



Updates on Statins

Benefits of statin therapy in breast cancer patients

A recent study comparing the efficacy and tolerability of atorvastatin in addition to endocrine treatment in patients with advanced breast cancer showed that statin therapy significantly enhances overall survival and breast cancer-specific survival when used both in the prediagnostic and the postdiagnostic setting compared with no statin use.

The study was a Swedish nationwide study headed by Signe Borgquist and presented at the San Antonio Breast Cancer Symposium (SABCS) 2017.

Statins are already proven to be effective for cardiovascular disease prevention. Studies have shown that extrahepatic function of the statins may affect the mevalonate pathway in cancer cells by targeting enzyme 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. HMG-CoA reductase is differentially expressed in breast tumors, with some tumors having an expression higher than others. However, it was noted that high levels of HMG-CoA reductase expression was associated with better outcomes in breast cancer, and may thereby be used as a predictive marker for statin response.

The study indicated that both prediagnostic and postdiagnostic use is beneficial if women were using a statin in either setting. In addition, if women were using statins regularly, they would have more benefits than those who were not regular users.

The study cohort included 20559 Swedish women diagnosed with breast cancer from July 2005 through 2008. Statin use was identified through the Swedish Prescription Registry, while breast cancer-specific death was identified from the national cause-of-death registry through the end of 2012.

Out of the 4678 patients that died during follow-up, 2669 deaths were considered breast cancer-specific deaths. The results showed that:

- compared with women not receiving statins at all, women who took a statin regularly before their diagnosis had a 23% lower relative risk of dying from breast cancer
- women who had been exposed to any statin use had a 17% lower relative risk of dying from breast cancer
- women who took an intermediate statin dose had a 26% lower relative risk for a breast cancer-related death
- women who took high-dose statin therapy before diagnosis had a 16% lower risk of reaching the same endpoint

The type of statin taken in the postdiagnostic setting did not affect the death rate in breast cancer and the relative risk was identical for both lipophilic and hydrophilic statins. In addition, the dosage of statins administered before breast cancer diagnosis did not appear to affect the risk of breast cancer-related death. It was also noted that administration of both lipophilic and hydrophilic statins after breast cancer diagnosis was associated with a 7% relative risk reduction in breast cancer-related mortality, and therefore, the type of statin administered may not play a role in the magnitude of risk reduction.

In this study, the researchers also demonstrated that statins inhibit not just the HMG-CoA reductase enzyme but also decrease systemic levels of a cholesterol metabolite known as 27-hydroxycholesterol (27HC). Since the metabolite binds to the estrogen receptor, the production of both cholesterol and cholesterol metabolite with estradiol-like capabilities is also inhibited. Considering the fact that 27HC serves as an estrogen receptor agonist in breast cancer cells, inhibition of cholesterol and its metabolite may have a mitigating effect on breast cancer progression and recurrence.

Another trial, BIG 1-98, reported that use of statins during adjuvant endocrine therapy improved disease-free survival, breast cancer-free survival intervals, and distant recurrence-free intervals in postmenopausal women with early-stage, hormone receptor-positive

breast cancer. This study thereby reiterated the fact that statins may help in preventing breast cancer recurrence.

The study group is now looking into conducting another trial—the Advanced Breast Cancer-Statins and Endocrine Treatment (ABC-SE) trial—comprising patients with metastatic breast cancer. In that trial, they will attempt to compare the efficacy and tolerability of atorvastatin, 40 mg, in addition to endocrine treatment in patients with estrogen receptor-positive advanced breast

cancer. The objective of the trial will be to assess whether statin therapy can boost the effectiveness of endocrine therapy by modulating pathways of cholesterol production. In future, it is necessary to conduct large-scale study to identify robust predictive markers to determine which women might benefit from a statin.

Source: Statins May Up Breast Cancer-Specific and Overall Survival - Medscape - Dec 08, 2017.