Deciding on the Appropriate Treatment

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“Cancer is one of the most curable chronic diseases in this country today.”
—Vincent T. DeVita Jr., M.D.

Medicine has now reached the stage where about half of all diagnosed cancers are cured. Of course, this statistic is an average. The cure rate for some cancers is much higher than for others. And some cancers can come back even after the five-years cancer-free interval that is often used to define “cure.”

But even with cancers still considered incurable, proper therapy often yields tremendous benefits. Treatment can add months or years to a reasonably normal life. It can also greatly improve the quality of your life by relieving pain or ensuring the relatively normal functioning of your body processes. Many people live a normal life span with chronic cancer before succumbing to some other disease.

Unfortunately, far too many people still think a cancer diagnosis is a death sentence. Far too many take the attitude that if it can’t be cured, there’s no point in undergoing treatment. What is even more unfortunate is that this attitude is found not only among people with cancer and the lay public but within the medical community.

In many cases, cancer truly is an incurable disease. But it’s not the only one. Diabetes and heart disease can’t be cured, but they can be treated on an ongoing basis. They’re treated all the time. Few people take the “Why bother?” attitude with either of them. Why? Because they know both can be managed day by day and that people with either disease can lead long, active, and productive lives. The same can be true for cancer patients.

The key to getting the chance for cure or successful management is getting the best treatment as soon as possible after your diagnosis. What that treatment is, you will have to help decide. Yes, you should rely on experts with training and experience in fighting cancer. But it’s your life on the line, and ultimately, the decisions must be yours. And you will have to base those decisions on a detailed analysis of your disease and the recommendations of your primary physician or cancer specialist.

What Are the Options?
A Treatment Overview

The three mainstays of cancer therapy over the years have been surgery, radiation, and chemotherapy. These have now been joined by biological therapy, which uses the body’s immune system to combat growing cancer cells. The goals, procedures, risks, and side effects of each of these kinds of therapy (sometimes referred to as modalities) are detailed in chapters 6 to 9. Here, the treatment options are briefly reviewed.
Surgery  This is the oldest and most successful approach to cancer treatment. If it is possible to cut it out safely and there is no residual disease, you may be cured. Two key questions have to be answered when deciding if surgery is the right thing to do:

- Is the tumor just in one place (localized)? Once the cancer has spread, surgery may or may not be appropriate.
- Can the tumor be removed without damaging vital organs or causing major functional problems? A cancerous lung or kidney can be removed because everyone has a spare. But a surgeon can’t cut out the whole liver or vital parts of the brain.

There are two surgical approaches. In the one-stage approach, the diagnostic biopsy might be followed immediately by the removal of the tumor while you are still under anesthesia. After the operation, you can discuss whether you need additional therapy and what the most effective method or sequence would be, particularly if several therapies might be realistic alternatives.

In the two-stage approach, only the biopsy is done. You then discuss the results with your doctor. If the biopsy shows cancer, you and your doctor plan the definitive cancer treatment. If surgery is an option, the operation to remove the tumor will then be carried out.

Radiation Therapy  The purpose of radiation is to make tumors shrink or disappear. Radiation does this by damaging the genetic structure (DNA) of the tumor cells so they can’t grow or divide. The damage is done by a beam of X-rays, gamma rays, or electrons aimed directly at the tumor from a high-energy X-ray machine set up at a specific distance from your body or by radioactive materials placed inside or close to the tumor.

There is no pain or discomfort during radiation therapy. Undergoing treatment is much the same as having a chest X-ray, except the machine is left on for several minutes instead of a second or two. Radiation may be the only treatment needed for some localized cancers, or it might be used along with other kinds of therapy.

Chemotherapy  This term is often misunderstood. What it means is treating some medical condition with chemicals (drugs). Treating cancer with 5-fluorouracil is chemotherapy. So is treating an infection with penicillin or a headache with aspirins.

Yet when chemotherapy is mentioned in connection with cancer, the term generates a lot of fear. Almost everyone has heard horror stories about serious side effects. These side effects can be unpleasant, but they are in general greatly exaggerated. It’s true that a few people cannot tolerate chemical therapy at all. But most can tolerate it reasonably well. Others have moderate to significant reactions. When approaching the subject, also keep in mind that many drugs are used in chemotherapy and not all of them have serious side effects. The side effects themselves can often be reduced or controlled by anti-nausea drugs or other medications.

Surgery and radiation treat cancers that are growing in one particular place (locoregional treatment), whereas chemotherapy is generally used for cancers that have traveled through the blood and lymph systems to many parts of the body (systemic treatment). In the past, chemotherapy was used only when surgery and radiation were no longer effective. But now it is the treatment of choice for some kinds of cancer and is often used in combination with surgery and radiation, especially for localized cancers.
Biological Therapy: This is a relatively new way to treat cancer. It takes advantage of recent research that shows that the immune system may play a key role in protecting the body against cancer. The immune system might even play a part in combating cancer that has already developed. Refer to chapter 9, “What Happens in Biological Therapy and Immunotherapy,” which provides a more in-depth look at biological therapy.

The immune system consists of white blood cells called lymphocytes that act as a defense system against foreign organisms such as bacteria and viruses. One type of lymphocyte—the T cell—is formed in the thymus gland and is a natural killer of foreign cells, including cancer cells. Another lymphocyte—the B cell—is produced in the bone marrow and lymph nodes and makes antibodies in response to stimulation by a foreign protein. B lymphocytes can also kill cancer cells. Another white cell—the monocyte—interacts with T and B cells.

Biological therapy encompasses a number of classes of therapeutic agents, including:

1. Highly purified proteins characteristic of natural proteins produced by the body, such as interleukin-2 (IL-2) and interferon, which boost the lymphocytes’ cancer-killing properties. These are used in certain tumor types, such as kidney cancer and melanoma.

2. Monoclonal antibodies that target various cancer proteins. Examples include trastuzumab (Herceptin) for breast cancer; rituximab (Rituxan), yttrium Y 90 ibritumomab tiuxetan (Zevalin), and iodine I-131 tositumomab (Bexxar) for non-Hodgkin’s lymphoma; gemtuzumab ozogamicin (Mylotarg) for acute myelogenous leukemia; alemtuzumab (Campath) for chronic lymphocytic leukemia; bevacizumab (Avastin), cetuximab (Erbitux), and panitumumab (Vectibix) for colorectal cancer; bortezomib (Velcade) in multiple myeloma and mantle cell lymphoma; cetuximab for head and neck cancer; dasatinib (Sprycel) for various forms of leukemia; and sorafenib (Nexavar) for renal cell cancer. In some cases, the monoclonal antibody is attached to chemotherapy drugs (“chemolabeled”), attached to radioactive particles (“radioimmunotherapy”), or attached to toxins (“immunotoxins”). Active research, including clinical trials, is in progress to discover the best way to use these new treatments, especially in combination with chemotherapy.

3. Cancer vaccines, which are specifically directed against cancer cells. These are created by various methods, some relatively nonspecific and others directed against specific proteins preferentially expressed on cancer cells. Similar in principle to vaccines used against various infectious diseases, vaccines are designed to stimulate a person’s immune system to attack and destroy the foreign agent (in this case, cancer cells).

Combination and Adjuvant Therapies

Twenty or thirty years ago, it was common to think about treating cancer only by surgery or radiation or chemotherapy, depending on the stage of the disease. Two or all three therapies might be used, but usually only one at a time and in the sequence mentioned—surgery if the tumor was localized, then radiation if there was an actual or potential recurrence, then chemotherapy if the cancer involved vital organs or had spread so far that surgery or radiation had to be ruled out.

Recently there has been great interest in using what is called combination or multimodality therapy. Multimodality therapy incorporates two or three of the standard treatment methods with the goals of increasing response rates, reducing the likelihood of tumor recurrence, and, of course, improving survival. For
many malignancies, there is no universal agreement on the best combination or best sequence, but several broad principles have emerged:

- **When tumors are large, locally aggressive, and touch adjacent structures, radiation and/or chemotherapy might be given before surgery.** The goals here are to shrink the tumor and make the surgical procedure much simpler. This is called neoadjuvant therapy. In hospitals with special radiotherapy equipment, radiation will sometimes be given during surgery (intraoperative radiation) to kill invisible or microscopic tumor cells that might cause the cancer to come back in the future.

- **Radiation and/or chemotherapy may be given after surgery,** referred to as adjuvant therapy. Radiation is given to reduce the chances of local recurrence of the tumor (recurrence in the area that the tumor originated), especially for tumors that are large and where surgical margins were close or positive. Chemotherapy is given to reduce the chances of systemic recurrence (metastases elsewhere in the body), by wiping out tumor cells that may be too small to be visible right now but that might cause a recurrence later on. For example, evidence is clear that adjuvant chemotherapy benefits women who have undergone surgery for breast cancer, especially those whose cancer has spread to the lymph nodes under the armpit (axilla).

- **Radiation and chemotherapy have also been combined in an attempt to produce a more powerful antitumor effect than either treatment can produce alone.** Certain chemotherapy agents act as radiosensitizers—they enhance the effects of radiation to make its cell-killing abilities even more potent. The dosages of both modalities, however, may sometimes have to be reduced to prevent major side effects that could result from their simultaneous administration.

- **The new biological therapies, as listed earlier, are being blended with standard radiotherapy and chemotherapy.** But research on these combinations is still in an early stage. We are still testing this form of therapy to discover what sequence, dosage, or combination is the most helpful and how adding biological therapies to the others can be made more effective than today's standard treatments.

**How Your Physician Decides on the Best Treatment**

Making the decision on which treatment to use is a stepwise process. It really begins with the suspicion of cancer aroused by signs or symptoms, then proceeds through the diagnostic process outlined in chapter 2, “How Cancer Is Diagnosed.” Once the diagnosis is confirmed by a positive biopsy, several factors have to be considered.

**The Stage**  How far along the tumor is in its development is the most critical factor. Sometimes the stage isn't known until a surgeon actually has a look at the tumor. But there are other ways to find out what stage the malignancy has reached.

During the staging process, many parts of the body will be searched for evidence of cancer. Tests will discover the extent of the spread and the involvement with other tissues at the primary site. This will involve blood tests to see how organs such as the kidneys and liver are functioning. Imaging techniques such as chest X-rays and CT scans will be used to see if there is any involvement of the lungs either directly or by spread.

Other specialized tests will be ordered according to the primary site and the type of tumor being investigated. Each type of cancer has a typical pattern of spread, so different specific areas of the body will be investigated in each case.

Prostate cancer, for example, can spread to bone, so bone scans, bone...
X-rays, and blood tests may be important diagnostic tests for advanced stages of the disease. Lung cancer can spread to the center of the chest (mediastinum), an area that can be mapped with a CT scan and looked at directly through a scope (mediastinoscopy). Cancers of the stomach and bowel commonly spread to the liver, so CT scans of the abdomen and blood tests will be needed to investigate those areas.

It is important to understand that when a cancer spreads, it remains the same cancer. A breast cancer that spreads to the bone does not become bone cancer. If it spreads to the lung, it does not become lung cancer. Wherever it lands, it grows as breast cancer. It’s like blowing the seeds off a dandelion—whether the seed lands in a field, a forest, or a crack in a sidewalk, what grows is still a dandelion.

This is important because the choice of cancer treatment is guided more on where the tumor starts than on where it lands.

The Biology of the Disease An analysis of the disease—its cell type, biology, and expected behavior—is an important factor to consider. The tumor’s biology strongly affects the likelihood of a particular therapy slowing down or stopping the disease.

State-of-the-Art Alternatives Once the staging process is completed, your doctor has to consider all the treatments that might be appropriate considering the type of tumor, the site of origin, and the stage of spread. In some cases, only one specific therapy may be generally accepted as appropriate. But in many cases, a variety of approaches might be used.

Cancer treatment is always evolving. Every year new discoveries are made and old methods are modified or discarded. It’s hard even for specialists to keep up with all the developments in the field. But there are several ways your primary physician can find out about the most current treatment methods that are considered state-of-the-art.

- Cancer specialists (medical oncologists) are often consulted at this stage. So are surgeons or specialists in radiotherapy.
- The most recent medical literature can be reviewed, perhaps along with a computer search of your disease via a database like PDQ (see chapter 47, “Cancer Information”).
- Physicians and specialists attend many of the hundreds of cancer meetings that take place every year where important research findings and other cancer information are presented.

Tumor Boards Another way for your doctor to review your case, get information, and discuss the best treatment, especially with unusual types of cancers, is to attend a meeting called a tumor board. These boards are held frequently in all hospitals where cancer treatment is offered. They allow a group of doctors specializing in cancer to meet, discuss particular cases, and give their opinions about the advantages and disadvantages of treatment alternatives. It is very common at such a meeting for biopsy results to be presented and explained by the pathologist and for the radiologist and nuclear medical specialists to present all the X-rays and scans.

Your primary physician or oncologist will present your case (anonymously) so that each physician there has the same information your doctor has in making his or her decision.

In many larger hospitals there are specialty tumor boards that review cases in one particular field—breast cancer, urologic cancer, gynecologic cancers, or head and neck cancers, for example.

When it comes to recommending treatment, then, your doctor has had the benefit of input and ideas from a wide range of professionals.
**Personal Factors: Benefits and Risks**

Which treatment is finally recommended will also depend on such personal factors as your age, your other medical problems (which might make surgery risky), and especially the possibility of significant side effects with one or another treatment.

Age comes into the decision because the patient who is forty years old may be able to tolerate the aggressive chemotherapy drugs that bring about a substantial rate of remission. The same drugs given to an eighty-year-old could be risky. At that age, the kidneys don’t function as well as they do earlier in life and the risk of therapy could outweigh the potential benefit. But each case has to be decided on its own merits.

Both you and your doctor have to consider the relative advantages and disadvantages of each therapy. You have to weigh the chances of achieving remission or cure against the risks and side effects of treatment. You and your family are partners with your physician in this decision-making process.

**Your Decision** In making the final decision on treatment, nothing replaces a good discussion between you and your doctor. He or she should be able to explain to you the staging process, the tests that were done, their results, and all the available methods of treatment.

He or she may present the information from any tumor board that was held. Or he or she can sometimes pass on the consensus of the informal consultations with other doctors that often take place in medical groups having several physicians involved in the cancer field. Your doctor should also have alternative forms of therapy in mind and should outline what could be done if your tumor doesn’t respond to treatment or if some other problem comes up.

**Informed Consent** There may be legal principles regarding “informed disclosure” that come into play during these discussions. In the state of California, for example, patients with breast cancer must be given a pamphlet published by the state describing the various methods of primary treatment and the advantages and disadvantages of each. Although this document appears to be comprehensive, its coverage of many important areas may be incomplete and outdated.

A brochure certainly cannot replace the important and key discussion between physician, patient, and family. Nothing can. This initial comprehensive discussion about deciding on therapy is the most important single meeting that you have with your physician. It forms the basis for all of the decision making that follows.

**When and How to Ask for a Second Opinion**

Even after you have met with the physician who has outlined your treatment plan (for example, the medical oncologist or surgeon), you may still feel insecure about the treatment options you’ve been given. You might want to discuss them with another physician. This is a perfectly acceptable, rational, and appropriate thing to do.

There should be no hesitation on your part in asking your doctor if he or she would have another specialist review all the material relating to your case. Second opinions are not unusual. Some insurance companies require them.

In view of your need for a continuing relationship with your primary physician or specialist, it would be helpful to express your satisfaction with his or her decision and care. You can simply say that you wish to have someone else review the case to assure yourself that your decision to accept treatment will be made on the most thoroughly informed basis possible.
**Whom to Consult** You may have a certain consultant in mind or you might ask your doctor to select a senior specialist in your city or at a major medical center, depending on your diagnosis. Many times, your oncologist may recommend a second opinion and refer you to a local specialist or a specific cancer center where researchers with a special interest in your disease are working. Your doctor should have no hesitation in making your case material, including pathology slides and X-rays, available to the second-opinion consultant. This consultation is generally done fairly quickly so it does not delay treatment.

It is not a good idea to get a second opinion “in secret.” Ultimately, it is not in your best interest. Second-opinion consultations are done by physicians for physicians. They are done to review and help improve your medical care. Consultants cannot evaluate your case properly unless they have at least the same information your primary doctor has, including the slides, X-rays, and results of laboratory tests and other procedures.

Don’t think your doctor will take offense or feel hurt. Your doctor should welcome the opportunity to satisfy your need for a second opinion. Please read chapter 5, which is dedicated specifically to second opinions, as this is a very important topic for you to know about.

**Considering a Clinical Trial**

Depending on the type and stage of your cancer, your doctor might recommend a new kind of treatment. The word *investigational* might come up. Or *experimental* might be the term used. If the standard treatment options available to you aren’t likely to be effective, your doctor might simply suggest that you take part in a *clinical trial*.

All these terms might make you feel more than a little anxious. They shouldn’t. Investigational treatments that are being given in a clinical trial are used only under very stringent conditions. They are important in moving the medical field forward and wouldn’t be used at all if there wasn’t some hope they might be as effective as or more effective than currently available treatments, especially if standard treatment options are limited.

**What a Clinical Trial Is**

Advances in cancer treatment are rarely made by one scientist or physician working with a single or even a few patients. Advances usually come about because of some innovative idea or concept for a new therapy, based on an expanding understanding of cancer biology. This idea is eventually tested in a large number of patients to find out two things: Is it effective? And is it as good as or better than conventional treatments?

It takes several hundred and sometimes several thousand patients to prove quickly and reliably whether a new treatment will work and is worthwhile. It is almost impossible to conduct a trial in any single hospital or cancer center. The concept of cooperative clinical trials was developed for just this reason. The rules and procedures for clinical trials are standardized and specific.

**The Clinical Protocol**

A clinical trial consists of an exact written description of a treatment program that is called the clinical protocol. This is formulated and written with great care. Not only do the researchers need to be sure that the trial will answer the two main questions about effectiveness, but the rights of the patients being treated have to be safeguarded, too. The risks involved have to be minimized and disclosed.

The clinical protocol outlines the criteria for patients who might participate in the trial. It also describes what tests will be done and how the researchers will determine if a tumor is responding. Systems for monitoring the patient and
checking for any adverse effects will be detailed. And there will be provisions for informed consent.

Who Approves the Trial The entire project has to be approved by a human use committee made up of physicians and nonphysicians who have no relationship with the study (commonly referred to as an IRB, or institutional review board). The members of this committee certify that the patients’ rights are protected, that the trial is reasonable and logical, and that the study will answer the question it is supposed to answer. This same committee reviews the study again during and after completion of the trial as originally proposed. The Cancer Therapy Branch of the National Cancer Institute also keeps watch on these investigational studies.

The Importance of Clinical Trials Almost every advance in cancer treatment over the past several decades has come about because of clinical trials. In fact, just about every chemotherapy drug and radiation treatment now considered standard therapy was first given in a clinical Phase I trial. These treatments were given to patients who were willing to be in the forefront of advances in medical knowledge.

The willingness of thousands of women to participate in clinical trials by the National Surgical Adjuvant Breast Project (NSABP), for example, has resulted in answers being given to extremely important treatment questions. These trials have formed the basis for adjuvant chemotherapy in breast cancer patients with a high risk for recurrence even though no apparent tumor is left after surgery. This has saved many lives.

The Three Phases of Clinical Trials Whether for surgery, chemotherapy, radiotherapy, or biological therapy, clinical trials are always conducted in three phases.

A chemotherapy clinical trial, for example, proceeds this way:

• Preliminary (Preclinical) After a new anticancer drug has been found to be effective against one or more experimental tumor systems in the lab, it is tested in rats or other small animals to find out which dosage might be both effective and reasonably safe.

• Phase I About twenty human patients are treated with the same drug. There is no assurance or certainty that a significant tumor response will occur, although, again, every single anticancer drug now useful in therapy was initially a Phase I agent. Patients selected for these trials are almost always in cancer research centers and have already received all known effective anticancer therapy. After the proposed treatment is explained to them, they may volunteer to receive the new treatment. Phase I studies are often not tumor specific; that is, patients with breast cancer, lung cancer, and colon cancer may all enroll in the same Phase I study of a new agent. Since there is "nothing to lose," it is hoped that this specific new agent may in fact prove effective.

This phase will often involve a “dose escalation” scheme, in which different patients receive increasing doses of the study medication(s). The primary objective here is to test for safety (but also to get some sense of the potential efficacy). The study is completed when no unusual problems or toxic effects have been found and the maximal tolerated dose has been determined. The study can then move to the next phase.

• Phase II This phase of clinical trial typically enrolls patients with one particular type of tumor. The goal here is to get a clearer picture of how effective the new agent or treatment regimen is against a certain type of cancer, by looking at the percentage of patients who respond...
to the therapy. The safety of the drug(s) being tested continues to be an important objective to evaluate. Phase II trials generally enroll twenty to fifty patients and can involve one or several medical centers.

- **Phase III** In this phase, the new therapy is compared with standard treatment (patients are randomly selected to receive one treatment arm or another) to see if there is an improvement in the response or if the same response rate is achieved but with less-toxic side effects.

A therapy tested in a clinical trial may involve a drug already in clinical use. A new treatment often consists of standard drugs used in a new combination or a new sequence, in new dosages, or even simply given in a new way. But if a new drug is involved and the Phase III trial is successful, the National Cancer Institute will approve the drug for general use. Eventually, the new therapy might become the standard therapy.

**Clinical Trials and the “Approved” Uses of Drugs** Every drug comes with an official package insert detailing what dose to use for what illness. This information is also listed in the *Physician's Desk Reference*. These summaries usually contain only the information “passed” by the government’s approval agencies. This is important to know because many drugs in standard use may not specifically be approved for a particular indication, even though experience with patients has shown they are effective. Oncologists will often use these drugs “off-label.” About half of all the current uses of anticancer drugs in the United States and Canada, in fact, are not given in the official inserts.

Since the inserts do not necessarily reflect the most up-to-date cancer research, the current standard use of these drugs, or even their optimum use, your doctor should not be restricted to printed drug-listing materials. In fact, appropriate uses of anticancer drugs may not be listed in such official sources.

That being said, there are three important points to consider: (1) A responsible physician should make treatment recommendations based on compelling evidence that has been presented or published, not just by “reaching off the shelf” for what he or she thinks might possibly work. (2) Insurance companies may or may not cover the cost of drugs that are being used off-label, especially with some of the newer agents that are extremely costly. (3) Some of these newer agents do carry significant risks, so should not be given cavalierly, especially beyond their known indications. Make sure you discuss these considerations with your physician carefully, so that you understand the rationale behind the treatment plan that is being recommended.