**1st CVD Anti-Inflammatory Canakinumab with Positive Phase 3 Results Announced – Studied in HIV at CROI**

**Studied in pilot HIV study:**

**CROI/2017: IL-1β (canakinumab) INHIBITION SIGNIFICANTLY REDUCES ATHEROSCLEROTIC INFLAMMATION IN TREATED HIV Priscilla Hsue**

University of California, San Francisco, San Francisco, CA, USA

[**http://www.croiwebcasts.org/console/player/33597?mediaType=slideVideo&**](http://www.croiwebcasts.org/console/player/33597?mediaType=slideVideo&)

this was a pilot study in only 10 HIV+ subjects. Patient study subjects were HIV+, 59 years old and 24 years HIV duration, with elevated lipids on a statin. Patients received a single subcutaneous injection in insulin syringe in this pilot study. In the followup randomized controlled study in 100 patients will receive 2 doses at baseline and week 12 and will be followed for 36 weeks to much better evaluate this therapy.

Hsue concluded "this is the first we believe this is one of the first immune based therapies to show a very profound reduction in inflammatory markers in the setting of treated HIV, one of the first to show improved arterial inflammation & bone marrow activity."

rst immune based therapies to show a very profound reduction in inflammatory markers in the setting of treated HIV, one of the first to show improved arterial inflammation & bone marrow activity."

---------------------

**1st CVD Anti-Inflammatory Canakinumab with Positive Phase 3 Results Announced**

Novartis announced heralded results from the big Phase III  called in the press "win in cardio it’s been searching for.” The drug is currently approved for rare autoimmune diseases and sold as Ilaris. “ACZ885 is the first and only investigational agent which has shown that selectively targeting inflammation reduces cardiovascular risk. Our priority now is to thoroughly analyze these important data and discuss them with regulatory agencies.”

The pharma giant’s canakinumab (ACZ885) significantly reduced the risk of a composite of cardiovascular death, non-fatal myocardial infarction and non-fatal stroke for patients with a prior heart attack and inflammatory atherosclerosis. The pharma giant is sticking with top line data for now, but with analysts skeptical that the 6-year, 10,000-plus patient study would come through, Novartis saw its shares jump more than 2% Thursday morning.

This drug works by inhibiting IL-1ß, a key cytokine, for a prolonged period, tamping down on inflammation to lower risk to patients.

Canakinumab is a human monoclonal IL-1β antibody indicated for treatment inflammatory disorders such as CAPS and Muckle-Wells syndrome

–Dosing is quarterly subcutaneous injection….Produces a rapid and sustained inhibition of inflammation with only minimal effects on lipids

[**https://www.forbes.com/sites/johnlamattina/2017/06/22/novartis-cantos-heart-trial-results-could-lead-to-drastic-drop-in-arthritis-drug-price/#130a01356bf3**](https://www.forbes.com/sites/johnlamattina/2017/06/22/novartis-cantos-heart-trial-results-could-lead-to-drastic-drop-in-arthritis-drug-price/#130a01356bf3)

**FDA PI attached above**



[**https://en.wikipedia.org/wiki/Canakinumab**](https://en.wikipedia.org/wiki/Canakinumab) - **Canakinumab** ([INN](https://en.wikipedia.org/wiki/International_Nonproprietary_Name), trade name **Ilaris**, previously **ACZ885**)[[2]](https://en.wikipedia.org/wiki/Canakinumab#cite_note-2) is a human [monoclonal antibody](https://en.wikipedia.org/wiki/Monoclonal_antibody) targeted at [interleukin-1 beta](https://en.wikipedia.org/wiki/IL1B). It has no cross-reactivity with other members of the interleukin-1 family, including interleukin-1 alpha.[[3]](https://en.wikipedia.org/wiki/Canakinumab#cite_note-3)

Canakinumab was approved for the treatment of [cryopyrin-associated periodic syndromes](https://en.wikipedia.org/wiki/Cryopyrin-associated_periodic_syndrome) (CAPS) by the U.S. [Food and Drug Administration](https://en.wikipedia.org/wiki/Food_and_Drug_Administration) (FDA) on June 2009[[4]](https://en.wikipedia.org/wiki/Canakinumab#cite_note-4) and by the [European Medicines Agency](https://en.wikipedia.org/wiki/European_Medicines_Agency) in October 2009.[[5]](https://en.wikipedia.org/wiki/Canakinumab#cite_note-5) CAPS is a spectrum of autoinflammatory syndromes including [familial cold autoinflammatory syndrome](https://en.wikipedia.org/wiki/Familial_cold_autoinflammatory_syndrome), [Muckle–Wells syndrome](https://en.wikipedia.org/wiki/Muckle%E2%80%93Wells_syndrome), and [neonatal-onset multisystem inflammatory disease](https://en.wikipedia.org/wiki/Neonatal-onset_multisystem_inflammatory_disease). On September 2016, FDA approved the use of canakinumab on 3 additional rare and serious auto-inflammatory diseases:[[6]](https://en.wikipedia.org/wiki/Canakinumab#cite_note-6) Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) and Familial Mediterranean Fever (FMF).

Canakinumab was being developed by [Novartis](https://en.wikipedia.org/wiki/Novartis) for the treatment of [rheumatoid arthritis](https://en.wikipedia.org/wiki/Rheumatoid_arthritis) but this trial was completed in October 2009.[[7]](https://en.wikipedia.org/wiki/Canakinumab#cite_note-7) Canakinumab is also in [phase I](https://en.wikipedia.org/wiki/Clinical_trial#Phase_I) [clinical trials](https://en.wikipedia.org/wiki/Clinical_trial) as a possible treatment for [chronic obstructive pulmonary disease](https://en.wikipedia.org/wiki/Chronic_obstructive_pulmonary_disease),[[8]](https://en.wikipedia.org/wiki/Canakinumab#cite_note-8) [gout](https://en.wikipedia.org/wiki/Gout) and [coronary artery disease](https://en.wikipedia.org/wiki/Coronary_artery_disease) (the CANTOS trial; [[9]](https://en.wikipedia.org/wiki/Canakinumab#cite_note-9)). It is also in trials for [schizophrenia](https://en.wikipedia.org/wiki/Schizophrenia).[[10]](https://en.wikipedia.org/wiki/Canakinumab#cite_note-10) In gout it may result in better outcomes than a low dose of a steroid but costs five thousand times more.[[11]](https://en.wikipedia.org/wiki/Canakinumab#cite_note-11)

Interestingly, canakinumab is already on the market for inflammatory conditions. [As explained by my *Forbes* colleague,](https://www.forbes.com/sites/matthewherper/2017/06/22/novartis-drug-becomes-first-to-prevent-heart-attacks-and-strokes-by-targeting-inflammation/#aede4c72b1a7) Matt Herper, canakinumab, under the trade name of Ilaris, is sold by Novartis to treat systemic juvenile idiopathic arthritis and also periodic fever syndromes. Ilaris is an expensive drug with a list price of $200,000 per year. However, it is dosed monthly. In CANTOS, canakinumab was only dosed every three months, so theoretically, Herper estimates that based on current costs, using this same drug for CV disease would cost $60,000/year/patient.

The drug in question is canakinumab (ACZ885), an antibody to the inflammatory protein, Il-1B. In a trial called CANTOS, Novartis tested canakinumab (plus standard of care) against standard of care alone in 10,061 patients who had previously suffered a myocardial infarction (MI) and who also had a high level of inflammation as evidenced by levels of high-sensitivity C-reactive protein in excess of 2mg/L. While specific results will not appear until later in the year, Novartis said that the “[Phase III CANTOS study](https://www.novartis.com/news/media-releases/novartis-phase-iii-study-shows-acz885-canakinumab-reduces-cardiovascular-risk) met the primary endpoint, a composite of heart attack, stroke and cardiovascular death, showing that ACZ885 (canakinumab) in combination with standard of care therapy reduces cardiovascular risk in people with a prior heart attack and inflammatory atherosclerosis.”

However, unless the CANTOS data are stunning, such a pricing scheme would be dead on arrival. That’s because we have already gone down this road with another class of compounds, the PCSK9 inhibitors Repatha (Amgen) and Praluent (Sanofi/Regeneron). These drugs have the amazing ability to lower LDL- cholesterol (LDL-c) levels to 30mg/dL when combined with statins. Furthermore, [Amgen’s FOURIER study](https://www.forbes.com/sites/johnlamattina/2017/03/22/ucsf-cardiologist-is-distrustful-of-amgens-cholesterol-drug-study/#1eb1a40a3826) with Repatha shows that this reduction in LDL-c  can meaningfully reduce heart attacks in people with serious heart disease. Yet, payers have been reluctant to add the PCSK9 inhibitors to their formularies because of their price. These drugs have list prices of about $14,000/patient/year. (Although industry scuttlebutt suggests that deals have been struck such that the actual negotiated prices are about $9,000.) Even with the negotiated price, Amgen has had to [provide money-back guarantees](https://www.forbes.com/sites/johnlamattina/2017/04/04/amgens-money-back-guarantee-for-its-cholesterol-drug-repatha/#5223f4ac35d4) for Repatha with payers in order to help gain formulary access.

Until the CANTOS data are published, one cannot compare the relative benefits of canakinumab to the PCSK9 inhibitors. But it is hard to believe that there will be a dramatic difference between the two classes of drugs. What is dramatically different, however, are the current prices of Ilaris compared to Repatha and Praluent. Thus, if the CV benefits are only comparable, it is unlikely that payers will include Novartis’ drug on their formularies unless it is priced similarly to the PCSK9s. Given the enormous potential of canakinumab in the CV market, Novartis would likely do just that.

However, Novartis would be hard pressed to make the case that Ilaris (canakinumab) for juvenile idiopathic arthritis should be priced at $200,000/patient/year, whereas using the same drug (undoubtedly with a different tradename) for CV disease can be priced at $9,000/patient/year. One can’t use the usual “costs of R&D” argument, as the CANTOS trial likely cost tens of millions of dollars more than all of the Ilaris trials combined. In addition, while the formulation and dosing schedule for “CV canakinumab” might well be different from that of Ilaris, it would in no way justify a major price difference for canakinumab in the different diseases.

In all likelihood, Novartis would bite the bullet and lower the price of Ilaris to the level set with “CV canakinumab”. That wouldn’t be a great hardship for Novartis because, as Herper pointed out, Ilaris sales are only about $250 million annually. But who would have thought at the results of a heart disease study could potentially provide an unexpected financial benefit to those patients with juvenile arthritis.

--------------------------

press release from Novartis

**Novartis Phase III study shows ACZ885 (canakinumab) reduces cardiovascular risk in people who survived a heart attack**

Jun 22, 2017

* *Phase III CANTOS study met the primary endpoint, a composite of heart attack, stroke and cardiovascular death, showing that ACZ885 (canakinumab) in combination with standard of care therapy reduces cardiovascular risk in people with a prior heart attack and inflammatory atherosclerosis*
* *Despite current treatments about 40% of heart attack survivors remain at increased risk of  recurrent heart attack, stroke or cardiovascular death because of high-risk inflammatory atherosclerosis[1]; 25% experience another event within five years[2]*
* *Full results will be presented at an upcoming medical congress; Novartis plans to initiate discussions with regulatory authorities*

**Basel, June 22, 2017 -**Novartis today announced topline results from the global Phase III CANTOS study investigating the efficacy, safety and tolerability of ACZ885 (canakinumab) in combination with standard of care in people with a prior heart attack and inflammatory atherosclerosis. With more than 10,000 patients enrolled in the study over the last six years, CANTOS is one of the largest and longest-running clinical trials in Novartis' history.

The CANTOS study met the primary endpoint, demonstrating that when used in combination with standard of care ACZ885 reduces the risk of major adverse cardiovascular events (MACE), a composite of cardiovascular death, non-fatal myocardial infarction and non-fatal stroke, in patients with a prior heart attack and inflammatory atherosclerosis. The full data from the study will be submitted for presentation at a medical congress and for peer reviewed publication later this year.

"Despite current treatment, about 25 percent of heart attack survivors will have another cardiovascular event within five years, making the outcome of the CANTOS study a promising new development for patients," said Vas Narasimhan, Global Head, Drug Development and Chief Medical Officer, Novartis. "ACZ885 is the first and only investigational agent which has shown that selectively targeting inflammation reduces cardiovascular risk. Our priority now is to thoroughly analyze these important data and discuss them with regulatory agencies."

Heart attack occurs in about 580,000 people every year in EU5 and 750,000 people in the United States alone[3],[4]. In 2015 there were an estimated 7.29 million heart attacks globally[5]. Despite standard treatment, people with a prior heart attack live with a higher ongoing risk of having another event or dying, and it has been shown that in about four in 10 people, this risk is directly related to increased inflammation associated with atherosclerosis[1]. The recurrent MACE in patients with inflammatory atherosclerosis are associated with increased morbidity, mortality and reduced quality of life and currently represent a major economic burden on patients and healthcare systems around the world.

**About CANTOS**

The Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS) (NCT01327846) is a randomized, double-blind, placebo-controlled, event-driven Phase III study designed to evaluate the efficacy, safety and tolerability of quarterly subcutaneous injections of ACZ885 (also known as canakinumab) in combination with standard of care in the prevention of recurrent cardiovascular (CV) events among 10,061 people with a prior myocardial infarction (MI) and with a high-sensitivity C-reactive protein (hsCRP) level of >=2mg/L. The study evaluated three different doses of ACZ885 vs placebo. The primary endpoint of the study was time to first occurrence of major adverse CV event (MACE), a composite of CV death, non-fatal MI, and non-fatal stroke. Secondary endpoints included time to first occurrence of the composite CV endpoint consisting of CV death, non-fatal MI, non-fatal stroke and hospitalization for unstable angina requiring unplanned revascularization; time to new onset type 2 diabetes among people with pre-diabetes at randomization; time to occurrence of non-fatal MI, non-fatal stroke or all-cause mortality; and time to all-cause mortality. The median follow-up time was 3.8 years. The study ran for approximately six years.

**About heart attack and inflammatory atherosclerosis**

 Heart attack occurs in about 580,000 people every year in EU5 and 750,000 people in the United States alone[3],[4]. In 2015 there were an estimated 7.29 million heart attacks globally[5]. Despite standard treatment, patients who have had a prior heart attack live with a higher ongoing risk of secondary major adverse cardiovascular events (MACE), a composite of cardiovascular (CV) death, non-fatal MI, and non-fatal  stroke. It has been shown that in about four in 10 people, this risk is directly related to the increased inflammation associated with inflammatory atherosclerosis as measured by a high-sensitivity C-reactive protein (hsCRP) biomarker level of >= 2mg/L[1]. The recurrent MACE in people with inflammatory atherosclerosis are associated with increased morbidity, mortality and reduced quality of life and currently represent a major economic burden on patients and healthcare systems around the world.

**About ACZ885**

ACZ885 (canakinumab) is a selective, high-affinity, fully human monoclonal antibody that inhibits IL-1ß, a key cytokine in the inflammatory pathway known to drive the continued progression of inflammatory atherosclerosis[6]-[10]. ACZ885 works by blocking the action of IL-1ß for a sustained period of time, therefore inhibiting inflammation that is caused by its over-production[11],[12]. ACZ885 is the first and only agent which has shown that selectively targeting inflammation significantly reduces cardiovascular risk in patients who have had a prior heart attack and have an increased cardiovascular inflammatory burden.