Cancer Smart Bomb: Part II Artemisinin Follow-Up (c) 2002 Brewer Science Library, All rights reserved Excerpted from New Horizons, Fall 2002 issue by Christina L. White, BA

(The full details of the discovery, development, research, toxicity, etc. is contained in Part I, an 8- page article in the summer 2002 issue of New Horizons)

As I promised, I have been following up on people who are taking ART compounds as part of their campaign against cancer in their bodies. A few months ago, I initiated an Artemisinin Results Survey, in the hope of being able to follow enough cases of particular cancers to get a clearer idea what dosage of ART compounds might be effective against those cancers.

So far I have only been able to speak with several people directly (under 10 people) about their experiences with ART compounds, as well as receive some e-mails from others indicating some degree of success.

I have spoken with people who are getting results with each and every ART compound, including artemisinin, artesunate, dihydroartemisinin, and artemether as oral products and also with people utilizing the injectible form. The various people I have spoken with are using dosages from 100 to 600 mg a day. Some people are simultaneously using both the injectible and the oral compound; most people are just using one form of the oral compound. There is no clear picture emerging yet.

The other issue that muddies up the results that can be accrued to artemisinin, is that everyone that I have spoken with is on a complex anti-cancer protocol, including diet, supplements and detoxification methods. Some are also receiving traditional cancer treatments like high-dose chemotherapy and radiation, or even non-traditional low-dose chemotherapy delivered by IPT (see article on page 12). I am, of course, happy for the success these people are experiencing, whatever compound, treatment or combination of protocols are responsible for it.

There are a few "pure" cases where the results can only be from use of the ART compounds. Dr. Narendra Singh, MBBS, one the Washington researchers involved in several of the ART studies, is also a medical doctor from India. He has followed several cases in India that have been treated only with ART compounds. One of his "pure" cases is that of a man with a brain cancer who had been in a coma for five months, who came out of his coma after 21 days of injections of artemether. This is a dramatic example of an initial response, but only time will tell if continuing improvement or even stabilization can be achieved in this case.

Another dramatic case reported by Dr. Singh is that of a 72 year old man with a laryngeal tumor (3 cm x 2.5 cm x 3 cm, stage II) who responded with a 70% reduction in tumor size within a week of treatment with artesunate. His

treatment regimen was initiated on day one with an oral capsule containing 150 mg of ferrous sulfate along with folic acid (0.5), and from day 1 to day 15, a 60 mg injection (IM) of artesunate was given every evening. Starting on day 16, the patient was switched to an evening oral tablet of artesunate (50 mg), which is being continued on a daily basis. The patient has regained his voice, appetite and weight, along with maintaining the tumor reduction.

Several stage III and IV breast cancer cases are doing very well on a complex protocol, with ART compounds as one of their primary tools against cancer. One person with pancreatic cancer has been doing well for over 16 months, but he has also done two rounds of chemotherapy, and recently added low-dose naltrexone to his regimen (refer to page 4 for LDN update).

It is unclear at this time how helpful ART compounds are for prostate cancer. Dr. Henry Lai, the researcher who had the original idea of testing artemisinin against cancer cells, has received several reports of substantial reductions of PSA's after using various ART compounds. On the other hand, one man (F.K.) who was following a small group of men with prostate cancer, reported an initial reduction of PSA by several of the men. Later he (F.K.) experienced a subsequent rise in his PSA following an emotionally upsetting family situation. He is still on ART compounds after a rest period from them of several weeks. A few other men who have high PSA's have decided to try higher amounts of ART compounds. Their results will be reported in subsequent issues.

Dr. Bernard Bihari, MD, has added ART compounds to the protocols of some of his cancer patients on LDN (read article on page 4 about LDN update). He reported that one lung cancer case returning for a follow-up office visit has shown a significant reduction (more than he would have expected on LDN alone) in her lung tumor size in three months. Other cancer cases he has placed on both LDN and ART compounds are expected in soon for their follow-up office visits; he promises to keep me updated. Dr. Bihari believes that these two compounds will not conflict with each other, and expects them to support each other in the control of various cancers.

It is important for people to realize that the complete pharmacokinetics of artemisinin compounds, which includes absorption, distribution, metabolism and excretion, has not been determined. The use of ART compounds in both malaria treatment as well as more recently in cancer treatment has spread before all the metabolic pathways of ART compounds have been completely understood. As more research information is examined and exchanged, a more complete understanding will develop among both researchers and practicing physicians. The following paragraphs examine some of the present considerations about absorption and distribution.

Absorption Resistance of Artemisinin In my first article on artemisinin, I mentioned some research that indicated that one study found that absorption

resistance built up very quickly at the intestinal wall. Many people have been upset, concerned and confused about whether they should cycle on and off ART compounds or take something that might enhance its absorption, or also do injections to by-pass this potential problem.

The study was conducted with 10, healthy male Vietnamese adults. They were given 500 mg of artemisinin a day, which is a common dosage amount given for short term treatment of malaria in several areas of the world. On average, plasma levels decreased by day 4 to 34% of the beginning absorption level, with a further decrease to 24% of original absorption by day 7. After a two-week washout period, 7 of the 10 subjects had almost normalized their plasma levels of absorption to the original levels. Of importance is the fact that this research also indicated that there is a high individual variability in absorption from person to person.

This research indicates at the least that a very rapid and significant reduction in absorption of artemisinin occurs in most individuals at high dosages of 500 mg a day. This same degree of resistance may not occur at daily dosages of 100 or 200 mg, and indications are that this resistance varies greatly among individuals.

ART compounds in many cases have been given at what might be considered to be a low daily dosage to cancer patients in India (review Dr. Singh's write-up on a cancer case in the following paragraphs), on a once daily dosing schedule. Dr. Lai still believes that twice daily dosing is the preferred protocol.

Grapefruit Concentrate Increases Absorption One study showed that artemether taken with 350 ml of grapefruit juice concentrate more than doubled the bioavailability in 6 healthy volunteers. Many drugs come with warnings about not consuming them with grapefruit juice as it will increase its absorption beyond what the physician has prescribed. Several doctors have now suggested their patients take the ART compounds with grapefruit juice to facilitate absorption. A following study discounts that proposition.

Another study with eight healthy male subjects reported that although grapefruit juice concentrate significantly increased the oral bioavailability of artemether, it did not prevent the reduction in bioavailability that has been shown to occur over time in other studies. On the 5th day of consuming 100 mg of oral artemether with 350 ml of double strength fresh frozen grapefruit juice there was still an average reduction to 30% of the original plasma levels.

Considering that 350 ml of grapefruit juice also contains a great deal of fruit sugar which is contraindicated in most anti-cancer dietary regimens, it appears that the benefits of grapefruit juice concentrate may be too limited to be of any significant benefit. Taking higher dosages of ART compounds may be a better solution.

Body Distribution of ART Compounds In the last article, I wrote that Dr. Lai considered the artemether form to be superior because of its long duration in the body. Research and communications with Dr. Guo-Qiao Li, the Chinese doctor who has been involved in artemisinin discovery and development since the beginning, has changed Dr. Lai's thinking about which artemisinin analog is the best for general use.

A comprehensive research paper on the Pharmacokinetics of Artemisinin-Type Compounds (Clin Pharmakinetic 2000 Oct; 39 {4}) summarizes much of the present knowledge about the pharmacokinetics of ART compounds and their distribution throughout the body.

It concluded from a survey of research data that the parent compound artemisinin has a more uniform distribution throughout the body. It can be absorbed through the blood brain barrier and has a half-life of 3-4 hours. Dr. Lai has presently concluded that the artemisinin compound may be the preferred compound to use, because a wider body distribution would protect more organs from metastasis. Dr. Lai considers his present position to be a tentative and changeable one that may be revised as new information becomes available. There continue to be many unknowns about ART compounds.

The summary of information on the artesunate analog indicates its high water solubility, and its rapid conversion to the compound artenimol. Rat studies found it to be distributed in highest concentrations to the intestine, "followed by the brain, liver, kidney, testicle, muscle, fat, heart, serum, eyeball, spleen and lung in decreasing order". After an hour, the tissue concentrations remained high in the intestine and brain, while dropping significantly in other tissues.

The summary of information on the oil-soluble artemether analog indicates that the highest concentrations after injection are found in brain tissue, demonstrating its easy passage through the blood brain barrier. Although some minor amounts of artemether were also found in lung tissue, very low concentrations were found in the liver or kidneys. From this it may be surmised that the artemether form would not be very protective against metastases occurring in the liver.

Artemether bioavailabiltiy was more than doubled when taken with a high fat meal. Most recommendations for taking ART compounds suggest taking it on an empty stomach, but the addition of fatty nutrients such as cod liver oil or CLA (conjugated linoleic acid), as Dr. Rowen has some of his patients use, should increase artemether absorption. Artemether also tends to bind to blood proteins more than the water soluble artesunate.

This research summary also mentions that there is some modest amount of covalent

binding of artemisinin and the derivative artenimol, with human plasma proteins, primarily albumin. This may have some relevance for cancer patients who may have low albumin levels, a common state in certain stages of cancer, and one that can be easily checked by a blood test.

An interesting side note in this research paper is that there may be a gender difference in the absorption levels of artemisinin; female rats had twice the blood levels as their male counterparts on the same dosage, although the half-life was the same for each.

Iron Supplementation Since iron is known to fuel cancer growth, cancer patients are obviously concerned about taking supplemental iron. It is assumed in most cases that the cancer cells have already sequestered adequate iron stores, so that supplemental iron is not needed. In the protocol for the laryngeal cancer patient, the patient was instructed to take a one-time 150 mg dose of ferrous sulfate. A few of the cancer patients that I have spoken to have taken 25 mg of iron for the first five days of their beginning use of ART compounds in oral or injectible forms. Since iron does potentiate the ART compounds, further research might validate a short use of supplemental iron. Dr. Lai reminds us that concurrent iron supplementation even in the test tube studies increased the effectiveness of ART's anti-cancer actions. All the dogs that were successfully treated for cancer with ART compounds were given supplemental iron.

Antioxidants Most of the people I have spoken with are taking various amounts of antioxidants while they are taking the ART compounds. Dr. Rowen responded to my question about this and wrote that he is only restricting vitamin E in his patients on ART compounds. Drs. Lai and Singh still believe that high levels of antioxidants may compromise the amount of damage that can be done to cancer cells from ART compounds.

Possible Contraindications This leads one to the confusing issue of mixing different anti-cancer protocols together. The chemistry of action of one cancer protocol may contradict or limit the effectiveness of another one. There is some mixing and matching of different protocols going on by both cancer patients and alternative practitioners.

One cancer patient called and inquired about taking artemisinin compounds at the same time as using a copper chelating compound called TM (tetrathiomolybdate). Copper is needed for the growth of blood vessels (called angiogenesis) to the tumor. Compounds that reduce the growth of blood vessels to tumors are therefore called anti-angiogenic compounds. Treatment with the TM compound is an anti-angiogenic treatment. The goal of treatment with TM is to lower the level of copper to approximately 20% of the original level, which would provide enough copper for basic functions, but hopefully slow down and reduce the growth of blood vessels to the tumor.

Reduced amounts of copper might compromise the effectiveness of artemisinin compounds. 1) First of all, copper is a critical part of the protein, hephaestin, that appears to act as a sort of pump to move charged iron molecules through the intestinal membrane to the bloodstream. Low copper levels could result in low levels of iron being absorbed, reducing the levels of cellular iron that is needed for activation of ART compounds. 2) If reduced copper levels do end up having an anti-angiogenic effect, the reduced blood flow to the cancer cells will also result in less iron and less artemisinin derivatives being able to get to the cancer cells to interact in their free radical cascade effect.

Several of the cancer patients I spoke with who are taking ART compounds are also doing IPT treatments. Some of them take their ART compounds orally at distinctly different times from the IPT treatment, but a few patients take an artesunate injection in conjunction with their IPT treatment. One of the primary uses of insulin in IPT is to increase cancer cell cycling.

A discussion with Dr. Lai indicates that this may be counterproductive to the artemisinin effect because the increased cell membrane cycling will actually reduce the time for the transferrin receptors to bind to iron. Dr. Lai pointed out that more iron will actually go into the cell if the process of membrane cycling is slowed down, not speeded up. Dr. Lai also pointed out that research has shown that a lot of transferrin receptors are empty when they go inside a cell because they are brought in passively.

Although the successful responses physicians are obtaining cannot be argued with, the present and admittedly incomplete understanding of transferrin receptor dynamics does not seem to warrant simultaneous use of IPT and injections of artesunate. Perhaps this brief discussion will stimulate further research to clarify this issue.

SUMMARY I had hoped that after a few months of following many cases that I would have more definitive information about the most effective type of ART compound to use, the specific dosages that were producing success, and would have clearer answers to questions about supplemental iron, antioxidant use, and cycling schedules that work to overcome absorption resistance.

In many cases, there does seem to be a significant initial response which levels off at a stabilization without complete resolution of the cancer. People can live a very long time in a state of homeostasis with the cancer, but everyone would obviously prefer a complete resolution of the cancer.

Although it is obviously tempting to blame increasing absorption difficulties that develop over time for this stabilization state, it may turn out that the cancer cells have found a way to modify the ART reaction. Still, I tend to focus on the intestinal absorption problem, because it is one that can be overcome through another means, the use of injections. One of the stage IV breast cancer

cases with extensive metastases I have been in contact with whose bone scans have become clear, continues to do at least one 60 mg injection of artesunate a day.

I have been unable to give up thinking about the man with prostate cancer in Belgium who tried a unique approach to treatment with ART compounds. One day a week he took a supplemental iron pill with one meal and then took 700 mg of ART compounds that evening. He reported a substantial reduction in his PSA with this unique treatment approach. Unfortunately, there is no contact information to follow up on his long term results with this innovative approach.

Dr. Lai is quite concerned about anyone taking such a high dosage, as it might lead to cardiotoxicity or neurotoxicity. Malaria treatment commonly uses 500 mg of ART compounds for the first day of a dosing cycle, and many of the adults in the tropical countries that it is used in are small, with low body weights. A once a week dosage might at least overcome the absorption resistance that seems to be a property of the present ART compounds in use.

Just last week I heard second hand from an acupuncturist that had visited two Chinese hospitals that they are using 1000 mg of ART compounds with cancer patients! That is an exceptionally high amount, raising concerns about toxicity. I am working on getting the complete information on this therapeutic approach. I am in no way suggesting that anyone dose at these high levels, just pointing out that dosing amounts are literally all over the map, so to speak.

One of the women I have spoken with recently who has recurrent breast cancer has decided to do a six week maximum use trial of ART. She has decided to use 60 mg injections of artesunate two times a day, and take 25 mg of supplemental iron for the first five days along with 50 to 100 mg of oral artemisinin twice a day. She will temporarily discontinue all the many antioxidants she has been taking for many years. She has also decided to discontinue her immune enhancing supplements because she said if her immune system isn't at peak function now, after all the supplements she has taken, it never will be. She plans on drinking plenty of water, and will continue on the low stress diet she has been on of raw salads two times a day, with protein sources from organic eggs, salmon, chicken, turkey, and undenatured whey powder. She will maintain her carbohydrate intake at under 30 grams a day. She will continue taking extra fatty acids from fish oils for their anti-inflammatory effects, and is considering silymarin for liver support. She will continue her nightly dose of 4.5 mg of low dose naltrexone. She has promised to keep me informed of her results on this trial protocol.

In summary, treatment of cancer with artemisinin is still in its infancy. The brave people who are trying different dosages and protocols with it are actually pioneers in its usage. Although it is unsettling to many people who want complete answers to their questions about all the dynamics of ART compounds, the truth is that no one knows all the answers yet, and that is just the way it is.

In a year or two we will all know far more than we do today.