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Best-Case Series for the Use of Immuno-Augmentation Therapy and Naltrexone for the Treatment of Cancer

Summary

Overview

This report presents an assessment of patients with cancer treated with either of two complementary and alternative medicine (CAM) therapies, immuno-augmentation therapy (IAT) or low-dose naltrexone. Some patients report that these treatments have improved their health-related quality of life. Two clinics that treat patients with these therapies were identified by staff at the National Center for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health. In selecting patients' records for review, the researchers used criteria developed by the National Cancer Institute for its "best-case series." These criteria require rigorous and objective evidence of the patient's clinical condition and treatment received. A "best-case series" can provide information on the efficacy of a treatment in the absence of a controlled clinical trial. The researchers judged nine cases in which patients received IAT and three cases in which patients received naltrexone, to best meet the "best-case series" criteria, and these cases are reported in detail herein. The authors also report on the difficulties identifying "best-case series" for these patients.

Methodology

The project's staff visited the two sites and asked the CAM providers to identify their best cases based on their belief that the patients benefited from the treatment. The staff screened these and additional patient files that were identified from the clinic records, based on the criteria for a best-case series established by the National Cancer Institute.

In a "best-case series," cases are not selected randomly and are not representative of the "average" or "typical" case. Furthermore, there are no control cases that would facilitate a comparison of patient outcomes with and without the treatment in question. A best-case series relies on assumptions about patient outcomes in the absence of treatment, and consequently requires very rigorous documentation of the patient's clinical status. This information is then used by clinical experts to make judgments about outcomes in similar patients treated with the best available conventional therapy. This is the basis for conclusions regarding the potential efficacy of the treatment in question. Best-case series are useful to help identify therapies that have sufficient promise of efficacy to justify the time and resources necessary for more rigorous study, such as a clinical trial.

For this study, the researchers used criteria developed by the Office of Cancer Complementary and Alternative Medicine (OCCAM), a part of the National Cancer Institute. These criteria require the following:

- *Documentation of the diagnosis of cancer.* The patient's cancer should be documented by obtaining tumor tissue and having it examined by a pathologist. The pathologist's report should be included in the case summary.
- *Evaluation of the appropriate antitumor endpoint.* The only reliable antitumor endpoint that can be documented in a best-case series is a demonstrable and reproducible

reduction of tumor size. Tumor measurements are made before treatment, during treatment, and after treatment is complete. An objective response is considered to be a decrease of at least 50 percent in the area of the tumor (i.e., the cross product of the diameters) with no increase in size of any other lesions.

- *The patient must not be receiving any other treatment for his/her cancer*. To document an antitumor effect based upon individual patient histories, the patient must have a documented, measurable tumor just before the CAM modalities are given. While the CAM modalities themselves may have multiple components, they must not be given together with any other cancer treatments.
- *A record of previous anti-cancer treatments.*
- *Documentation of sites of the cancer.* At least one recurrent or metastatic cancer should be documented histologically. The date at which recurrence or metastatic disease was first noted should be provided.
- *Description of the patient's general medical condition.* The age, sex, and any other previous or concurrent illnesses or significant medical conditions should be carefully documented.
- *Description of the treatment administered.* The treatment that was felt to result in the antitumor response should be described.

Promising cases were identified, and these patients were contacted to obtain permission for the researchers to abstract their files. After consents were obtained, patients were interviewed by telephone; for deceased patients, their next of kin were interviewed. All data collected from abstraction forms and the interview were summarized on a case report form. The most pertinent clinical data (radiology studies, pathology slides) were identified, and original clinical material was requested from the appropriate institution. If the original clinical material was still available, it was sent to the Southern California Evidence-Based Practice Center (SCEPC).

Several instruments were developed specifically for this project: Cancer Best-Case Series Abstraction Form; Case Report Form; and IAT and Naltrexone Patient Interview Questionnaires. The patient questionnaire includes a health-related quality-of-life instrument, the European Organization for Research and the Treatment of Cancer Quality-of-Life Questionnaire (QLQ-C30).

Findings

For IAT, the researchers reviewed in detail 30 cases (out of 60 promising cases) that had the potential to be included in a best-case series. Of those, nine cases are presented that the researchers consider the most complete or appropriate in terms of the NCI criteria for a best-case series. These cases include the following types of cancer: Hodgkin's lymphoma, non–small-cell carcinoma of the lung, nodular lymphoma (poorly differentiated), peritoneal mesothelioma (two cases), ovarian adenocarcinoma, squamous cell carcinoma of vocal cord (two cases), and adenocarcinoma of the colon.

For naltrexone treatments, three cases of the 21 that the researchers reviewed in depth best met the NCI criteria. These include the following cancers: melanoma, pancreatic cancer, and endometrial adenocarcinoma with a second primary breast adenocarcinoma (single case). These cases represent the best that the authors were able to assemble using the currently accepted NCI best-case method.

Conclusions

With regard to the two best-case series, this review supports the following conclusions:

- The IAT cases provide sufficient indications for the recommendation that IAT warrants further study.
- The naltrexone cases provide insufficient indications to determine the likely benefit for naltrexone at this time.

For IAT, this review suggests there is sufficient evidence to recommend that either a random controlled trial or a prospective case series could be considered. For naltrexone, a prospective cohort case series should be considered.

While the researchers' work demonstrates that a best-case series can be constructed for CAM therapy, it also demonstrates that to do so requires considerable resources, time, and effort. Assembling documentary evidence through retrospective case analysis is difficult, even with a trained research staff. The researchers encountered several difficulties trying to establish a "best-case" series: the quality of the records; confirmation of the diagnosis and the disease; documentation of treatment; self-selection of patients; and use of multiple treatment methods.

Future Research

This review was based on the assumption that a proactive approach by researchers to creating a best-case series might be more productive than relying on practitioners to create their own best-case series. The authors' review established that this work is extremely time consuming and expensive. This lead them to the conclusion that it is not feasible to expect health providers to create such a series—especially CAM providers, who may not be trained in research. An alternative approach might be to establish a prospective case series where the protocol for treatment and the documentation can be established prior to the treatment.

Availability of the Full Report

The full evidence report from which this summary was derived was prepared for AHRQ by the Southern California RAND Evidence-based Practice Center under contract number 290-97-0001. It is expected to be available in spring 2003. Printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295.

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