.
- I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to the John Hunter Hospital concerning my disease and treatment for the purposes of this study. I understand that such information will remain confidential.
- I understand that my name and personal contact details will be given to study staff at the John Hunter Hospital for purposes of making study-specific telephone calls to me to collect information from me about my asthma symptoms for the purposes of this study.
- I have had an opportunity to ask questions and I am satisfied with the answers I have received.
- I freely agree to participate in this research study as described and understand that I am free to withdraw at any time during the study without affecting my future health care.
- I understand that I will be given a signed copy of this document to keep.
- I understand that, if I decide to discontinue the randomly prescribed treatment, a member of the research team may request my permission to obtain access to my medical records for collection of follow-up information for the purposes of research and analysis.

- I understand that I may participate in the main part of this research study without giving my consent to participate in the optional sub-studies.

☐ **Optional residual samples consent.** By signing this consent form and checking ☒ this box, I also give permission for **any residual samples** to be used by the researchers for future research after HREC approval.

SUB-STUDY INVOLVEMENT

I would like to volunteer for the following sub-studies in addition to the main study (please check ☒ the box(es) that applies):

☐ Sub-study 1: sputum induction (V1 and V2) John Hunter & Princess Alexandra Hospitals only.

☐ Sub-study 2: PBMCs (V1 and V2), PaxGene (V1 and V2), SpiroNOSE (V1 and V2)

☐ Sub-study 3: PBMCs, PaxGene, SpiroNOSE (V1, V2 & Weeks 4 & 12)

Name of Participant (please print) _____

Signature _____ Date _____

Declaration by Study Doctor

I have given a verbal explanation of the research study, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor (please print) _____

Signature _____ Date _____

Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation - *Adult providing own consent*

[Insert hospital name]

TITLE: **CHOOSING BETWEEN BIOLOGICAL AGENTS FOR SEVERE ALLERGIC EOSINOPHILIC ASTHMA**

Short Title	Choosebetweenamab
HREC Number2019/ETH01231	
Coordinating Principal Investigator	Professor Peter Wark
Principal Investigator	[insert PI name]
Location	[insert hospital address]

Declaration by Participant

I wish to withdraw from participation in the above research study and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with the **[insert hospital name]**.

❑ **I do not want to continue in the study (main and sub-study):**

Check ☒ all that are applicable:

☐ I agree to be contacted by telephone if required after my withdrawal from the study.

☐ I agree that my Study Doctor collects information regarding study related health from available sources, such as medical records.

For a participant wishing to withdraw from a Sub-study only but remain in the main study:

I do not want to continue in the sub-study and hereby withdraw my consent to participate in the sub study:

☐ Sub-study 1 ☐ Sub-study 2 ☐ Sub-study 3

Participant Name (please print): ……

Signature: …… Date: ……

Study Doctor Name (please print): ……

Signature: …… Date: ……

Declaration by Study Doctor

I have given a verbal explanation of the implications of withdrawal from the research study and I believe that the participant has understood that explanation.

Note: All parties signing the consent section must date their own signature.