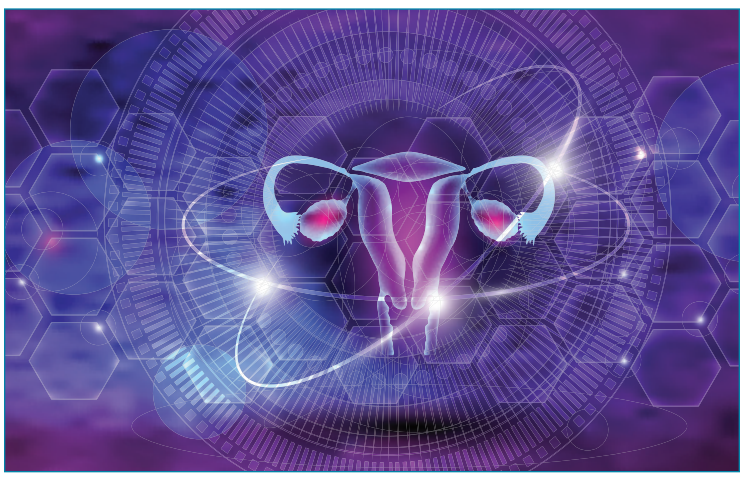
The Role of Lipophilic Statins in Reducing Epithelial Ovarian Cancer

BY WARREN FROELICH

In a study of more than 10,000 women, a team led by researchers at Johns Hopkins University found that lipophilic statins, a commonly prescribed drug used to control high cholesterol, was associated with a 40 percent reduction in mortality from epithelial ovarian cancer.

The findings, presented during a press briefing at the 2020 American Association for Cancer Research (AACR) Virtual Meeting II held online June 22-24, showed reductions in mortality across all subtypes, including the most common and aggressive forms of the disease.

"Our results consistently showed that among women with epithelial ovarian cancers, statin users compared to never-users had a significant reduction in ovarian cancer mortality, particularly those taking lipophilic statins," said Kala Visvanathan, MD, MHS, Professor of Epidemiology and Oncology at Johns Hopkins Bloomberg School of Public Health and Sidney Kimmel Comprehensive Cancer Center, who outlined the findings for the research team.



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The researchers emphasized that a randomized controlled trial was needed to conclusively demonstrate that statin use resulted in improved survival in ovarian cancer patients.

"They make it clear in their conclusion that this hypothesis needs to be tested in a randomized trial," said Antoni Ribas, MD, PhD, Director of the Tumor Immunology Program at the Jonsson Comprehensive Cancer Center at UCLA and President of AACR who co-chaired this press briefing.

"But this is a great start and a good way to go because these are agents with low toxicity and they achieved the goal of increasing needs for ovarian cancer (treatments) in a randomized trial," he added. "That would be a great outcome."

Studying Statins

Ovarian cancer is a rare cancer type, accounting for only about 1.2 percent of cancer cases diagnosed each year in the United States. About 90 percent of ovarian tumors stem from the transformation of epithelial cells, as opposed to those originating from germ cells or sex cord-stromal tissues, and are thus designated as epithelial ovarian cancers.

The disease has a 5-year survival rate of less than 50 percent and is frequently diagnosed in an advanced stage when surgery is no longer an option.

"There are no proven screening strategies [for ovarian cancer] and there is an urgent need to find cheaper effective treatment alternatives," Visvanathan said.

According to a recent survey, about 40 million individuals in the United States—representing nearly 28 percent of adults older than 40 years of age—use statins to control cholesterol. The drugs come in two categories, based on their solubility: lipophilic statins, such as simvastatin and lovastatin, dissolve in fats; while hydrophilic statins, such as pravastatin and rosuvastatin, dissolve in water.

Statins first attracted interest among cancer researchers in the early 1990s when some animal studies suggested a link between their use and cancer growth. But subsequent randomized controlled safety and observational studies in patients failed to find this connection. In fact, these studies found that individuals taking statins were less likely to be diagnosed with prostate cancer and were living longer after a diagnosis with breast, colorectal, kidney, and lung cancer than individuals not taking statins.

Animal studies suggest statins may impact several complex cellular processes and underlying molecular mechanisms to accomplish this feat, including angiogenesis, inflammation, immunological changes, and inhibition of HMG-CoA reductase, the rate limiting enzyme in the synthesis of mevalonate (the fatty acid intermediate in cholesterol biosynthesis).

When asked about the potential mechanism statins might use to reduce ovarian cancer mortality, Visvanathan noted: "It's likely not one specific mechanism. There are actually multiple mechanisms being associated with statins in the preclinical setting."

She further noted that two previous observational studies examining the association between statins and ovarian cancer and mortality yielded mixed results. The large sample size of this current study allowed researchers to evaluate different statins and their impact on multiple subtypes of ovarian cancer.

Research Details

In all, the study population for this study included 10,062 women aged 18 and older diagnosed with incidence of epithelial ovarian cancer between 1995 and 2015. The researchers used the Finnish National Cancer Registration and Finnish National Prescription Claims Database for high quality and completeness, allowing them to stratify for age, statin use, cancer subtype, and concurrent medications.

A total of 2,621 patients were statin users of which 80 percent took lipophilic statins as a treatment. The median age at diagnosis among all patients was 63 years and 67 among statin users. The medium duration of statin use was 7.5 years.

Overall, the study found that ovarian cancer mortality among ever-statin users was reduced 40 percent compared to never-users Those who took lipophilic statins to treat their cholesterol—specifically simvastatin and atorvastatin—showed a 43 percent reduction in mortality from this disease.

Women with all subtypes of ovarian cancer experienced a reduction in mortality, but the magnitude of reduction varied. The most significant reductions in mortality occurred in those with high-grade serous carcinoma (40% reduction in mortality) and endometrioid ovarian cancer (50% reduction in mortality). Serous epithelial ovarian cancer is the most common and aggressive form of the disease.

Visvanathan said the improved survival data across all ovarian cancer subtypes were encouraging. But she noted data for the rarer ovarian cancer subtypes were less robust. Some women initiated the use of lipophilic statins after receiving an ovarian cancer diagnosis, and they, too, experienced reduced mortality.

"Our results support further evaluation of lipophilic statins in women with epithelial ovarian cancer in a randomized trial in conjunction with existing therapies," she said. "Our results also reinforce the value of examining existing therapies that are well-tolerated and inexpensive to reduce worldwide cancer occurrence." OT

Warren Froelich is a contributing writer.