**Lay Summary**

Metastasis, the spread of cancer cells to distant parts of the body, is the most common cause of death in patients with breast cancers. Remarkable progress made in the field of immune-oncology over the past decade has provided tremendous hope to patients with advanced and metastatic cancer. Immune checkpoint inhibitors that unleash the patient’s T lymphocytes to attack cancer can cause durable long-lasting responses in a significant number of patients with various cancers. However, only a fraction of patients with locally advanced and metastatic breast cancer receive clinical benefit from immune checkpoint inhibitors.

One major limitation of this approach for breast cancer is the lack of T lymphocytes in the tumor for immune checkpoint inhibitors to be effective. To overcome this limitation, we have developed a new combination treatment that involves injection of immune-stimulating drugs into the tumor and radiation therapy to generate T lymphocytes attacking breast cancer metastasis. The goal of this project is to investigate if our new strategy can be effective in patients with locally advanced and metastatic breast cancer, and if this strategy can be more effective in combination with immune checkpoint inhibitors.

Since we received generous support from METAvivor, we had a chance to publish our results from pre-clinical studies (Oba et al., ***Cancer Research***, (2021); 81(24):6183-6195, and Yokoi et al., ***Scientific Reports***, (2021); 11(1):21992), and opened a Phase I clinical study (NCT04616248) for metastatic breast cancer patients in January 2023 at the USC. We have recently submitted an abstract to ASCO to introduce our clinical study to medical oncologists in the U.S.

Results from this research are expected to help patients with metastatic breast cancer by providing the foundation for developing significantly improved combination immunotherapy, and for future personalized cancer treatment to improve survival.