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-- PRESS BRIEFING SUNDAY, JUNE 4, 12:00 PM EDT --

ADVANCES IN CANCER SURVIVORSHIP AND PATIENT CARE

-- Yoga Can Improve Quality of Life During Breast Cancer Treatment; Modafinil Improves Quality of Life for Patients with Brain Cancer; Genetic Polymorphisms Predict Likelihood of Heart Failure after Childhood Cancer --

Atlanta, GA—Advances in the treatment and long-term care of cancer survivors and people living with the disease were released today at a press briefing at the 42nd Annual Meeting of the American Society of Clinical Oncology (ASCO).

"With progress in treating cancer comes a new and unique challenge—ensuring the long-term health and quality of life for the growing number of cancer survivors in this country," said Patricia A. Ganz, MD, Director for Cancer Prevention and Control Research at Jonsson Comprehensive Cancer Center at UCLA, and moderator of the press briefing. "While recent studies paint a stark picture of some of the long-term health problems faced by survivors, other research, like those studies being discussed today, suggest that new drugs and even yoga can significantly improve quality of life for both cancer survivors and those living with the disease."

Study findings include:

- Inclusion of yoga as part of the treatment plan for breast cancer patients undergoing radiation therapy improves quality of life, both physically and emotionally.
- Modafinil (Provigil), a drug used to treat sleep disorders, improves cognitive function, mood, and fatigue in patients with brain tumors.

- more-

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- Variations in genes that control the metabolism of some cancer drugs may explain why some pediatric cancer survivors experience severe cardiac toxicity in the years following treatment.

For consumer-oriented information on these studies and more than 90 cancer types, please refer your readers to www.plwc.org.

This study is embargoed until 12:00 PM EDT, Sunday, June 4.

ORAL PRESENTATION
MONDAY, JUNE 5, 10:00 AM EDT
ROOM B305

Lead Author:
Lorenzo Cohen, PhD
The University of Texas
M. D. Anderson Cancer Center
Houston, TX

Yoga Can Improve Quality of Life During Breast Cancer Treatment

A new study shows that participating in a yoga program while undergoing radiation therapy for breast cancer improves many aspects of patients' quality of life.

"This is the first study to incorporate yoga as part of the treatment plan for cancer patients," said Lorenzo Cohen, PhD, Associate Professor and Director of the Integrative Medicine Program at the University of Texas M. D. Anderson Cancer Center, and the study's lead author. "Because yoga deals with both mind and body, we hypothesized that cancer patients would benefit both physically and emotionally, and we found that to be the case."

Researchers developed a yoga program for breast cancer patients undergoing radiation therapy that included stretching, breathing exercises, and other relaxation techniques. Sixty-one women were randomly assigned either to attend the biweekly classes during the entire course of radiation treatment or to be on a waiting list (the control group). The average patient was 52 years old; 48% of patients had undergone breast-conserving surgery, and 75% had received chemotherapy.

Patients were surveyed about aspects of their well-being after radiation therapy had been completed. Adjusting for factors such as stage of disease and time since diagnosis, participants in the yoga program reported significantly better physical functioning, social functioning, and general health perceptions than the control group, and lower levels of fatigue and sleep disorders. However, researchers found no differences between the two groups in depression and anxiety, another area of quality of life assessed in the study.

The team is now planning a study with an "active" control group, in which patients who are not participating in yoga will take a class that teaches general stretching exercises. This will allow investigators to determine if the benefits seen in the current study are the result of unique mind-body aspects of yoga or the emotional and social support received from participating in the class.

***8505**
Randomized trial of yoga in women with breast cancer undergoing radiation treatment.
L. Cohen, K. Chandwani, B. Thornton, G. Perkins, E. Rivera, B. Arun, N. Raghuram, H. Nagendra

Background: Yoga, an ancient Indian science, incorporates stress-reduction techniques that include regulated breathing, visual imagery, and meditation, as well as various postures that may be useful for cancer patients.
Methods: A yoga program was developed that including loosening and breathing exercises, postures, alternate nostril breathing, a deep relaxation technique, and meditation for patients with breast cancer who were undergoing radiotherapy. Women participated in bi-weekly classes during their 6 weeks of radiation treatment. Sixty-one women with breast cancer were randomly assigned to either the yoga program or to a waitlist control group. Patients completed measures of intrusive thoughts and avoidance behaviors (Impact of Events Scale: IES), depressive symptoms (CES-D), sleep disturbances (Pittsburgh Sleep Quality Index), fatigue (BFI), and quality of life (SF-36) at baseline, 1 week, and 1 and 3 months after the last radiation therapy. We report on the outcomes 1 week after the end of radiotherapy.
Results: The average age of the women was 52, 3% stage 0, 28% stage I, 43% stage II, and 26% stage III, 48% had undergone breast-conserving surgery, and 75% had received chemotherapy prior to starting radiotherapy. Analysis of covariance, controlling for baseline, revealed that the yoga group had significantly better SF-36 physical function scores (adjusted means: yoga 81.8 vs. control 68.6, $P < 0.01$), significantly higher SF-36 general health scores (adjusted means: yoga 78.3 vs. control 67.9, $P < 0.03$), marginally better SF-36 social functioning scores (adjusted means: yoga 85.3 vs. control 76.0, $P > 0.1$), significantly lower levels of sleep-related daytime dysfunction (adjusted means: yoga 0.5 vs. control 1.2, $P < 0.04$), and

marginally lower levels of fatigue (adjusted means: yoga 1.9 vs. control 3.1, $P < 0.06$) than the control group. There were no other group differences on the SF-36 subscales or for the CES-D or IES scores.
Conclusions: The results indicated that the yoga program was associated with statistically and clinical significant improvements in aspects of quality of life.

Disclosures: nothing to disclose.

This study is embargoed until 12:00 PM EDT, Sunday, June 4.

ORAL PRESENTATION
MONDAY, JUNE 5, 3:00 PM EDT
GEORGIA BALLROOM 3

Lead Author:
Thomas A. Kaleita, PhD
University of California, Los Angeles
Los Angeles, CA

Drug Used for Sleep Disorders Improves Quality of Life for People with Brain Tumors

Early findings from a recently completed UCLA study show for the first time that the drug modafinil, generally used to treat sleep disorders, enhanced quality of life in patients with brain cancer by improving cognitive functions, mood, and fatigue levels, with a low incidence of negative side effects.

Modafinil is used for treatment of narcolepsy, shift-work sleep disorders, and obstructive sleep apnea, and is increasingly being used to supplement anti-depressants in the treatment of depression. It is also prescribed by physicians for other conditions, including fatigue associated with multiple sclerosis, Parkinson's disease, stroke, and HIV infection.

The 30 patients in the study had a variety of brain tumor types, and most were categorized as having severe attention, memory, and fatigue problems. All of the patients had received some combination of neurosurgery, radiation therapy, and chemotherapy treatments, and several patients were receiving chemotherapy while participating in the study. The first part of the study was double-blind, and patients were randomized between two different dosage levels of the drug for three weeks. After a one-week period in which the patients did not receive the drug at all, there was an eight-week "open-label phase" in which all patients received modafinil at what was determined to be each patient's optimal dose, which varied between 50 and 600 mg per day.

Patients were evaluated at specified times with various measures, including standardized tests of concentration and attention, fatigue self-ratings, and a structured interview to evaluate mood and identify specific symptoms of depression. In addition, patients received comprehensive neurological examinations at specified times, and brain MRIs were performed before, during, and after completion of this therapeutic trial.

Comparing patient scores before they started taking modafinil to their scores after they had been on it for two to three months, the majority of patients showed clinically meaningful improvements in all areas. Test scores in cognitive abilities improved by an average of 21%, mood improved by 35%, and fatigue improved by 47%. The site of the tumor or psychological factors were believed to be responsible for a lack of response to the drug in three patients. Modafinil was generally well tolerated, and there were no serious adverse events. The most common side effects were headache (42%), insomnia (26%), dizziness (23%), and nausea (13%). These side effects were considered mild to moderate in severity, and typically resolved after adjustments in dose and scheduling of medication.

"This study shows there is hope for people with brain cancer, and that there are interventions that can improve their quality of life," said Thomas A. Kaleita, PhD, Assistant Professor of Psychiatry at the University of California, Los Angeles, and the lead author of the study. Dr. Kaleita noted that the next step is to determine long-term outcomes, and to verify that modafinil does not create a tolerance or lose efficacy over time.

***1503**
Pilot study of modafinil for treatment of neurobehavioral dysfunction and fatigue in adult patients with brain tumors.
T. A. Kaleita, D. K. Wellisch, C. A. Graham, B. Steh, P. Nghiemphu, J. M. Ford, A. Lai, S. Peak, T. F. Cloughesy

Background: Patients with brain cancer develop neurobehavioral dysfunction and fatigue that compromise their performance of daily activities. We report results from evaluating the efficacy and safety of modafinil treatment for tumor/therapy sequelae in this medically fragile patient population.
Methods: Patients- 21-65 years old with primary malignant disease or nonmalignant cerebral tumors treated with neurosurgical resection, radiotherapy, and/or chemotherapy. Clinical Global Impression of Severity ratings of mild to severe attention/memory impairment and/or fatigue. Measures: Trail Making (TM) A and B, Symbol Digit Modalities (SDM), Verbal Fluency (VF), Hamilton Depression Scale (HAM-D), Fatigue Severity Scale (FSS), Visual Analogue Fatigue Scale (VAFS), Modified Fatigue Impact Scale (MFIS). Design: Double-blind dose-controlled randomization (200 or 400 mg/day modafinil in divided doses) 3 wks; Washout 1wk; Open label extension 8 wks. Statistical analyses: Changes from baseline at scheduled visits (1, 3, 4, 8, 12 wks) using paired t-tests or Wilcoxon Signed Rank tests as appropriate. **Results:** Thirty patients, 63% male, mean age (SD) = 45.3 (11.7) yrs were accrued from 6/03-10/05. Illness severity: moderate 3 (10%), marked 13 (43%), severe 14 (47%). Tumor histology: glioblastoma multiforme 8 (27 %), anaplastic glioma 10 (33 %), low grade glioma 10 (33 %), meningioma 1 (3%), CNS lymphoma 1 (3%). Treatment: neurosurgical resection 93%, radiotherapy 87%, chemotherapy 70%. Table 1 shows relationships of nine variables at baseline and 8 and 12 weeks after initiation of modafinil. Adverse events reported by ≥4 patients: headache 13 (42%); insomnia 8 (26%); dizziness 7 (23%); dry mouth 7 (23%); depressed consciousness 5 (16%); nausea 4 (13%). **Conclusions:** Results show improvement across cognitive, mood, and fatigue outcome measures. Modafinil was generally well tolerated, with a low incidence of adverse events. Greatest improvements in outcomes were observed 8 wks after baseline.

TABLE 1: NEUROBEHAVIORAL AND FATIGUE OUTCOME MEASURES

VARIABLE	BASELINE Mean (SD)	+ 8 WEEKS Mean (SD)	p value	+12 WEEKS Mean (SD)	p value
TM-A	35.5 seconds (16.0)	29.7 seconds (21.7)	.01	28.8 seconds (16.3)	.002
TM-B	95.5 seconds (47.2)	68.0 seconds (36.5)	<.0001	73.6 seconds (45.0)	<.0001
SDM-Oral	50.4 (15.3)	61.5 (22.7)	.0002	58.1 (21.6)	.006
SDM-Manual	44.3 (13.3)	54.2 (20.0)	<. 0001	50.7 (18.9)	.004
VF	32.5 (15.9)	42.3 (15.6)	<.0001	39.2 (15.3)	.002
HAM-D	17.8 (9.0)	10.4 (6.5)	<.0001	12.8 (8.5)	.007
FSS	5.2 (1.4)	3.6 (1.5)	<.0001	3.5 (1.6)	.0003
MFIS	50.2 (17.0)	30.5 (16.7)	<.0001	28.9 (21.0)	<.0001
VAFS	4.0 (2.4)	6.7 (2.6)	.0001	6.7 (3.0)	.0005

Disclosures: research funding from Cephalon, Inc.

This study is embargoed until 3:00 PM EDT, Saturday, June 3.

ORAL PRESENTATION
SATURDAY, JUNE 3, 3:00 PM EDT
ROOM B211

Lead Author:
Richard Aplenc, MD
University of Pennsylvania
Philadelphia, PA

Genetic Variations May Explain Why Some Childhood Cancer Survivors Suffer Severe Cardiac Side Effects in the Years Following Treatment

A new study shows that variations in genes that control the metabolism of certain cancer drugs may explain why some patients who received those drugs as children experience severe cardiac side effects later in life while others do not. Anthracylines are a class of chemotherapy drugs used to treat a variety of pediatric cancers. The use of these drugs has resulted in significantly improved rates of survival, but can also cause damage to the heart; such damage may not appear until 10 to 15 years after treatment has been completed.

In this study, a multi-institutional team looked at 5,739 patients enrolled in the Childhood Cancer Survivor Study, a comprehensive long-term follow-up study funded by the National Cancer Institute. Researchers identified 47 patients with congestive heart failure and selected 195 childhood cancer survivors without cardiac problems as controls, matched for demographics, follow-up, and treatment.

Researchers collected DNA samples from the patients and studied genes related to two metabolic pathways. The researchers looked for variations in genes that control the metabolism of anthracyclines and in genes that control the elimination of oxygen free radicals (a form of oxygen that can damage cells), which are believed to be the cause of the heart damage associated with anthracyclines. They found several genetic variations, also called polymorphisms, that appeared to be risk factors for heart disease in these patients. Variations included several specific mutations in the *GSTP* and *CBR3* genes, which control the body's processing of free radicals and anthracyclines, respectively.

"We can't say based on this study that we're ready to start testing patients for these variations. We need to look at more patients and look for additional polymorphisms that may be important," said Richard Aplenc, MD, Assistant Professor of Pediatrics at the University of Pennsylvania School of Medicine, Attending Physician at Children's Hospital of Philadelphia, and the study's lead author. "However, our hope is that one day we might use this type of information to guide treatment decisions and to determine which cancer survivors should be more closely monitored for cardiac problems in the years following treatment."

***9004**
Polymorphisms in candidate genes in patients with congestive heart failure (CHF) after childhood cancer: A Report from the Childhood Cancer Survivor Study (CCSS).
R. Aplenc, J. Blanco, W. Leisenring, S. Davies, M. Relling, L. Robison, C. Sklar, M. Stovall, S. Bhatia

Background: In cancer survivors, CHF associated with the use of anthracyclines is an important clinical complication. Risk factors for anthracycline associated cardiac toxicity, including cumulative dose, gender, and age, have been described. However, these risk factors do not fully explain the observed clinical variability. Notably, the potential role of genetic risk factors has not been studied. A recent "unifying hypothesis" postulates that the early cardiac damage is mediated mostly by oxidative stress while the more chronic type of toxicity is induced by anthracycline alcohol metabolites synthesized by carbonyl reductases (CBRs). Therefore we hypothesized that genetic polymorphisms in genes encoding for enzymes involved in oxidative stress pathways, and the metabolism of anthracyclines may impact on the risk of anthracycline-related cardiotoxicity.
Methods: We conducted a nested case-control study within a cohort of 5739 patients enrolled in the CCSS. Forty-seven cases with CHF and 195 matched controls (matched for demographics, follow-up and treatment) were genotyped for 10 genetic polymorphisms in 7 genes: catalase (*CAT*), *GSTP, GSTT, GSTM*, superoxide dismutase (*SOD 1*), *NQO1*, and *CBR3*.
Results: In the subjects who received anthracyclines, multivariable analyses of CHF risk, adjusted for gender, smoking history, recurrence, and family history of heart disease, showed the GSTP +313A>G polymorphism was a significant risk factor, HR = 5.0, p = 0.01 for the A/G genotype vs. A/A; HR = 3.3, p = 0.19 for the G/G genotype vs. A/A. In addition, a suggested association between

CBR3 V244M polymorphism and the risk of CHF after treatment with anthracyclines, HR=10.2, p=0.06 for G/G vs. A/A; HR = 4.0, p=0.18 for G/A vs. A/A was seen in an identical multivariable analysis.
Conclusions: These data suggest that specific polymorphic genetic variants on a panel of candidate genes relevant to the anthracycline pharmacodynamics may modify the risk of CHF in childhood cancer survivors. Future studies to further refine the role of these novel genetic risk factors affecting a large population are warranted.

Disclosures: nothing to disclose.

Moderator, Patricia A. Ganz, MD, had nothing to disclose.

The American Society of Clinical Oncology (ASCO) is the world's leading professional organization representing physicians of all oncology subspecialties who care for people with cancer. ASCO's more than 20,000 members from the United States and abroad set the standard for patient care and lead the efforts to discover more effective cancer treatments, increase funding for clinical and translational research, and, ultimately, improve cancer care for the estimated 10 million people diagnosed with cancer worldwide each year. ASCO publishes the *Journal of Clinical Oncology* (*JCO*), the preeminent, peer-reviewed, medical journal on clinical cancer research, and produces People Living With Cancer (www.plwc.org), a comprehensive consumer website providing oncologist-vetted cancer information to help patients and families make informed health-care decisions.

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