

## Beta-blockers Or Placebo for Primary Prophylaxis of oesophageal varices (BOPPP Trial).

## Participant Information Sheet (Trial) – Summary

**We invite you to take part in a clinical trial called BOPPP**

- Before you decide if you want to take part, it is important for you to understand why this research is being done, and what it will involve.
- Please take time to read this and to discuss with friends or relatives, if you wish.

## Important things you need to know

- You are entirely free to decide whether to take part or not.
- Deciding not to take part will not affect your care.
- You can stop taking part at any time.
- Support will be given to you throughout the trial.

## Trial Design

- We want to find out if a widely prescribed beta blocker medication will help prevent bleeding of small blood vessels (or varices) in patients with cirrhotic liver disease.
- Participants will be given either a beta-blocker medication or a dummy drug ('placebo') for 3-years.
- We would meet with you every 6 months in line to your routine NHS appointments.
- There are **no additional tests** other than those you will have as routine clinical care.
- Your participation could help future medical treatment in this condition.
- If you are interested in knowing more please read pages 2-8.
- For further information please contact the BOPPP Trial Nurse on <<INSERT DETAILS>.

## Contents

1. Why are we doing this clinical trial?
2. Why have I been invited? Can I say no?
3. What will happen to me if I take part?
4. How many visits are there and how long will it take?
5. Are there any benefits to taking part?
6. Is the treatment safe?
7. What if I am pregnant or want to get pregnant?
8. What happens if my varices progress?
9. What happens when the trial stops?
10. What if new information becomes available?
11. What will happen if I don't want to carry on?
12. Will my details be kept confidential?
13. Linkage to records of hospital procedures.
14. What will happen to the results of the clinical trial?
15. Who is organising this clinical trial?
16. Who has reviewed this clinical trial?
17. What if there is a problem?



# Participant Information Sheet (Trial) – Detailed

## 1. Why are we doing this clinical trial?

- People with long standing liver disease called cirrhosis (scarring of the liver) can develop swelling of veins in the gullet (food pipe) known as ‘oesophageal varices’.
- People with medium or large oesophageal varices have a 1 in 3 chance of these veins bleeding and treatment with beta-blocker medication to prevent bleeding is recommended.
- People with small varices have a lower risk of bleeding but we are not sure whether treating people with beta-blockers helps to prevent bleeding in the future. **This clinical trial will address this important question.**
- We will investigate whether giving a beta-blocker to people with small varices reduces the risk of bleeding.
- Beta-blockers slow down the heart rate and lower blood pressure. The main beta-blockers currently prescribed are Carvedilol and Propranolol. Both of these medications lower pressure in the varices which reduces the risk of bleeding.
- Carvedilol has been used for many years to treat high blood pressure and some forms of heart disease. Research studies have shown Carvedilol is also very effective at lowering the pressure in large varices in the gullet. In addition, is considered more effective than Propranolol at lowering the pressure in the veins (the lower the pressure, the lower the risk of bleeding).
- However, the evidence in people with small varices is lacking – which is why we are conducting the BOPPP trial.
- We will involve 1,200 patients from over 30 hospitals around the United Kingdom.

## 2. Why have I been invited? Can I say no?

- You have been invited because you have liver disease with small oesophageal varices that have not previously bled.
- Can you say no? Yes - it is entirely your decision whether you take part in this trial.
- You will be given time to decide whether or not to take part.
- If you decide to take part, you will be asked to sign a consent form. Your consent form will stay on record in the trial file, be noted in your medical records and a photocopy will be given to you to keep.
- If you decide not to take part, your normal treatment will not be affected in any way and you will continue to be cared for by your normal medical team.

## 3. What will happen to me if I take part?

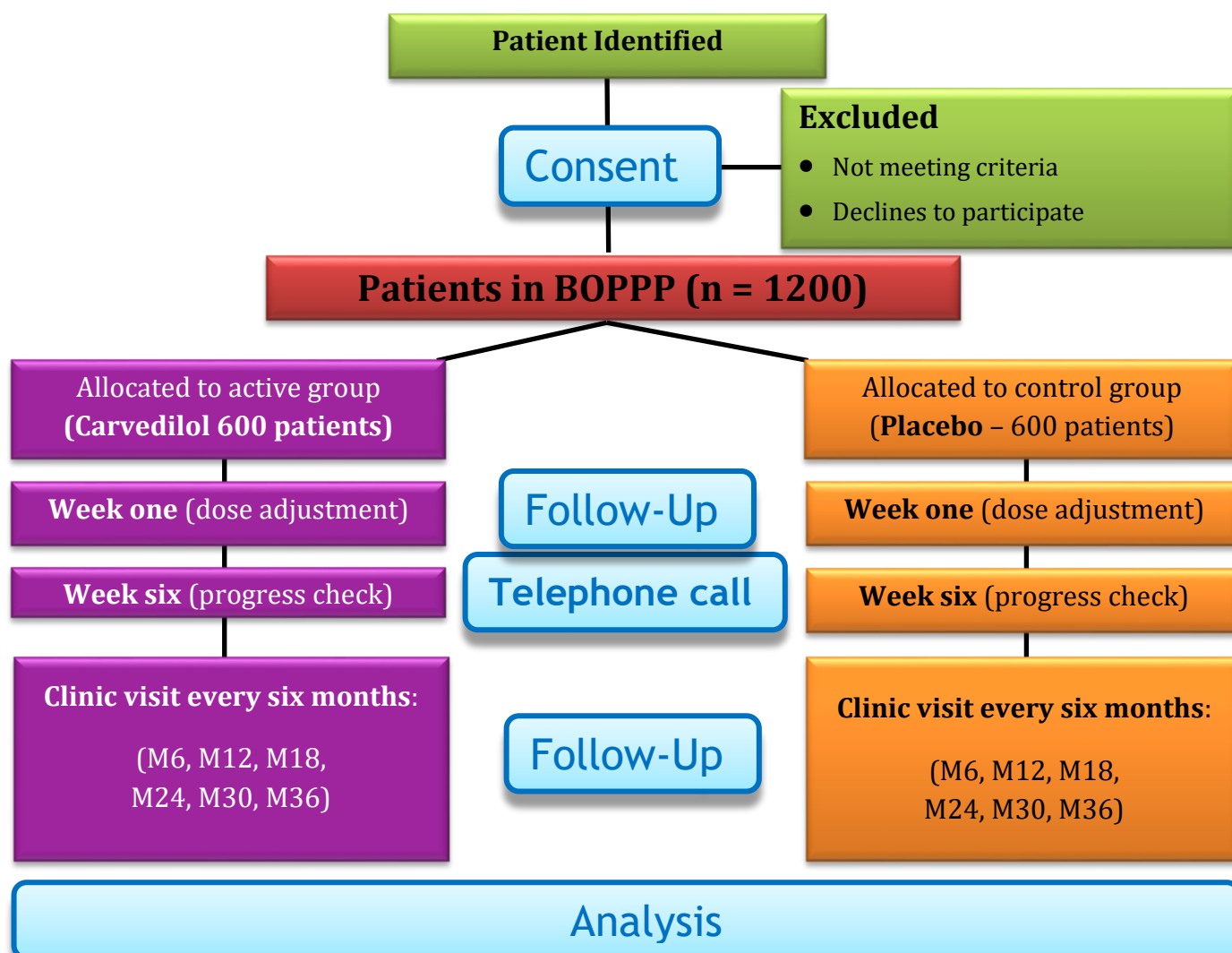
- Sometimes we do not know which treatment is best. To find out, we compare different treatments by putting patients into groups with each receiving a different treatment.
- To ensure the groups are the same to start with, each patient is put into a group by chance i.e. randomly, selected using a computer that has no personal information about the patient.

- One group is called the ‘active’ group and will receive Carvedilol and the other group, called the ‘control’ group, will receive a placebo treatment.
- There is a one in two chance of being allocated to either treatment (like flipping a coin).
- The placebo treatment is a blank (or dummy) treatment and will be made to resemble a Carvedilol tablet. Placebo does not contain any active drug.
- Using a placebo is called a ‘placebo controlled trial’ and ensures that the trial results are reliable by checking that any effects are actually due to the active drug and not influenced by you or your doctor expects to happen.
- Neither you nor the research team nor the medical team will know which treatment you are receiving so this does not influence the trial results. This is called ‘blinding’. However, should we need to know what treatment you are on, there are mechanisms in place to ‘unblind’ if necessary.
- All participants will be followed up at regular intervals and will have various routine tests.
- All of the tests in BOPPP are standard as part of your normal medical care when you have liver disease (cirrhosis).
- There is one research specific measurement which is a Quality of Life questionnaire.
- Trial treatment will be started at a small dose and increased after one week if required.
- You will be supported by a research nurse through your participation in the trial. This will not include conventional clinical care.

#### **4. How many visits are there and how long will it take?**

- Participants will provide informed consent at a “baseline visit” and eligibility will be confirmed. The trial drug will be given to the participant.
- Participants will come to clinic one week after starting the treatment, to adjust the dose of the drug if necessary according to blood pressure and heart rate.
- Participants will receive a telephone call 5 weeks later to check progress.
- After this, participants will be seen in the liver clinic as per usual practice every 6 months to assess well-being and to make sure everything is OK and for routine blood tests.
- Participants will undergo annual endoscopies as part of their routine medical care to assess their varices.
- There are no special life style restrictions needed if you take part in this trial, and other medications should be continued as usual.
- We will supply the trial medication from our Hospital pharmacy for duration of the trial.
- Routine blood samples and an ultrasound scan will be taken at each visit with gastroscopy at yearly intervals.
- These tests are part of your standard medical care so there is no additional burden to participate in BOPPP and are safe.
- Blood samples will not stored for the purposes of BOPPP.

- Your GP will be kept informed of your participation in the trial. By consenting to take part, you will agree to us sharing your progress in the trial with your GP, as needed for your clinical care.
- A summary of the trial schedule is illustrated below.



## 5. Are there any benefits to taking part?

Although there may be no direct benefits to you for taking part in this trial, the results of the trial will lead to the best treatment being offered to prevent bleeding in patients with cirrhosis and small varices in the future.

## 6. Is the treatment safe?

- Carvedilol is a drug that has been used for many years in many different types of patients and conditions, and is well tolerated in the majority of people.
- The safety profile of the drug is well known and as with any drug, there are potential common side effects that might occur in 1 in 10 to 1 in 100 patients:
  - bronchitis, urinary tract infection, anaemia, weight increase, increase in cholesterol, impaired blood glucose control in patients with pre-existing diabetes, depressed

mood, headache, dry eye, low blood pressure, shortness of breath in predisposed patients, low blood pressure causing dizziness, and upset stomach.

- Other less common side effects affecting 1 in 100 to 1 in 1,000 patients include abnormal vision, slow heart rate, fatigue and impotence.
- Serious complications that occur in 1 in 10,000 patients are very rare but include allergic reactions, reductions in white blood cell count, skin reaction and changes in liver enzyme levels.
- Please note:
  - We will carefully monitor any side effects and take action where needed.
  - You can contact the trial team at any time to discuss these problems, should they arise.
  - You will be given a contact phone number for your research site for such issues.
- Should unacceptable side effects develop the treatment will be modified or stopped.
- There is an independent safety committee in place to ensure that possible side effects do not outweigh the potential benefits of the drug and that your safety is paramount.

## 7. Pregnancy

- It is possible that carvedilol may harm an unborn child in pregnant women.
- Pregnant women must therefore not take part in this trial and neither should women who plan to become pregnant during the trial.
- Women who could become pregnant must use barrier contraception during the trial.
- If you find you have become pregnant while taking part, you should immediately tell the research doctor.
- We will need to follow you up during your pregnancy and information about the outcome of your pregnancy will be collected from yours and your baby's medical notes.
- There is no risk to children born to fathers taking this medicine.

## 8. What happens if my varices progress?

- It is possible that your oesophageal varices may grow in size as a natural progression of your liver disease.
- If your varices are confirmed to have grown in size (which could suggest and increase in bleeding), your clinician will withdraw you from the trial and you will return to standard clinical care, which may also involve you being considered for other complementary trials.
- Whilst you would have no further involvement in the BOPPP trial, we would seek your permission to continue to collect information on your progress, by accessing your medical records and via NHS Digital Hospital Episode Statistics (see sections 12 and 13 for further information about how we protect your confidentiality, and data management).

## 9. What happens when the research trial stops?

After the trial finishes, your clinical care will continue to be provided by your medical team (your Consultant and your General Practitioner) using the current standard care for patients with cirrhosis and small oesophageal varices that have not bled.

## 10. What if new information becomes available?

Sometimes we get new information about the treatments being studied. If this happens, your research doctor will tell you and discuss whether you should continue in the trial. If the trial is stopped for any other reason, we will tell you and arrange your continuing care.

## 11. What will happen if I don't want to carry on?

- You can withdraw from the trial at any time without giving a reason. Please contact your research nurse or Principle Investigator using their contact details on the last page.
- However, we would like to keep in contact with you to let us know your progress.
- Information collected until your withdrawal will still be used, unless you ask us not to.

## 12. Will my details be kept confidential?

King's College Hospital NHS Foundation Trust is the sponsor for this trial and based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study. King's College Hospital will act as the data controller for this trial. This means that King's College Hospital is responsible for ensuring your information is stored and used properly. Your research site will keep identifiable information about you **for 15 years after the trial has finished**.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the trial, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information

<https://www.kch.nhs.uk/about/corporate/data-protection>

- 1) Your research site will keep your name and contact details i.e. postcode, confidential and will not pass this information to King's College Hospital or 2) Your research site will keep your name and contact details i.e. postcode, confidential. <<Delete option 1) and the number 2) if King's College Hospital is a trial site.>>
- Your research site will use this information as needed, to contact you about the research trial, and make sure that relevant information about the trial is recorded for your care, and to oversee the quality of the study.
- Your research data will be inserted into a database that is maintained on a secure server at the King's College London Clinical Trials Unit. As such, King's College London will act as a data processor.



- Certain individuals from King's College Hospital, King's College London and regulatory organisations may look at your medical and research records to check the accuracy of the research trial.
- The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.
- There will be an open-access BOPPP trial website <<INSERT DETAILS>> which contains information about the trial. No identifiable personal information will be on this website.
- If you wish to raise a complaint on how we have handled your personal data, you can contact your Data Protection Officer <<INSERT DETAILS>> who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

### 13. Linkage to records of hospital procedures

The NHS collects data on all inpatient, outpatient and emergency care provided by hospitals and funded by the NHS. This data is collected to pay hospitals for the treatments they provide. It is also used for health research purposes and for planning health services. In England, the body that oversees the collection and release of this type of data is NHS Digital, and the data is known as Hospital Episode Statistics or HES. Data for patients can be linked to deaths recorded by the Office for National Statistics (ONS) using Civil Registration Mortality data.

- We would like to ask for your permission to access relevant HES data that might be held about you regarding treatments you have received, and any record of your death.
- HES data will include information about your inpatient, outpatient and emergency care provided by hospitals, such as number of appointments and treatments received. Civil Registration Mortality data includes the date of death and the cause as noted on the certificate.
- HES data does NOT include any observations or notes made by doctors (medical notes). However, we may want to contact your clinician and review the notes related to your liver treatment.
- We will use HES data to estimate the cost of the treatments you have received as a whole.
- This will allow us to understand the impact of beta blockers on the overall cost of care for your condition.
- NHS Digital will use your NHS number and date of birth to identify any records of care you received in hospital and send this information back to us.
- This data will be stored on a secure server at the King's College London Clinical Trials Unit.
- In order for the BOPPP research team to access the information held about you in HES, we will ask your permission to share your NHS number and your date of birth with King's College London and NHS Digital to identify you.
- The transfer of this information will be subject to strict confidentiality and information governance policies.

#### 14. What will happen to the results of the clinical trial?

- At the end of the trial, we will report trial results to the Department of Health and we will publish summary data in appropriate academic and professional journals and at conferences.
- We will contact you with the trial results once it is finished.
- The publications will be available to the general public on free to access websites.
- You will not be identified in any publication.

## 15. Who is organising and funding the clinical trial?

- BOPPP is funded by the Department of Health, through the National Institute for Health Research Health Technology Assessment Programme (Project Number: 17/32/04).
- Department of Health and Social Care Disclaimer - The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

## 16. Who has reviewed the clinical trial?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your rights, interests and wellbeing. This trial has been reviewed and given favourable opinion to proceed by the York and Humber (Leeds West) Research Ethics Committee

## 17. What if there is a problem?

- If you have a concern about any aspect of this trial, you should ask to speak to the researchers who will do their best to answer your questions **(see contact details on the last page)**.
- If you remain unhappy and wish to complain formally, in England and Wales you can do this by contacting the Patient Advice and Liaison Services (PALS). In Scotland, you can contact your local hospital's Patient Experience Team.
- Contact details are: << INSERT LOCAL DETAILS HERE>>.
- In the unlikely event that something does go wrong and you are harmed during the research due to someone's negligence, then you may have grounds for legal action and compensation against the Sponsor but you may have to pay your legal costs.
- The normal NHS complaints mechanisms will still be available to you, if appropriate.

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

**If you have any questions, please contact the trial research nurse on <INSERT CONTACT DETAILS HERE> or Principle Investigator on <INSERT CONTACT DETAILS HERE>**

**Alternatively, you can contact the Chief Investigator for the BOPPP trial:**

Dr Vishal Patel (Consultant Hepatologist)

Institute of Liver Studies, King's College Hospital, Denmark Hill, London SE5 9RS

[kch-tr.BOPPPTrial@nhs.net](mailto:kch-tr.BOPPPTrial@nhs.net)

