

LAY ABSTRACT

Sacituzumab govitecan (SG) is an antibody attached to a drug which releases the drug when it encounters the tumor cell. The antibody recognizes Trop2, which is a protein not expressed in normal adult tissues but highly expressed in triple negative breast cancer (TNBC). In women with metastatic TNBC who are treated with this drug, one of three will have a decrease by at least 30% of their tumors despite having failed multiple lines of prior treatment. These responses happen early at around 2 months, and persist for 9 months on average. Based upon these findings, SG has received an expedited review by the FDA with accelerated approval anticipated to occur later this year (2019).

A significant problem with TNBC is the development of brain metastases. Nearly half of the women with advanced TNBC will develop spread of cancer to the brain, and there are no drugs specifically approved to treat TNBC brain metastases. Survival remains poor for these women. It is unknown if SG is actively able to reach tumors within the brain due to a blood brain barrier. We believe that this particular antibody-drug combination has particular potential to treat brain metastases. The molecule portion that attaches the drug to the antibody spontaneously breaks when exposed to more acidic conditions, which is a situation commonly seen in tumors. The drug which is attached to the antibody is known to readily cross the blood brain barrier, so that when released in the vicinity of the tumor should attack the tumor cells.

This trial will assess the concentrations of drug in women with breast cancer undergoing surgery as part of their standard care for brain metastases, after receiving a dose of drug. In the first part of the study, a total of 20 women will be treated. The day prior to surgery the drug they will receive the drug. The following day, when the tumor is removed by a neurosurgeon, the tissue will be immediately collected and frozen within the operating room. A sample of blood and spinal fluid will also be collected. Specimens will undergo analysis for the concentration of SG by a process that measure the weight of all compounds called mass spectroscopy. The relative amount that is in the tumor relative to the blood will be compared, to determine how much actually enters the brain tumors, as well as compared to known concentrations necessary to kill tumor cells. Once women recover from surgery, they will continue to receive SG as long as their tumors do not grow. We will also measure the amount of Trop2 protein and oxygen levels in the tumors to provide more information on the importance of these two biomarkers to the drug in tumors and time before tumors grow. This will help clarify if this drug may be useful for patients with breast tumors in the brain, and extend the potential impact of this new targeted therapy to improve lives of women with breast cancer.