Bristol Vaccine Centre
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Participant Information Sheet (12-15 years): Com-COV3

Comparing COVID-19 Vaccine Schedule Combinations in adolescents

A single-blind, randomised, phase II multi-centre study to determine reactogenicity and immunogenicity of heterologous prime/boost COVID-19 vaccine schedules in adolescents

An update on the Com-COV3 study

Thank you very much for taking part in the Com-COV3 study.
This section tells you some new information about what is happening in the study.

(a) A new part to the study

We plan to add a new part (or "cohort") to the study. Your part of the study will be called Cohort A. The new part will be called Cohort B.

The aim of this new part of the study (Cohort B) will be to look at the options for a third dose of COVID-19 vaccine in young people. We aim to recruit 380 participants aged 12 to 15½ years, who have already received two standard doses of Pfizer vaccine in the community. They will be allocated to 5 groups, each of which will be given a different vaccine schedule. We will be using the same vaccines as in the first part of the study (Pfizer and Novavax). As well as looking at responses to the full adult dose of these vaccines, we will also be looking at responses to a lower dose of the Pfizer vaccine given in two different ways.

We hope to start enrolling participants to the new part of the study in May or June 2022.

(b) Recruitment to the first part of the study (Cohort A)

Following advice from Trial Steering Committee, it has been decided not to recruit any more participants to the original part of study. This decision was influenced by the announcement of the Joint Committee on Vaccination and immunisation (JCVI) that all 12 to 15 year-olds would be offered a second dose of Pfizer vaccine.

You have already enrolled in the study and may continue with your remaining visits, as planned.

(c) Results of the first part of the study (Cohort A)

We are analysing information from blood tests and study diaries from participants in the first part of the study. The results are being prepared for publication.

Please note that the rest of this information sheet is unchanged from the previous version.

Some background information

1. What are vaccines?

Vaccines are medicines which are injected to prevent you from becoming unwell from certain diseases. They also help to stop you spreading disease to your friends and family. They protect you and those around you.

2. What is COVID-19?

COVID-19 is a new disease, which since early 2020 has spread around the world. It has caused many deaths and has made many more people seriously unwell.

COVID-19 vaccines that have been shown to work are now being used. They are helping to prevent people from becoming seriously ill or dying from the disease. They also reduce the chance of people spreading the infection to others.

In this country, most adults have now been vaccinated against COVID-19. Older people are much more likely to be seriously ill from COVID-19 than young people. However, children and teenagers do occasionally become very unwell if they catch the disease.

It was announced on 29th November 2021 that all 12 to 15 year-olds in this country will be offered two doses of a COVID-19 vaccine. Immunisation of adolescents against COVID-19 is also occurring in some other countries such as the USA, Australia and Israel.

What is the purpose of this research study?

The purpose of our study is to find out how well young people (aged 12-16 years) respond to two doses of COVID-19 vaccine.

When we designed the study we wanted to find out if using different vaccines for the first and second dose was as good as using the same vaccine for both doses. We knew that in adults some combinations of vaccines worked well and wanted to find out if the same was true for younger people.

At the start of the study there were three different options being studied for the second dose including a COVID vaccine produced by Novavax. However following the JCVI recommendation on 29th November 2021 that all 12 to 15 year olds should be offered a second dose of the Pfizer vaccine, the study design has been amended to focus on different options for the Pfizer vaccine. This was not done because of any concern regarding the safety of the Novavax vaccine in this or other studies.

We want to find out if using different vaccines for the first and second dose is as good as using the same vaccine for both doses. We know that in adults some combinations of vaccines work well. We want to find out if the same is true in younger people.

We are interested in looking to see how well young people respond to smaller doses of the standard adult dose of the Pfizer vaccine. We know that one-third of the standard adult dose of Pfizer vaccine works well in children aged 5 to 11 years. We would like to know if the same is true in adolescents.

If smaller doses and different combinations of vaccine can be used, this could help to vaccinate more people with the available vaccine supplies. It could also help to minimise the unwanted side-effects of vaccination.

Our study will also be trying to find out whether young people who have previously had COVID-19 infection respond differently to the vaccines than people who have not been infected.

If you take part in our study, we will look at how your body responds to vaccination. One way in which we do this is to ask you to fill in a diary, where you record any symptoms you may have after the vaccine. If, for example, you have a sore arm, a temperature or a headache, you will record this in the diary. Another way is to test your blood. Your blood contains antibodies and white blood cells, which help your body to resist infections. We will take a blood test each time you visit us. The blood will be sent to a laboratory for special tests which show how well your body can resist COVID-19 infection.

What happens in the study?

We initially designed our study to look at three different possibilities for the second vaccine dose: a standard or lower (one-third) dose of Pfizer vaccine or a standard dose of Novavax vaccine. However, since starting this study, the national guidance has changed and it is now recommended that young people aged 12-16 years should receive two doses of Pfizer vaccine. As a result, we have changed what happens in the study.

The following information applies if you haven't yet had your second COVID-19 vaccine:

We will look at two possibilities for the second vaccination. The standard dose of Pfizer vaccine will be given for the first vaccination. The second vaccination, given 8 weeks after the first, will be one of the following:

1. Standard dose of Pfizer vaccine
2. One-third standard dose of Pfizer vaccine

There is an equal change (50%) of receiving one of these two vaccine options as the second dose.

The following information applies to you if you have already had your second COVID-19 vaccine:

We will look at three possibilities for the second vaccination. The standard dose of Pfizer vaccine will be given for the first vaccination. The second vaccination, given 8 weeks after the first, will be one of the following:

1. Standard dose of Pfizer vaccine
2. One-third standard dose of Pfizer vaccine

3. Novavax vaccine

There is an equal chance (one-third) of receiving one of these three vaccine options as the second dose.

Can I take part in the study?

Not everyone can take part. For example, if you have certain health conditions you are not able to participate. This is for safety, and also to make sure that the results we obtain are reliable. Your parent/ legal guardian can fill in a short online questionnaire to see if you would be suitable for this study.

What happens if I do want to take part?

If you decide to take part, we will ask you to visit us up to six times over the period of one year. The visits will be arranged to take place outside of school hours. The visits will take place at the Clinical Research Facility at 60 St Michael´s Hill, Bristol, BS2 8DX.

At the **first visit**, we will make sure you are happy to be in the study. We will answer any questions you want to ask about it. We will ask your parent/legal guardian to sign a consent form and will ask you to sign an assent form.

We will check your temperature, height, weight and briefly examine you to make sure that you are well enough to have the vaccine.

If you are a girl, we will ask you to give us a urine sample to check you are not pregnant. We must do this before giving you a new vaccine (one reason for this is that pregnancy may affect the results of the study). Anyone who could possibly be pregnant (considered to be any female aged 12 and above) must provide a urine sample to check before they receive the vaccination. All female participants who have started their periods must make sure they do not become pregnant while they are in the study.

We will take a blood test. This can sometimes be uncomfortable, but we can give you some cream or spray to help numb your skin first, if you want. Having a blood test can make some people nervous, but it can help if they have something fun to distract them, such as listening to music or reading.

We will be taking samples of fluid from the nose and saliva from some children in this study. You do not have to give these samples, it is up to you. We will discuss what it involves when we see you. If you decide to let us take these samples, we will do so at the first three visits.

We will give you a dose of vaccine (into your arm). Like the blood test, this can also be a bit uncomfortable for a short while.

We will give you a diary to record your symptoms and explain how to use it. We will also give you a thermometer and tape measure. We will want you to record symptoms such as pain, redness or swelling where you had the injection, and also more general symptoms, such as fever, headache or diarrhoea. Not everyone has symptoms after a vaccination.

If you have already had your first dose of a COVID-19 vaccine in the community, at the first visit the study team may only ask you to have a medical check-up and for you and your parent/legal guardian to sign a consent form. Alternatively, we may arrange for both the "first" and "next" visits to happen on the same day.

At the **next visit,** you will have the second dose of vaccine. This will be at about 8 weeks after your first COVID-19 vaccine dose, whether this was given in the community or in our study. We will take a blood test before this second vaccine. For girls, we will check a urine pregnancy test. We will decide which sort of vaccine you will be given for your second dose. This is done in a way that relies on chance. You will not be able to choose the vaccine, nor will your parent/legal guardian.

We will ask you to record your symptoms in the diary after this second dose of vaccine.

At the **rest of the visits**, you will only have a blood test and brief health check. (Saliva and nasal fluid samples will be taken at the third visit if you have agreed to this). These will be arranged at about 2 weeks, 4 weeks, 4 months and 7 months after your second COVID-19 vaccination.

What if I change my mind?

Taking part in research is entirely **your** choice. You are free to change your mind at any time. You can decide to stop being in the study, even if your parent/legal guardian thinks you should continue.

What are the disadvantages of being in the study?

After the blood test and/or vaccine, your arm may be sore and you may have a bruise.

Vaccines, like all medicines, can sometimes cause unwanted side-effects. Usually these are a minor nuisance (like a sore arm) and they disappear within a few days. Very occasionally the side-effects can be much more serious.

Common side-effects after vaccination include pain, redness and swelling where the injection has been given. Other common side effects include: tiredness; headache; aches in joints and muscles; feeling sick; vomiting.

We now know that the Pfizer-BioNTech vaccine can, extremely rarely, cause a serious condition called myocarditis (inflammation of the heart muscle). It seems that this is more likely to occur in boys and young men shortly after their second dose of the vaccine (but, even then, it is very rare).

The Novavax vaccine is currently only used in medical studies. It is not routinely used for the general public. Because it has been used in fewer people, we know less about the very rare side-effects it might cause than we do about the Pfizer-BioNTech vaccine.

What are the advantages of being in the study?

In this country since 29th November 2021, healthy young people aged 12 to 15 years have been advised to receive two doses of a COVID-19 vaccine. By taking part in this study, you will still receive two doses of COVID-19 vaccine. However, you will be able to receive your second vaccine 8 weeks after your first dose instead of having to wait 12 weeks like other people your age. This is likely to mean that you are better protected against the disease than if you were unvaccinated. You may also be less likely to pass the infection on to people around you. However, you should remember that vaccination doesn't guarantee that you will be protected from COVID-19; you should continue to take care to protect yourself.

By taking part in this study, you would be helping us to learn more about how well young people respond to standard and lower doses of the Pfizer vaccine and which vaccine combinations work best in young people. The results might help to guide future decisions about how best to use vaccines in children and young adults.

I want to be part of this study, what should I do?

If you want to take part in this study, then let your parent/legal guardian know and they will get in touch with us.

Remember that taking part in the study is up to you. Even if your parents want you to take part, you can say no if you don't want to be in the study.

Thank you for thinking about helping us.