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Review of the Best Case Series Methodology: Best Case Series Results of East-West Cancer Center

Hwa Seung Yoo, OMD, PhD, Chong Kwan Cho OMD, PhD, and Michael S. Hong, BS

Purpose. To assess the efficacy of the best case series program methodology as a preliminary evaluation of complementary and alternative programs. Setting. East-West Cancer Center (EWCC) is a traditional oriental cancer center located in Daejeon, Korea. Cancer patients received Wheel balance therapy (WBT), which focuses on rediscovering homeostatic harmony with dietary therapy, metabolism-activating therapy, antiangiogenesis and immune system therapy, and controlled breathing and psychotherapy. Methods. Summaries of 6 cases in which patients showed longer survival without progression and were treated with WBT without conventional treatments were submitted for review to the National Cancer Institute (NCI) Office of Cancer Complementary and Alternative Medicine. Each case was then classified by the NCI review panel with pathologic confirmation of disease and radiologic confirmation of complete response or partial response not attributable to conventional treatments. Results. Two of 6 cases were classified as evaluable NCI best cases; the other 4 cases were classified as unevaluable. Except for a patient with squamous cell lung carcinoma, no patient showed further progression as of July 2007. Conclusion. The best case series program provides a preliminary evaluation of complementary and alternative medicine programs. But the method will only find treatments that have effects similar to those of conventional methods such as surgery, chemotherapy, and radiation therapy. Therefore, in future studies, BCSP reviewers should additionally consider assessing tumor dormancy and efficacy of combination therapies for Best Case qualification.

Keywords: cancer; best case series; traditional Oriental medicine; complementary; alternative; complete response; partial response; tumor dormancy

Since 1990, complementary and alternative medicine (CAM) therapies have been widely incorporated in medical applications and now make up 20% to 40% of treatments in use worldwide. Types and frequencies of CAM are different in each country and depend on the country’s culture and customs. Among these alternative practices, traditional Oriental medicine (TOM), including traditional Korean, Chinese, and Japanese medicine, provides elaborate and accountable theories backed by thousands of years of experience, an abundant source of herbal medicine, and a variety of different clinical treatments. Attributable in part to differences of culture and theoretical basis, however, many CAM cancer clinics have yet to develop an evidence-based, standardized treatment, thus hindering the application of TOM in conventional practice.

To help account for these CAM treatments, the best case series method was adopted by the National Cancer Institute (NCI) in 1991 to evaluate the degree of documentation in support of complex cancer CAM therapies. The Best Case Series Criteria for Optimal Case Studies, published by the NCI Office of Cancer Complementary and Alternative Medicine (OCCAM), specifies that every case to be reviewed must be fully documented with evidence of cancer diagnosis and disease response in the form of pathology slides and radiographic images, respectively. The CAM treatment must follow a treatment protocol specified by the CAM practitioner’s regimen and there must be no presence of confounders of conventional treatment, neither recently nor concurrently. A best case or persuasive case is defined as a case that has pathology confirmed by the National Institutes of Health (NIH) or NCI and radiographic response resulting in complete remission. A supportive case is defined as a case with NIH/NCI-confirmed pathology and radiographic response resulting in partial response or stable disease. In this report, we describe the results of East-West Cancer Center’s (EWCC) best case review from March 2005 to January 2007. We also review the BCSP methodology’s efficacy and limitations as a preliminary evaluation of CAM therapies and give recommendations for improvements, based on our experience with BCSP. The EWCC is a renowned traditional oriental cancer clinic in South Korea and has treated...
more than 30,000 cancer patients in the past 15 years with its unique cancer fighting program, wheel balance therapy (WBT), based on principles of TOM.

Methods

Review Procedure

We selected cases for review with consent from participating patients and submitted a summary of each case to NCI OCCAM for review. Patient medical records accompanied the summaries, including pathology slides and radiological examinations from all institutions where patients received diagnostic assessments or cancer treatments, so that all relevant data could be reviewed. Pathology slides were reviewed by the NCI Laboratory of Pathology to confirm cancer diagnosis. Radiologists at the NIH Diagnostic Radiology Department reviewed imaging studies in various formats to assess patients’ status before and after WBT. Based on these results, reviewers at the NCI OCCAM selected cases for further study that satisfied the NCI best case criteria.

East-West Cancer Center

The EWCC was established in 1991. It is located in the Dunsan Oriental Hospital at Daejeon University (Daejeon, South Korea). Incorporating traditional Korean treatments with conventional cancer treatments, EWCC is one of the major cancer clinics using TOM in Korea.

Philosophy

TOM theories view the body’s physiology as networks of interdependent organ systems. Therefore, health is defined as a condition of stable balance among these networks where the metabolism of each organ system occurs in harmony with others. TOM therapies focus on restoring homeostasis by synchronizing networks of metabolic pathways and thus creating a favorable environment for the immune system to function properly. Conventional modes of cancer treatments mostly target tumors, whereas WBT is an indirect approach that targets physiological environments to induce cancer regression and tumor dormancy.

Wheel Balance Therapy Program

A complete review of patient history and physical examination are completed by the physician within 2 weeks after cancer diagnosis and/or conventional treatment. Physical examination includes electrocardiogram, laboratory studies (complete blood count, platelet count, differential, tumor marker, and liver and renal function tests), and radiology tests. Based on results of these studies, patients are entered into one of the following 4 subprograms of WBT. (Only patients in the basic treatment program were evaluated for BCSP.)

1. Basic treatment: Patients who refuse conventional therapy due to old age or side effects of conventional treatment are entered into this intensive TOM herbal and acupuncture therapy.
2. Combination therapy: Patients who are physically in good condition may opt to receive the basic treatment while being treated with conventional cancer therapy.
3. Metastasis/recurrence prevention: Patients who have completed tumor mass reductive procedures and are in a physically weakened state receive this treatment program, which consists of components of the basic treatment but with milder dosages.
4. Terminal patient care: Analgesics and supportive care are provided for terminal patients with less than 6 months life expectancy.

Basic Treatment

Diet. All patients at the EWCC followed diets composed of constitution-specific foods, with serving proportions balanced accordingly. Patients were recommended to take green vegetable juice twice a day. Patients were encouraged to avoid meat, tobacco, caffeine, and alcohol.

Metabolism activation. Patients received herbal enema, acupuncture and moxibustion, hydrotherapy (herbal steam baths), herbal hot pack therapy, and pharmacopuncture (herbal acupuncture) treatments.

Antiangiogenic agents and immunotherapy. Daily antiangiogenic and immune system-stimulating agents, including Hang-Am-Dan (HAD) capsules, a medication produced by grinding 9 herbal ingredients (Coix lachryma Semen, Panax notoginseng Radix, Hippocampus kelloggi, Cordyceps militaris, Cremastra appendiculata Tuber, Panax ginseng Radix, Bos taurus Calculus, Pteria martensii, and Moschus moschiferus) and mixed into powder form, were orally administered. First developed at the EWCC, HAD has been routinely used for treatments of solid tumor patients at EWCC for the past decade.

Controlled breathing and meditation. Under a physician’s supervision, patients exercise their mind and body through meditation, controlled breathing, and Qigong exercises based on Tai Chi.

Results

Summaries of the 6 cases reviewed are shown in Table 1. Two of 6 cases were classified as evaluable in the NCI BCSP.

Pathology Review

To determine whether the 6 cases satisfied the NCI best case criteria, original histological analysis was reviewed by pathologists. Cases 2 and 3 in Table 1 were histologically confirmed as small cell lung cancer and endometrial cancer by the NCI Laboratory of Pathology.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Primary Site</th>
<th>Gender</th>
<th>Age at Diagnosis</th>
<th>Date of Diagnosis</th>
<th>Conventional Treatment</th>
<th>Last Conventional Treatment</th>
<th>Date of EWCC Visit</th>
<th>First Visit to EWCC</th>
<th>Status at First Visit</th>
<th>Status at Last Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Best cases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Endometrium</td>
<td>F</td>
<td>72</td>
<td>July 2002</td>
<td>None</td>
<td>NA</td>
<td>September 2002</td>
<td>September 2002</td>
<td>Vaginal discharge, severe bleeding</td>
<td>Alive and well as of June 2007</td>
</tr>
<tr>
<td><strong>Not best cases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Endometrium</td>
<td>F</td>
<td>46</td>
<td>October 2002</td>
<td>Surgery (hysterectomy), chemotherapy</td>
<td>July 2003</td>
<td>October 2003</td>
<td>Palpable mass in right breast and left side of neck (progression after chemotherapy)</td>
<td>Alive and well as of June 2007</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Colon</td>
<td>F</td>
<td>48</td>
<td>September 1997</td>
<td>Surgery (anterior resection of sigmoid colon), chemotherapy</td>
<td>September 2000</td>
<td>November 2000</td>
<td>Side effects from chemotherapy (progression after chemotherapy)</td>
<td>Alive and well as of June 2007</td>
<td></td>
</tr>
</tbody>
</table>

NOTES: EWCC = East-West Cancer Center; M = male; F = female; NA = not available; CT = computed tomography.

*Cases reviewed by the National Cancer Institute Office of Cancer Complementary and Alternative Medicine. Cases 2 and 3 were classified as evaluable cases. Cases 4 through 7 did not meet the criteria attributable to lack of documentation or confounder.
Table 2. Results of Pathology Reviewa

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Primary Site</th>
<th>Dates</th>
<th>Original Histologic Diagnosis</th>
<th>Histologic diagnosis on review</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Lung</td>
<td>September 11, 1998</td>
<td>Small cell carcinoma</td>
<td>Small cell carcinoma</td>
</tr>
<tr>
<td>3</td>
<td>Endometrium</td>
<td>July 30, 2002</td>
<td>Adenocarcinoma</td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>4</td>
<td>Endometrium</td>
<td>October 22, 2002</td>
<td>Adenocarcinoma</td>
<td>Moderately to poorly differentiated adenocarcinoma</td>
</tr>
<tr>
<td>5</td>
<td>Liver</td>
<td>July 9, 1996</td>
<td>Hepatocellular carcinoma</td>
<td>Consistent with hepatocellular carcinoma, grade III/IV, chronic hepatitis</td>
</tr>
<tr>
<td></td>
<td>Liver</td>
<td>August 3, 1998</td>
<td>Hepatocellular carcinoma</td>
<td>Fibrous and neuronal tissue with detached clusters of abnormal cells</td>
</tr>
<tr>
<td>6</td>
<td>Lung</td>
<td>September 8, 1997</td>
<td>Specimen not available</td>
<td>NA</td>
</tr>
<tr>
<td>7</td>
<td>Colon</td>
<td>September 8, 1997</td>
<td>Adenocarcinoma</td>
<td>NA</td>
</tr>
</tbody>
</table>

NOTE: NA = not available.

a Results of the pathology review conducted by the National Cancer Institute Laboratory of Pathology. Cases 2 through 5 had confirmed malignancies. Pathologic slides were not available for case 6.

Case 4 was histologically confirmed as endometrial cancer but was considered an unevaluable case because slides that demonstrated metastasis to liver and lymph nodes were not available. In case 5 (liver), the first tumor was confirmed as hepatocellular carcinoma, but the recurrent tumor could not be determined. The pathology specimen of case 6 (lung) was not available for review. OCCAM did not request full review of case 7 (colon), even though histological slides are available at the EWCC.

Radiology Review

Table 3 shows results of radiology reviews. Case 2 (lung) was classified as persuasive, but the X-ray image was considered suboptimal. The scan that was available for this case was an underpenetrated single anteroposterior chest radiograph without diagnostic qualities, and thus study of this case was limited. Based on the evidence of tumor remission, however, it was classified as a persuasive case, and NCI OCCAM suggested a case–control study of survival of patients with non–small cell lung carcinoma (stage IIIb and IV) and small cell lung carcinoma (limited and extensive stage) treated with WBT at the EWCC. This study is ongoing.

In case 3 (endometrium), tumor response was stable during a 4-year period. It was classified as a supportive case by the NCI reviewer. Magnetic resonance imaging (MRI) dated August 23, 2002, showed the endometrium irregularly thickened with extension into the myometrium, whereas another MRI dated January 21, 2005, showed grossly stable appearance of the uterus with thickened endometrium.

MRI and positron emission tomography (PET) whole-body scans of case 4 (endometrium) showed metastasis. A PET scan dated November 20, 2002, showed evidence of endometrial cancer with multiple hypermetabolic lesions in the supraclavicular lymph node (LN) area, multiple hypermetabolic lesions in para-aortic LN chains, mild hypermetabolic lesions in pelvic cavities, and mild hypermetabolic activities in inguinal LNs. A PET scan dated April 24, 2003, also reported a hypermetabolic lesion in the left supraclavicular area and small multiple hypermetabolic lesions in right internal jugular LN chain. A pelvic CT dated July 28, 2003, reported 2 new nodules shown in the liver's caudate lobe after chemotherapy. Despite these radiological findings, case 4 was classified as an unevaluable case because pathology slides that demonstrated metastasis to liver and lymph nodes were not available.

Case 5 (liver) showed evidence of an initial response with disease stabilization. A CT scan dated June 15, 1996, showed a mass in the posterior right lobe of the liver. Lobectomy was performed in 7/8/1996 and histopathologic type was hepatocellular carcinoma. An abdominal CT scan on July 15, 1998, demonstrated a 2-cm ovoid hypoattenuation nodule in the portahepatic space. A laparotomy was attempted on August 3, 1998, but resection was not possible due to difficulty in approaching the tumor and an abdominal tissue biopsy from the site revealed hepatocellular carcinoma as determined by Young Nam University Medical Center pathology laboratory, but reviews by the NCI Pathology Laboratory revealed fibrous and neuronal tissue with detached clusters of abnormal cells. No further surgical intervention was possible at that time, and the patient did not receive any additional conventional therapy. A July 3, 2000, CT scan showed a 2.5-cm lymph node in the portahepatic region. A CT scan on April 28, 2004, showed that the node remained stable at a size of 2.4 cm. The recurrent tumor could not be confirmed, and the case was classified as unevaluable.

The case 6 (lung) patient reportedly showed metastasis in a right chest CT, but the image was not available because hard copies of films are disposed of after 10 years. Thus, the presence of measurable radiographic abnormalities could not be determined. On September 1, 1999, recurrence from the primary lung tumor was suspected, and a CT scan reportedly revealed multiple nodules in the superior segment of the left lower and upper lobes. No biopsies were performed because chemotherapy was not possible attributable to the patient's old age. A chest CT scan performed on July 16, 2000, demonstrated no interval change. A January 13, 2004, CT reportedly showed new development of consolidation, disappearance of nodules in the left lower lobe, no change in patchy nodule in the left upper lobe lingular
segment, no change in lymphadenopathy seen previously in the para-aortic region, and no change in emphysema-related lung appearances. A December 21, 2004, chest CT reportedly showed multifocal pneumonic infiltrations in both lungs.

In case 7 (colon), diagnostic-quality images were not available. Furthermore, there was a potential confounder of chemotherapy that ended 2 months prior to the initiation of the alternative regimen. In August 2000, a new lesion was suspected in the right lobe of the liver with CT scan. After 1 cycle of CPT-11 chemotherapy was given on September 4, 2000, CPT-11 was terminated because of nausea, vomiting, and chest discomfort. A CT scan was performed on November 20, 2000, which showed disease progression, but the report was not in the case file. On February 13, 2001, a reduction in the size of liver metastases was reportedly noted on abdominal CT scan. Further abdominal scans, which were performed on January 6, 2002, and February 28, 2005, demonstrated no recurrence or metastases.

Discussion

Through formal, independent, and retrospective reviews, the BCSP method has provided a means of standardizing the review of documentation in support of the use of CAM modalities in the treatment of patients with cancer. The screening criteria are based solely on tumor regression, which allows for efficient yet unbiased evaluation without calculation of response rates or survival comparison studies.

Although the requirements are rather relaxed compared with standard research procedures, many CAM institutions have experienced difficulties in tracking medical histories and gathering the necessary documentation for BCSP eligibility. This is a common obstacle for any retrospective study because practitioners often select cases for which a considerable amount of time has passed. Medical charts, radiographic scans, or pathology specimens are usually difficult to locate for these cases. Even when found, the scans and images exist as developed films and inevitably would be of limited quality attributable to degradation after considerable time has passed.

Realizing the importance of evidence-based medicine, EWCC incorporated X ray and CT as routine diagnostic procedures when it was established in 1991. An electronic charting system (ECS) was instated in 2004 when EWCC moved to its current location, but many hard copies of charts and scans were either lost during the move or disposed of after 10 years, making it difficult to find successful cases with fully documented evidence.

Additionally, most cancer patients usually receive diagnosis and treatment at primary health care centers before entering TOM hospitals. Therefore, to compile a case summary for BCSP, EWCC had to obtain missing medical records, including charts, slides, and scans, from institutions where the patient had previously received diagnosis and treatment. This process took more than 2 years, which is a considerable time to invest in a preliminary evaluation. Nonetheless, these steps provide a substantial basis for evidence-based medicine and scientific approaches to CAM therapies. BCSP participants will have to accept the time-consuming burden of tracking down old charts and scans for now but should consider adopting evidence-based methodologies and ECS.

Table 3. Results of Radiology Review

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Primary Site</th>
<th>Modality</th>
<th>Dates</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Lung</td>
<td>Chest X ray</td>
<td>November 13, 2000</td>
<td>Bilateral hilar prominence that could be related to pulmonary vessels</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chest X ray</td>
<td>May 14, 2004</td>
<td>No fullness in the left hilar area</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chest X ray</td>
<td>May 31, 2004</td>
<td>Very limited; not diagnostic</td>
</tr>
<tr>
<td>3</td>
<td>Endometrium</td>
<td>MRI, pelvis</td>
<td>August 23, 2002</td>
<td>Endometrial carcinoma; 1.5-cm cystic lesion posterior to the uterus on the left</td>
</tr>
<tr>
<td>4</td>
<td>Endometrium</td>
<td>PET/CT, chest</td>
<td>December 10, 2004</td>
<td>Uptake in bilateral lower cervical areas (near thoracic inlet) consistent with adenopathy</td>
</tr>
<tr>
<td>5</td>
<td>Liver</td>
<td>CT, abdomen</td>
<td>June 15, 1996</td>
<td>Mass in posterior right lobe of liver</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CT, abdomen</td>
<td>June 15, 1998</td>
<td>Right lobe of liver had been resected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CT, abdomen</td>
<td>July 15, 1998</td>
<td>Right lobe of liver had been resected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CT, abdomen</td>
<td>November 26, 1999</td>
<td>Right lobe of liver had been resected</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CT, abdomen</td>
<td>July 3, 2000</td>
<td>Lymph node in the portacaval region that measured 2.5 cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CT, abdomen</td>
<td>April 23, 2003</td>
<td>Node remained stable measuring 2.4 cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CT, abdomen</td>
<td>April 28, 2004</td>
<td>Node remained stable measuring 2.5 cm</td>
</tr>
<tr>
<td>6</td>
<td>Lung</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>7</td>
<td>Colon</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

NOTES: MRI = magnetic resonance imaging; CT = computed tomography; PET = positron emission tomography; NA = not available.

* Results of the radiologic review conducted by the National Cancer Institute Diagnostic Radiology Department. Cases 2 through 5 showed partial response or stable disease. Scans for case 6 and 7 were unavailable, and treatment response could not be confirmed.
Even with evidence-based methodologies in place, however, there are limitations to securing pathology slides, as in case 6 (lung) and case 7 (colon). Although biopsies of superficial lymph nodes may be considered, clinics do not usually perform invasive procedures such as biopsies of internal organ metastasis when radiological imaging diagnosis is possible following successful treatment of cancer. For this reason, it is hard for many CAM clinics to secure pathology slides of past cases. BCSP is a retrospective review of successful cases of the past, and requiring rare pathology slides of metastatic sites in internal organs overly restricts the number of cases to be considered. Consequently, many important cases may be overlooked. We therefore recommend that the requirement of securing pathology slides for sites of metastasis be relaxed. Instead, diagnostic images should be allowed to replace pathology slides for supportive case criteria when slides for metastatic sites of internal organs are unavailable.

In case 7 (colon), the patient had received chemotherapy 2 months prior to initiation of WBT. According to the BCSP exclusion criteria, there must be no confounders when the CAM therapy begins, and thus the case was considered unevaluable. This exclusion criterion was instated in order to evaluate the efficacy of the CAM therapy as an independent regimen. But many cancer patients first enter primary health care centers to receive conventional cancer therapy until the treatment fails to improve their condition. Patients will then consider CAM therapies, but the impending nature of the disease usually forces patients to make the transition as soon as possible. So only a small number of cases satisfy this criterion.

Although efficacy of individual regimens is important and should always be considered a priority, combinations of conventional medicine and CAM should not be overlooked in the search for curative practices. Most CAM therapies are composed of multiple treatment arms, often providing support for the immune system, spa services, psychosocial programs, and customized meals. Such a multimodality design is common for CAM programs, and regimens like WBT are designed not only to be effective independently but also to complement many other methods of treatment, including conventional modalities.

This concept of combination treatment was incarnated when TOM physicians were faced with treating cancer patients who had received conventional treatment but were forced to discontinue because their physical strength had weakened to a point where the immune system began to fail. TOM’s greatest strength may lie in improving immunological activity and restoring homeostasis. Recognizing the potential symbiotic relationship of conventional and TOM cancer therapies, EWCC designed WBT to complement conventional cancer treatments and began conducting research on its clinical effects.

A recent retrospective analysis of 62 patients with stage III/IV gastric cancer treated at EWCC compared overall survival and disease-free survival of combination treatment (surgery and/or chemotherapy with WBT) with those of WBT alone. Both treatment groups were selected using the same inclusion/exclusion criteria. Increased overall survival and disease-free survival were observed for combination treatment, but no significance was found between the 2 groups. The study is limited in that it was not a prospective, randomized clinical trial and involved a wide range of known or unknown prognostic factors, which are characteristics of retrospective studies done on multimodal regimens. Nevertheless, the study may provide an initial estimation of potentially synergistic effects brought about by combining conventional treatments with WBT or other CAM regimens.

The increased survival found in the above-mentioned retrospective analysis could be attributable to the symbiotic relationship between WBT and conventional treatments, where conventional treatments remove or reduce the tumor and WBT keeps the tumor dormant thereafter by preventing primary and secondary tumor growth. The proposed mechanism of tumor dormancy is largely based on theoretical and philosophical views of TOM, and many TOM institutions have conducted some laboratory studies and clinical trials on the synergistic effects of herbal medicine and conventional treatment. Additional research has been carried out at EWCC research facilities to scientifically observe the effects of HAD on tumor cells, the immune system, and other physiological environments.

*Cordyceps militaris*, one of the main ingredients of HAD, has been found to promote macrophage production of nitric oxide and cytotoxicity of natural killer cells and enhance gene expression of natural killer cells. In addition, it has antiangiogenic properties that may inhibit tumor growth when used on cancer patients. Unlike conventional methods, which directly remove tumor cells via surgery and radiation therapy, WBT was designed to indirectly treat cancer by stimulating immune system activity and modulating the physiological environment.

These indirect methods may not always result in tumor regression, but it could be hypothesized that they keep the tumor dormant so that the patient can survive longer with a higher quality of life, as shown in many of our cases. Except for the patient with squamous cell lung carcinoma (case 6), who died in September 2006, all of the patients reviewed here had survived independently with no recurrences or metastasis as of June 2007. From the time of disease progression or the start of WBT up to June 2007, the patients reviewed here had survived 8 years 9 months (case 2), 4 years 10 months (case 3), 3 years 9 months (case 4), 8 years 10 months (case 5), 6 years 10 months (case 6), and 6 years 8 months (case 7). Although duration of survival is not a criterion for best case status and cannot provide any substantial evidence of treatment efficacy, the fact that these patients were still alive with stable disease and that their survival far surpassed average expected survival is noteworthy.

The BCSP standard for determining response was based solely on actual tumor regression, whereas other hypothesized benefits of CAM, such as induction of tumor...
dormancy, improvement in quality of life, prevention of metastasis, and lessening of side effects of chemotherapy and radiation, were not considered. This might be inevitable, because mass reduction is a critical step in the beginning stages of cancer treatment, but once the mass has been removed, mass reduction is no longer needed and the cellular toxicity of conventional methods actually becomes a hindrance to the patient's well-being. Furthermore, mass reduction does not always lead to tumor dormancy, as shown by the persistent nature of cancer even after conventional treatment. Tumor dormancy must be sustained thereafter by upholding the immune system integrity to restore the body's natural ability to inhibit tumor growth.

Treatment of cancer should therefore be a 2-step process consisting of mass reduction followed by sustaining of dormancy. Conventional methods already provide effective means of removing tumor mass or reducing tumor size. However, inducing or sustaining dormancy has not been a priority in the search for cancer treatments. Tumor dormancy may be a key factor in determining survival outcomes and should not be neglected when assessing efficacy of CAM regimens.

Survival was once used as an end point by reviewers of BCSP, but it posed some issues concerning cancer's variability among different patients and the possibility of spontaneous regression. However, if the proposed mechanism of combination therapy can be proven to be true and survival prolongation along with stable disease does indeed adequately reflect the degree of induced dormancy, then perhaps survival can be a practical end point for preliminary studies of CAM regimens, especially when numerous documented cases of prolonged survival (compared with average survival observed when treated with only conventional medicine) are presented.

Because of the nature of retrospective case studies, BCSP is prone to both false positives and false negatives, and therefore strict criteria must be applied to the program to minimize these errors. With the current best case criteria in place, introducing survival as a criterion may decrease the number of false positives, making the screening process more efficient. The number of false negatives may also increase attributable to the reinforced criteria and inaccurate reporting of survival, which can compromise the potential of finding more numbers of effective regimens.

**Conclusion**

With its strict screening criteria, BCSP provides a preliminary evaluation of vast numbers of CAM programs around the world. But because the assessment of treatment efficacy was based on tumor shrinkage, the method will only find treatments that have effects similar to the effects of conventional methods. As history has shown, cancer cannot be overcome solely through methods that directly target tumor cells.

Indirect methods of modulating the physiological environment seem to be a common theme among CAM therapies, but BCSP only allows for evaluation of tumor regression, which may be a redundant effort in the development of cancer treatments. Therefore, in future studies BCSP reviewers should additionally consider assessing tumor dormancy, defined as stable disease with significant extension of survival, and efficacy of therapies used in combination with conventional methods. Cancer is a difficult disease to overcome, and we believe that the joint efforts of cancer institutions to build a combination treatment composed of effective regimens from around the world will provide the answer.

**References**