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10 Steps to 'End Cancer As We Know It'

BY PEGGY EASTMAN

A 28-member Blue Ribbon Panel has released a scientific report with 10 sweeping recommendations designed to accelerate progress against cancer under the Cancer Moonshot initiative established by President Obama. Implementing the cutting-edge recommendations depends on Congress' willingness to provide adequate funding.

In his State of the Union address in January 2016, the President announced the Cancer Moonshot, whose goal is to speed advances in diagnosis, treatment, and patient care. The President appointed Vice President Joe Biden—whose son Beau Biden died of brain cancer—to head the Cancer Moonshot Task Force. In accepting the charge, Biden stated that "the goal of this initiative is simple: to double the rate of progress. To make a decade's worth of advances in 5 years."

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Relationships, Intimacy, & Body Image After Breast Cancer

CME Article

BY MARGARET FLOWERS, PHD, & MARC HURLBERT, PHD

Patients diagnosed at any stage of cancer seek to maintain their quality of life both during and after treatment. The American Cancer Society (ACS) and ASCO developed and released breast cancer survivorship care guidelines to provide recommendations to assist primary care and other clinicians in the care of female adult survivors of breast cancer (***J Clin Oncol 2016;34:611-35***). Quality of life is a significant concern for patients living with metastatic cancers who are on continual treatment, often for years, until the end of life.

In the U.S., it is estimated that 3.5 million women are living with a history of invasive breast cancer. An additional 246,600 women and 2,600 men will be newly diagnosed with invasive breast cancer this year. The ACS/ASCO Breast Cancer Survivorship Care Guidelines

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Patients With Advanced Lymphoma in Remission After T-Cell Therapy

Patients with non-Hodgkin lymphoma participating in an early-phase immunotherapy trial led by Fred Hutchinson Cancer Research Center, Seattle, had their advanced tumors disappear completely after their immune cells were genetically engineered into cancer fighters, despite having previously exhausted multiple conventional cancer treatments. These short-term results, published in *Science Translational Medicine* (***2016:8;355ra116***), are the latest from a closely watched study of these CAR T cells for treating blood cancer.

Thirty-two participants in the trial received an infusion of CAR T cells following chemotherapy that was given to make space in the patients' bodies for the infused CAR T cells. The team found that the CAR T cells most effectively knocked out the cancer in a group of 11 patients who received a two-drug combination chemo followed by an intermediate dose of the engineered T cells. Seven of these participants, or 64 percent, went into complete remission.

These data demonstrate how dialing in the treatment parameters can make these cells more effective cancer fighters in patients with this particular type of cancer, said Cameron Turtle, MBBS, PhD, FRACP, FRCPA, an immunotherapy researcher at Fred Hutch and one of the study leaders.

"The main message is that you can treat patients with non-Hodgkin's lymphoma with CAR T cells and get very good response rates with optimization of the CAR T-cell dose and lymphodepletion," Turtle said.

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PERIODICALS

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summarized current literature and evidence for the assessment and management of physical and psychosocial long-term and late effects of breast cancer and treatment.

All breast cancer treatments—surgery, radiation, chemotherapy, hormonal therapy, and targeted therapy—can have long-term and late effects that impact physical and psychosocial well-being of women. A long-term effect is something that starts during treatment and does not subside. A late effect is something that develops much later. Some of the physical effects of treatment are summarized in the **Table**.

According to the ACS/ASCO report, long-term and late psychosocial effects after breast cancer treatment include depression, distress, worry or anxiety, fear of recurrence, fear of pain, end-of-life concerns, loss of sexual function, and/or desire, challenges with body image and self-image, relationship, and other social role difficulties and concerns with finances and return-to-work.

Body Image Concerns

Between one- and two-thirds of breast cancer survivors express concerns over body image and appearance changes. This is a particular concern to young women who have undergone breast cancer treatment. Loss of a breast, scarring or disfiguration due to surgery or treatment, lymphedema, hair loss, sexual dysfunction (due to loss of libido, vaginal dryness or pain with intercourse), and chemotherapy-induced early menopause can all affect how a woman feels about her body and subsequently, her intimate relationships.

The ACS/ASCO Breast Cancer Survivorship Care Guidelines recommend active surveillance by primary care physicians to assess body image concerns so appropriate interventions can be initiated. Options include oral pentoxifylline and vitamin E in patients with radiation-associated breast/soft-tissue scarring, breast-reconstructive surgery to improve breast symmetry, breast forms, prostheses or special lingerie to help a woman recover her pre-cancer self-image. The report further recommends women with body image concerns be referred for psychosocial care.

Sexual Health

The reported rates of sexual health problems after breast cancer treatment range widely and include sexual desire disorder/decreased libido (range of 23-64% of patients), issues with arousal or lubrication (20-48% of patients), orgasmic concerns (16-36% of patients), and difficult or painful sexual intercourse (35-38% of patients). Patients treated with chemotherapy tend to report more of these sexual concerns than those treated only with surgery and/or radiation. Changes in body image due to breast cancer treatment or loss of skin sensitivity after radiation can also affect sexual health.

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Menopausal symptoms can be induced in young women treated with chemotherapy that affects ovarian function or that targets estrogen production or function. Younger women typically experience more vasomotor symptoms (hot flashes or night sweats) because of the abrupt changes in hormones and more than half of women taking tamoxifen report hot flashes.

The Breast Cancer Survivorship Care Guidelines recommend the clinical care team counsel patients about the possibility of sexual dysfunction and premature menopause due to breast cancer therapy and discuss treatment options to manage side effects. Non-hormonal, water-based lubricants and moisturizers remain the primary recommendation for vaginal dryness. Selective serotonin reuptake inhibitors, gabapentin, or lifestyle modifications may mitigate symptoms of premature menopause.

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Learning Objective for This Month's CME Activity: After participating in this CME activity, readers should be better able to delineate the breast cancer survivorship care guidelines recommended by the American Cancer Society and American Society of Clinical Oncology.

TABLE: Physical Effects of Treatment

Treatment Type	Possible Long-Term & Late Effects
Surgery	Lack of skin sensitivity, body image issues, sexual dysfunction, numbness, pain, limited range of motion, weakness, poor cosmetic outcome, lymphedema, neuropathy
Radiation therapy to the breast, chest wall, or regional lymph nodes	Fatigue, skin discoloration, skin sensitivity/pain, sexual dysfunction, pain, pneumonitis, poor cosmetic outcome, breast atrophy/asymmetrical breast volume, lymphedema, numbness or weakness of the upper extremity
Chemotherapy	Cognitive impairment, increased risk of cardiovascular disease, fatigue, ovarian failure with or without menopausal symptoms, sexual dysfunction, change in libido, infertility, weight gain, obesity, neuropathy, oral health issues, hair loss
Hormonal therapy—tamoxifen	Hot flashes, changes in menstruation, mood changes, increased triglycerides, increase risk of stroke, endometrial cancer, and blood clots
Hormonal therapy—aromatase inhibitors	Vaginal dryness, decreased libido, musculoskeletal symptoms/pain, cholesterol elevation, increased risk of osteoporosis, and fractures
Targeted therapy—trastuzumab	Increased risk of cardiac dysfunction

Source: American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline (*CA Cancer J Clin 2016;66:43-73*)

EXPERIMENTAL THERAPEUTICS

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"MR-HIFU is essentially an MRI machine with an ultrasound transducer built into the table. The MRI is used to image a patient and the focused ultrasound delivers energy into the interior of the body to cause localized heating in a noninvasive manner," explained Laetsch.

The resulting effect of the localized heating is vasodilation and increased vascular permeability. The study is utilizing those effects, in conjunction with a modified chemotherapy agent, as a method to increase the dosage and specificity of treatment. One drug they are studying is an investigational medication consisting of doxorubicin encapsulated in a heat-sensitive liposome. Localized heating by MR-HIFU destabilizes the liposome, releasing doxorubicin directly into the area of the tumor.

"In studies with a preclinical tumor model, we have been able to concentrate the effective dose delivery up to 25-fold compared to unheated tumors. In some tumor models this results in a significant tumor growth delay," said Laetsch. Although doxorubicin is a commonly used chemotherapy agent, a particular concern in children is limiting cumulative dose to prevent irreversible myocardial damage. This method has the potential to increase exposure of the tumor to the chemotherapeutic agent while limiting myocardial exposure.

Based on their present results, Laetsch has put together a clinical trial to evaluate the safety of MR-HIFU in combination with liposomal doxorubicin to treat pediatric patients diagnosed with refractory solid tumors. The study should open shortly.

Bone & Soft Tissue Sarcoma

Leavey has a longstanding interest in bone and soft tissue sarcoma and is currently leading a multi-site study to develop a new system to interpret tumor necrosis in osteosarcoma. He noted that "although osteosarcoma is a rare disease, with only 400 newly diagnosed cases per year in the U.S., it is the most common malignant bone sarcoma in children and adolescents, and despite 3 decades of effort, we've essentially been unable to increase the likelihood of a more favorable outcome for our patients."

The current conventional treatment for patients diagnosed with osteosarcoma is 10 weeks of chemotherapy, followed by a surgical procedure to remove the tumor, then followed by an additional 6 months of chemotherapy. In diseases like childhood leukemia, analysis of the treatment response comes quickly and is critical to decision-making for children with this disease, allowing tailoring of therapy for patients based on response. For children with osteosarcoma, pathological response evaluation comes only after 10 weeks of treatment and involves an extensive process in the pathology laboratory, necessitating a manual examination of up to 50 sections of each resected tumor. Leavey hypothesizes that sophisticated computational systems will transform histological interpretation from a binary outcome to an earlier biomarker that will identify patients to be considered for novel treatment.

"Rather simply defined, a biomarker is a measurable characteristic that can be used as an indicator of the normal or diseased state—thus allowing us to quantitate the effect of a therapeutic intervention," noted Leavey.

> There are still certain diseases, such as biologically high-risk subsets, cases with advanced disease stage or cases of relapse, where there is just no effective therapy available. An experimental therapeutics program can make a difference by testing new treatment approaches in "bench-to-bedside" strategies.

The initial objective is to develop a computerized image analysis tool that will interpret tumor response at the time of surgery, using histology samples. The study has brought together a multidisciplinary team of investigators, including computer scientists at the University of Texas at Dallas, and pathologists and radiologists at UT Southwestern and Children's Health and the Imaging Center and the 3D Printing Laboratory at Children's Health. While a similar automated pathological evaluation system has been used in certain other types of cancer, their system would be absolutely novel in osteosarcoma.

The ultimate goal of the group is to greatly expand the utility of their innovative image pattern recognition software, essentially dependent on artificial intelligence, to interpret MRI features that predict tumor response.

"This would significantly speed up response analysis and address many of the limitations of our current system," said Leavey. Briefly, the steps toward that goal are to digitize individual pathology slides and to utilize the computer system to build a tumor map, or whole tumor image, for each patient. Using 3D-printed tumor models, Leavey's team will be able to identify co-planar areas for MRI and histological interpretation. Leavey indicates the group is currently 1.5 years into the study and has exciting results they are preparing to share with the research community soon. OT

BREAST CANCER

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The clinical care team should evaluate any reported concerns about sexuality and sexual health following breast cancer treatment. Patients experiencing sexual health issues after cancer care should be referred to psychosocial interventions such as brief psychoeducational support, group therapy, sexual counseling, marital counseling, or intensive psychotherapy.

Unique Challenges for Young Women

Young women with a high risk of breast cancer recurrence face unique challenges in achieving intimacy and quality of life after breast cancer treatment. In particular, for young women diagnosed with BRCA-breast cancer, mastectomy and prophylactic removal of the ovaries are recommended to decrease the chance of breast cancer recurrence or future ovarian cancer. The loss of one's breasts will affect a woman at any age but for young women still dating, it can create new layers of complexity in intimate relationships and family planning. Likewise, young women facing the prospect of removal of the ovaries may have a heightened sense of urgency to start a family.

Many women who have undergone breast cancer treatment are relieved that the cancer was treated and are eager to resume their lives. However, the post-treatment experience will be unique to each woman and all women undergoing breast cancer treatment, or who have completed treatment, should feel empowered to talk about all health issues, including sexual health, body image, and other psychosocial issues, with their clinical providers—their oncologist, primary care doctor or gynecologist. Medical practitioners should assess these issues in their patients and the ACS/ASCO Breast Cancer Survivorship Guidelines provide a framework to better understand the issues and recommendations for care based on the current medical evidence. OT