

## DCA (dichloroacetate) Frequently Asked Questions

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Medicor Cancer Centres was the first cancer clinic in North America to begin prescribing DCA "off label" to cancer patients under the full supervision of a medical team. We have consulted with the relevant regulatory bodies in Canada and are following their guidelines and policies. We would like to thank everyone who has expressed an interest in our DCA therapy. We appreciate your feedback and encouragement. We would also like to acknowledge and extend a special thanks to two of our patients who brought DCA to our attention, and motivated us to begin DCA treatments.

## **Background**

In 2007 it was discovered that the drug DCA (dichloroacetate sodium) induced the death of human breast, lung and brain cancer cells that were implanted into rats, while being non-toxic to healthy cells. This research was published in *Cancer Cell, 11, 37–51, January 2007*. DCA has been found to kill cancer cells by a newly discovered mechanism that appears to be common to several types of cancer. DCA works by turning on the natural cell suicide system which is suppressed in cancerous cells, thus allowing them to die on their own. It also alters the cancer cell's use of glucose, starving the cell of energy.

Newer research shows that DCA also kills many other types of cancer cells, and can boost the cancer-killing effects of radiation. The first formal human cancer research using DCA was published in May 2010. It confirmed that DCA is an effective anti-cancer drug for treating glioblastoma patients (*Metabolic Modulation of Glioblastoma with Dichloroacetate, Science Translational Medicine, Vol 2, Issue 31*).

Further research to determine how well DCA works against various cancers within the human body is ongoing: http://clinicaltrials.gov/ct2/results?term=dichloroacetate+cancer

## What types of cancers does DCA work on?

Several publications demonstrate that DCA works in a variety of cancers. These include human studies / case reports and lab studies (rat and *in vitro*):

Publication	Date	Cancer Type(s)
Role of SLC5A8, a plasma membrane transporter and a tumor suppressor, in the antitumor activity of dichloroacetate. <i>Oncogene. 2011 Sep 22;30(38):4026-37.</i>	2011	colon, breast, prostate
Dichloroacetate Induces Apoptosis of Epithelial Ovarian Cancer Cells Through a Mechanism Involving Modulation of Oxidative Stress. <i>Reprod Sci.</i> 2011 Jun 23.	2011	ovarian
DCA inhibits neuroblastoma growth by specifically acting against malignant undifferentiated cells Int J Cancer. 2011 May 9. doi: 10.1002/ijc.26173	2011	brain (neuroblastoma)
Use of Oral Dichloroacetate for Palliation of Leg Pain Arising from Metastatic Poorly Differentiated Carcinoma: A Case Report. J Palliat Med. 2011 Apr 12	2011	poorly differentiated / unknown primary
Synergistic antitumor effect of dichloroacetate in combination with 5-fluorouracil in colorectal cancer <i>J Biomed Biotechnol. 2011;2011:740564. Epub 2011 Feb 20.</i>	2011	colon
In vitro cytotoxicity of novel platinum-based drugs and dichloroacetate against lung carcinoid cell lines. <i>Clin Transl Oncol. 2011 Jan;13(1):43-9.</i>	2011	lung (carcinoid)
Dichloroacetate shifts the metabolism from glycolysis to glucose oxidation and exhibits synergistic growth inhibition with cisplatin in HeLa cells. Int J Oncol. 2011 Feb;38(2):409-17. doi: 10.3892/ijo.2010.851.	2010	uterus (cervix)

Non-Hodgkin's Lymphoma Reversal with Dichloroacetate.  J Oncol. 2010;2010. pii: 414726. Epub 2010 Sep 16.	2010	lymphoma (non-Hodgkins)
Metabolic modulation of glioblastoma with dichloroacetate. Sci Transl Med. 2010 May 12;2(31):31ra34.	2010	brain (glioblastoma)
Reversal of the glycolytic phenotype by dichloroacetate inhibits metastatic breast cancer cell growth in vitro and in vivo. <i>Breast Cancer Res Treat.</i> 2010 Feb;120(1):253-60.	2010	breast
Dichloroacetate (DCA) sensitizes both wild-type and over expressing Bcl-2 prostate cancer cells in vitro to radiation. <i>Prostate.</i> 2008 Aug 1;68(11):1223-31.	2008	prostate
Dichloroacetate induces apoptosis in endometrial cancer cells. Gynecol Oncol. 2008 Jun;109(3):394-402.	2008	uterus (endometrial)
A mitochondria-K+ channel axis is suppressed in cancer and its normalization promotes apoptosis and inhibits cancer growth. <i>Cancer Cell.</i> 2007 Jan;11(1):37-51.	2007	breast, lung, brain (glioblastoma)

## **Observational DCA Data**

For the first time in the world, on Dec 7, 2007 we publicly shared our observational data from the treatment of 118 cancer patients with DCA. We updated our data in 2009 from treating over 347 patients. This can be found at: <a href="http://www.medicorcancer.com/dca-data.html">http://www.medicorcancer.com/dca-data.html</a>. As of Oct 2011, we have treated over 800 cancer patients with DCA, the most of any center in the world. Since clinical trial data is now emerging, we are no longer collecting observational data. Instead, we are focusing our efforts on publishing our findings in reputable peer-reviewed medical journals. Our first publication is: "Use of Oral Dichloroacetate for Palliation of Leg Pain Arising from Metastatic Poorly Differentiated Carcinoma: A Case Report." This can be viewed here: <a href="http://www.liebertonline.com/doi/pdfplus/10.1089/jpm.2010.0472">http://www.liebertonline.com/doi/pdfplus/10.1089/jpm.2010.0472</a>

### Is DCA safe?

DCA has been used in humans to treat a rare disease called "congenital lactic acidosis", and found to have some mild to moderate side effects. Our experience so far suggests that DCA is safe to use in cancer patients under close medical supervision. Some animal studies show that DCA can itself cause liver cancer. These studies used doses which are over 100 times higher than what would be prescribed for cancer treatment. We think that DCA can have 2 main categories of side effects.

## Neurological:

Nerve injury in the hands and feet ("peripheral neuropathy"). Neuropathy typically takes several weeks to months to develop, and is reversible if it is caught early. In the existing literature, neuropathy from DCA has been shown to be reversible. We use vitamin B1 (benfotiamine or thiamine), acetyl L-carnitine and R alpha lipoic acid to prevent and reduce the severity of peripheral neuropathy. Our own data on frequency of neuropathy in our patients confirms that these supplements are effective. If neuropathy develops, supplement doses are increased and iv R alpha lipoic acid treatment may be added (performed by our naturopathic doctor).

Sedation, confusion, hallucinations, memory problems, mood changes, hand tremors. These side effects are temporary and appear to be dose-dependent and age-dependent. This finding is consistent with existing human research on DCA that we have reviewed. We use benfotiamine (a type of vitamin B1), acetyl L-carnitine and R alpha lipoic acid to prevent/reduce these side effects. If you are a Medicor patient, you will receive our latest dosing guidelines for these supplements. Due to potential interference with other ongoing treatments like radiation or chemotherapy, certain supplements may not be recommended. Medicor patient will receive detailed information specific to their treatment plan.

### Gastrointestinal:

Heartburn, nausea, vomiting, indigestion. These side effects may occur with DCA, and we prescribe a "proton pump inhibitor" antacid medication (e.g. pantoprazole) as needed to treat them.

### Other Side Effects:

Some patients experience pain at the sites of their tumour(s) within the first few days of starting DCA. This may be an indicator of the effectiveness of DCA. About 1-2% of patients have mild liver toxicity (increase in liver

enzymes noted without symptoms). We have not observed any drop in blood cell counts due to bone marrow toxicity, or any other significant organ toxicity. Note that leukemia patients may see a drop in their high white blood cell count, indicating destruction of the cancerous white cells.

Most side effects reported so far have been mild or moderate. Patients experiencing moderate side effects are usually taken off DCA as a precaution. Most side effects typically resolve within days after stopping DCA. Neuropathy can take weeks or months to resolve, and is reversible.

## **TLS (Tumour Lysis Syndrome)**

This is a condition in which a large number of tumour cells are rapidly killed, causing a sudden release of the contents of the dead cells into the bloodstream. It can result in abnormal heart rhythms, and kidney failure. A detailed reference article can be found here: <a href="http://www.emedicine.com/MED/topic2327.htm">http://www.emedicine.com/MED/topic2327.htm</a> TLS occurs most commonly in patients with a large mass of tumour cells in the body who receive chemotherapy, especially with lymphomas or acute leukemia. We have not had a single case of TLS in our patients treated with DCA alone. Since DCA can enhance the effect of chemotherapy in certain cases, it may be more likely to occur if DCA is combined with chemotherapy (especially without medical supervision).

## **DCA-Drug Interactions**

We have observed that drugs that can cause confusion or hallucinations have a potential to interact with DCA. This may include cannabinoids, benzodiazepines and other CNS drugs, especially if they are already causing some neurological side effects. Patients who receive consultations by our physicians will be assessed for potential drug interactions, and specific medical advice will be given. All Medicor patients who receive DCA will be closely monitored by our physicians for drug side effects with routine check-ups, comprehensive lab tests, and imaging studies. We take into account our patients' general condition, other medications, past medical history, and concurrent health problems.

### **DCA** and Caffeine

We have received a large number of inquiries about caffeine following some anecdotal reports of enhanced DCA effect with excessive tea/caffeine intake. After conducting a limited review of our DCA patients, we have noted that a few patients with high tea/caffeine consumption (> 10 cups per day) have shown no response to DCA. Also many patients who have shown an excellent response to DCA do not take tea/coffee or caffeine or take it in minimal amounts.

There are a number of potential harmful effects of consuming high doses of caffeine including increased likelihood of seizures in brain tumour patients, abnormal heart rhythms, anxiety, and insomnia. Even though there is new data to show that intravenous high dose caffeine can enhance chemotherapy, the potential for caffeine to enhance DCA therapy is unverified. We are presently recommending against the use of high dose caffeine, unless it is done with medical supervision. Patients should use moderation with consumption of caffeinated drinks and check with their own doctor, naturopath or dietician for specific advice.

## **DCA and Chemotherapy**

For the first time in North America, Medicor and Advanced Cancer Theranostx (<a href="www.act-inc.net">www.act-inc.net</a>) began conducting ChemoFit tests with DCA and chemo combined (in 2008). This means eligible patients can have a sample of their own tumor analyzed to see if combinations of DCA and chemo will work, and if they will work better than chemo or DCA alone. The accuracy of the ChemoFit test ranges from 85-95%.

We have already had some exciting results showing that DCA can, in some cases, dramatically enhance the cancer-killing effects of chemo. However, there is a possibility that DCA can interfere with chemo as well. This is similar to single agent chemo being better than combination chemo for some patients. Published lab research now confirms our findings.

If you are a patient who is thinking of combining DCA and chemotherapy, we recommend you review our ChemoFit web page at: <a href="http://www.medicorcancer.com/chemofit.html">http://www.medicorcancer.com/chemofit.html</a> and discuss the test with your oncologist. We also have more detailed information for physicians at <a href="http://www.medicorcancer.com/chemofit4doctors.html">http://www.medicorcancer.com/chemofit4doctors.html</a> Malignant ascites fluid samples and malignant pleural effusion samples can now be tested with ChemoFit, eliminating the need for a biopsy in some patients.

If you are not able to have the ChemoFit test, a treatment plan can be developed to safely combine DCA with most chemotherapy drugs with minimal risk of interference (depending on the chemotherapy schedule).

### What is the status of DCA clinical trials?

The first phase 2 clinical trial of DCA in glioblastoma was completed but was not published as a trial, possibly because the DCA doses were too high and resulted in a large number of patients dropping out (our opinion, actual reason not disclosed by the authors). See <a href="http://www.medicorcancer.com/news.html">http://www.medicorcancer.com/news.html</a> for detailed commentary on this trial.

Several DCA clinical trials are presently ongoing. These can be reviewed at: http://clinicaltrials.gov/ct2/results?term=dichloroacetate+cancer

Even though we have seen clear evidence of DCA's effectiveness in several types of cancer, Medicor physicians believe that it is essential for formal clinical trials to be conducted. DCA is different from other drugs that undergo clinical trials because it is not a "new" drug. It has already been used for decades in humans, and has a relatively safe profile. This means that the trials may take less time, but may still take years. Many cancer patients cannot wait this length of time. We are hopeful that information obtained from our experiences with DCA will supplement clinical trials, and help patients and the medical community.

# Can I take DCA on my own?

We are aware of many patients who are currently self-medicating with DCA. DCA can be purchased as a lab chemical not suitable for human use. This DCA contains impurities that make it unsafe for patients to take. DCA can also be purchased by various internet companies. Buyers should be aware that these companies are not regulated and may be selling fake DCA or contaminated DCA. One owner of a web-based company has already been convicted of internet fraud for selling counterfeit DCA, and is serving a jail term. <a href="http://www.cbc.ca/news/story/2010/06/01/con-dca-gaber.html">http://www.cbc.ca/news/story/2010/06/01/con-dca-gaber.html</a>

Cancer is complex and so is its treatment. DCA is a prescription medication. We strongly recommend DCA to be obtained only by a doctor's prescription and taken only under the supervision of a medical doctor.

## Do I Qualify for DCA Treatment?

Patients with a documented diagnosis of cancer (any type) under the following categories qualify for treatment:

- a. failed conventional, scientifically proven treatments
- b. told by their doctor that there is no safe or effective treatment for their cancer
- c. waiting to start conventional treatment, and would like to do something in the interim
- treated for cancer, and would like to prevent recurrence (where no proven recurrence prevention is available)
- e. receiving therapy which has a poor chance of success and would like to strengthen their treatment

## What is the duration of treatment?

In order to determine if DCA is effective in treating your cancer, we recommend at least 6 to 8 weeks of treatment. For slow growing cancers, longer treatment is needed. If your cancer responds to the drug, therapy may continue indefinitely. If you experience significant side effects, treatment will be stopped and may be restarted later.