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ATERONON BRIEFING SPONSORED SYMPOSIUM AT THE BRITISH CARDIOVASCULAR SOCIETY ANNUAL CONFERENCE

June 3rd 2014

Introduction

There are now many good quality epidemiological studies supporting the use of lycopene, normally derived from tomatoes, to improve cardiovascular health. We are extremely lucky to be able to assemble today at the British Cardiovascular Society a panel of leading world lycopene experts to discuss the latest lycopene research findings and their significance.

For lycopene to be effective, we know that it has to be readily absorbed by the body, or 'bioavailable'. Processed tomatoes have been shown to be more bioavailable than raw tomatoes. One way to raise lycopene levels significantly is the unpalatable prospect of eating 100g of tomato paste every day. Alternatively, as the research which Professor Sesso is announcing today shows, a daily supplement of Ateronon will achieve the same result.

Ateronon is based on LactoLycopene, which is a patented form of lycopene designed to make it highly bioavailable. In the largest randomized, double-blind placebo-controlled clinical trial to be done on any lycopene or tomato product, Professor Howard D. Sesso of Harvard Medical School is announcing today the preliminary findings of his work. Initial findings are that Ateronon was extremely well tolerated by the patient group and that over a 12 month period, a daily capsule of Ateronon raised blood levels of lycopene by up to 20%. The comprehensive data gathered on the group of 213 patients provides Professor Sesso plenty of further data analysis opportunities which will likely be the subject of several peer-reviewed scientific papers.

Sesso's work complements a separate independent clinical trial of Ateronon by Dr. Joseph Cheriyan (of Addenbrooke's Hospital, Cambridge), examining the potential beneficial effect of Ateronon on endothelial function. Publication in a peer-reviewed journal is expected imminently.

There is clearly more work to be done to support the exciting research already undertaken. Lycopene seems likely to have strong cardiovascular benefit if it can be absorbed by the body and LactoLycopene, in the form of Ateronon, is proven to deliver bioavailable lycopene. We expect to focus further research effort and analysis on Ateronon's role in primary prevention of cardiovascular disease and in particular how it may impact key vascular risk factors such as cholesterol, high blood pressure and diabetes.

Tim Dye

CEO
Ateronon

OUR FOUR KEY SPEAKERS

Peter Kirkpatrick, FRCS (SN) FMedSci

Mr Peter Kirkpatrick is a neurosurgeon based in Cambridge with about 12 years' experience. His specialist practice in carotid disease and cerebral vascular disease, including aneurysm surgery. He was awarded Hospital Doctor Award in 1999. In addition, he has clinical and research interests in head injury and all aspects of spinal disease, including lumbar and cervical disc disease. He is a member of the stroke association and works on their specific board. He has gathered over £3 million of research income and supervised a number of higher degrees. Mr Kirkpatrick has been published in over 200 publications and sits on a number of working parties to improve neurosurgical and spinal care. Approximately 50 per cent of his additional work relates to medico-legal issues for all aspects of neurosurgery.

Venket Rao, M.Sc. Ph.D

Dr. Rao completed his M.Sc. and Ph.D. degrees in Food Science at Oregon State University, USA. After being a Full Professor in the Department of Nutritional Sciences, Faculty of Medicine, he currently holds the position of Professor Emeritus at the University of Toronto. He has established a major focus in the area of diet and health, particularly focusing on the role of oxidative stress and antioxidants in the causation and prevention of chronic diseases. He is one of the pioneering researchers to study the bioavailability, metabolism, mechanisms of action and biological role of lycopene, a carotenoid antioxidant present in tomatoes, other fruits and vegetables and nutritional supplements. The main focus of his research is to study the role of lycopene in the prevention and management of cardiovascular disease, cancer and osteoporosis. He is credited with bringing international awareness to the role of lycopene in human health.

Joseph Cheriyan, MBBS

Dr. Joseph Cheriyan has been a Consultant Physician and Clinical Pharmacologist at Addenbrooke's Hospital, Cambridge, UK since 2006, and an Associate Lecturer in the Department of Medicine, University of Cambridge. He trained initially in Sheffield, and subsequently in Nottingham and London before completing his specialist training in Cambridge.

He is an active clinical researcher with interests in cardiovascular medicine, particularly vascular function and inflammation. He is one of a few clinical trialists working on early phase experimental medicine studies of novel therapeutics, and has a unique post which combines close collaboration with industrial partners on the Addenbrooke's Biomedical Campus.

His clinical service commitments are to the Department of Acute Medicine at Addenbrooke's Hospital. He is the Vice Chair of the local Research Ethics Committee, a member of the Management Board of the Cambridge Clinical Trials Unit and is seconded as a Senior Physician and Clinical Pharmacologist to the GSK CUC in Cambridge.

He has also co-authored the Oxford Specialist Handbook on Hypertension.

Howard D. Sesso, ScD, MPH

Dr. Howard D. Sesso is an Associate Epidemiologist at the Divisions of Preventive Medicine and Aging at Brigham and Women's Hospital (BWH), an Associate Professor of Medicine at Harvard Medical School, and an Associate Professor of Epidemiology at the Harvard School of Public Health in Boston, MA. He received his BA in Human Biology from Stanford University, an MPH in Epidemiology from The George Washington University, and a ScD in Epidemiology from the Harvard School of Public Health. Dr. Sesso specialises in the epidemiology and prevention of cardiovascular disease (CVD) and its major risk factors, including hypertension and obesity. His research focuses on the role of dietary factors, including vitamin supplements, lycopene, and flavonoids, as well as the role of nutritional biomarkers. He is also interested in the roles of diet and lifestyle in the prevention of cancer.

Ateronon briefing Sponsored Symposium at the British Cardiovascular Society Annual Conference

June 3rd 2014

BACKGROUND ANALYSIS OF PREVIOUS WORK INDICATING THE SIGNIFICANT CARDIOVASCULAR BENEFITS FROM RAISED LYCOPENE INTAKE.

Commentary by Howard D. Sesso, Professor of Medicine, Harvard Medical School; Associate Epidemiologist, Brigham and Women's Hospital, Division of Preventive Medicine

The consumption of a diet rich in fruit and vegetables has been consistently associated with a reduced risk of cardiovascular disease (CVD)[1] in a variety of populations. This effect is believed to be a consequence of dietary factors reducing the rate of atherosclerosis or clogging of the arteries, which is a main underlying mechanism leading to CVD.

Atherosclerosis damages the functions of the endothelium, the sensitive layer of cells lining the blood vessels, which transmit messages relating to blood flow requirements.

This damage reduces the responsiveness of blood vessels to blood flow demand, which in turn causes further stress and damage in other organs.

It is critically important to identify specific components among fruits and vegetables that influence these risk factors, reduce atherosclerosis, improve endothelial function, and decrease the risk of developing CVD.

An identifiable key compound with these properties is lycopene, the carotenoid that gives tomatoes their red colour.[3]

Tomato products represent a major component of fruit and vegetable intake, and provide more than 80% of the intake of dietary lycopene.[2]

Lycopene is known to be a potent antioxidant and 'mopper-up' of potentially harmful unpaired oxygen molecules called free radicals.[6] These molecules are programmed to search for another electron to pair up with, and this search initiates an uncontrolled chain reaction that can damage the natural function of healthy cells and lead to cardiovascular disease.

The need for antioxidants in our daily life is becoming more critical because of increased exposure to free radicals from environmental pollution. Illness and stress can also increase the body's production of free radicals.

Studies have shown that lycopene cooked and consumed with oil in tomato paste, tomato sauce, or pizza, is better absorbed by the body than raw tomato.[4] Therefore, dietary lycopene is more 'bioavailable' in processed tomato products.[5] The new product Ateronon uses a novel component called LactoLycopene which was originally developed by scientists at the food multinational Nestlé.[16] It is absorbed up to twice as efficiently as natural lycopene and has been shown to produce as much bioavailable lycopene as would be present in a large daily dose of cooked tomato paste.

This patented compound has been licensed to the biotech company CamNutra and is now being produced under the Ateronon brand name.

It is expected that Ateronon's uniquely bioavailable LactoLycopene will enable scientists to build on results achieved by several recent studies which have shown an exciting association between higher levels of dietary and blood lycopene and a lower risk of cardiovascular disease and also a lowering of other measurable risk factors.[10-14]

The large-scale Women's Health Study in the USA found middle-aged and older women consuming large quantities of tomato products had up to 32% reduced risk of CVD compared to women consuming the lowest levels.[15]

The Framingham Offspring Study in America also showed through repeated measures of dietary lycopene intake over 10 years, that the nutrient was associated with a lower risk of developing CVD. A 2.7-fold difference in dietary lycopene intake was associated with a 17% reduction in CVD and a 26% reduction in coronary heart disease.[19]

Other studies have also reported an association between blood lycopene levels and a reduced risk of heart attack,[12, 21] CVD[12, 22, 23] and aortic atherosclerosis.[10]

Dietary lycopene has also been associated for many years with reduced stroke risk[17] and most recently with a reduction of stroke risk of up to 55% in 1,031 Finnish men aged 46 to 65. Additional analyses in the same volunteer group also found a significant association between serum lycopene and reduced risk of heart attack.[24]

The thickness of the intima-media cells lining the carotid arteries in the neck can be measured by ultrasound (IMT testing), and is also a predictor of coronary disease.[26] In the Kuopio Ischaemic Heart Disease Risk Factor study[27] of 1,028 Finnish men aged 46 to 64 years, those with lowest blood lycopene levels had significantly worse thickening or hardening of this artery compared with other men.

The authors concluded that higher blood lycopene concentrations may reduce rates of atherosclerosis. Karppi et al[28] extended these findings in the same cohort of eastern Finnish men to examine the progression of carotid IMT. In a seven-year study, they found that high lycopene levels significantly reduced the thickening and hardening of the IMT.

Other investigations of blood serum lycopene and intima-media thickness reinforce these findings.[29-32, 33, 11, 34, 35]

Given the increasing scientific evidence and interest in the role of lycopene on CVD, a key research question is understanding the mechanisms for this effect.[36]

Suggested possibilities include lycopene's beneficial effect on low density lipoprotein-cholesterol[37-41] or on C-reactive protein,[42] a marker of inflammation. Other studies have investigated the effects of dietary lycopene on low density lipoprotein-cholesterol.[37-41]

Commentary on results from studies of Ateronon use so far

Ateronon is a lycopene supplement using LactoLycopene, which has been developed with the understanding that the potential clinical effectiveness of lycopene depends on how well it is absorbed. A single daily tablet of Ateronon provides more bioavailable lycopene than a litre of tomato juice or 100g of tomato paste, because it is absorbed more efficiently. In all patients studied to date, it has also been found to inhibit the atherogenic lipid oxidation process that leads to clogging of the arteries. In contrast, tomato paste only partially inhibits this atherogenic lipid oxidation process.

These promising data highlight the pressing need to improve our understanding of the mechanisms through which Ateronon may reduce the risk of developing CVD. In particular, it is especially important to understand the long-term absorption and vascular effects of Ateronon on sophisticated biomarkers of CVD, along with traditional risk factors for heart disease, such as raised blood pressure.

In an analysis among 39,876 women initially free of CVD and cancer already involved in the Women's Health Study, my own group looked at 483 CVD cases and 483 matched controls during a mean of 4.8 years of follow-up.[13] Higher plasma lycopene levels were associated with a reduced risk of CVD in women, with those in the upper versus lower half of plasma lycopene having a 34% reduction in CVD risk. In some circumstances this risk reduction rose to 50%.

Most recently, we have used Ateronon to carry out the largest randomized, double-blind, placebo-controlled clinical trial to date of any lycopene or tomato-based intervention

We compared a 7mg per day Ateronon dose with a placebo in a trial involving 213 patients with stable coronary heart disease. They were followed up for 12 months, to look for changes in carotid intima media thickness, blood pressure, and a specified group of coronary disease biomarkers. We found that Ateronon increased average blood levels of lycopene at both 6 and 12 months follow-up by up to 20%. These findings reflect the bioavailability of Ateronon.

At 6 months, there was some improvement in carotid IMT in the group taking Ateronon and a slight worsening of carotid IMT in the group taking the dummy or placebo treatment. Only about half of the participants completed the 12 month assessment, at which point differences in carotid IMT were neutral.

The magnitude of change seen so far in coronary biomarkers is small, but this is likely to be because trial participants were already taking statins, blood-pressure lowering drugs, and aspirin.

Analyses to investigate the effect of Ateronon on changes in carotid IMT are ongoing.

More than 90% of volunteers completed the trial reflecting the fact Ateronon is well tolerated and safe. Importantly, we also found no differences comparing Ateronon versus placebo for any self-reported symptoms or potential adverse events and there were no long-term safety concerns among those taking Ateronon versus placebo.

Analyses are ongoing to delve further into the effects of Ateronon and its capacity to reduce key cardiovascular risk factors.

This completed trial testing Ateronon represents a tremendous opportunity to expand our knowledge on the cardiovascular effects of Ateronon use in men and women with pre-existing coronary heart disease. Comprehensive data have been collected on lifestyle, clinical, and dietary factors, along with blood pressure records and data from the completed carotid ultrasounds. We also have stored blood samples from trial participants available for further analysis.

Beyond the primary findings to be reported from the Ateronon trial, many other important analyses will be conducted to clarify the mechanistic effects and potential benefits of Ateronon in the prevention of CVD.

We have seen a glimpse of what benefits may be achieved and we expect to report shortly on the results of our further analysis. The first of these reports will shortly be submitted for publication in a leading peer-reviewed academic journal.

Beyond our trial, additional research should consider the effect of Ateronon in those without cardiovascular disease but with early signs of high cholesterol, diabetes, or high blood pressure as a means of primary prevention.

Forthcoming publication

Dr Joseph Cheriyan Associate Lecturer in Medicine, University of Cambridge Clinical Pharmacology Unit; Consultant Physician and Clinical Pharmacologist, Cambridge University Hospitals NHS Foundation Trust.

Here he explains some of his work on the effects of Ateronon on blood vessel function, which has already been presented as an abstract at the American Heart Association. It has now been accepted for publication and will appear shortly in the journal PLoS ONE, the open access peer-reviewed scientific journal published by the Public Library of Science.

The process by which cardiovascular disease begins is initially varied and involves a range of stimulants including cardiovascular risk factors such as smoking, high cholesterol, high blood pressure, inflammation and so on which results in endothelial dysfunction. The endothelium is the inner lining of the blood vessels across the whole circulatory system, and acts as a barrier between blood and the rest of the blood vessel and tissue, as well as mediating blood clotting, the formation of new blood vessels, vasoconstriction, blood pressure control, and the repair of damaged or diseased organs. Endothelial dysfunction, which occurs when normal function is impaired, is thought to be the hallmark of cardiovascular disorders, and eventually leads to the development of stiffer blood vessels (arteriosclerosis), the deposition of lipid plaques (atherosclerosis), which can then go on to rupture causing thrombosis (ie occlusion of blood vessels) which can present as a sudden heart attack, stroke or peripheral vascular disease.

In order to test the effects of lycopene on endothelial function, a randomized, double blind, placebo controlled trial was conducted. The hypothesis was that lycopene would improve endothelial function in two groups namely those with cardiovascular disease and healthy volunteers.

There are many ways of measuring endothelial function including ultrasound methods (eg flow mediated dilatation), radial tonometry (using applanation techniques) but the gold standard remains forearm plethysmography. The different techniques vary in their suitability and reliability but only forearm plethysmography has been shown to have a linear relationship with cardiovascular outcomes in a landmark study comparing the three methods.[18]

Our study also measured a range of other parameters of health including blood pressure, lipid profiles, systemic markers of inflammation, blood vessel stiffness and so on.

The groups (n=36 each) were randomized in a blinded manner to either 7mg per day lycopene or placebo, and treated for approximately 2 months. Dietary intake was not restricted throughout the study to allow a pragmatic study design.

Baseline measurements of endothelial function were taken at the beginning and repeated at the end of treatment. In the cardiovascular group (who were already on evidence-based drugs including statins) we were able to show an improvement in endothelial function, comparing change from baseline, when corrected for placebo effects.

Serum lycopene levels also increased significantly in the active therapy group when compared to placebo.

The results of this study suggest that lycopene may be able to improve endothelial function in patients already on established therapies. We did not test a higher dose, and cannot establish if a higher dose may have had different effects or whether indeed there is a dose response relationship. To determine if these effects translate to clinical benefits to patients (such as preventing ill health or future events) a much larger outcome study will need to be conducted.

There is a strict press embargo (i.e it cannot be reported, broadcast, published or discussed on social media until this embargo is lifted by PLoS One at 10pm GMT (5pm US EST) June 9th, 2014, after which the article will be available at http://dx.plos.org/10.1371/journal.pone.0099070):

Potential implications for the general population and next steps for Ateronon research

Commentary by Peter Kirkpatrick, consultant neurosurgeon, Addenbrooke's Hospital NHS Trust, Cambridge, and honorary lecturer in Neurosurgery, Cambridge University, with a special interest in strokes, carotid artery disease and cerebral vascular disease.

Future research on Ateronon will focus on the effects of Ateronon in a primary prevention setting for CVD, to investigate how Ateronon can counter the development of key vascular risk factors including high cholesterol, high blood pressure, and diabetes. Many people are initially diagnosed with early stages of these conditions, for which lifestyle and dietary changes are recommended before initiating what may become lifelong treatments. Ateronon may have strong effects in these individuals for whom there is an opportunity to lower vascular risk factors without the use of costly pharmaceutical medication.

Plans are being drawn up for wider-ranging comparison of the effects of Ateronon on the endothelial function of healthy people and those with pre-existing heart disease.

Dr. Andrew Carson, Associate Dean for GP training in the West Midlands, has been asked to recruit patients for the trial through the university's primary care research network. He believes that if Ateronon has an effect on endothelial function, then it could have a beneficial effect on virtually every inflammatory disease process, including conditions such as cancer, arthritis and diabetes.

As results from epidemiological research on the cardiovascular effects of blood lycopene continue to emerge, evidence points encouragingly towards lycopene as a key component in the prevention of heart and circulatory disease. Ateronon represents a highly bioavailable and safe lycopene formulation that has now been comprehensively and successfully tested in the largest trial to date of any lycopene or tomato-based intervention.

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Dr. Peter Kirkpatrick

Consultant and Honorary Lecturer in Neurosurgery, Addenbrooke's Hospital, University of Cambridge.

LEADING INTERNATIONAL EXPERT ON THE MECHANISMS INVOLVED IN STROKES, AND SCIENTIFIC ADVISOR TO CAMNUTRA THE MANUFACTURERS OF ATERONON.

Hundreds of studies have now shown the benefits of lycopene in boosting the immune system and reducing the incidence of a variety of conditions. There is now convincing evidence that high levels of plasma lycopene can reduce the risk of heart attack and stroke by 20% to 30%.

This symposium is investigating the evidence so far for how this protective mechanism works and the importance of bioavailability in delivering lycopene into the blood.

We are now engaged in a programme to prove that the benefits of raised blood lycopene can best be provided by Ateronon, the first supplement to deliver lycopene to the body in a consistent, reliable way, and to have scientifically proven and validated benefits.

We are finding the specific formulation of lycopene present in Ateronon provides a unique method of reliably raising blood serum lycopene. If it can reduce incidence of heart disease and stroke at a population level by the percentages indicated, widespread use of this treatment could save the NHS vast sums of money.

The latest data indicates heart disease and stroke costs the National Health Service well over £30bn. Anything that cuts that bill is to be welcomed.

The company has so far concentrated on demonstrating Ateronon's efficacy as a treatment for heart disease and stroke, though in collaboration with the University of Texas, we are now planning to investigate its capacity to slow down the progression of metabolic syndrome leading to diabetes.

We believe Ateronon is at the forefront of the relatively new concept of nutraceuticals - safe, food-based compounds which are ingested with, or as foods, and which have a measurable biological effect.

We know from hundreds of published studies that high blood serum lycopene levels are linked with protection from a variety of diseases. Natural lycopene is poorly absorbed. Ateronon's LactoLycopene formulation is a uniquely bioavailable form of lycopene that is well absorbed, and the exciting results from our first placebo controlled studies have already shown evidence of its beneficial effect.

We are already collaborating with respected world-class scientists from my own institution the University of Cambridge, and professors from Harvard University and University of Texas in the United States. Announcements of further collaborations will appear in due course.

Dr. Venket Rao

Professor Emeritus Department of Nutritional Sciences, University of Toronto

A NEW WAY TO REDUCE INCIDENCE OF HEART DISEASE AND STROKE BY 25-30%

Cardiovascular disease (CVD) causes almost a third of all deaths.

Finding ways to prevent and manage the condition is important for improving quality of life and overall life expectancy.

Although several risk factors influence the incidence of CVD, in recent years oxidative stress induced by lifestyle factors such as smoking, poor diet, exercise and excessive alcohol consumption, has been recognized as playing an important role.

Oxidative stress generates unpaired oxygen molecules called free radicals. These molecules are programmed to search for another electron to pair up with, a process which initiates an uncontrolled chain reaction that can damage the natural function of healthy cells and lead to oxidation of the LDL cholesterol and the formation of fat-containing foam cells and plaque deposits in the arteries.

Preventing LDL oxidation will therefore significantly reduce risk of CVD.

Recently there has been a great deal of interest in using natural antioxidants to do this, which may be a safe and effective strategy for the prevention and management of CVD and play a complementary role to traditional therapeutic drugs.

Lycopene, a fat soluble carotenoid, found in significant concentrations in tomatoes and tomato products, has emerged as a very powerful natural antioxidant.

Many more clinical studies have now investigated the role of lycopene in the prevention and management of CVD.

The evidence to support its efficacy comes from epidemiological, in vitro and animal studies as well as human intervention studies.

There is now convincing evidence to suggest the consumption of lycopene and maintaining high level of serum lycopene, is effective in reducing the incidence of CVD by an impressive 25-30%.

Tomatoes and tomato products are the main sources of lycopene in human diets. Several studies from around the world have shown that daily intake of lycopene in a variety of populations is far below this recommended level.

Nutritional supplements containing lycopene can play a significant role in filling this gap, but until now a major problem in achieving a beneficial effect from supplements has been the fact that lycopene is poorly absorbed. Recently a new lycopene product called Ateronon has been introduced as a nutritional supplement.

This product has a unique patented LactoLycopene formulation produced by a novel manufacturing process that maximizes the stability and bioavailability of lycopene.

Studies investigating the efficacy of this product in lowering the risk of CVD have already been carried out. Speakers at this symposium following my talk will present results from recently completed and ongoing studies.

The important take home message is that there is convincing scientific evidence to suggest intake of lycopene that is stable and bioavailable, can significantly reduce the risk of CVD and improve quality of life.

Joseph Cheriyan

Associate Lecturer in Medicine, University of Cambridge; Consultant Physician and Clinical Pharmacologist, Cambridge University Hospitals NHS Foundation Trust.

THE BIOLOGICAL EFFECT OF LACTOLYCOPENE

After decades of research to establish why Mediterranean populations have lower rates of heart disease and stroke, experiments have identified lycopene a key nutrient in tomatoes, as a principal source of this health benefit.

Our research team at Cambridge has found that using Ateronon, a newly developed version of modified lycopene improves absorption of the compound into the blood, and boosts the elasticity and efficiency of blood vessels, improving blood flow and reducing the hardening of the arteries that occurs with age.

It was this modified lycopene called LactoLycopene, that was shown to improve flexibility of blood vessels by up to 50%.

Our two-month study compared the effect of LactoLycopene on 36 patients with pre-existing heart disease, who were already taking cholesterol-lowering statin drugs, and 36 healthy volunteers. Both groups had an average age of 67 and comparable blood pressure readings, though those with heart disease already had demonstrable blood vessel damage.

The compound was shown to dramatically improve the function of the cells of the endothelium, the layer of cells lining the blood vessels, in the group of patients suffering from heart disease.

Increasing blood lycopene levels boosted the endothelium's sensitivity to nitric oxide, the gas that triggers the dilation of the blood vessels in response to exercise and the body's demand for increased blood flow in healthy people.

Our study was selected for presentation at a recent American Heart Association meeting. The full results will appear in a scientific journal next week, and I am unable to elaborate further until they are made public, but we're hoping this growing interest in LactoLycopene will inspire other groups to undertake further studies.

There is already a large body of research pointing to the benefits of increased lycopene intake. The main problem has been finding a way to increase its absorption. Lactolycopene is better absorbed than the less stable unmodified compound found in tomatoes, which is called trans-lycopene.

There is now enough evidence to indicate that if entire populations increased their blood serum lycopene levels to those of the highest 25% of the population, levels of heart disease and stroke would fall dramatically. Some authorities including Sudhir Kurl's group at the University of Eastern Finland, have suggested optimum lycopene level could cut the risk of these diseases by 20-30%.

If the results we achieved are replicated in larger groups of patients, the use of the LactoLycopene pill Ateronon, could revolutionise the treatment of patients at risk.

Howard D. Sesso

Sc.D., M.P.H. Associate Epidemiologist, Brigham and Women's Hospital Associate Professor of Medicine, Harvard Medical School

LACTOLYCOPENE RELIABLY ELEVATES BLOOD LYCOPENE TO A LEVEL ASSOCIATED WITH MAXIMUM PROTECTION BY STUDIES

We used Ateronon, a LactoLycopene supplement, because of its proven track record to increase plasma lycopene, to carry out the largest randomized, double-blind, placebo-controlled clinical trial to date of any lycopene or tomato-based intervention.

We gave 7mg daily of either Ateronon or placebo to 213 patients with existing coronary heart disease. Patients were followed for up to 12 months, to look for changes in carotid intima media thickness (IMT), blood pressure, and a pre-specified group of coronary biomarkers.

We found that those taking Ateronon increased their average blood levels of lycopene at either 6 or 12 months follow-up by up to 20%, reflecting the excellent bioavailability of Ateronon.

Compliance with taking Ateronon was very high, exceeding 90%, reflecting the fact that Ateronon was well-tolerated and easily taken by participants. Importantly, we found no differences comparing Ateronon versus placebo for any self-reported symptoms or potential adverse events and there were no long-term safety concerns among those taking Ateronon versus placebo.

At 6 months, there were small improvements in carotid intima media thickness in the group taking Ateronon. About half of the participants completed the 12 month assessment at which differences in carotid IMT were neutral. The magnitude of change seen so far in coronary biomarkers is small, but this is likely to be because trial participants were already taking statins, blood-pressure lowing drugs, and aspirin.

This completed trial represents a tremendous opportunity to expand our knowledge on the cardiovascular effects of Ateronon in men and women with pre-existing coronary heart disease. Full reports of this work will shortly be submitted for publication in a leading peer-reviewed academic journal.

In our trial, comprehensive data have also been collected on lifestyle, clinical, and dietary factors, along with stored blood samples, blood pressure and other clinical assessments. Analyses are ongoing to investigate further into the effects of Ateronon on these other cardiovascular risk factors, along with the potential for expanded data from the completed carotid ultrasounds.

In addition to the primary findings from the Ateronon trial, to be submitted to a major peer-reviewed journal, many other important analyses and studies will be completed from our trial to clarify the mechanistic effects of Ateronon in the prevention of CVD.

Beyond our trial, additional research should consider the effect of Ateronon in those without cardiovascular disease but with early signs of high cholesterol, diabetes, or high blood pressure as a means of primary prevention.