Anti-inflammatory Drug May Fight Cancer as Well as Heart Disease

Canakinumab was associated with lower lung cancer risk in a large cardiovascular study.

August 30, 2017 By Liz Highleyman

An experimental drug that reduces inflammation was associated with a lower risk of lung cancer and reduced cancer-related mortality in a clinical trial designed to evaluate cardiovascular outcomes.

Findings from the CANTOS study, presented at the European Society of Cardiology conference this week in Barcelona, support the idea that inflammation plays a key role in cancer as well as cardiovascular disease.

Cancer occurs when cells grow out of control. While a number of factors can cause cancer, including toxic chemicals (such as those found in tobacco smoke), viruses (such as human papillomavirus) and inherited genetic mutations, a growing body of evidence suggests that inflammation promotes cancer development and progression.

Paul Ridker, MD, of Brigham and Women's Hospital in Boston, presented findings from the Phase III CANTOS study, a randomized clinical trial designed to test whether the monoclonal antibody canakinumab would reduced the occurrence of heart attacks, strokes and cardiovascular death.

The primary cardiovascular results were published in The New England Journal of Medicine. Ridker's team also conducted a preplanned exploratory analysis of the effect of canakinumab on cancer in people with atherosclerosis. These findings were published in The Lancet.

"As an inflammatory biologist and cardiologist, my primary interest is heart disease, but CANTOS was a good setting to explore a previously observed link between cancer and inflammation," Ridker said in a press release issued by the European Society of Cardiology. "The data on cancer rates point to the possibility of slowing the progression of certain cancers, but these are exploratory findings that need replication."

Produced by Novartis, canakinumab is a monoclonal antibody that targets interleukin-1 beta (IL-1β), a cytokine (cell-signaling molecule) that triggers inflammatory responses. It is currently approved under the brand name Ilaris for treatment of juvenile arthritis and rare inherited immune diseases. It is being studied for a number of conditions involving inflammation, including HIV.

CANTOS enrolled more than 10,000 participants who had a previous myocardial infarction (heart attack) and an elevated blood level of high-sensitivity C-reactive protein, a marker of inflammation; they did not have a cancer diagnosis at study entry. The participants were randomly assigned to receive one of three doses of canakinumab or a placebo by injection every three months.

The primary study results at 48 months showed that people who received canakinumab had a modest decrease in cardiovascular events, compared with those who received the placebo (up to a 15 percent reduction). This effect was not related to changes in blood cholesterol, so canakinumab did not work like statins. Those who received canakinumab had reduced levels of C-reactive protein and the inflammatory cytokine interleukin 6 (IL-6).

“For the first time, we’ve been able to definitively show that lowering inflammation independent of cholesterol reduces cardiovascular risk,” Ridker said. “This has far-reaching implications. By leveraging an entirely new way to treat patients—targeting inflammation—we may be able to significantly improve outcomes for certain very high-risk populations.”

Blocking IL-1β interferes with the immune system’s ability to fight infection. People who received canakinumab had a higher rate of fatal infections than placebo recipients. However, canakinumab recipients had fewer cancer deaths, so the overall death rates were similar.

The exploratory cancer analysis found that cancer-related mortality during 3.7 years of follow-up was significantly lower among people who received canakinumab: 0.31 per 100 person-years in the highest dose group versus 0.64 per 100 person-years in the placebo group.

Those who received the highest dose of canakinumab were 67 percent less likely to be diagnosed with lung cancer and 77 percent less likely to die from it. Participants who were diagnosed with lung cancer during follow-up had higher C-reactive protein and IL-6 levels, and those who saw the largest reductions in these markers benefited more. Smokers also seemed to gain the most benefit.

The researchers said that canakinumab seemed unlikely to have a direct effect on the development of new lung cancers, although this possibility cannot be ruled out. Instead, they suggested, “a more biologically plausible explanation is that canakinumab reduced the rate of progression, invasiveness and metastatic spread of lung cancers that were prevalent but undiagnosed at trial entry.”

This is consistent with previous research showing that cytokines such as IL-1β can promote tumor growth and angiogenesis, or development of new blood vessels to feed a growing tumor.

Studies have shown that long-term use of aspirin and other nonsteroidal antiinflammatory drugs is associated with a reduction in death from certain cancers, but the beneficial effects of canakinumab on lung cancer incidence and mortality in the CANTOS study was seen in a much shorter time frame, they noted.

“Our hypothesis-generating data suggest the possibility that anti-inflammatory therapy with canakinumab targeting the interleukin-1β innate immunity pathway could significantly reduce incident lung cancer and lung cancer mortality,” the study authors concluded.

Novartis said it plans to seek approval of canakinumab for cardiovascular disease this year and will further test the drug as a treatment for lung cancer in additional Phase III studies.

Click here to read the full article in The New England Journal of Medicine.

Click here to read a summary of the article in The Lancet.

Press releases about the cardiovascular results and cancer findings are available online.
