Placebos in Cancer Clinical Trials [1]

A placebo is an inactive drug or treatment in a clinical trial and is often referred to as a ?sugar pill.? A placebo-controlled trial compares a new treatment with a placebo; people who receive a placebo are in the control group. The use of placebos in cancer clinical trials is rare. Cancer.Net previously talked with Richard L. Schilsky, MD, in 2008 to learn more about the emerging use of placebos in cancer clinical trials. This article was updated in 2012.

Q. Why are some cancer researchers now using placebos in clinical trials?

A: In past years, it was generally not necessary or possible to use placebos in cancer clinical trials because most chemotherapy treatments caused obvious tumor shrinkage and striking, sometimes severe, side effects that could not be produced by a ?sugar pill.? However, many of the newer, targeted drugs slow tumor growth but may not cause tumor shrinkage. Testing these drugs requires that clinical trials have a control group, so that researchers can tell whether stabilization of the tumor growth is an effect of the treatment or just reflects the natural behavior of the tumor. Further, many of the newer drugs are given orally (by mouth) and have side effects that are hard to distinguish from the symptoms of cancer itself, such as fatigue. When clinical testing of new a drug begins, it is not known whether the drug will be effective against any kind of cancer. Because new drugs are often tested in patients who have already received all known, effective treatments, comparing a new drug with a placebo may be appropriate and allows researchers to easily and definitively determine the good and bad effects of the new drug.

Q. Why are these clinical trials necessary for the advancement of cancer research?

A: The fastest way to improve access to new cancer treatments for all patients is the timely completion of well-designed, definitive clinical trials that provide evidence of the safety and effectiveness of a new drug and lead to marketing approval. In some circumstances, such clinical trials may require the use of placebo controls to provide convincing evidence of drug safety and clinical benefit.

Q. How can the design of a clinical trial address some of the ethical concerns around using placebos?

A: Placebos should be used in cancer clinical trials only when it is scientifically necessary, ethically appropriate, and when patients have been clearly informed that they will receive a placebo and whether they will receive the active drug at some point during the clinical trial, if not immediately. Use of placebo controls may be justi?ed to prove effectiveness of a new treatment for diseases with high placebo response rates; in conditions that alternately become worse or better, have spontaneous remissions (the disappearance of the signs and symptoms of cancer, but not necessarily the entire disease), or have an uncertain and unpredictable course; when existing therapies are minimally effective or have serious side effects; or in the absence of any effective therapy. Furthermore, patients randomly assigned to a placebo must not be substantially more likely than those in active treatment group(s) to: die; suffer irreversible illness, disability, or other substantial harms; suffer reversible but serious harm; or suffer severe discomfort. Thus, placebo-controlled trials should also ensure that patients receive outstanding supportive care [2] during their participation in the study. Specific clinical trial designs can be used to minimize the chances that a patient receives a placebo. For example, the clinical trial may permit crossover to the active drug at the time of disease progression (the point at which the cancer continues to grow or spread). In such clinical trials, all patients have the opportunity to receive the new treatment, although some receive it sooner than others.

Q. What are some examples of when it is*not* appropriate for a person with cancer to participate in a placebo-controlled trial?

A: Placebo-controlled trials are never appropriate when a highly effective or potentially curative therapy is available for a patient, unless the trial allows the patient to receive the new treatment/placebo in addition to the potentially curative therapy. For example, let's say that a promising new treatment is in development for advanced testicular cancer, a disease that is curable in many cases with the use of chemotherapy. It would not be appropriate for a clinical trial to randomize patients between the new treatment and placebo because potentially curative chemotherapy already exists. However, it might be appropriate to randomize between standard chemotherapy *plus* the new drug or standard chemotherapy *plus* placebo because in both cases, patients will receive the standard, potentially curative treatment.

Q. What are some recent examples of placebo-controlled clinical trials for cancer?

A: Several new drugs were tested against placebos in the clinical trials that proved their effectiveness. These include sorafenib (Nexavar) for the treatment of kidney and liver cancers, erlotinib (Tarceva) for the treatment of pancreatic cancer, and sunitinib (Sutent) for treatment of gastrointestinal stromal tumors (GIST). It is also important to note that many placebo-controlled trials have been performed in recent years to definitively prove that a promising new therapy was not an effective treatment. Indeed, a search of the *Journal of Clinical Oncology* [3] for the years 2009-2012 revealed nearly 50 published reports of randomized trials testing new drugs to treat cancer that used placebos in control groups.

Q. What questions should patients ask their doctor about placebo-controlled clinical trials?

A: The main questions that patients should ask are about their treatment options. If a patient has already received all known, effective therapies for their disease, options may include supportive care or participation in a clinical trial. If participation in a clinical trial is an option, patients should understand the rationale and goals of the trial, whether it involves use of a placebo, and the likelihood of receiving the drug being studied or a placebo. It is also important to ask about the likelihood of benefit from the investigational treatment and the potential side effects. If a placebo is administered as part of the trial, patients should ask whether there will be an opportunity to receive the study drug at any point in the trial, if not immediately upon enrollment.

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More Information

Clinical Trials [4]

ASCO Expert Corner: Informed Consent [5]

Links:
[1] http://www.cancer.net/navigating-cancer-care/how-cancer-treated/clinical-trials/placebos-cancer-clinical-trials
[2] http://www.cancer.net/node/25282
[3] http://jco.ascopubs.org/
[4] http://www.cancer.net/node/24863
[5] http://www.cancer.net/node/24386