# Cancer Chemotherapy



Cancer cells are everything we would like healthy cells to be: They quickly adapt to toxic environments, they readily alter themselves to assure their continued survival, and they utilize biologic mechanisms to promote cellular immortality. All of these factors make cancer an extremely difficult disease to treat.

Chemotherapy drugs have a high rate of failure because they usually kill only specific types of cancer cells within a tumor or the cancer cells mutate and become resistant to the chemotherapy. Cancer chemotherapy could save more lives if the latest scientific findings were incorporated into clinical medicine.

What concerns us is that respected cancer journals are publishing articles that identify safer and more effective treatment regimens, yet few oncologists are incorporating these synergistic methods into their clinical practice. Cancer patients often suffer through chemotherapy sessions that do not integrate the latest scientific findings. Our objective is to provide the patient with more options to discuss with their oncologist and to bring about multimodality approaches to improve the probability of a successful outcome.

It is impossible to design a single chemotherapy protocol that is effective against all types of cancer. The oncologist might need to administer several chemotherapy drugs at varying doses because tumor cells express survival factors with a wide degree of individual cell variability. This protocol conveys the findings from published scientific studies so that a cancer patient will have a logical basis to augment the effects of chemotherapy and also reduce the potential for side effects.

**How Does Chemotherapy Work?**
According to the National Cancer Institute, almost all normal cells grow and die in a controlled way through a process called apoptosis. Cancer cells, on the other hand, keep dividing and forming more cells without a control mechanism to induce normal apoptosis.

Anticancer drugs destroy cancer cells by stopping them from growing or dividing at one or more points in their growth cycle. Chemotherapy may consist of one or several cytotoxic drugs that kill cells by one or more mechanisms. The chemotherapy regimen chosen by most conventional oncologists is based on the type of cancer being treated. As you will read later in this protocol, there are factors other than the type of cancer that can be used to determine the ideal chemotherapy drugs that should be used to treat an individual patient.

The goal of chemotherapy is to shrink primary tumors, slow the tumor growth, and kill cancer cells that may have spread (metastasized) to other parts of the body from the original, primary tumor. However, chemotherapy kills both cancer cells and healthy normal cells. Oncologists try to minimize damage to normal cells and to enhance the cell killing (cytotoxic) effect on cancer cells. Too often, unfortunately, this delicate balance is not achieved.

Clinical studies show that for certain types of cancer chemotherapy prolongs survival and increases the percentage of patients achieving a remission. A partial remission is defined as 50% or greater reduction in the measurable parameters of tumor growth as may be found on physical examination, radiologic study, or by biomarker levels from a blood or urine test. A complete remission is defined as complete disappearance of all such manifestations of disease. The goal of all oncologists is to strive for a complete remission that lasts a long time--a durable complete remission, or CR. Unfortunately, the vast majority of remissions that are achieved are partial remissions. Too often, these are measured in weeks to months and not in years. Some types of cancer do not show any meaningful response to chemotherapy.

## CHOOSING THE BEST CHEMOTHERAPY DRUGS TO KILL YOUR TUMOR



It is highly desirable to know what drugs are effective against your particular cancer cells before these toxic agents are systemically administered to your body. A company called Rational Therapeutics, Inc., performs chemosensitivity tests on living specimens of your cancer cells to determine the optimal combination of chemotherapy drugs.

Dr. Robert Nagourney, a prominent hematologist/oncologist, founded Rational Therapeutics, Inc., in 1993. Rational Therapeutics pioneers cancer therapies that are specifically tailored for each individual patient. They are a leader in individualized cancer strategies. With no economic ties to outside healthcare organizations, recommendations are made without financial or scientific prejudice.

Rational Therapeutics develops and provides cancer therapy recommendations that have been designed scientifically for each patient. Following the collection of living cancer cells obtained at the time of biopsy or surgery, Rational Therapeutics performs an Ex-Vivo Apoptotic (EVA) assay on your tumor sample to measure drug activity (sensitivity and resistance). This will determine exactly which drug(s) will be most effective for you. They then make a treatment recommendation. The treatment program developed through this approach is known as assay-directed therapy.

At present, medical oncologists, according to fixed schedules, prescribe chemotherapy. These schedules are standardized drug regimens that correspond to specific cancers by type or diagnosis. These schedules, developed over many years of clinical trials, assign patients to the drugs for which they have the greatest statistical probability of response.

Patients with cancers that exhibit multidrug resistance will likely receive treatments that are wrong for them. A failed attempt at chemotherapy is detrimental to the physical and emotional well being of patients, is financially burdensome, and may preclude further effective therapies.

Rational Therapeutics' EVA assay uses your living tumor cells to determine which drug or drug combination induces

apoptosis in the laboratory. Each patient is highly individualized with regard to sensitivity to chemotherapy drugs. A patient's responsiveness to chemotherapy is as unique as their fingerprints.

Rational Therapeutics, leading the way in custom-tailored, assay-directed therapy, provides personal cancer strategies based on the tumor response in the laboratory. This eliminates much of the guesswork prior to the patient undergoing the potentially toxic side effects of chemotherapy regimens that could prove to be of little value against their cancer. Rational Therapeutics may be contacted at:

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Long Beach, CA 90806
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In addition to the EVA chemosensitivity testing, we advocate immunohistochemistry testing of your tumor to provide additional data that will assist in making treatment decisions. The importance of the immunohistochemistry test is described in the Cancer Treatment: The Critical Factors protocol. The immunohistochemistry test can be done if your physician sends a specimen of your tumor to a specialty laboratory called Impath (www.impath.com). Impath can be reached by calling (800) 447-5816. Impath also performs chemosensitivity testing of living tumors (fresh specimens). Because many chemotherapy patients' primary tumors were previously removed or irradiated, Impath can perform the immunohistochemistry test with a frozen or parraffin-preserved tissue sample that is accessible through the pathology laboratory that examined your previous tumor(s).

### Protecting Against Anemia

The importance of maintaining or enhancing the oxygen-carrying capacity of blood cannot be overemphasized. Blood oxygen-carrying capacity may be the single most important factor in determining whether chemotherapy is successful.

In response to a low-oxygen environment, cancer cells send out growth signals that result in increased angiogenesis (blood vessel growth into the tumor). Oxygen deprivation not only induces angiogenesis, but also causes cancer cells to express additional survival factors that make them highly resistant to the toxic effects of chemotherapy.

It is an established fact that a low-oxygen environment (hypoxia) promotes tumor growth. If nothing else in this protocol is followed, correcting a hypoxic state could vastly enhance the odds of long-term survival.

The first step in correcting hypoxia is to guard against anemia. Anemia is common in cancer patients, and the result is that less oxygen is delivered to the tumor, that is, hypoxia occurs. The importance of avoiding anemia is well established in scientific literature. A study was conducted to systematically review and obtain an estimate of the effect of anemia on the survival of cancer patients. This study found that the increased risk of mortality in cancer patients who were anemic was an astounding 65% (Caro et al. 2001)!

Chemotherapy often induces anemia that then exacerbates hypoxia in the tumor. The best way of evaluating blood oxygen-carrying capacity is to measure hematocrit and hemoglobin levels. These are standard components of the complete blood count (CBC) test that should be routinely performed in all cancer patients.

Since cancer cells thrive in a hypoxic environment, the cancer patient's hematocrit and hemoglobin should be maintained in the upper one-third of normal range prior to the initiation of chemotherapy. Table 1 describes the optimal ranges of hematocrit and hemoglobin for cancer patients.

***Table 1: Optimal Ranges of Cancer Patients' Hematocrit and Hemoglobin Levels***

Based on findings from survival studies, cancer patients should fall within the optimal ranges of the following two blood tests that measure the oxygen-carrying capacity of blood:

| **Blood measure** | | **Normal Laboratory Reference Range** | **Optimal Range For Cancer Patients** |
|---|---|---|---|
| Hemoglobin | (men) | 12.5-17 grams/dL | 15.5-17 grams/dL |
| | (women) | 11.5-15 grams/dL | 13.83-15 grams/dL |
| Hematocrit | (men) | 36-50% | 45-50% |
| | (women) | 34-44% | 41-44% |

*Normal reference ranges based on Labcorp's standards as of May 14, 2002.*

Hypoxia (low oxygen) promotes tumor growth by inducing angiogenesis and causing cancer cells to express survival factors that interfere with the ability of chemotherapy to kill them. Chemotherapy drugs are supposed to promote apoptosis. In a hypoxic environment, however, cancer cells develop survival mechanisms that protect them against apoptosis.

There are nutrients that help improve anemic states, but any cancer patient who does not have his or her hematocrit and hemoglobin in the upper one-third of the normal range (as described in Table 1) should consider the drug Procrit (or Epogen) to achieve such levels. Procrit is a natural erythropoietin that stimulates the production of red blood cells. There is also a new long-acting erythropoietin agent approved by the FDA called Aranesp, which allows dosing every 2 weeks instead of weekly injections.

If an oncologist fails to address anemia, the patients should assume the role of advocate, demanding that attention be paid to the quality of his blood counts.

A problem that cancer patients will encounter is that oncologists normally view low blood counts as normal in cancer patients and are reluctant to prescribe Procrit unless anemia is demonstrated. Because Procrit is an expensive drug, most insurance companies refuse to pay for it unless a cancer patient is severely anemic (<10g/dL). Remember, anemia means hematocrit and hemoglobin are below the low-normal laboratory reference ranges. A cancer patient, on the other hand, should aim to have levels in the high upper-third range of normal for hematocrit and hemoglobin. Some insurance companies will not pay for Procrit until hematocrit levels are at least 20% below the lowest normal range. Is it any wonder that chemotherapy fails for so many cancer patients?

Since most insurance companies will not pay for Procrit for the purpose of boosting hematocrit and hemoglobin to the upper ranges of normal, patients may have to pay for this drug as an out-of-pocket expense. The first hurdle is convincing the oncologist to prescribe Procrit. The good news is that most cancer patients may only need Procrit for a few months, so the high cost does not have to be borne indefinitely.

The Life Extension Foundation has located pharmacies that will sell Procrit at lower prices. If your insurance company will not reimburse for this costly drug, call (800) 544-4440 for referrals to pharmacies that may charge less than conventional retail prices.

**Inhibiting the COX-2 Enzyme**
Some progressive oncologists are prescribing cyclooxygenase-2 (COX-2) inhibitor drugs along with chemotherapy to improve the odds of successful treatment. COX-2 is an enzyme that many types of cancers use in order to propagate. COX-2 and its byproducts such as prostaglandin E2 (PGE2) have been shown to help fuel the growth of cancers such as colon, pancreas, estrogen-negative breast, prostate, bladder, and lung cancer.

Drugs that inhibit the cyclooxygenase enzyme are known as COX-2 inhibitors. Celebrex and Vioxx are two popular COX-2 inhibitors. Both Celebrex and Vioxx are nonsteroidal anti-inflammatory drugs (NSAIDs) that are usually prescribed to treat the symptoms of rheumatoid arthritis and osteoarthritis. There appears to be more research about Celebrex in the treatment of cancer than Vioxx.

Since chemotherapy can cause gastrointestinal bleeding, careful physician monitoring is needed when using a COX-2 inhibiting drug such as Celebrex. Caution is urged for those with known kidney disease, poor heart-lung function, liver disease, or susceptibility to stress-induced ulcers. The protocol entitled Cancer Treatment: The Critical Factors has a detailed description of the connection between COX-2 and cancer and why inhibiting the COX-2 enzyme is so important in treating many cancers.

In 1996, Life Extension recommended that most cancer patients take a COX-2 inhibiting drug because of solid evidence that cancer cells use the COX-2 enzyme to sustain their rapid division. In 1996, Americans had to import a COX-2 inhibitor named nimesulid from other countries because this class of drug was not widely available in the United States.

Experiments in laboratory animals suggest that drugs such as Celebrex could help cure cancer, especially if combined with chemotherapy or radiation (Hsueh et al. 1999; Pyo et al. 2001; Swamy et al. 2002). There are 100 separate cancer studies involving COX-2 inhibitors going on worldwide at this time.

Doctors are predicting that COX-2 inhibiting drugs may become standard therapy in 5-10 years. There was adequate evidence in 1996, however, to recommend COX-2 inhibiting drugs available to cancer patients. There are three potent COX-2 inhibiting drugs on the American marketplace. You may ask your physician to prescribe one of the following COX-2 inhibitors:

Lodine XL, 1000 mg once a day or
Celebrex, 200-400 mg every 12 hours or
Vioxx, 12.5-25 mg once a day