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Trial Rationale

So the Apollo Trial is designed to treat a lipid disorder that has been very resistant to treatment for a very long time and that's elevated Lipoprotein . About 20% of the world population have this lipid abnormality. And it is a cause for premature atherosclerotic cardiovascular disease and aortic stenosis. We really wanted to find treatments for it.

Mechanism of Action

What we studied is what's known as a short interfering RNA, it's a double stranded RNA and it's given subcutaneously. It is attached to a sugar that helps to transport it into the liver. It's taken up actively by the liver, is cleaved, and then one of the RNA strands degrades the messenger RNA that codes for the protein that's essential to the formation of lipoprotein.

Study Design and Inclusion Criteria

Well first of all this was a phase one trial so it's small. It was really designed primarily to look at safety but of course we do look carefully efficacy and we took people without known cardiovascular disease over the age of 18 men and women who had an elevated lipoprotein of at least 150 nanomoles per litre. And we ended up actually with the values even higher than that.

Key Findings

Well, first of all, key findings include we did not see any serious safety issues. The drug at the highest dose, we studied four different doses, at the highest dose it reduced lipoprotein by 98%. In the second to highest dose, it reduced it by 96%, but impressively, that effect was durable. And if you go on a 150 days, five months, was still 81% reduced in the top dose group and 70% reduced in the next highest dose group. So very effective lowering, very durable lowering.

Next Steps

So when you do these studies you have to plan the next phase, which is phase two. Right now we're doing what is known as a multiple dose study, where instead of giving a single dose, we give a couple of doses. We'll need to see what happens to the durability and to the efficacy when we give somewhat smaller doses but do it more than once. After that's completed we'll enter phase two and ultimately phase three.

Take-home Messages

This is part of the kind of routine approach to drug development. Take home message is that lipoprotein is important. It needs to be measured in more patients. There are therapies coming, the therapy we studied and at least two others. And ultimately this is that last frontier of a lipid disorder that we've never been able to treat and we're soon going to be able to treat.