Welcome to the second of our newsletters for people taking part in REVEAL.

It's been more than three years since we began the study, so we are now well past the halfway mark, and we are delighted to say that REVEAL is progressing really well.

In one of your more recent visits, your study coordinator will have taken a middle of study blood sample from you, which has been sent to the Central Coordinating Office laboratories in Oxford to be analysed. These blood samples, together with the information you have provided at your follow-up visits, are vital to us in assessing how the study is progressing.

We do need to know how you are getting on, even if you are no longer taking the tablets. Please do keep going to your clinic appointments every six months so the study staff can check how you are, and update you on the progress of the study. It is anticipated that the study will continue until around the end of 2016, and we may wish to keep in touch with you from time to time after that, just to see how you are doing.

Thank you once again for taking part in REVEAL. With your help, we hope we will be able to answer a really important scientific question that could improve and extend the lives of many thousands of people around the world.

“What can I do to make REVEAL a success?”

Congratulations on passing the half way mark of the REVEAL study! At the outset, REVEAL was scheduled to run for a whole five years with follow up beyond that point.

We’re very grateful that you have been so generous with your time and commitment in agreeing to be part of the study. To ensure the study results are as reliable as possible, it’s important that we follow you up so we know how you’re doing.

The best way to do this is to attend your clinic appointments twice a year and to keep taking the REVEAL tablets wherever possible. The REVEAL clinic staff are always keen to see you!

If this isn’t possible, the clinic staff would still like to stay in touch with you, maybe by telephone so that you can tell us how you are getting on, or via a friend or relative who can tell us how you are.

If you move house or change your telephone number, don’t forget to let us know so we can keep in touch.

We hope to see you again in clinic soon!
Your safety

The welfare of our participants has always been our top priority and we monitor safety in the trial in several ways.

Blood tests in clinic

At every clinic visit we check a blood test to make sure that you are not developing any liver or muscle problems. Rare side effects of atorvastatin (the statin that is used in REVEAL) are muscle pain and/or weakness, and abnormal functioning of the liver.

Do tell your study coordinator if you experience any unusual or unexplained symptoms. When the study coordinator enters the result from your blood test onto the study laptop, the computer does an automatic check and warns them if the result is high. It also advises if other tests should be checked.

Study doctors in Oxford

In Oxford, there is a dedicated team of REVEAL study doctors who review the results of blood samples taken at follow-up visits, and offer guidance if anything abnormal is identified.

The study doctors are also available to advise and provide reassurance to participants and other healthcare professionals if there are concerns about new diagnoses or the prescription of other drugs at the same time as the study medications. It is always a good idea to bring your list of other medications with you each time you come to clinic, so the study coordinator can check it.

There is a list of other drugs that should not be taken with the study treatments on the back page of this newsletter.

Independent Data Monitoring Committee

In addition, the progress of the trial is watched by a group of doctors and statisticians called the Data Monitoring Committee (DMC), who look at the study data while the trial is ongoing. They are the only people who are allowed to know who is taking the active anacetrapib treatment and who is taking the placebo (“dummy”) tablets.

The DMC work independently of Oxford’s daily trial team, and they review information about how many study participants report any new medical problems during the study. For example, they look at how many people experience liver problems during the study, and compare the number in those who are taking the active anacetrapib with those who are on the placebo, to check that the study tablets do not seem to be causing any illnesses.

The DMC review study information every three months. Each time, there is a huge amount of new accumulated data and they are in a very good position to watch for emerging safety concerns. Based on their review, they can recommend changes to the way the trial is being run.

So far this has not been necessary because the study medications appear to be very well-tolerated. But, as always, we do encourage you to report any new symptoms to us – either directly or via your study coordinator or nurse.
REVEAL the Oxford team

As you will know the REVEAL study is centrally coordinated at Oxford University’s Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU).

Within CTSU, the Oxford team, also known as the Central Coordinating Office, comprises a wide range of expertise and many years of experience.

These groups (shown right) work closely together to support the study through Regional Coordinating Centres in your country and Local Clinical Centres where you attend for your appointments.

The supply and delivery of your study medication is one of the things organised by the ‘Supplies & Equipment’ team. See below for more information about where your study medication comes from.

Where your study drugs come from

Have you ever wondered where your REVEAL tablets are produced and what happens to them before they reach you?

The production, packaging and distribution of study medication is a complex process, which has to meet the rules, regulations and standards of all the countries taking part in REVEAL.

Large batches of tablets are packaged about twice a year for REVEAL, some in the USA and some in Europe.

The batches are tested several times during production to check that they meet the approved standards.

We keep detailed records to ensure that we know exactly what went into each bottle and where that bottle ends up.

We also keep track of storage temperatures and expiry dates to be certain that the tablets are in excellent condition.

The team in Oxford uses information in our database to help co-ordinate the delivery of large shipments of study drugs from the packaging factories to regional hubs, and then of boxes to be sent to every clinic so that the bottles are there in time for your appointment.

So far we have packaged over 100 million tablets into over 1 million bottles. If we could stack those bottles up, they would reach a height of more than 12 times that of Mount Everest.
A healthier you!

- A diet rich in fresh fruits and vegetables is a great way to fight bad cholesterol and will help you to a healthier heart.
- Oily fish once or twice a week is a great treat and good heart-health food as well!
- Steaming, grilling and boiling your food is generally better than frying and roasting.
- Creating your own dishes can be cheaper (and quicker!) than buying ready meals and take-aways, and allows you to control what you eat more carefully.
- Going for a walk with friends and family is a lovely way to exercise and catch up on all the news.
- 20 minutes of physical activity, equivalent to a brisk walk, should be possible for most people to include in their daily routine.

A reminder of drugs that should generally NOT be taken with one or other of the study treatments

If you are taking one of the following drugs, please contact your study nurse or doctor or ring the Freephone service on 0800 585 323 for further advice.

<table>
<thead>
<tr>
<th>1. FOR LOWERING CHOLESTEROL</th>
<th>2. ANTIBIOTICS</th>
<th>3. ANTI_FUNGALS</th>
<th>4. PROTEASE INHIBITORS</th>
<th>5. OTHER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statins:</strong> if your own doctors wish to change the atorvastatin dose you are receiving in REVEAL, or change to a different statin, please contact your study clinic first.</td>
<td><strong>Erythromycin</strong> (Arpimicin, Erymax, Erymin, Erythrocin, Erythropeid, Ilosone, Tiloryth)</td>
<td><strong>Itraconazole</strong> (Sporanox)</td>
<td><strong>Atazanavir</strong> (Reyataz)</td>
<td><strong>Ciclosporin</strong> (Neoral, Sandimmun, SangCya)</td>
</tr>
<tr>
<td><strong>Fibrates:</strong></td>
<td><strong>Clarithromycin</strong> (Biaxin, Claripen, Clarixin, Crixan, Fromilid, Klabax, Klacid, Klaricid, Vikrol)</td>
<td><strong>Posaconazole</strong> (Noxafil)</td>
<td><strong>Posamprenavir</strong> (Telzir)</td>
<td><strong>Fusidic acid</strong> (excluding creams or eye/ear drops)</td>
</tr>
<tr>
<td>Bezafibrate (Bezalip, Bezalip Mono, Bezagen XL, Fibrazate XL, Liparol XL, Zimbacol XL)</td>
<td><strong>Telithromycin</strong> (Ketek)</td>
<td></td>
<td><strong>Lopinavir</strong> (Kaletra)</td>
<td><strong>Nelfinavir</strong> (Viracept)</td>
</tr>
<tr>
<td>Ciprofibrate (Modalim)</td>
<td><strong>Daptomycin</strong> (Cubicin)</td>
<td></td>
<td><strong>Darunavir</strong> (Prezista)</td>
<td><strong>Ritonavir</strong> (Norvir)</td>
</tr>
<tr>
<td>Fenofibrate (Fenogal, Lipantil, Lipantil Micro, Supralip)</td>
<td></td>
<td></td>
<td><strong>Saquinavir</strong> (Invirase, Fortovase)</td>
<td><strong>Tipranavir</strong> (Aptivus)</td>
</tr>
<tr>
<td>Gemfibrozil (Lopid)</td>
<td></td>
<td></td>
<td></td>
<td><strong>Indinavir</strong> (Crixivan)</td>
</tr>
<tr>
<td><strong>High dose niacin:</strong> (more than 100 mg per day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicotinic acid (Niaspan)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acipimox (Olbetam)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

We hope you have found this newsletter interesting and helpful. If you have any feedback, or ideas about subjects you would like us to cover in future editions, please write or email to the following address.

**REVEAL Central Coordinating Office**

CTSU, Nuffield Department of Population Health, University of Oxford
Richard Doll Building, Old Road Campus, OXFORD OX3 7LF, UK
Tel: 0800 585 323 (toll free from UK), +44 1865 743 882 (from outside UK)
Email: ccoreveal@ctsu.ox.ac.uk

Participant Newsletter Issue 2, Summer 2015