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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

After More Than 150 Years, Recent Progress in Atherosclerosis Treatment

AFTER MORE THAN 150 YEARS, RECENT PROGRESS IN ATHEROSCLEROSIS TREATMENT

For more than 150 years, medical researchers have known atherosclerosis has an inflammatory component, but why hasn't there been anything done about it. Welcome to The Clinician's Roundtable on ReachMD XM 157, The Channel for Medical Professionals. I am Bruce Japsen, the healthcare reporter of The Chicago Tribune, and with me today is Dr. Lawrence Cohen. He is the President and Chief Executive Officer of VIA Pharmaceuticals. Dr. Cohen has served as President and CEO since VIA's formation in 2004 and before that he had a long resume in the Biotech Industry for 2 decades holding various executive roles including that as CEO of Zyomyx a proteomics technology company he joined in 1999 as Chief Operating Officer. Dr. Cohen received a PhD in microbiology from the University of Illinois and completed his post doctoral work in molecular biology at Dana-Farber Cancer Institute and the Department of Biological Chemistry at Harvard Medical School. He joins us today from VIA's offices in lovely San Francisco right on Battery Street.

BRUCE JAPSEN:

Dr. Cohen, welcome to ReachMD XM 157, The Channel for Medical Professionals.

DR. LAWRENCE COHEN:

Thank you very much Bruce, it's a pleasure.

BRUCE JAPSEN:

So tells us a little bit about, a lot of our listeners definitely are clinicians and have heard of atherosclerosis, but if you could tell us a little bit about this and why this inflammatory component, there just hasn't been anything new to treat this in this last century and a half really.

DR. LAWRENCE COHEN:

Our founder of VIA pharmaceuticals, Dr. Thomas Quertermous of Stanford University likes to point out that it was <_____>, I think in 1852 that published the first paper that characterized atherosclerosis as an inflammatory disease. Part of the distinction though, nobody really knew whether it was cause or effect. So they thought it was a lipid deposition disease. They thought it was sort of inert, if you will lipid deposition on the vessel wall and to some degree I think people thought that the inflammatory component was a response to the deposition of lipid on the vessel wall, although we now know that it is more causal than it is a response. So the first issue was not knowing whether it would be an effective way to treat the disease or not. Secondly about 20 years ago statins came in the market. These are very effective at lowering LDL and they had a serious impact on the disease process itself. In fact, many people thought that we would see the end of heart disease based on the development of statins, and of course, we now know that not to be the truth. I think the third component here is that it has been very difficult to define which of the inflammatory pathways are working in vessel wall. Inflammation comes in many flavors and it has only been recent work in the past perhaps 5 years have really defined what the most appropriate targets would be if you like to inhibit information in the vessel wall.

BRUCE JAPSEN:

And so the role of inflammation, could you narrow that down to, I mean, it is believed to be that it is a key contributor to the cardiovascular disease or we just don't know for sure.

DR. LAWRENCE COHEN:

I think that it's pretty well accepted in this day and age that inflammation is involved in the initiation of atherosclerosis. It is involved in the progression of the disease and it's also involved and those events that ultimately lead to major adverse cardiac events such as heart attack or stroke. So, it's really involved in every stage of the disease process.

BRUCE JAPSEN:

And it is a surprise to you that given the fact that it has been known about for so long that there haven't really been any therapies to address it?

DR. LAWRENCE COHEN:

I think only because our understanding of the disease has really changed recently that the people now understand the role that inflammation plays and I think they always assumed it was a component, but I think it's really recent work that has been done, again over the past 5 years, perhaps may be a little bit longer, which has really underscored the importance of the process to controlling the disease.

BRUCE JAPSEN:

Can you talk about some of this work, I mean for our listeners out there, even, you know, consumers, or specifically medical professionals what they might know and how they would be familiar with it?

DR. LAWRENCE COHEN:

I mean, there are number of centers around the country that have focussed a lot on this. VIA Pharmaceuticals specifically was focussed on work, and again like I mentioned before, that came out of Stanford University and this was a large significant grant to our founder Thomas Quertermous, and specifically what he had was he had access to all of the human hearts that were coming out of the Stanford Heart Transplant Unit. So if your heart was replaced or transplanted at Stanford, the excipient heart that was being replaced essentially ended up in the study and that is an unprecedented amount of tissue for the characterization of atherosclerosis and coronary vessels and it really led to the ability to do a very detailed molecular analysis to identify that yes inflammation was present and also to identify which molecular targets would be appropriate. So there is work from Stanford, there is work from many places all over the country, a lot of it has been done, but a lot of it has also been done in animal models both mice and rabbits of atherosclerosis.

Well, if you are just joining us or even if you are new to our channel, you are listening to the Clinician's Round Table on ReachMD XM 157. I am Bruce Japsen, the healthcare reporter with The Chicago Tribune and joining me from his offices in San Francisco is Dr. Lawrence Cohen. He is the chief executive officer of VIA Pharmaceuticals and we are talking about chronic inflammation in the vessel wall in the arteries or atherosclerosis and Dr. Cohen was just telling us about how we have known a lot about this condition for a long time, but there really have not been any therapies to address it and he was giving us some of the landscape into some of the research.

BRUCE JAPSEN:

If you could continue on doctor and tells us more about kind of where this is and where it may be headed.

DR. LAWRENCE COHEN:

So I think people now pretty well understand we have a good basal understanding. I think we'd never have a complete understanding of the role that inflammation plays and cells that are contributing to that inflammatory process. So it really starts with monocytes that are circulating in the bloodstream. They attach themselves to the endothelial cells, to the vessel wall. They actually transverse through that vessel wall. They turn into macrophages and that really starts the inflammatory process and it really starts the development of plaque and so it is pretty well now understood what the basic molecular and cellular events are around the process and I think because of that understanding that is which allowed us to think about that we can start to develop actually drug therapies for treating the inflammatory component of atherosclerosis.

BRUCE JAPSEN:

Now, a lot of primary care doctors and other health professionals might be listening in and say, well, you know what, it just seems like you statins that have been out there for so long would be considered more or less miracle drugs in reducing the risk of heart disease and we know that the number of deaths from heart disease have dropped, all you have to do is look at the CDC numbers, but the statins do not address this issue of the inflammation?

DR. LAWRENCE COHEN:

The statins actually have what we could call for the purposes of conversation a side effect so that they do have an anti-inflammatory component to their mechanism, but certainly the statins as a class of drugs were never optimized for that anti-inflammatory component. If you think about statins today, they are miracle drugs. They are very widely prescribed. Obviously, they are very safe. They are effective at reducing LDL in the majority of people. However, if you look at the published clinical trial results for those drugs, they are really reducing only somewhere between 20 and 30% of the relative risk of having heart attack. So if you have had a heart attack in this country, you are put on standard of care which includes aggressive statin therapies, your risk of having that second heart attack within 12 months has only been reduced by about 25 to 30%. So there is still a significant on that medical need and that's one of the reasons why the community has been looking at anti-inflammatories perhaps to fill that need.

BRUCE JAPSEN:

And could you give us an example of some of the anti-inflammatories out there that could be used because we're all of a sudden hearing about a lot of major drug companies looking at various ways to attack heart disease through combination pills, you know the triglyceride levels and looking at that as well.

DR. LAWRENCE COHEN:

If you look at the drugs that are accredited so obviously nothing on the market yet to treat inflammatory component of

atherosclerosis, but if you look at the programs that are being conducted in pharmaceutical companies and also in biotechnology companies, I think that they sort of broadly can be categorized into 2 areas, one is the innovation of leukotriene metabolism. So leukotrienes are pro-inflammatory mediators, and I like to think of them as sort of stoking the fire and keeping it burning once the inflammatory process has started. So there are a number of programs trying to develop leukotriene metabolic inhibitors and the second is cell adhesion molecules where, you know, we talked about monocytes circulating through the blood seeing an injured vessel wall attaching to that wall and then ultimately actually transversing through that and starting the process of atherosclerosis and there are some people that are also focussed on trying to inhibit that initial attachment of the monocyte. So I am sure there are other programs, but I think the majority of the programs that I know about are really focused on those two mechanisms.

BRUCE JAPSEN:

And are these types of compounds being developed, are they molecular in nature, are they pills, capsules, what are we talking about here?

DR. LAWRENCE COHEN:

I think the majority of the programs are small molecule drugs to be taken orally. I can think of one or two perhaps antibodies it's a little less obviously convenient. We are talking about a chronic therapy. This is something that if you had had a heart attack, you are probably going to have to take for the rest your life and so, you know, the convenience of once a day small orally available drug is really the focus of most of these programs.

BRUCE JAPSEN:

And that would certainly be good news for patients and so would you see potentially given the market out there that is changing so rapidly and a lot of the big pharmaceutical companies are developing combination pills to attack this, I would think that this could fit into that genre.

DR. LAWRENCE COHEN:

I mean if you think about you are living in the United States, you've had a myocardial infarction, you've had a heart attack, you've had a stroke, you're admitted to the hospital, you are put on a pretty serious regimen of drugs following that, I mean, you're basically given a statin, you're probably given an antihypertensive to reduce your blood pressure, you're given platelet aggregation inhibitors. It could be, you know, baby aspirin. It could be something like clopidogrel that's now on the market for that and so there is a regimen of drugs you are put on, and you can imagine that just out of convenience at some point, combination therapies would involve a number of these mechanisms which are complementary would be one way to go.

BRUCE JAPSEN:

You know, you bring up an excellent point really because when you <_____> things that are recommended, you know, if you have a heart history take a baby aspirin, it would only make sense that some of the things that are going on such as your company's efforts in this arena to look at the atherosclerosis it certainly would make sense just to add another component, because that's basically what has been done in the history of treating heart disease.

DR. LAWRENCE COHEN:

That's right, I mean, I think that the anti-inflammatories that are being developed today will be used on top of standard of care. So they are not going to replace on of the current approaches we have, but they are just going to be one more arm in that attack on coronary vessel disease.

BRUCE JAPSEN:

And how close are we to seeing something like this on the market?

DR. LAWRENCE COHEN:

There are a number of programs that have completed phase II and probably will begin phase III trials next year.

BRUCE JAPSEN:

And so if all goes to plan, potentially, 5 years?

DR. LAWRENCE COHEN:

Yeah, I would say less than 5 years. I mean, VIA Pharmaceuticals, our drug is completing its phase II clinical program. There are two trials actually that are

INCOMPLETE DICTATION