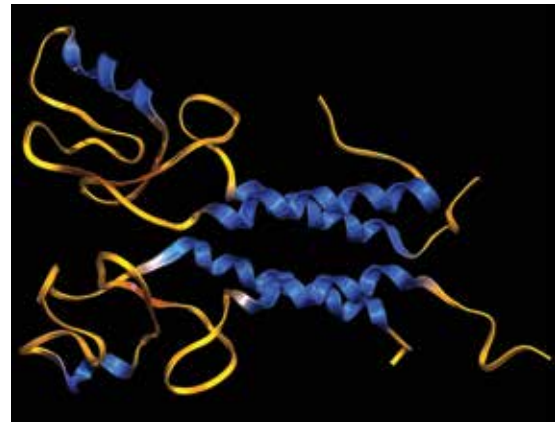
BMN 673 promising in BRCA cancers

AN INVESTIGATIONAL new PARP inhibitor, BMN 673, is showing early responses in patients with heavily pretreated, advanced, BRCA-related breast and ovarian cancers. Phase I clinical trial results were presented in Boston, Massachusetts, at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, held October 19-23, 2013.

The proteins, PARP 1 and PARP 2, recruit proteins that can repair the damage associated with loss of BRCA proteins. Mutations in BRCA genes often result in inefficient repair of damaged DNA, which increases the risk for developing certain cancers, including cancers of the breast and ovary. Inhibiting PARP, therefore, prevents the repair of damaged DNA, leading to cell death. Although some PARP inhibitors have been tested in various settings, none are approved to date.

Zev A. Wainberg, MD, assistant professor of medicine at the Jonsson Comprehensive Cancer Center of the University of California Los Angeles School of Medicine reported that BMN 673, the most potent PARP inhibitor in clinical development, has optimized pharmaceutical properties. It is well-absorbed orally, has substantial single-agent antitumor activity, and has a long half-life allowing once-daily dosing. High objective and clinical benefit response rates were observed in BRCA-related breast and ovarian cancers at low, oral, once-daily doses. "The clinical data to date are promising and compare favorably with results from clinical trials with other PARP inhibitors," said Wainberg.



Molecular model of the BRCA1 protein

Based on this phase I study, Wainberg and colleagues feel there is a good chance that patients with BRCA-related cancers who meet the study eligibility criteria can achieve disease control for a meaningful period of time with relatively few side effects. Wainberg added that randomized trials are still necessary.

The phase I trial evaluated the safety and efficacy of BMN 673 in a two-stage dose escalation/expansion study. So far, Wainberg and colleagues have recruited 39 and 41 patients to the escalation phase and expansion phase, respectively. Patients were 18 to 82 years old and had undergone one to 13 prior therapies.

Fifty participants—18 with breast cancer, 28 with ovarian cancer, three with pancreatic cancer, and one with prostate cancer—had BRCA mutations in their tumors. To date, among the patients with BRCA mutations in their tumors, 44% of those with ovarian cancer and 44% with breast cancer had an objective response. Overall, 82% of the ovarian cancer patients and 72% of the breast cancer patients had clinical benefit.

In patients receiving the 1-mg dose recommended for future trials, 50% of the breast cancer patients with BRCA mutations had an objective response and 86% had clinical benefit. Of the three patients with pancreatic cancer, two have had stable disease.

Fewer than 20% of the patients had grade 3 adverse events including fatigue, anemia, neutropenia, and thrombocytopenia. One patient had a grade 4 toxicity.

Given the high objective and clinical benefit response rates in breast cancer patients, the investigators have recently initiated a phase 3 trial in metastatic breast cancer with BRCA mutations. ■

BMN 673 is well-absorbed orally, has substantial single-agent antitumor activity, and has a long half-life allowing once-daily dosing.

LLLT improves common HNSCC side effect

A DEFINITIVE TRIAL has indicated that low-level laser therapy (LLLT) reduces the occurrence of canker sores and improves quality of life in patients with head and neck squamous cell carcinoma (HNSCC) who are undergoing concurrent chemoradiotherapy.

Almost all patients with HNSCC develop canker sores resulting from different modalities of treatment.

No effective preventive strategy is currently available for canker sores, but prospective trials of LLLT in patients with HNSCC undergoing chemoradiotherapy showed promising results.

The trial, led by Héliton Spindola Antunes, DDS, MSC, PhD, at the Brazilian National Cancer Institute (INCA) in Rio de Janeiro, Brazil, was conducted with 94 patients with HNSCC undergoing chemoradiotherapy. One group of 47 patients received LLLT, and the other 47 patients received a placebo.

Only three patients receiving LLLT developed severe canker sores, whereas 19 patients in the placebo group developed severe canker sores. In the LLLT group, 59.6% of patients were free of canker sores compared with 21.3% in the placebo group. The LLLT group had less severe oral pain and, as a result, used fewer opioid analgesics. They were also less likely to require gastrostomy throughout the cancer treatment. ■

NCONN

Navigator Notes

The National Coalition of Oncology Nurse Navigators (NCONN) is the first association to identify, support, and connect nurses in oncology who navigate patients through the cancer continuum. There are many definitions of the role of the navigator that range from clinical nurses to volunteer survivors. Oncology nurse navigators (ONNs) are clinical professionals acting as a map or compass through the confusing process of diagnosis, treatment, and survivorship.

A navigation program ideally, should include a multiple disciplinary team of professionals working in parallel with one another to address every aspect of a patient's needs. The primary role of the navigator is to remove barriers and obstacles that patients encounter. Barriers may be real or perceived. In these economic times, understanding the ways in which navigation can improve the patient experience and outcomes is essential for all types of health care providers, and can play a part in health care reform.

This discipline is dedicated to the holistic care of the patient with cancer. These patients and their families are in need of physical, mental, emotional, psychosocial, and spiritual support throughout the cancer continuum. There are numerous health care professionals involved in every patient's care, but none is there throughout the entire journey to navigate the patient and family around barriers, identifying resources and services needed to improve quality of life, trust, and satisfaction in the system.

ONN interventions can help reduce gaps in care. Through a streamlined approach, clients have access to timely delivery of services, diagnosis, and treatment.

Navigator roles vary widely, some work primarily with clients who have a diagnosis of cancer, however, many work in the community. These community nurse navigators have worked diligently to develop trusting relationships and interventions that are essential to improving the overall well-being of the greater population. Primary intervention strategies involve development of community health screening and educational programs. Many ONNs collaborate with community partners including congregations, not-for-profit programs, health clinics, and statewide organizations to provide screening and education to the high-risk under- and uninsured clients who may be unable to access health services due to cultural, financial, or linguistic barriers. The goal of these types of programs is to educate people on the importance of prevention and early detection techniques that can help to reduce late-stage cancers.

Collaboration, communication, advocating on behalf of our patients, and translating the medical information is essential to our clients making the most informed decisions about their care. The essence of what ONNs bring to the nursing forum is more than just course plotting. These nurses bring knowledge, individualism, trust, critical thinking, and handholding, as well as a variety of other important skill sets, that help patients make educated decisions concerning their treatment planning in a timely manner. Most importantly, ONNs build relationships within their communities that foster trust in the health care system and improve education and screening, thus improving the health and well-being of the people they serve. To learn more about ONNs and the NCONN, visit www.nconn.org or email info@nconn.org. ■

FDA Update

Obinutuzumab (Gazyva) received FDA approval for use in combination with chlorambucil to treat patients with previously untreated CLL. The drug is approved with a boxed warning regarding Hepatitis B virus reactivation and progressive multifocal leukoencephalopathy.

FDA granted orphan drug designation to **ADXS-HPV** for the treatment of HPV-associated head and neck cancer. ADXS-HPV is an immunotherapy that target cells expressing the HPV gene E7

Ibrutinib (Imbruvica) received FDA approval for the treatment of mantle cell lymphoma, a rare and aggressive blood cancer, in patients with MCL who have received at least one prior therapy.

Crizotinib (Xalkori) capsules were granted FDA regular approval for the treatment of metastatic NSCLC in patients whose tumors are ALK-positive as detected by an FDA-approved test.

FDA expanded the approved uses of **sorafenib (Nexavar)** to treat late-stage (metastatic) differentiated thyroid cancer. The new use is intended for patients with locally recurrent or metastatic, progressive differentiated thyroid cancer that no longer responds to radioactive iodine treatment. ■

Breast cancer survivors troubled most by postmastectomy pain

WOMEN WITH breast cancer who undergo surgery rate persistent postmastectomy pain as the most troubling symptom. Surgery is part of the treatment for more than 40% of the 200,000 US women with breast cancer.

Researchers from the University of Pittsburgh evaluated 611 women who had undergone total or partial mastectomy and were treated with chemotherapy, radiation, and/or hormone therapy. The objective was to determine which factors—demographics, tumor size, pain severity, treatments, stress, and psychological factors—contribute to postmastectomy pain. Their study was published in *The Journal of Pain* (2013;14[10]:1185-1195).

Previous research has provided little consensus regarding the most important determinants of pain following mastectomy. Earlier studies had small sample sizes and focused on just one group of variables. For this research, the authors used a much larger sample, which allowed them to study a large number of variables at the same time.

Applying distress-lowering measures or medications can help women avoid developing persistent pain after mastectomy.

Results showed no evidence linking the type of mastectomy performed, tumor size, or the occurrence of treatment side effects with the development of postmastectomy pain. However, psychosocial variables were found to be important predictors, specifically anxiety, depression, impaired sleep, somatization, and catastrophizing.

The researchers stated that providing those patients who are at highest risk with more intensive perioperative therapy, applying cognitive-behavioral therapy, or applying other distress-lowering measures or medications may help these women to avoid developing persistent pain after mastectomy. ■