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Draft information sheet (to be translated and distributed before screening)

A PHASE IIIbCOMPARATIVE TRIAL OF SEASONAL VACCINATION WITH THE MALARIA VACCINE RTS,S/AS01, SEASONAL MALARIA CHEMOPREVENTION AND OF THE TWO INTERVENTIONS COMBINED.

Information Sheet

Introduction

Malaria is a serious problem in Burkina Faso/Mali and affects mainly children. Malaria is spread by mosquitoes and can be partially prevented by sleeping under a mosquito net that incorporates an insecticide that kills mosquitoes, an ITN. All children should be encouraged to sleep under an ITN. However, ITNs are not perfect and some children who sleep under an ITN still get malaria.

Malaria can also be prevented by taking drugs. Research conducted in several countries in Africa, including Burkina Faso and Mali, has shown that when children take antimalarial medicines three or four times during the rainy season, they gain at least 50% protection against malaria even if they are already sleeping under an ITN. Therefore, the World Health Organisation now recommends that all children under the age of five years living in countries like Burkina Faso and Mali, where malaria occurs mainly in the short rainy season, should be given a combination of two antimalarial medicines (SP and amodiaquine) three or four times during the rainy season to prevent malaria, even if they are well. This is called seasonal malaria chemoprevention (SMC) which you probably know about.

Recently, a study conducted in several countries in Africa showed that three doses of a malaria vaccine called RTS,S/AS01 given to 5-17 month old children, provided about 30% protection against malaria during the four years after vaccination. Protection was much higher (about 70%) in the first few months after vaccination but after that, the vaccine gradually lost its effect. Children who received a booster dose of the vaccine when they were 18 months old had more protection than those who did not. The malaria vaccine caused some side effects, so WHO has recommended further testing of this vaccine in children before it is introduced into the regular vaccination programmes. We propose to investigate whether the vaccine could be used to prevent seasonal malaria in countries, such as Burkina Faso and Mali, where malaria occurs during only a few months of the year.

Giving three doses of SP+AQ four times every year requires a lot of time and effort from the caretakers and health care providers. In addition, malaria parasite may become resistant to SP+AQ in few years time and then SMC with SP+AQ would become ineffective because these drugs no longer kill the malaria parasite. In contrast, seasonal vaccination with a malaria vaccine would require only one visit just before the rainy season and would be less demanding for children and their parents. Therefore, we are planning to do a study of these two possible ways of protecting children from malaria and to see which is best and whether

using both approaches together might provide some extra protection against malaria. We need your help in addressing these important questions.

The trial

If you agree that your child can join the trial, your child will be allocated to one of the three study groups by lottery.

Group 1. In year one of the study, children in group 1 will receive 3 doses of the malaria vaccine and 4 rounds of dummy tablets that look like SP+AQ. In years 2 and 3 of the study, children in this group will receive one dose of the malaria vaccine and 4 rounds of dummy tablets that look like SP+AQ.

Group 2. In year one of the study children in group 2 will receive 3 doses of a vaccine that protects against rabies and 4 rounds of SP+AQ. In years 2 and 3 of the study, children in this group will receive 1 dose of hepatitis A vaccine that can protect against jaundice and 4 rounds of SP+AQ

Group 3. In year one of the study children in group 3 will receive 3 doses of the malaria vaccine and 4 rounds of SP+AQ. In years 2 and 3 children in this group will receive one dose of the malaria vaccine and 4 rounds of SP+AQ.

Your child will be eligible to receive any other vaccines appropriate for their age recommended by the national EPI programme.

Druing year one of the study you will be asked to bring your child to a study health centre once a month for three months (from April to June in 2017) to receive the study vaccines. In addition, during the rainy season you will be asked to bring your child to a central place in the village on four occasions, at monthly intervals, where the children will be given either SP and AQ or matching dummy tablets depending on their study group.

In years 2 and 3 of the study you will be asked to bring your child once, in June, to receive either the malaria vaccine or a vaccine against hepatitis A depending on the group of your child. Then you will need to bring your child to a central place in the village four times during the rainy season each year to receive SP+AQ or dummy tablets.

To test whether the tablets and the vaccine are having a good effect against malaria and other severe illnesses and are safe, children in the trial will be investigated for malaria and other illnesses when they attend a clinic because they are sick. Some children will be visited at home to check if they have malaria and all children will be examined at the end of the rainy season each year to check for malaria.

The funds needed to conduct this trial are being provided by a grant from the UK's Medical Research Council, Department for International Development and the Wellcome Trust. The IRSS, Bobo, and Malaria Research and Training Centre, Bamako working with the London School of Hygiene & Tropical Medicine are responsible for the conduct of the trial.

What happens if your child becomes sick?

If your child becomes sick you will be asked to take him/her to a local clinic and show the nurse or doctor your vaccination card. He/she will examine your child to find out what is wrong with him/her and treat the child with the correct medicines. As part of the examination, few drops of blood sample will be collected by pricking the child's finger to see if the child has malaria parasites in the blood or is anaemic (thinning of blood). A sample of blood on paper will be stored to test whether the malaria parasites in your community are still sensitive to the drugs used for SMC. If the child has either malaria or anaemia s/he will be given effective treatment against these conditions. Any child with a severe illness will be referred to hospital and receive appropriate treatment, for example investigation and treatment of meningitis, according to national guidelines.

Will my child be followed up in other ways?

Malaria can be present without making a person feel sick. Therefore, 90 children will be visited at home each month to check if they have malaria by testing a drop of blood even if they are feeling well. In addition, all children will be asked to attend a survey at the end of the rainy season. During these surveys, all children will be examined by a doctor and a finger prick blood sample will be collected to see if malaria parasites are present or if the child is anaemic. If either is found, the child will be treated with effective antimalarial medicines and/or medicines that treat anaemia.

In addition, a sub-group of about 160 children will be selected through a lottery to help us in determining how well the vaccine is producing changes in the blood that provide protection against malaria. In these children, a teaspoonful (2 ml) of blood will be taken from a vein, using a small needle, twice each year. In year 1, a sample will be taken before the first dose of the vacccine is given and then one month after the third dose of vaccine is given. In years 2 and 3, a teaspoonful of blood will be taken from these children before and one month after a booster dose of vaccine is given.

Are the drugs and vaccines that will be given to my child safe?

Both of the antimalarial drugs that will be given to your child are very safe and are recommended by WHO for the prevention of malaria in children, although they may occasionally cause some minor side effects such as dizziness and vomiting and, very rarely, SP can cause a serious skin rash.

Like nearly all vaccines, the malaria, rabies and hepatitis vaccines that will be used in this study may sometimes cause redness, pain and swelling at the site of the injection and some fever. A few children, about 1 per 1,000, who received the malaria vaccine developed a convulsion associated with fever after their injection but all these children recovered rapidly and none had any permanent harm. In a large trial of the malaria vaccine a few more children than expected developed meningitis (brain fever) – it is not known whether this was a chance finding or related in some way to the vaccine. Therefore, we will follow carefully each child to detect any such cases and treat them promptly. The rabies and hepatitis A vaccines that will be given to children who do not receive the malaria vaccine are licensed vaccines which only very rarely cause serious side effects, such as an allergic reaction to the vaccine, (less than 1:1,000 children vaccinated).

What will happen to the information collected during the trial?

Personal information obtained about children in the trial will be available only to the team of scientists involved in conducting the research, including some who are based in Europe. Once the results of the trial have been obtained, a member of the research team will come to your community and explain what was found. Once the trial is finished, information about how the drugs and vaccines affected the health of children who have participated in the trial, for example how many got malaria, may be made available to other scientists interested in the results who have obtained approval to look at this information but these scientists will not be able to identify your child becaue all personal information that could be used to identify your child will be removed when sharing data with other scientists.

What will happen to the blood samples collected during the trial?

The blood will be used to measure how your child responds to the malaria vaccines and drugs. It will also be used in tests to learn more about the parasites that are causing malaria. Any remaining blood samples left after doing these tests will be stored in a repository and might be used to carry out tests against other infections as well as malaria in the future, if a good reason for doing this occurs.

What happens if I decide that my child should not join the trial?

You are completely free to decide if you would like your child to be join this trial or not. If you agree initially that your children can join the trial, you are free to withdraw him/her from the trial at any time if you wish to do so. If you decide not to let your child join the trial, s/he will continue to receive all the treatment and routine vaccinations that your child is eligible to receive, including SMC.

Will I receive payment for allowing my child to enter the trial?

You will not receive any direct payment for allowing your child to enter the trial. However, if your child becomes sick and needs treatment the costs of this, either in the health centre or hospital, will be met by the study and you will not have to pay for these expesnses.

What happens after the trial?

After the trial is over your child should continue to receive the antimalarial drugs SP and AQ during the rainy season from the National Malaria Control programme as this is now national policy. The Ministry of Health and WHO will be asked to review the results of the trial and on the basis of these results decide what is the best way of preventing malaria in children in your area and whether this should include the use of the malaria vaccine being tested in this study.

Further questions

Do you have any questions about the trial? If you want more information now or at any time during the trial please contact [To follow with contact telephone numbers]

CONSENT FORM
(to be adapted at each site)

A COMPARATIVE TRIAL OF SEASONAL VACCINATION WITH THE MALARIA VACCINE RTS,S/AS01, SEASONAL MALARIA CHEMOPREVENTION AND OF THE TWO INTERVENTIONS COMBINED.

I confirm that the nature of this study on the malaria vaccine RTSS and seasonal malaria prevention with SP and amodiaquine has been explained to me in a language that I understand, that I have had an opportunity to consider this information, to ask questions and to have these answered to my satisfaction.

I understand that I am under no obligation to enter my child into the trial and that if I do not do so, my child will not be penalised in any way. I understand that I can withdraw my child from the trial at any time if I wish to do so without a penalty of any kind.

I understand that my child will receive 3 doses of either the malaria vaccine or rabies vaccine in year one of the study and one dose of the malaria vaccine or hepatitis A vaccine in years 2 and 3. In addition my child will receive antimalarial treatment (SP+AQ) or similar looking dummy tablets that do not contain any medicines against malaria, on four occasions during the malaria season over the three year study period. I also understand that it will be necessary to take a small, finger-prick blood sample from my child once a year at the end of the rainy season and whenever the child is sick and brought to a clinic to see if your child has malaria or anaemia even though s/he seems to be well. In addition about 160 children selected by lottery will be asked to provide a small blood sample (a teaspoonful) before and after vaccination each year (a total of six samples) to see whether the vaccine has led to the production of substances in the blood that protect against malaria and to learn more about what causes malaria and I understand that my child might be one of those selected.

I understand that the information collected about my child will be available only to the medical staff who are undertaking the trial and to doctors in London who are co-ordinating this study. I understand that once the trial is finished, information about children who have participated in the trial may be made available to other scientists interested in the results who have obtained approval to do so, but these scientists will not be able to identify your child.

I agree that my child [NAME] can enter this study on new ways of preventing malaria.

Printed name of the parent or legal guardian giving consent:

Signature or thumbprint of the above:

Date:

I certify that the nature of this trial has been explained to the respondent in a language that s/he understands, that s/he has been given an opportunity to ask questions about the study and that s/he has given her/his consent for her/his child to enter the trial.

Printed name of witness:

Signature of witness:

Date:

Chandramohan D, *et al. BMJ Open* 2020; 10:e035433. doi: 10.1136/bmjopen-2019-035433