# Alternative Chemotherapy

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Conventional cancer treatment for advanced stage cancers consist of maximum tolerated dose chemotherapy, as well as radiation for local control. Unfortunately, five year survival for the advanced stage solid tumors has minimally improved over the last 50 years (Morgan G, Ward R, Barton M, Clinical Oncology, 2004), despite the development of targeted drugs and targeted agents.

For nearly half a century, systematic cancer treatment has been dominated by the use of maximum tolerated dose chemotherapy. While progress has been modest in terms of curing or significantly prolonging the lives of patients, it comes at a high price. Toxic side effects are frequently associated with MTD-based (Maximum Tolerated Dosage) chemotherapy and the improvement is often time minimal at best.

In addition, the long breaks between maximum dose treatment cycles can also allow cancer cells to recover and even develop resistance, ultimately resulting in treatment failure and cancer progression. Unless a cytotoxic therapy eradicates all cancer cells, its application to a tumor population produces natural selection forces that select for cells that are resistant to the therapy. In essence, repeatedly administering maximum tolerated chemotherapy produces a more resistant cancer that will eventually not respond to any chemotherapy (this is analogous to treating a bacterium with multiple antibiotics, until the bacterium becomes resistant to all antibiotics).

Other causes for chemotherapy failure include poor blood supply to the tumor (which inhibits chemotherapy delivery) and low tumor oxygen concentrations, which increases resistance to chemotherapy while it encourages the spread of tumors in search of a better blood supply. A fundamental principle of chemotherapy is to use drugs that are more toxic to rapidly dividing cells. However, since these drugs do not specifically target tumor cells, but rather interfere with cell division, they tend to do damage to the normal dividing cells of rapidly regenerating tissues, e.g. bone marrow, gut mucosa, and hair-follicle cells.

Also, tumors are heterogeneous (meaning they consist of different types of cells); the outer rim consists of replicating cells, which are susceptible to being killed by chemotherapy, while the inner mass consist of cells in quiescent or non-dividing state. The cells on the outer rim of the tumor are the most readily targeted by cytotoxic therapies (due as much to their proximity to blood vessels as to their fast growth).

Because of this, integrative cancer physicians are turning away from the historical one-size-fits-all approach and are beginning to seek out personalized chemotherapy. It has become apparent to many physicians and researchers worldwide that cancer treatments, in order to be most effective, must be individualized. For this reason, ICT utilizes a broad array of treatment modalities designed to address the individual's cancer, as well as the environment in which the cancer exists (the patient's body).

## Chemotherapy Sensitivity Testing

Cancer is a disease characterized by uncontrolled cell growth and proliferation. Because cancer develops when genes regulating cell growth and differentiation undergo certain aberrant alterations, this testing

is essential to customize the appropriate treatment plan for each patient. In order to first diagnose and treat a patient's cancer, Chemotherapy Sensitivity Testing is performed to identify the optimal protocol for each individual patient. A preserved tissue sample from prior surgical procedures or live tissue from a new biopsy (when available) is used to complete molecular profiling and chemotherapy sensitivity testing.

Laboratory Evaluation

Extensive laboratory evaluation is necessary for personalized cancer treatment. In conventional cancer treatment, the treatment is determined simply by the origin of the cancer. For example, every patient with pancreatic cancer could potentially get the same treatment regimen, regardless of other potentially confounding factors. The following is a list of only some of the labs that will be tested to help determine an appropriate cancer treatment regimen:

1 Ceruloplasmin levels; ceruloplasmin is the copper storage protein. Copper is necessary for activation of growth factors for cancer. Many cancers sequester copper to accomplish angiogenesis, which is the development of new blood vessels to feed the cancer. Elevated ceruloplasmin levels should be treated with a copper lowering substance, such as ammonium tetrathiomolybdate.

2 Lymphocyte subset panel; as cancer progresses, the quantity of different types of white blood cells tends to change, to favor the proliferation of the cancer. Typically, neutrophils increase while lymphocytes decrease. Cytotoxic T cells will often become low, which decreases the ability of the individual's immune system to fight cancer. Measuring these white blood cells allows us to appropriately strengthen the immune system.

3 Vascular Endothelial Growth Factor (VEGF);stimulates the growth of new blood vessels and perhaps the most commonly over-expressed growth factor for cancers. Elevated levels require techniques, such as the use of hyperbaric oxygen, ammonium tetrathiomolybdate, and/or Avastin to lower VEGF levels.

4 Glucose, insulin, and HgbA1C levels; elevated glucose and insulin levels promote growth of glycolytic cancers. Elevated levels should be treated with dietary changes (low carbohydrate or ketogenic diet), as well as drugs and/or nutraceuticals that lower blood sugar and insulin levels.

5 Heavy Metals; elevated heavy metals in the urine should be chelated with oral and/or IV medicines because the heavy metals increase oxidative stress, which interferes with the proper function of normal tissues.

6 Circulating Tumor Cells (CTCs); although this test is not typically ordered by most oncologists, it is perhaps one of the most important diagnostic tests for individuals with advanced-stage cancers. Most patients don't succumb to the primary tumor, rather they die from metastatic disease. The circulating tumor cells are the next generation of disease which will eventually result in further metastasis. Patients with high levels of CTCs require aggressive treatment.

Therapy

ICT delivers Low-Dose Metronomic Chemotherapy to our patients. Low dose metronomic chemotherapy is the prolonged, repetitive, and more frequent use of low doses of chemotherapy drugs to target the endothelium. The endothelium supports the formation of new blood vessels and/or tumor stroma (the abnormal connective tissue which feeds the cancer), rather than targeting the tumor itself. Unlike conventional maximum tolerated dose chemotherapy, this approach does not require the long breaks between treatment cycles to allow the patient to recover. Research suggests that it may be during these long "break" periods in which cancer resistance develops.

The benefits of this approach are decreased toxicity and inhibition of angiogenesis (the development of blood vessels that feed the tumor). During angiogenesis, new endothelial cells are extremely fragile as they branch off from existing blood vessels, multiply, migrate into a tumor, and eventually form into tubular structures to give rise to new vessels. The endothelial cells engaged in angiogenesis are extremely sensitive to killing by these cytotoxic drugs; much more so than most cancer cells. Thus, when low-dose chemotherapy is administered on a regular schedule (hence "metronomic" like the steady beat of a metronome), the continual death of endothelial cells attempting to form new blood vessels can substantially disrupt the angiogenic process.

Additionally, one of the particular merits of this approach centers on cancer drug resistance. Whereas conventional, high-dose chemotherapy accelerates the development of chemotherapy resistant cancer cells, metronomic low dose chemotherapy targets endothelial cells rather than cancer cells. This technique is often associated with less resistance.

Recently, a further benefit of metronomic chemotherapy has been established. It tends to selectively kill a population of immune cells, called "T-reg cells," that function to suppress the activity of immune cells capable of attacking the tumor. T-reg cells often congregate within tumors and secrete hormone-like factors that "turn off" the immune cells, trying to attack the cancer. Thus, metronomic chemotherapy has emerged as a useful adjuvant to the therapeutic strategies intended to boost the tumor-killing capacity of NK and T-cytotoxic cells.

Low dose metronomic chemotherapy may be effective in treating the outer rim of the tumor with less toxicity, but it does not address the interior of the tumor which is anaerobic, hypoxic, and lacks blood supply. By combining this therapy with techniques such as pH Manipulation Therapy, eradication of both the inner and outer sections of the tumor may be possible.

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IV Therapies

Immune system boosters and anti-oxidants are administered to aid in recovery, to support the overall health of the patient, and to maximize the effectiveness of cytotoxic chemotherapeutics.

Myer's "cocktail": energy boosting nutrients including B5, B6, B12, Magnesium, Calcium,

Ascorbic Acid

Ascorbic Acid (megadose): At high doses, Ascorbic Acid functions as a pro-oxidant to kill cancer

Immune -boosting IV cocktails:

Please Note: While most patients will be scheduled for supportive care following a treatment day, patients may be scheduled for supportive care prior to, as well as, post treatment days.