Improved Novel VaccIne CombinaTion InflUenza Study
SUB-COHORT
VOLUNTEER INFORMATION LEAFLET

We would like to invite you to take part in INVICTUS.
Before you decide if you would like to take part it is important that you understand why we are doing this research and what it would involve for you.

Please take time to read the following information carefully and decide if you wish to take part.

You may like to talk to others, friends or family members, about the trial. Please ask if there is anything that is not clear or if you would like more information.

EudraCT number:2017-001103-77

INVICTUS
Improved Novel VaccIne CombinaTion inflUenza Study

What is the purpose of the trial?

Flu and older adults

Flu is a commonly used term that refers to different influenza viruses and strains that are highly infectious. Flu occurs every year and can affect anyone.
However, some groups of people are more likely to get it, and may feel more unwell, if they do. One of these groups are older adults. In this age group, current vaccines are less effective than for other at risk groups. And so as the need for a new vaccine that is effective is much higher in this group, we will be recruiting adults 65 years and over to test the INVICTUS trial vaccine.

Current Vaccine

Existing flu vaccines use 'surface proteins' from the outside of the flu virus that stimulate your immune system to produce antibodies. These antibodies protect you from getting sick with the strain of flu virus or viruses whose 'surface proteins' you were injected with.

As the seasonal flu virus changes its 'surface proteins', the flu vaccine needs to change too. This is so your body receives the new surface proteins and is able to produce the relevant antibodies that will protect you from the changed flu virus.

This means that with the current vaccine you are only protected against the flu virus(es) your body has antibodies for.

The current vaccine, given before the flu season starts, is based on a prediction of the strain of flu that will be circulating for that flu season.

Trial Vaccine

The trial flu vaccine consists of two proteins from the 'core proteins' of the flu virus and a vaccine delivery system. This new vaccine stimulates a different part of your immune system called T - cells. We have found from previous research studies that **T cells fight flu viruses that your body has no antibodies for** and can reduce the severity of your symptoms as well as the time you have been experiencing them.

So even if you did get a flu virus you do not have antibodies for, the trial vaccine could still offer you protection from severe illness.

Also, as the 'core proteins' of the flu virus(es) **remain virtually unchanged every flu season**, the immune response your body elicits upon receiving the trial vaccine might be able to better protect you from many different flu strains even if they do change their 'surface proteins' periodically.

Aim

In previous studies, we have tested the trial vaccine as well as the combination of the trial vaccine with the existing flu vaccine and have found that the participants that received both had a stronger immune response.

So, the purpose of this trial is to find out whether the combination of the trial flu vaccine together with the existing flu vaccine will:

a. better protect older adults from flu-like illness
b. reduce the severity and duration of flu-like symptoms
than the current flu vaccine alone.

The INVICTUS study will be the first time the vaccine has been investigated in a clinical population.

Can I take part?

To take part you need to be aged 65 and over and be eligible to receive the flu vaccine.

Do I have to take part?

Participation is entirely voluntary. It is up to you to decide to take part in the trial or not.

What will happen if I do not want to continue with the trial?

If you decide to take part, you can still withdraw at any time without giving a reason. Information collected up to that point may still be used.

The decision to leave or not take part will not affect the standard of care you receive from your surgery in any way, now or in the future.

If you wish to withdraw from the study, please contact the trial team using the contact details on page 13.

What will happen to me if I take part?

Screening Visit

We will book you in for a screening visit where an Investigator (a doctor or nurse) will go through the information sheet with you and answer any questions that you may have .

You will be asked to sign a consent form

With your consent we will contact your GP to inform them that you are taking part in the trial and to ask if there are any medical reasons why you should not take part.

Vaccination Visit:

On the day of vaccination, we will check that there have been no changes in your health since your screening visit and take your temperature.

We will take a blood sample

You will be randomly allocated to receive either:

· The standard flu vaccine + the trial vaccine

· The standard flu vaccine + saline (placebo)

Follow-up: After your appointment

You will complete a diary for 7 days telling us about any symptoms you might be experiencing and how the injection site is healing.

We will book you in for an appointment a week after the vaccination and we will take another blood sample.

We will contact you on days 1-3 and 7-9 to see how you are getting on with your diary. You will continue to report any symptoms for 3 weeks after completing your Week 1 Diary

Follow-up: Flu Season

If you have any flu-like symptoms at any point throughout the winter, you will fill in a Flu Symptoms diary telling us how you feel.
We will contact you to remind you about this via text and/or email according to your preference. We will also call you periodically to make sure follow-up is going well.

Follow-up: Further appointments

You will have three more appointments: 7 days, 3 weeks and 26 weeks after your first appointment. At these appointments we will check how you are feeling and take blood samples.

What will happen to me if I take part? More details.

If you are interested in taking part, you will first need to attend a screening visit. When you come for the visit, you will be met by a member of the trial team who will ensure you understand what to expect by taking part, the risks involved and what side effects you may experience. We will provide answers to any questions you may have so you can make an informed decision about entering the study or not. We will take your temperature and ask you to sign a consent form. The screening visit usually takes between 60 and 90 minutes and will be arranged at a time that is convenient to you.

Once your screening visit is complete and it is confirmed that you are eligible to take part, we will make an appointment for you to receive your vaccination.

At the vaccination appointment:

- We will check that there have been no changes in your health since the screening appointment
- We will take your temperature.
- We will take a blood sample
- You will then be **randomised*** to either:
  - the **trial treatment**: the trial vaccine and the seasonal flu vaccine or,
  - the **control treatment:** the placebo saline (salt water) vaccine and the seasonal flu vaccine. Both injections will be given into one of your arms.
- The injection area will be covered with a sterile dressing for at least 10 minutes.
- As this new vaccine is an investigational product, which has been developed using a weakened modified virus, staff administering the vaccine will be required to use standard protective equipment (gloves, apron and goggles) in order to comply with current regulations.

***Randomised means that you will have an equal chance of receiving either treatments. You will not be able to choose the treatment you prefer.**

- You will be given a thermometer and a tape measure (to measure the extent of redness of the site) to take away so you can monitor your temperature and any redness at the injection site in the following 7 days after the vaccination.
- You will be asked to record your symptoms on a web-based diary that you can access from a mobile phone, tablet or computer. We will give you some paper versions to use as a back up (e.g. if you are on holiday and do not have internet coverage).

The entire visit will take between 50-60 minutes on average.

Follow-Up

The trial team will be in touch regularly and an out of hours number will be available (See Page 13) for Contact Information).

- **Week 1-4 Diary**

You will be asked to record any symptoms you may experience and your temperature daily for 7 days after the vaccination. Day 0 is the day of vaccination.

Completing your diary takes just a few minutes per day. After the first week, you will continue to tell us about any ongoing symptoms or anything unusual after your vaccination for the following 3 weeks.

- **Daily Diary & Flu Symptoms Diaries**

Once the flu season begins (1st of November) and until the end of April, you will have to record whether or not you have had flu-like symptoms in your daily diary.

If you start having any flu-like symptoms, you will have to keep a daily record of your temperature, the symptoms and any medication you are taking to treat them, in your Flu Symptoms Diary. You will continue to record the above until you feel completely better.

Detailed instructions on how to fill in your diaries can be found in the Frequently Asked Questions document you will receive at your appointment.

Follow-up Appointments

You will attend further visits at week 1, week 3 and week 26 after your first appointment. We will ask you about how your health has been since we last saw you and take another blood sample at each of these visits.

Reminders

A trial team member will call you twice during the first 7 days to ask about your symptoms. We will also be calling you every 3-4 weeks during the flu season to make sure all is well with completing your diaries and see if you have had any flu-like symptoms.

You will also be given the opportunity to choose to have a reminder sent to you either daily or weekly via text message or email.

What are the possible disadvantages or side effects of taking part?

With any vaccine, including licensed ones, there is a rare risk of serious reactions. These may be related to the immune system, like allergic reactions. Severe allergic reactions to vaccines are rare but can be fatal.

The investigators are trained in treating allergic reactions and will have the appropriate medication available in the clinic room. We also keep you in the clinic for at least 10 minutes after vaccination as severe allergic reactions happen soon after vaccination.

Reactions in the nervous system are also extremely rare, but can cause an illness called Guillain-Barré syndrome. This is a condition in which people can develop severe weakness and can be fatal.

These symptoms have not been seen in other people who have received the trial vaccine.

Side effects of the trial vaccine

- The most common side effect is discomfort at the site of vaccination. This discomfort can last for a few days and is experienced by most peo-

ple. The vaccination site may also become red and swollen but this usually subsides within 2-3 days.

- In the first 1-2 days after vaccination, most people have some general symptoms such as tiredness, headache, feeling hot, muscle and/or joint aches. These are usually mild and resolve by themselves.

With any new treatment there is always a possibility of an unexpected side effect. If you experience unexpected events or become in any way concerned you can contact one of the trial doctors (See Page 13 for contact details). We will ask you to record these symptoms too.

What are the possible benefits of taking part?

By taking part in this trial, there is the possibility that the trial combination of vaccines may give you better protection against the flu over this winter season. However, we will not know if this is the case until after the trial is finished. You will also be contributing towards the development of a new treatment that may help protect your peers from getting the flu or minimise the duration and severity of symptoms if they did fall ill.

Expenses and Payments

You will be reimbursed for your participation through gift vouchers. You will receive the first voucher (£15) at the end of the vaccination visit and the second voucher (£15) via post at the end of the follow-up period.

You will be compensated for your time, the inconvenience of having blood tests and your travel expenses. The total amount of compensation received will be approximately £190-215 depending on the exact number of visits and whether any repeat or additional visits are necessary.

What if there are any problems?

The investigators recognise the important contribution that volunteers make to medical research and will make every effort to ensure your safety and wellbeing.

If you have any questions about this trial, please contact the Trial Manager (See Page 13 for contact details).

If you have a concern about any aspect of this trial or wish to complain about any aspect of the way in which you have been approached or treated during the course of this trial, you should firstly contact the Trial team (See Page 13 for contact details).

Alternatively, you may contact Vaccitech (See Page 13 for contact details). Vaccitech has arrangements in place for any harm arising from participation in the study.

What will happen to any samples I give?

If you consent, some of your leftover blood samples will be stored and may be used for further studies of the human body's immune response and/or the vaccines used in this study, and/or your safety. Any such tests will have an appropriate ethical review. Upon your request at any time, your remaining blood samples will be destroyed. Your participation in this study will not be affected by your decision whether to allow storage and future use of your leftover samples.

Your study visit blood tests will be analysed in the hospital laboratories and Oxford University research laboratories. Other blood tests to look at the response of your body to the vaccine may be done with collaborating laboratories in the UK and in other countries. Any samples or data sent to them would be anonymous.

Will any genetic tests be done?

We may do genetic tests on your blood samples to look at the patterns of genes that regulate your own individual immune response (these are called Human Leukocyte Antigen genes). Doing this helps us to work out which aspects of the immune response to vaccines are due to genetic differences between individuals. We may also look at the expression of certain genes which relate specifically to the immune response to flu, but no genetic tests concerning diseases or conditions other than Flu. You can opt out of 'genetic

tests' if you wish, without any effect on your participation in the trial.

Will my participation be kept confidential?

Your personal information will be kept strictly confidential. Neither your individual results nor you would be identified in any report or publication.

Yes. All data will be kept according to the Data Protection Act 1998. The contact details that you provide will be kept securely in a restricted access location within the Clinical Trials Unit, Department of Primary Care Health Sciences, University of Oxford. Access will be granted only to appropriate members of the trial research team.

The information you provide at the vaccination appointment and follow-up will be coded with a trial identification number so you cannot be identified from it by anyone other than the research team. Responsible members of the University of Oxford, the NHS Trust, the Medicines and Healthcare products Regulatory Agency (MHRA) and Vaccitech may be given access to anonymous data for monitoring and/or audit of the trial to ensure we are complying with regulations.

With your permission your GP will be informed about your participation.

What if relevant new information becomes available during the trial?

Sometimes during the course of a research project, new information becomes available about the treatment that is studied.

If this happens, the trial team will tell you about it and discuss with you whether you want to continue in the trial or not.

If you decide to continue you would be asked to sign an updated consent form.

What will happen to the results of the trial?

We will use the information collected through INVICTUS to apply for a new license for the trial vaccine. We may publish the results in medical journals and present them at scientific meetings.

Who is organising and funding the research?

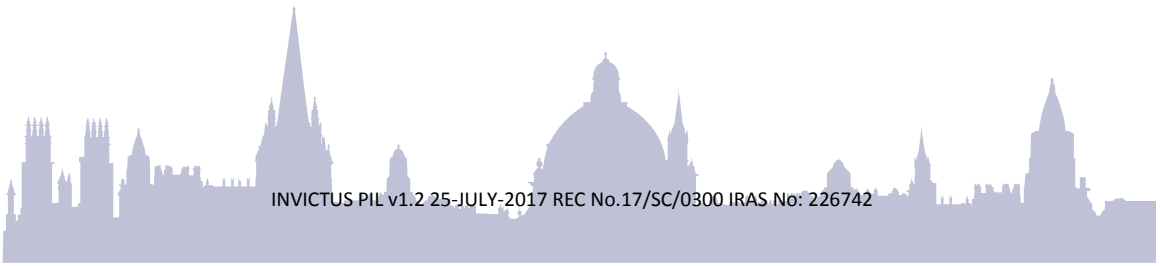
Funding has been provided by Vaccitech, a spin-out company of the University of Oxford.

INVICTUS has been set up by the Primary Care Clinical Trials Unit and the Jenner Institute of the University of Oxford.

Who has reviewed the trial?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee (REC). The REC is there to protect your safety, rights, wellbeing and dignity. This trial has been ethically reviewed and was approved by the South Central Berkshire Research Ethics Committee A.

This trial has also received approval from the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA regulates the use of all medicines in the UK and has granted permission to use the combination of the existing flu vaccine and the trial vaccine in this clinical trial.



Thank you for taking the time to read this information leaflet and considering taking part in this study.

If you would like any further information about this trial, you can contact the trial team here:

Trial Team Doctor 24/7:

Tel.: 01865 818805

Trial Address:

INVICTUS Trial
Nuffield Department of Primary Care Health Sciences
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Radcliffe Observatory Quarter-
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