

## **RESULTS: Question and Answers about the SHARP trial**

### **What do the results from the SHARP study show?**

The main findings of SHARP were:

- The patients who were allocated to take ezetimibe plus simvastatin had one-sixth fewer heart attacks, strokes or operations to unblock arteries (“major atherosclerotic events”), with similar reductions observed in all types of patient studied.
- During this long trial the proportion of patients who stopped taking their allocated treatment was about one third, but this was not generally due to side-effects and was the same for both real and dummy treatments. If taken without interruption, however, ezetimibe plus simvastatin could have even larger effects than observed in SHARP, potentially reducing risk by about one quarter.
- For every 1000 kidney patients taking this cholesterol-lowering treatment for 5 years about 30-40 would avoid major atherosclerotic events, and the benefit would be even bigger in kidney patients who already have heart disease.
- Adding 10mg daily of ezetimibe to 20mg daily of simvastatin produced a large reduction in LDL (“bad”) cholesterol safely. This combination treatment may be particularly good for kidney patients, who may experience side-effects with high statin doses.
- There was no support for previous concerns with ezetimibe about possible adverse effects on cancer, and no evidence of an increased risk of muscle or liver problems.

### **Why are the results from SHARP important?**

People with chronic kidney disease tend to have a very high risk of developing heart disease or experiencing a stroke. Until now, there has been a lack of information about how to prevent these conditions in kidney disease patients. The SHARP results are important because they provide the first reliable evidence that this high risk of cardiovascular disease can be lowered by reducing blood cholesterol levels.

### **How important are the results from SHARP?**

Chronic kidney disease affects about one in 10 people worldwide. Consequently, it is likely that the SHARP results will result in cholesterol-lowering treatment being used widely in this large group of high-risk people who were previously not being given such treatment. This could lead to at least 250,000 people with chronic kidney disease avoiding heart attacks, strokes or operations to unblock arteries each year worldwide.

### **Are the SHARP results consistent with previous studies?**

Yes. A large number of randomized trials had shown previously that reducing low-density lipoprotein (LDL; or “bad”) cholesterol in patients with normal kidney function reduces the risk of heart attacks, strokes and operations to unblock arteries in people. Previous trials of cholesterol-lowering in patients with kidney disease have not been able to demonstrate benefit, but it now seems likely that they were too small to demonstrate the benefits. The SHARP trial, which studied many more kidney disease patients, shows that reducing LDL cholesterol levels safely produces comparable benefits to those observed in people with normal kidney function.

**Are the results only relevant to kidney patients?**

No. The SHARP results are also relevant to people who don't have chronic kidney disease. The combination of ezetimibe and a statin produced similar benefits to those resulting from the same LDL cholesterol reduction achieved with a high dose of a statin. Since the lower the cholesterol the bigger the risk reduction, these results suggest that patients who remain at high risk of major atherosclerotic events despite maximal statin therapy may benefit further from adding ezetimibe to their current statin regimen.

**What do these results mean for a patient with kidney disease?**

Patients with kidney disease should consult their own doctors to find out whether cholesterol-lowering treatment might be helpful for them. SHARP shows that lowering cholesterol is beneficial for a wide range of people with chronic kidney disease, so many patients may now begin cholesterol-lowering therapy.

**Is this treatment suitable for all patients with kidney disease?**

SHARP included a wide range of different types of patients with less than 50% of their normal kidney function, and the benefits of lowering cholesterol were similar in all types of patient studied. Previous studies have shown that lowering cholesterol is beneficial for people with less severe kidney disease, so such treatment is likely to be beneficial for the majority of people with chronic kidney disease.

**Were there any adverse effects of treatment?**

No. The frequency of serious adverse effects was monitored very intensively during the SHARP, but there was no evidence that either of the active drugs (ezetimibe and simvastatin) in the study tablets caused any serious side effects in the muscles, liver, pancreas, kidneys, or any other organs. In particular, the previous suggestion that ezetimibe might cause cancer was not supported by the SHARP results.

**Do kidney disease patients need to take the particular treatments studied in SHARP, or could they take other cholesterol-lowering treatments?**

The key thing is to ensure that any cholesterol-lowering treatment used produces a big reduction in LDL (or "bad") cholesterol. Use of the combination of ezetimibe 10mg daily plus simvastatin 20mg daily can reduce LDL cholesterol by an average of 1.3 mmol/L (50mg/dL). An LDL cholesterol reduction of this size could also be achieved by high doses of one of the newer, more potent, statins (e.g. atorvastatin or rosuvastatin). SHARP indicates that this reduction in LDL cholesterol would reduce the risk of major atherosclerotic events by about one quarter, and shows that the combination of ezetimibe 10 mg daily plus simvastatin 20 mg daily is safe.

**Is there anything else that can be done to lower cholesterol levels?**

Reducing the fat content of one's diet can reduce cholesterol, but this is unlikely to be as effective as taking medication to lower cholesterol. Moreover, people with kidney disease are often instructed to follow very specific diets, so they should NOT change their diet without consulting their dietician or kidney doctor.

**Can people who took part in SHARP find out whether they received active cholesterol-lowering treatment or dummy "placebo" treatment?**

We do not plan to tell participants routinely what they received. The main reason for not doing so is that it minimises the risk of bias in the assessment of any long-term

follow-up of their health. (Someone's knowledge of which treatment they had may affect what they later report.) But, if the kidney specialist (nephrologist) caring for a patient who was in SHARP definitely wants to find out what treatment their patient received, they will be able to do so.

**What happens next?**

It is planned to publish the main study findings in a leading medical journal in early 2011. Further information about any such publications will be posted on the SHARP website ([www.sharpinfo.org](http://www.sharpinfo.org)).