

The focus of this column is to describe published research studies of interest to professional oncology nurses.



Cannabinoids May Be Therapeutic in Breast Cancer

Cannabinoids are a group of compounds synthesized exclusively by the *Cannabis sativa* plant, commonly known as marijuana. In 1990, the first cannabinoid-specific membrane (CB1) was characterized and cloned (Matsuda, Lolait, Brownstein, Young, & Bonner, 1990), which catapulted biomedical research on these unique compounds. Cannabinoids refer to both marijuana-derived compounds with the active ingredient of 9-tetrahydrocannabinol (THC) and also the synthetic molecules that activate the same primary targets as THC. Therapeutic properties of marijuana have been well established; however, the clinical use of either plant-sourced or pure cannabinoids remains limited. The anticachexia properties of cannabinoids are found in tetrahydrocannabinol (oral capsules of synthetically generated THC) and are used to manage weight loss, wasting syndrome, and nausea and vomiting associated with cancer treatment.

Preclinical evidence has indicated that these compounds demonstrate antitumor effects in several cancers, ranging from cell cultures to xenografted and genetically engineered mice (Velasco, Sánchez, & Guzmán, 2012). Antitumor action by cannabinoids depends on the deliberate blockade of tumor progression. They are known to inhibit uncontrolled cancer cell growth by halting cancer cell proliferation and by inducing cancer cell death by apoptosis. In addition, they are able to impair tumor angiogenesis and ultimately metastasis. Because the effects of cannabinoids are observed in many different types of cancer cell lines, they are considered to have general rather than site-specific tumor type affinity.

Breast cancer remains the most common malignancy among Western wom-

en (DeSantis, Siegel, Bandi, & Jemal, 2011). Mortality rates have dropped significantly since the 1990s because of refined adjuvant treatment, as well as earlier screening and prevention. However, certain breast tumors continue to be resistant to conventional regimens. Caffarel, Andradás, Pérez-Gómez, Guzmán, and Sánchez (2012) acknowledged the pivotal need to develop new therapeutic strategies that focus on three main breast cancer subtypes according to molecular profiles: hormone receptor-positive, HER2-positive, and triple-negative tumors. Laboratory evidence indicates that cannabinoids may demonstrate significant therapeutic effects for those subtypes.

The review provided resources demonstrating that cannabinoids modulate key tumor progression-related aspects of estrogen receptor (ER) or progesterone receptor (PR)-positive breast cancer cells. Cannabinoids also impair ER/PR cancer cell migration and culture invasion. That finding might indicate cannabinoid modulation of hormone-sensitive breast cancer metastasis.

Another histopathologic subtype of breast tumors are those that express the tyrosine kinase receptor HER2. Patient outcomes for those individuals have improved since the clinical use of trastuzumab for breast cancer began in 2006 when trastuzumab received U.S. Food and Drug Administration approval in combination with doxorubicin, cyclophosphamide, and paclitaxel for the adjuvant treatment of women with node-positive, HER2-overexpressing breast cancer. Strong preclinical evidence suggests that cannabinoids may be useful for the treatment of this patient population (Caffarel et al., 2010). Two different cell lines were injected either subcutaneously in immune-deficient mice or orthotopically in immune-competent FVB mice and treated with THC and/or

CB2 selective agonists. In both instances, a significant reduction in tumor growth was observed per animal (including those with lung metastases), as well as a reduction in the number of tumor blood vessels, indicating that THC impairs tumor angiogenesis.

No standard targeted therapy exists for triple-negative breast cancer. Prognosis for this cohort is poor, and intense efforts have been made to improve chemotherapy responses with a variety of agents. In vitro and in vivo preclinical evidence indicates that cannabinoids may play a future role in the treatment of this patient population as well. Synthetic cannabinoids have been tested in triple-negative breast cancer and all have produced an inhibition of cell proliferation. Cannabinoids in this setting impact cancer cell proliferation, as well as angiogenesis. Another important feature of these compounds is the low toxicity and high safety profile when used either as single agents or in combination with standard regimens.

Caffarel et al. (2012) suggested the introduction of clinical trials that would incorporate cannabinoids with standard regimens to achieve synergistic and therapeutic outcomes. As the review article indicated, cannabinoids have demonstrated antitumor activity in preclinical breast cancer models. Practicing oncology professionals need to be aware of the clinical potential of these agents, including antiproliferative, proapoptotic, antimigratory, and anti-invasive actions on cancer cells. Bench-to-bedside clinical practice is the assurance that patients will have access to current knowledge and the potential therapeutic benefit of enhanced, scientifically based clinical cancer care.

Caffarel, M.M., Andradás, C., Mira, E., Pérez-Gómez, E., Cerutti, C., Moreno-Bueno, G., . . . Sánchez, C. (2010). *Molecular Cancer*, 9, 196. doi:10.1186/1476-4598-9-196

Caffarel, M.M., Andradás, C., Pérez-Gómez, E., Guzmán, M., & Sánchez, C. (2012). Cannabinoids: A new hope for breast cancer therapy? *Cancer Treatment Reviews*, 38, 911–918. doi:10.1016/j.ctrv.2012.06.005

DeSantis, C., Siegel, R., Bandi, P., & Jemal, A. (2011). Breast cancer statistics, 2011. *CA: A Cancer Journal for Clinicians*, 61, 409–418. doi:10.3322/caac.20134