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Novel Selective Estrogen Mimics for Extending Survival Times of Tamoxifen-Resistant Breast Cancer Patients

Technology Overview

Approximately 230,000 new cases of breast cancer (BC) appear in the US each year making BC the most common type of cancer in women and the second deadliest type of cancer in the United States. Up to 80% of BC's are estrogen receptor positive (ER+) in which estrogen promotes tumor growth and patients with hormone receptor-positive metastatic breast cancer (MBC) typically undergo endocrine therapy as the initial therapeutic option. Tamoxifen (TAM) is a selective estrogen receptor modulator (SERM) used in most premenopausal patients with MBC and has been the standard of care (SOC) for this patient group.

Unfortunately, TAM patients invariably develop tumor TAM resistance resulting in today's lowered 5- year patient survival rates which have never been able to match the metrics of legacy treatments using high dose estrogen and diethystilbestrol (DES) employed in the 1960- 70s . DES is no longer used because of unacceptable side effects so there is an urgent need to develop new agents to address the survival gap with TAM but without the systemic toxicity associated with cytotoxic chemotherapy, and legacy therapies. These refractory cancers often over-express a biomarker, PKCα which is associated with Tamoxifen resistance.

Details

Scientists at the UIC College of Pharmacy have developed a unique and promising new compound series that promises to bring back the advantages of more effective classic therapies but without the risks.

TTC-352 is a unique Selective Estrogen Mimic (SEM) that interacts with nucleus-localized Estrogen Receptor (ER) and causes receptor externalization. Externalized ER is unable to signal normally and unlike TAM and estrogen, TTC-352 does not cause endometrial thickening which is associated with gynecological carcinogenesis and uterine cancer. Current efforts are directed at designing an anti-thrombotic functionality into this core to overcome cancer-associated thrombosis, another complication of BC. TTC-352 is a promising development candidate for ER+, TAM-resistant breast cancer, with enhanced safety profiles over SOC and classical therapies, and supported by a validated companion diagnostic biomarker.

Applications

- Premenopausal women with breast cancer who are failing Tamoxifen therapy
- Strong potential for use in Triple Negative Breast Cancer
- Potential use in Prostate Cancer

Benefits

- Potential for improving 5-year survival metrics for ER+ breast cancer patients
- Avoids toxicity MOA like classical chemotherapy
- Safer to use than existing SOC therapies

TECHNOLOGY QUICK FACTS

Reference Number
DG042

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Publications
Selective Estrogen Mimics for the Treatment of Tamoxifen-Resistant Breast Cancer Poster ME Molloy et al February 2013

IP Status
Provisional Patent Application

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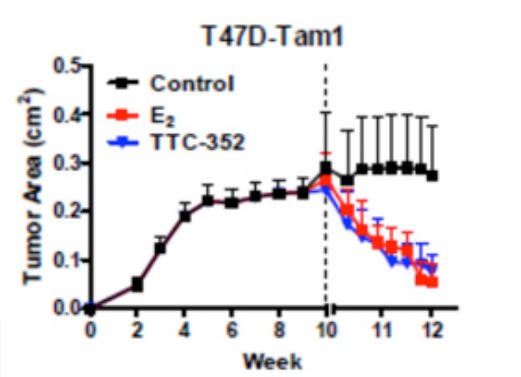
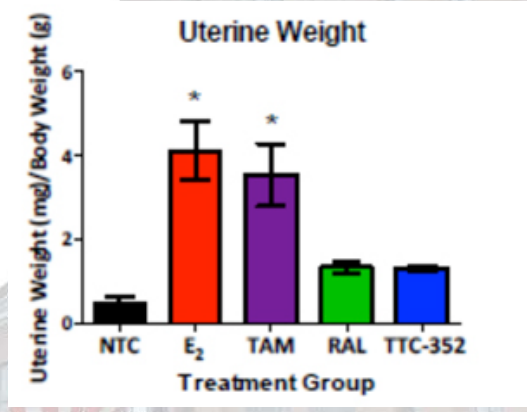
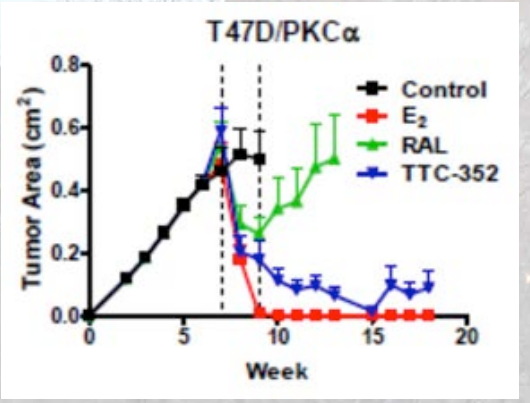
Supporting Data



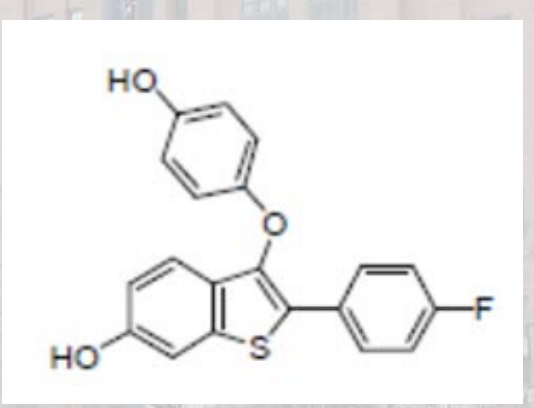
Treatment with estrogen or TTC-352 reduces an endogenously Tamoxifen-resistant tumor implanted in a xenograft animal model of breast cancer



TTC-352 does not promote uterine tissue growth like TAM and Estrogen predicating greater safety and lower risk of promoting uterine tumors.



A tumor cell line overexpressing PKCa which confers TAM resistance, is effectively suppressed in an animal xenograft model by estrogen and TTC-352 but not permanently by Raloxifene, a SERM from Eli Lilly



Future Development

As part of a Proof of Concept project sponsored by the UIC OTM, work is being done to develop novel compounds incorporating anti-thrombotic functionality into the molecule to address the cancer associated thrombosis risk of current therapies.

The TTC-352 analogs developed under the current POC funding program are envisioned to have a fast-track designation under the UIC Cancer Center and Center for Clinical and Translational Science.

The development pathway can be accelerated based on availability of a companion biomarker, PKCa, discovered by UIC scientists as a validated patient inclusion criterion for identifying breast cancer patients who are failing Tamoxifen therapy.